EPIDEMIOLOGY
RESEARCH GROUP IN
ORGAN TRANSPLANTATION

JOHNS HOPKINS
MEDICINE

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

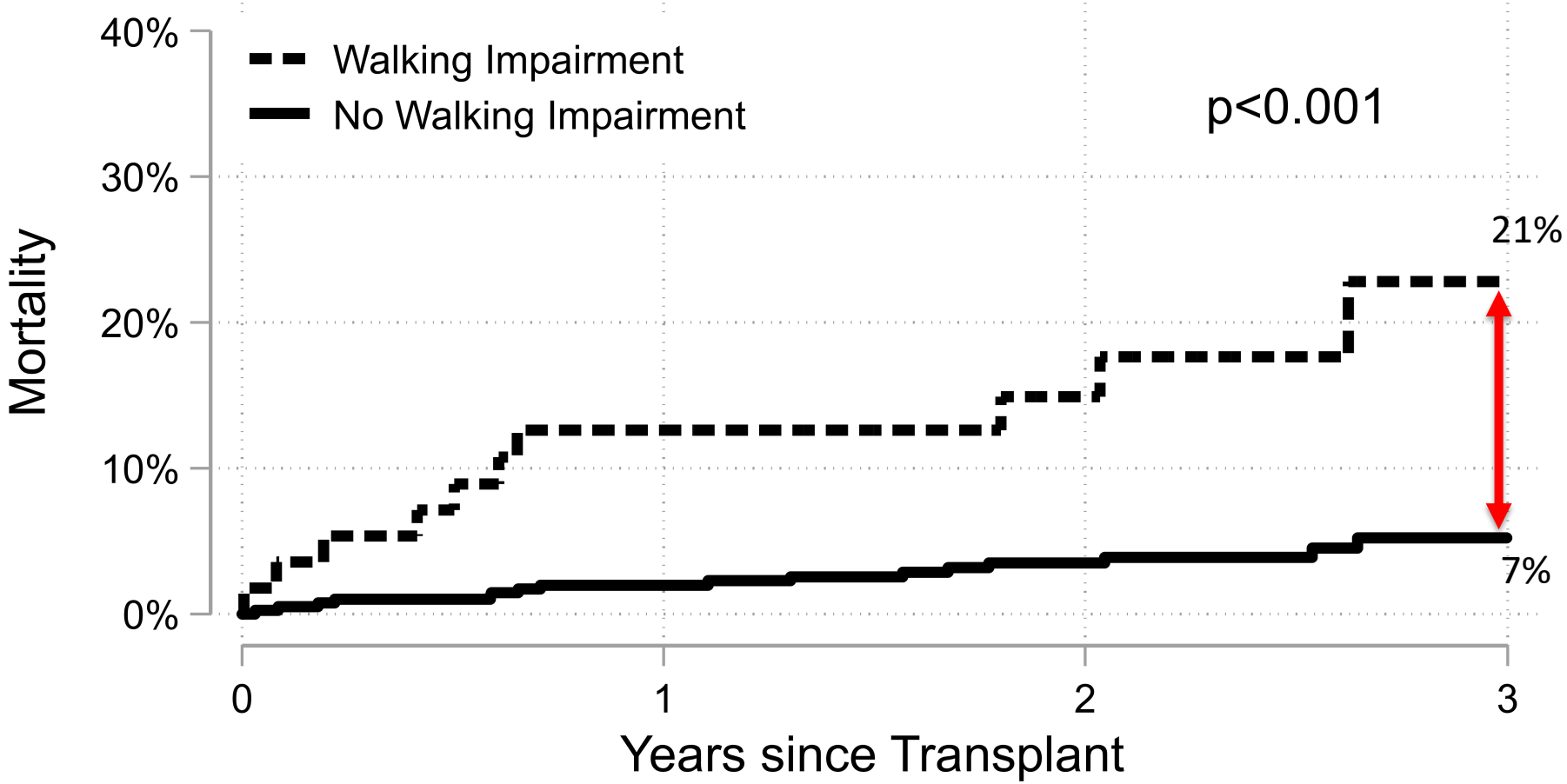
Pre-transplant Care Management Approaches

Mara McAdams-DeMarco, PhD
Director of Clinical and Outcomes Research
Associate Professor
Departments of Epidemiology and Surgery

