The Global Renal Exercise (GREX) Phenomenon: Lessons learned and future directions for exercise in End Stage Kidney Disease

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Global Renal EXercise

Objectives

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1. Introduce the Global Renal Exercise (GREX) network and its mission and vision
2. Educate attendees on the current status (including shortcomings) of physical activity, lifestyle, and rehabilitation in people living with ESKD and kidney transplantation
3. Provide an overview of up-to-date evidence base and examples of successful programs from around the globe
4. Discuss the need for change, and how to bring about this change; including policies that need to be implemented to make physical activity/exercise/rehabilitation a pragmatic, sustainable, and efficacious endeavor;
5. Better understand how we all can collaborate and learn from each other to better help people with ESKD to live well through physical activity, exercise, and appropriate rehabilitation

What does it mean to have kidney failure?

- CKD is a continuum: CKD stage 1-4 (Renal insufficiency); Stage 5 (Kidney Failure)
- Kidney Failure – 2 Options: 1) Transplant; 2) Dialysis (hemo or peritoneal)
  - Most undergo in-center Hemodialysis 3 days/week for ~4 hours
- Little urine production. **Interdialytic weight gain in HD = 2–3 kg**
- Average pill burden in U.S. dialysis patients: 19 pills/day (BP meds, P binders)
- Common co-morbidities include muscle wasting, CVD, bone disorders, cognitive dysfunction
  - < ¼ of dialysis patients are well enough to return to work
- Transplant recipients: no longer need dialysis, and have much improved health ad QOL, *but still face many challenges*
  - Poor physical function, elevated CVD risk, low re-employment rates, etc.
- **Across the globe, individuals with kidney failure are NOT being rehabilitated**

Can Exercise Help? Of Course!

CKD Stage	Systematic Reviews and/or Meta-analysis
ALL CKD stages	1) Barcellos CKJ 2015;8(6):753-65; 2) Heiwe AJKD. 2014;64(3):38 3) Heiwe. Cochrane Reviews. 2011(10):CD003236.
Dialysis	1) Clarkson. AJP 2019 (In press); 2) Smart N 2005;25(4):352-64.; 4) Chan. AJN. 20 6; 6)Sheng AJN. 2014;40(5):478-90.; 7) Pu. R Rehab. 2018;32(9):1189-202; 9) Chung. JCN 65(1):4-15. 11) Ferreira 2019 APMR (In Pr 13) Cheema AJN. 2016;44(1):32-45; 14) Bess want. Phys Can. 2014 16(1): 44-53
Transplan	6;

IF IT WORKS SO GREAT ....
THEN WHY ARE SO FEW DOING IT ????

Sur **oves muscle strength, physical function, QOL, etc.**

- **Reg** ***stage of disease*** **(non-dialysis CKD, dialysis, transplant)**

- ***Regardless of the mode of exercise (Resistance, endurance, yoga, balance, flexibility)***

A Skeptical/More Realistic View:

- It doesn't always work as well as we want:
  - Improvements in strength/physical function are modest/inconsistent….
  - CV benefits also inconsistent… though recent studies suggest reduced arterial stiffness and myocardial stunning

- Significant limitations in most studies:
  - Small sample sizes, short intervention periods, and/or lack control groups
  - LOW volume/intensity of exercise (energy expenditure < 70kcal/session)

- We have amazing anecdotes (which keeps us going)

- ***But implementation is extremely poor (with a few exceptions globally)***
  - ***"renal rehabilitation" is NOT reimbursed in most of the world***

- If we are going to improve our data… we have to admit our data is not ideal…. AND FIND A BETTER WAY FORWARD

My "AHA moment"

- Conducting NIH-funded exercise and nutrition-related RCT in dialysis patients
  - 1 year protein supplementation and "**intradialytic cycling**"
  - Primary outcomes: 1) cardiovascular function; 2) physical function

- One Monday…I noticed one of our patients (DJ) had interdialytic weight gain of **15kg!**

- Why? On previous Friday… he was cramping, got saline… and got thirsty

- Summary: A little bit of protein… and a little cycling during dialysis… is NOT GOING TO WORK
  - ***Comprehensive behavior change is needed***

- Evidence? At end of study, he started exercising more, changed diet, lost 40lbs and got a transplant

- ***I have amazing anecdotes… and some bad clinical trial data (including "failed" NIH trial)***

I had two choices:

Stay the course **OR…** **Find a new way**

$NIH & patient health

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History of GREX

- Started with 5 minute discussion at the end of 2015 ASN exercise symposium
- Discussed plans for an "Exercise in CKD Working Group." *Q&A took an hour*
- Lots of interest, but no funding. ***Needed to find who was serious about helping***
- Started having meetings in food courts and bars… and a network started
- Today: several international collaborations (pilot studies) and frequent meetings
- Goals: leverage this pilot data to acquire funding for large, multinational ***outcomes studies***, and tackle ***implementation*** issues (show cost-effectiveness)

Recent Update!

- Go GREX!
- Clara Bohm (U of Manitoba Nephrologist and GREX collaborator) just received a $500K grant from the Canadian Institute of Health Research
- Purpose: conduct a multinational RCT to examine effects of exercise in dialysis patients on "myocardial stunning"
- 23 investigators from Canada, USA, and Australia will be involved.
- **THIS is what GREX was made to do!**

GREX Mission and Vision

Mission: Foster collaborative research & innovation across multiple disciplines to develop effective/feasible strategies to increase PA and exercise participation in order to optimize health outcomes in people with CKD.

Vision:

- Facilitate the completion of rigorous, international, multidisciplinary, exercise and physical activity research
- Support the development/implementation of multidisciplinary, collaborative models and strategies to promote behavioral and lifestyle change, both locally and globally
- Increase awareness of therapeutic benefits of PA in people with all stages of kidney disease, among patients, their caregivers, and healthcare providers

What has GREX been doing?

