Canadians Seeking Solutions and Innovations to Overcome Chronic Kidney Disease (Can-SOLVE CKD)

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Overview

• Perspectives

• Context

• What we are doing

• How we are doing it
Perspectives

• Patients living with kidney disease(s)
• Clinicians
• Researchers
• Administrators/Policy-makers
Context: Chronic kidney disease

- Affects 4 million Canadians
  - Vulnerable populations: Indigenous peoples, children and the elderly
- Costs Canadian health care system >$50B per year
- Survival and quality-of-life in advanced CKD worse than metastatic breast or lung cancer
Chronic kidney disease

- Majority of people with CKD have multiple co-morbidities
  - Diabetes, hypertension, cardiovascular disease
  - Depression, anxiety and uncertainty
- CKD patients often excluded from clinical studies due to complexity of condition
- Uptake of evidence into clinical practice has been slow
Understanding variations in outcomes and care

• Patients with chronic kidney disease (CKD) have variable outcomes
  o Time to dialysis or death
  o Trajectories of progression
  o Accumulation of burden of disease over time

• Patients with CKD do not always receive care consistent with guidelines:
  o Complexities in CKD condition
  o Variation in CKD management practice
    • Resources, attitudes and philosophies
  o Lack of randomized trial data to inform care
  o Lack of access to and methods by which to disseminate best practice
The CKD Story:
Not where we would like to be

• Achievements to date
  o Definitions and classification system
  o Increasing awareness of CKD as public global health problem
  o Growing number of consortia and collaborations for basic and clinical science
  o New therapies for some specific conditions/etiologies of CKD
  o Genetic and molecular mechanisms being more carefully studied and understood

• BUT……Gaps in knowledge
  o Mechanisms of disease(s); responders and non-responders
  o Epidemiology and burden in different locations
  o Genetic and environmental interactions
Current State of CKD Research and Care

• Limited possibilities to influence the course of the disease
• Failure of trials (study design, populations, size, duration)
• Insufficient number of mechanistic targets identified: limited new agents for hope
• Culture of clinical trials and inquiry lacking

• But….needed and wanted by many....
Strategy for Patient-Oriented Research (SPOR)

- A coalition of federal, provincial and territorial partners dedicated to the integration of research into care
- Objective:
  - Foster *evidence-informed health care* by bringing innovative diagnostic and therapeutic approaches to the point of care, so as to ensure *greater quality, accountability and accessibility of care*
Strategy for Patient-Oriented Research (SPOR)

- Provincial SPOR SUPPORT Units
- National SPOR Networks
  - Mental Health
  - Primary Care
  - Chronic Disease Networks
What we did and are doing

• We submitted a 45-page grant (135 pages with appendices)

• We raised money to match the $12.5M required (and more…)
  o $21 million in cash
  o $6.9 million in kind

• We have formed:
  o National Patient Council
  o Indigenous Peoples’ Engagement and Research Council
  o Training and mentoring committee
  o Scientific Advisory Committee

• We have been meeting regularly to establish
  o Processes, timelines
  o Operational plans
Can-SOLVE CKD

• One of five SPOR Networks in Chronic Disease
• 5 year funding announced CIHR in April 2016
• >150 members
  o Patients, researchers, policy-makers, clinicians
• >30 partner organizations across Canada
• 18 research projects
Vision

By 2020, every Canadian with or at high risk for chronic kidney disease (CKD) will:

• receive the best recommended care
• experience optimal outcomes
• have the opportunity to participate in studies with novel therapies, regardless of age, sex, gender, location, or ethnicity
Pan-Canadian infrastructure and resources: developing

Resources include:

**NATIONAL SYNERGISTIC CORE RESOURCES**

- Canadian Network for Kidney Research Using Linked Data Holdings
- Patient-reported outcomes in Canadian Organ Replacement Registry
- National Nephrology Clinical Trials Network
- Laboratory for development of novel knowledge translation tools
- National biorepository with longitudinal laboratory & clinical outcomes
- Kidney REsearch Scientist Core Education and National Training program (KRESCENT)

**HUMAN RESOURCES**

- Patients, families and caregivers
- Health care providers
- Researchers
- Sex and gender champions
- Policy and decision-makers
Priority questions

Research priorities are based on key issues identified by patients over three years of priority-setting discussions.