Post-transplant Outcomes are Impacted by Pre-transplant Impairments

- Mortality and graft loss risk are elevated in patients with pre-transplant:
  - Frailty
  - Lower extremity impairment
  - Walking impairment
  - Cognitive impairment
  - Obesity/unintentional weight loss

KT Recipients by Walking Impairment



Number at risk				
Impairment	56	45	32	10
No Impairment	405	369	251	86

Thomas/McAdams-DeMarco, NDT 2020

PRE-TRANSPLANT INTERVENTIONS TO IMPROVE FUNCTIONING

Prehabilitation

- Surgery is a significant physiologic stress
  - Comparable to intense exercise
  - Causes increased metabolism/catabolism, increased oxygen uptake, stress hormone production, increased inflammation
- Prehabilitation: “Training” for surgery
  - Interventions seeking to enhance a patient’s functional capacity to tolerate upcoming surgery
  - Commonly includes an exercise component with strength, aerobics, and stretching components
  - Sometimes includes nutritional or psychological components
- Shifts the focus to optimization prior to surgery rather than rehabilitation afterwards

Transplantation is an ideal setting for prehabilitation.

- Long waiting periods for a deceased or living donor transplantation
- While patients wait, there is a profound loss of physical function due to:
  - Aging
  - Frailty
  - Comorbidity
  - Stress of undergoing dialysis
- Prehabilitation can mitigate this loss of physical function (Sheshadri *et al*)