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- WEBINARS and Journal clubs: highlighting "hot" research papers and other topics. Including a focus on student/trainee presentations.

- Collaborative Research Studies and Publications
  - International Delphi Survey on Exercise Priorities in CKD. KI Reports. https://pubmed.ncbi.nlm.nih.gov/33732980/
  - Global Policy Barriers and Enablers to Exercise and PA in CKD. JReN 2021. https://pubmed.ncbi.nlm.nih.gov/34393071/
  - Physical Activity in Peritoneal Dialysis
    - PD Physical Activity and Exercise Recommendations (Scoping Review). PDI 2021. https://pubmed.ncbi.nlm.nih.gov/34743628/
    - PD Clinician Survey (assessing practitioners perspectives on exercise in CKD). In progress
    - PD Patient Survey (assessing patient perspectives on exercise in CKD). In Progress
  - Identifying Common Physical Function Outcomes in CKD Exercise trials (systematic review, in progress)
  - Cognition and Physical Activity in CKD Delphi Survey (in progress)

- Education/Training Programs
  - "Exercise in CKD: A training program for fitness and health professionals" (in progress).
  - Goal: to train individuals to implement exercise programs for patients across the spectrum of CKD.

- Collaborative Research Grants
  - "Trial of Intradialytic Cycling as Kidney Exercise Rehabilitation for cardiac Stunning in Hemodialysis (TICKERS_HD)" (PI: Clara Bohm)

Global Renal Exercise Network (GREX)

2021 Activities

grexercise.kch.illinois.edu

BEST PRACTICES FOR EXERCISE IN PERITONEAL DIALYSIS (PD)

In collaboration with The International Society for Peritoneal Dialysis, a group of 22 PD experts developed and published a comprehensive set of practice points for physical activity and exercise for people receiving PD.

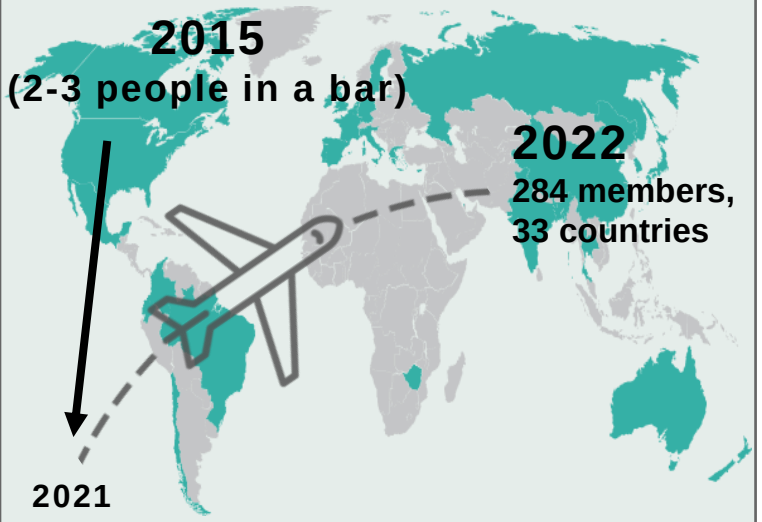
PHYSICAL ACTIVITY, COGNITION, AND CHRONIC KIDNEY DISEASE

Using large, population-based datasets we are exploring the relationship between physical activity and cognition in CKD and have launched a Delphi Survey to gather and prioritize the top research questions relevant to cognition in CKD.

GLOBAL POLICY BARRIERS, ENABLERS AND STRATEGIES

Our report on key policy-related enablers, barriers and strategies to increase exercise and physical activity participation for people living with CKD was published https://bit.ly/3rTKlVU

CONTINUED NETWORK EXPANSION



GREX YOUNG

GREX Young consists of trainees and early career researchers and clinicians committed to supporting the goals of GREX. Its aim is to organize webinars, share engaging information and to showcase and support early career researchers, students, and health care professionals in the field.

COMMUNITY ENGAGEMENT

3 trainee webinars, with 9 Masters, PhD, Post-Doc trainees and early career researchers presenting

A GREX working group was awarded an ISPD to survey clinicians and patients evaluating exercise in PD

2 conference presentations / sessions (Australian and New Zealand Society of Nephrology, Joint ISN/GREX symposium)

1 journal club on twitter (#NephJC), 1 joint webinar with ISRNM, 1 GREX webinar

2 virtual symposiums with invited speakers (researchers, people living with CKD, & trainees)

945+ followers on our twitter account (@GREXercise), where we routinely post the latest research and news

GREX is supported by an unrestricted grant from Satellite Healthcare

Session Overview

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Time	Title	Speaker
13:00-13:15	Introduction to GREX and the state of play in those living with kidney disease – what is the problem and what is being done about it?	Ken Wilund
13:15-13:30	Patient perspective: Rehabilitation in ESKD is still NOT a reality	Kevin Fowler
13:30-13:45	Overview of the new lifestyle and exercise clinical practice guidelines for kidney disease	Tom Wilkinson
13:45-14:00	Bringing about real-world change: Policy considerations and practical approaches to translating evidence to practice	Paul Bennett
14:00-14:40	Examples of novel and practical approaches to exercise programming for ESKD: 1) Lessons from Sustained Exercise Programs in CKD 2 & 3) Lessons from the Calgary Kidney Transplant Clinic 4) A Lifestyle Medicine Approach for Kidney Rehabilitation	1) Joao Viana 2) Stefan Mustata 3) Theresa Cowan 4) Giorgos Sakkas
14:40-15:00	**LIVE Roundtable discussion**	**All**