Patients ask:

How can we identify those at highest risk for CKD progression?

How can we identify and treat those at highest risk for adverse outcomes?

What are the best treatments to improve outcomes for CKD patients?

What strategies can reduce symptom burden in patients with advanced CKD?

What model of care will best deliver evidence-based personalized care?

How can we better enable self-management of CKD?

What is the best way to help patients access the best treatment for their kidney failure?
Patient-generated questions
direct research projects

Figure 3: Can-SOLVE CKD Themes, Priorities and Research Projects Overview
3 research themes

Theme 1
IDENTIFY KIDNEY DISEASE EARLIER AND SUPPORT THOSE WHO ARE AT HIGHEST RISK OF NEGATIVE OUTCOMES.
1.1A Defining CKD risk in youth with diabetes
1.1B Identifying diabetes and CKD in Indigenous communities
1.2 Personalizing treatment of patients with GN and ADPKD
1.3A Integrating risk-based care for patients with CKD in the community
1.3B Risk prediction to support shared decision-making for managing heart disease

Theme 2
DEFINE BEST TREATMENTS TO IMPROVE OUTCOMES AND QUALITY OF LIFE.
2.1A Impact of novel interventions to prevent CKD progression
2.1B Aldosterone inhibition and enhanced toxin removal in hemodialysis patients
2.2 Assessing and optimally managing symptoms in patients with advanced CKD

Theme 3
DEFINE THE OPTIMAL WAYS TO DELIVER PATIENT-CENTERED CARE IN THE 21ST CENTURY.
3.1 Restructuring kidney care to meet the needs of 21st century patients
3.2 Strategies to enhance patient self-management of CKD
3.3A Improving patient knowledge about treatment options
3.3B Increasing the use of living donor kidney transplantation

RESULT
The right patient receives the right treatment at the right time
The partners

- Extensive partnership across the country and internationally
- Kidney, cardiovascular, diabetes, and Indigenous peoples’ organizations
Organizational structure

- Patients are centre
- Patient Council and Indigenous Peoples’ Engagement & Research Council
Patient Council

- 3 co-chairs (rotating)
- >30 members with national representation of:
  - Indigenous and non-Indigenous peoples living with kidney disease
  - Kidney donors
  - Women and men of all ages

- Executive Patient Council + 4 working groups

  - Research Projects & Recruitment
  - Curriculum & Training for Patient Participation in Research
  - Knowledge Translation, Communications & Outreach
  - Measurement & Metrics
Indigenous Peoples’ Engagement & Research Council

- Co-chaired by Indigenous patient partners and MD/policy-maker
- ~15 members including Indigenous patients, caregivers, researchers and policy/administrative leaders within Indigenous communities
  - Indigenous patient partners are also part of Patient Council
- Links and communication with National indigenous organizations, including First Nations, Métis and Inuit
Patient engagement

- Building on 3 years of work
  - James Lind Alliance priority setting exercises
  - Patients on or nearing dialysis and patients with early CKD

- Development of key questions for the network
  - 2 workshops with patients, researchers and policy makers
  - Lay summaries and presentations
  - Question and Answer with Patient Council and the Indigenous Peoples’ Engagement & Research Council (IPERC)
  - Voting and vetting

1. Form priority setting partnership (Steering Committee)
2. Gather research uncertainties through national surveys
3. Steering Committee processed and collated submitted research uncertainties:
   - Combine duplicates
   - Reduce to top 30 list
4. Final priority setting workshop
James Lind Alliance
priority setting