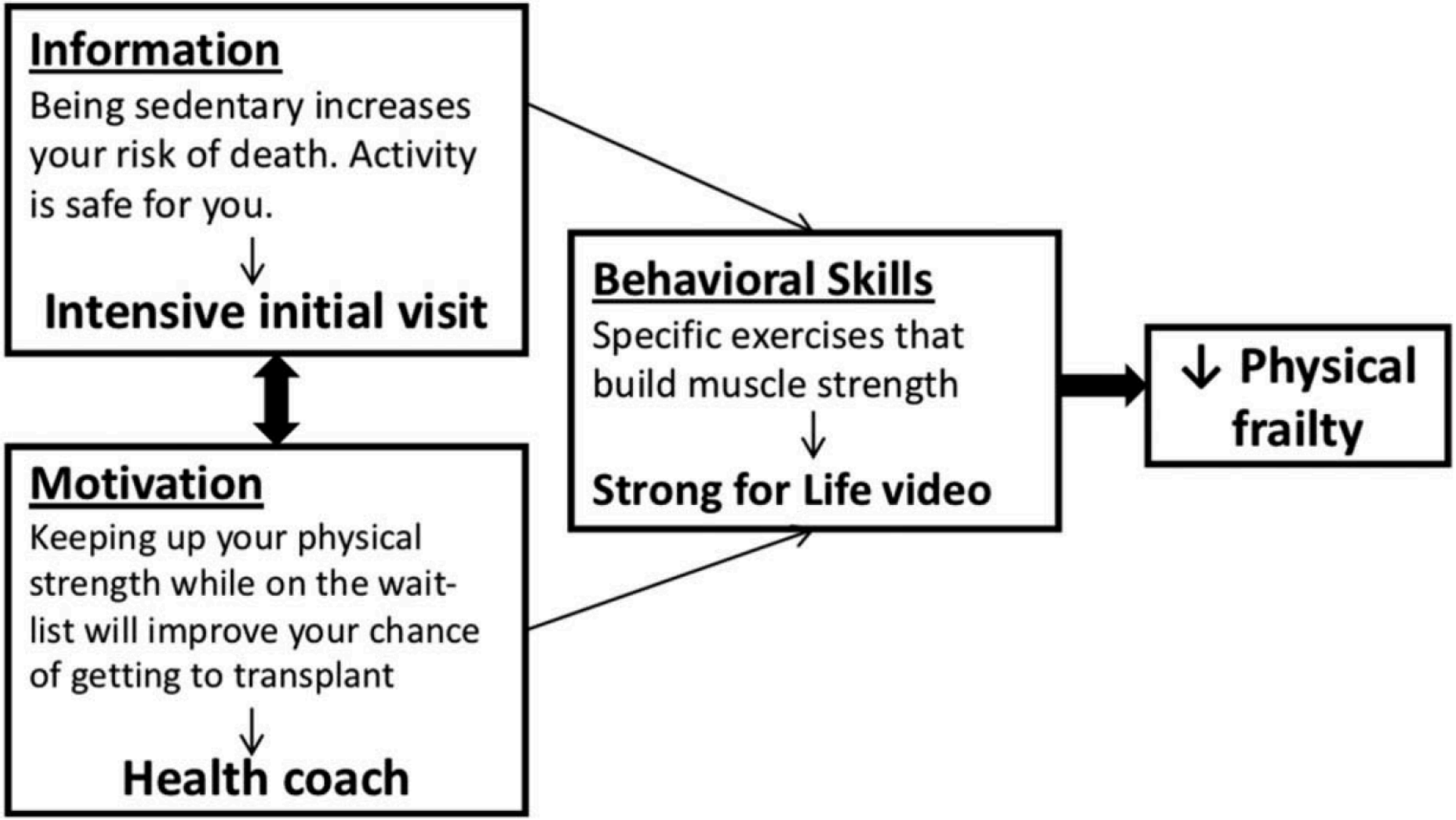


Figure 1. The 3 components of the strength training intervention for liver transplant patients (STRIVE) based on the Information-Motivation-Behavioral Skills conception model for modifying individual health behaviors (8).

Lai *et al*

Prehabilitation vs. Rehabilitation

- Transplant candidates may be more motivated to exercise knowing that they will be undergoing major surgery in the coming months

- Intervening through exercise post-transplant is not optimal
  - Steep decline in physical activity in the first year after transplantation
  - Poor adherence/compliance with prescribed rehabilitation (ie high dropout rates in clinical trials of transplant exercise)
  - Many transplant patients have prolonged recovery and are rehospitalized in the early postoperative period
  - Transplantation allows for return to work or school, which reduces the time for exercise

Physicians and patients support prehabilitation for transplant candidates.

	Physicians (n=41)	Patients (n=460)
Patients would be interested in prehabilitation	97.1%	80.2%
Prehabilitation would make ESRD patients less frail	97.1%	84.5%
Prehabilitation would help ESRD patients	100%	93.8%

RESEARCH ARTICLE Open Access

Engaging clinicians and patients to assess and improve frailty measurement in adults with end stage renal disease

Sarah Van Pilsum Rasmussen[1], Jonathan Konel[1], Fatima Warsame[2], Hao Ying[1], Brian Buta[3], Christine Haugen[1], Elizabeth King[1], Sandra DiBrito[1], Ravi Varadhan[4], Leocadio Rodríguez-Mañas[5], Jeremy D. Walston[2], Dorry L. Segev[1,5*] and Mara A. McAdams-DeMarco[1,5,6*]

Van Pilsum Rasmussen/McAdams
BMC Neph, 2018.