**Figure 4: Can-SOLVE CKD Patient-Oriented Priority Setting Process**

**Steps**

1. Form priority setting partnership (Steering Committee)
2. Gather research uncertainties through national surveys
3. Steering Committee processed and collated submitted research uncertainties:
   - Combine duplicates
   - Reduce to top 30 list
4. Final priority setting workshop

**Early Chronic Kidney Disease (2014)**
- Steering Committee:
  - 6 patients, 3 clinician scientists, 1 KFOC representative
- 309 patients and caregivers surveyed
  - 2241 priorities identified
- 148 unique research priorities identified
- 12 patients, 6 caregivers, 7 health care professionals

**Advanced Chronic Kidney Disease (2012-2013)**
- Steering Committee:
  - 5 patients, 4 clinician scientists, 1 KFOC representative
- 210 patients and caregivers surveyed
  - 1570 priorities identified
- 259 unique research priorities identified
- 11 patients, 5 caregivers, 18 health care professionals

**TOP 10 RESEARCH PRIORITIES (Early Chronic Kidney Disease)**
1. What are the most effective new interventions and treatments to prevent the development and progression of kidney disease?
2. What is the best diet to slow progression of kidney disease and what are the benefits and risks of specific diets (e.g., phosphate restriction, protein restriction, low salt, etc.) in terms of kidney disease progression and quality-of-life?
3. What are the causes of symptoms in patients with chronic kidney disease, including fatigue, low energy, sleeping problems, depression, anxiety, and sexual dysfunction, and how can these be treated to improve quality of life?
4. What are the optimum strategies, such as having access to health information (e.g., lab test results, sharing of information), and/or improving communication, to help patients manage their health condition(s) themselves and to improve patient experience and outcomes, and delay the need for renal replacement therapy?
5. What is the role of lifestyle factors (e.g., exercise, stress) or risk of developing kidney disease, kidney disease progression and quality of life?
6. What are the optimal strategies for the management of CKD (i.e., those undertaken by the primary care physician, nephrologist, other health care professionals) to delay progression and improve outcomes?
7. What are the harmful effects of medications used in patients with CKD, and in particular the combinations of medications used to treat other diseases (such as diabetes and high blood pressure)?
8. What are the optimal approaches for the prevention and treatment of cardiovascular disease in patients with CKD?
9. What is the best strategy (e.g., screening programs targeting high-risk groups, programs to increase public awareness) to identify kidney disease early?
10. How do we ensure that patients with CKD have equitable access to care (e.g., nephrologists, allied health clinic) irrespective of location of residence or socioeconomic status?

**TOP 10 RESEARCH PRIORITIES (Advanced Chronic Kidney Disease)**
1. What is the best way to enhance communication between healthcare professionals and patients and to maintain patient participation in decision-making with regards to the advantages and disadvantages of different forms of dialysis, and access to test results to facilitate self-management?
2. How do different dialysis modalities compare in terms of their impact on quality-of-life, mortality and patient acceptability, and are there specific patient factors that make one modality better for some patients with kidney failure than others?
3. What are the causes and effective treatment(s) of ways to prevent, treat, or reduce in dialysis patients?
4. What is the best strategy to increase kidney transplantation, including access to transplantation, increasing the efficacy of the transplant program, and increasing the availability of donor kidneys?
5. What is the psychological and social impact of kidney failure on patients, their family, and other caregivers and can this be reduced?
6. What are the best ways to promote heart health in dialysis patients, including management of blood pressure?
7. For people with kidney failure, what is the impact of each of the dietary restrictions (sodium, potassium, phosphorus) separately, and when taken in combination, on important outcomes including quality-of-life?
8. What are the best ways to manage symptoms in people in or near the end stage of dialysis including poor energy, nausea, cramping, and restless legs?
9. What are the causes and effective treatment(s) of depression in dialysis patients?
10. What is the best vascular access (among both new and existing types of access) for people on hemodialysis?
Patient engagement

• Integrating patient perspectives and voices into research training and mentoring activities for all projects and infrastructures

• Ensuring patients are partners in:
  o Study design
  o Study execution
  o Study interpretation
  o Study result dissemination…and more!
Partners

• >30 patient partners
• >120 investigators at 8 major universities
  o Translational, basic science, clinical researchers in nephrology, pharmacy, social sciences, nursing, engineering
  o Extensive partnership across the country and internationally
• Kidney, cardiovascular, diabetes, Indigenous peoples’ organizations
Research projects

- PIs
- Co-leads
- Patients
- Collaborators

USA
UK
Australia
## Research projects

### Theme 1: Identify kidney disease earlier and support those who are at greatest risk of negative outcomes

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<tbody>
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### Research projects

**Theme 2: Define best treatments to improve outcomes and quality of life**

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<th>2.1A</th>
<th>Impact of novel interventions to prevent loss of kidney function: Cell therapy</th>
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<td>2.1A</td>
<td>Impact of novel interventions to prevent loss of kidney function: Re-purposed drug for polycystic kidney disease</td>
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<tr>
<td>2.2</td>
<td>Assessing and optimally managing symptoms in patients with advanced CKD</td>
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## Research projects

**Theme 3: Define optimal ways to deliver patient-centred care in the 21st century**

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<td>Improving patient knowledge about treatment options</td>
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<td>3.3B</td>
<td>Increasing the use of living donor kidney transplantation (LKDT)</td>
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Some of the projects of Can-SOLVE CKD

- Increase the proportion of Indigenous people screened for CKD and diabetes within select communities, targeting those at highest risk, and demonstrate improved outcomes
- Identify adults with GN and polycystic kidney disease at highest risk of CKD progression and determine the effectiveness of novel therapies for personalized treatment
- Design and evaluate new models of care in CKD with a focus on enhancing self-management to improve outcomes and satisfaction
- De-prescribing medications: patient and provider perspectives
Research projects

Project 1.1A: Defining CKD risk in youth with diabetes

Project leads: Jim Scholey, Allison Dart, Etienne Sochett, Farid Mahmud, Brandy Wicklow

Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT)

- Observational Study: 450 youth (C 258 & 80 controls)
- RCT (Medication) Study: 450 (C 123) youth with Type 1 diabetes UK, Canada and Australia

Improving Renal Complications in Adolescents with Type 2 Diabetes through Research (iCARE)

- First Nations youth: Manitoba/Northwestern Ontario with Type 2 diabetes, n=200, 50 controls
- National Expansion (8 sites): BC, Alberta, Ontario, Quebec, Nova Scotia
Project 2.1A: Novel interventions to prevent loss of kidney function: Clinical trials of promising re-purposed drugs for autosomal dominant polycystic kidney disease (ADPKD)

Project lead: York Pei

- Two pilot randomized controlled trials to test the possible effect of two promising re-purposed drugs/compounds
- Selected cohort of ADPKD patients at highest risk of progression to enroll in clinical trials
- Patient partners will:
  - provide input on the design of PROMs
  - promote patient participation
Research Projects

Project 2.1B: Aldosterone inhibition and enhanced toxin removal in hemodialysis patients

Project lead: Mike Walsh

- Randomized controlled trial with 2 x 2 factorial design to evaluate:
  - Cardiovascular outcomes
  - Patient symptoms on dialysis
Project 3.3A: Improving patient knowledge about treatment options

Project leads: Joanne Kappel, Beth Horsburgh

- Using focus groups and other methods to co-develop culturally appropriate tools for informing patients with advanced CKD about treatment options for kidney failure
- Educational approaches will be tested in two Indigenous populations in each of BC, SK, and ON
  - Prospective study with pre and post test design over two years
- Outcome measures:
  - Research engagement, patient/family satisfaction, patient/family knowledge
  - Impact on use of home dialysis, transplantation and non-dialysis supportive care
Different Methodologies

- Stepped wedge cluster randomized controlled trial
- 2 x 2 Factorial RCT
- Qualitative methods
- Registry-based studies
  - Pragmatic large simple studies
- Pre and Post
Infrastructure being established

- Linked Canadian biorepositories in glomerulonephritis, diabetes and PKD
- National Nephrology Clinical Trials Network and national registry of patients interested in participating in RCTs
- Laboratory for the development of novel KT tools
- Achieving increased patient and researcher engagement in POR activities
  - KRESCENT multidisciplinary training and mentoring program
Knowledge translation

• Formal survey of all project leads re:
  o KT knowledge and KT needs

• iKT Laboratory supporting creation of tools to inform health care decision-making
  o Prioritizing Can-SOLVE CKD Network projects
  o Developing online support tools and patient decision aids
  o Using human factors engineering and informatics research to shape tools and interventions for network projects
Recent & ongoing activities

• Kick-off meeting and workshop at annual CSN conference (Halifax – May 2016)
Recent & ongoing activities

- Detailed work plan developed and submitted to CIHR (August 2016)
- Development of core operations team
- Policies and terms of reference for each committee and project
What we have learned

• Not all patients like the idea of RCTs
  o Have and have nots
  o Alternative designs may be more acceptable (SWD)

• Consent forms are too long and don’t make sense to most people (not patient-centred)

• Patients want to help answer important questions
What we have learned

- Patients have good questions
- Informing clinical trial design with patient input is essential for enrollment/uptake
- Lay summaries are essential to facilitate engagement and understanding
- Patients want to participate in research:
  - Some of our processes are prohibitive
Research projects transforming care

• Answering important questions about:
  o How to identify, triage and treat early CKD
  o Whether novel or other therapies are effective in delaying progression in specific diseases
  o How to improve symptoms and outcomes for those on dialysis
  o How to improve living donor transplantation experience and rates
Research:
Robust methods to evaluate usefulness of strategies and treatments

• Complex patient groups often excluded from clinical trials

• Need for evidence-informed therapy:
  o Participation in clinical studies
  o Disseminating results
  o Facilitating uptake into clinical practice
Outcomes, impacts and metrics

By 2020, Can-SOLVE CKD will realize:

i. better identification of individuals with CKD across Canada, by moving innovative diagnostics from the bench to clinical testing using the Network’s national registry (Theme 1);
ii. improved access to better therapies for all patients (Theme 2); and
iii. better health system efficiency for Canadians with CKD by creating, testing and implementing standardized models of care, new educational tools, and technology to optimize communication between providers and patients (Theme 3).

The costs of strategies will be carefully measured so that economic implications (including any cost savings) are fully understood prior to health system implementation.
Aspirational deliverables for transformative study and care of CKD in Canada

• Within 5 years, all family members of people with kidney failure, and all Aboriginal Peoples (includes First Nations, Métis and Inuit) will be offered the opportunity to be tested for CKD

• We will establish firm targets, based on baseline data, to increase the percentage of patients with diabetes and cardiovascular disease who are evaluated and treated for CKD

• Double the number of CKD patients involved in clinical trials and observational studies

• Ensure that 85% of those with CKD receive the right medications at the right time
Bridging the valleys and focus on the patient voice

- Spectrum of CKD
- Native and transplant kidneys
- All age groups
- Translational science(s)
- Health care system delivery
- Models of care
- Evaluation in real time
“Information is data arranged in meaningful patterns. It becomes knowledge only when it is interpreted in a context.”

• Can-SOLVE CKD is committed to knowledge transfer
Listening, learning, leading

To patients, caregivers, policy-makers, researchers & clinicians

From patients, caregivers, policy-makers, researchers & clinicians

With patients, caregivers, policy-makers, researchers & clinicians
Thanks

- Patient partners
- Researchers, policy makers and other partners
- Core operations team
- Funding sources
  - CIHR—SPOR Networks in Chronic Disease
  - The Kidney Foundation of Canada
  - Juvenile Diabetes Research Foundation
  - Provincial renal agencies
  - Private donors
  - Industry sponsors
  - Many others
Questions?
info@cansolveckd.ca

Learn more and get involved:
www.cansolveckd.ca