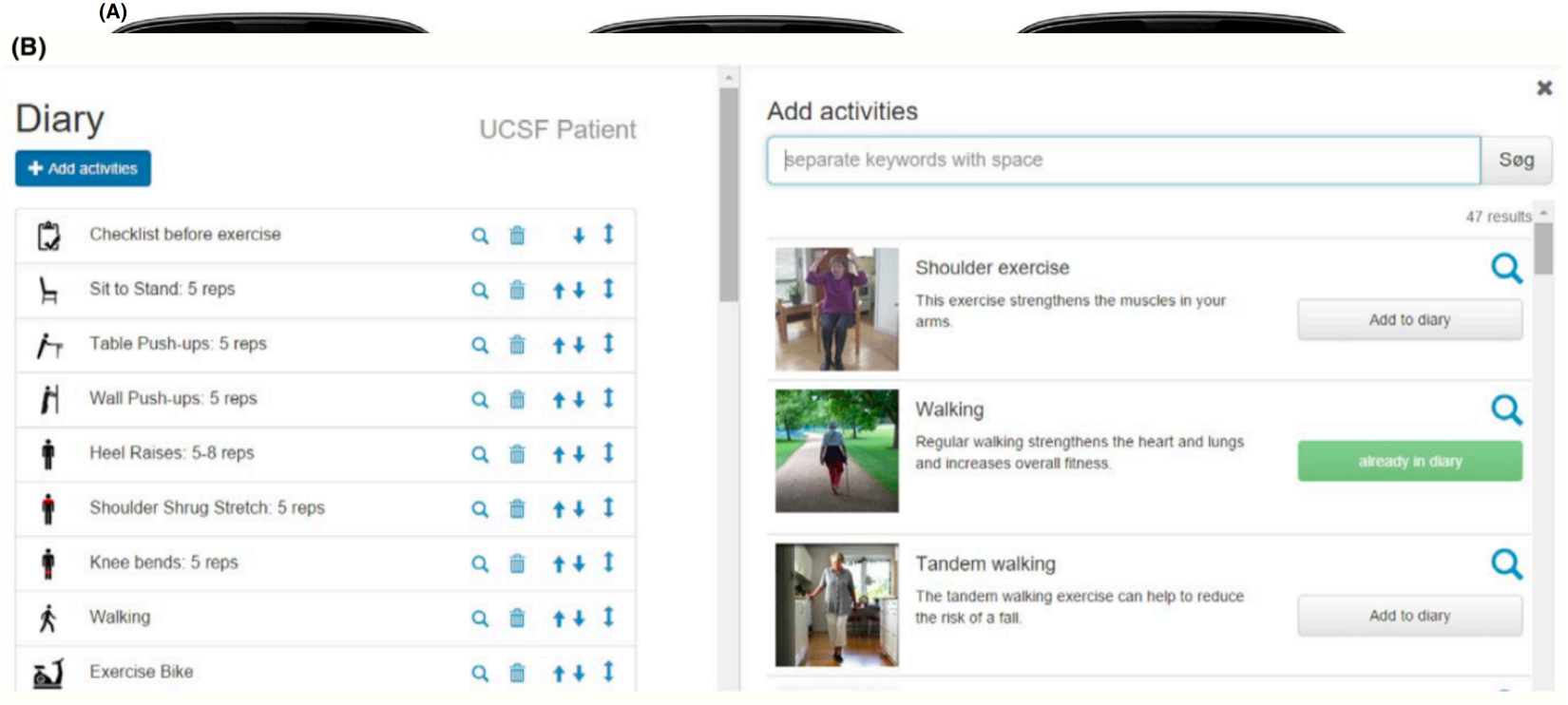
PRE-TRANSPLANT INTERVENTIONS IMPROVE FUNCTIONING

Pulmonary Rehabilitation of Lung Transplant Candidates

Study Design	Duration	Aerobic exercise	Other exercises	Outcomes	Author
Retrospective study (n=345)	1.5-2.0 hours 3 times/week	Treadmill	Resistance	Exercise capacity Quality of life	Li *et al*
Prospective study (n=58)	90 minutes 3 times/week	Treadmill	Muscle strength Breathing	Exercise capacity Quality of life	Florian *et al*
Trial (n=60)	3 week inpatient	Cycle interval training	-	Exercise capacity Quality of life	Gloeckl *et al*
Retrospective study (n=811)	5-6 days per week	Cycle endurance training	Muscle strength Breathing	Exercise capacity Quality of life	Kenn *et al*

Other Prehabilitation Interventions for Lung Transplant Candidates

- Among 13 patients, home-based prehabilitation using mobile health technology was safe and may improve frailty (Singer *et al*)



Other Prehabilitation Interventions for Lung Transplant Candidates

- Among 62 patients, prehabilitation improved the number of chair stands but not hospital length of stay (Wickerson *et al*)

- Among 159 patients, home-based exercise prehabilitation improved 6 minute walk distance for 26% of participants which was associated with (Massierer *et al*):
  - Less time on mechanical ventilation
  - Total hospital length of stay
  - Intensive care unit length of stay

EL-FIT (Exercise & Liver FITness) for Liver Transplant Candidates

- Feasibility study of novel exercise smartphone app for 25 participants (Duarte-Rojo *et al*)
- Exercise prescription:
  - Daily step goals
  - Exercise videos which increase in intensity over time

- Patients reported satisfaction with the device
- Engagement with it led to a significant increase in physical performance for 35% of patients

STRIVE for Liver Transplant Candidates

- Pilot study of a home-based exercise and strength training program (Lai *et al*)
- Targeted physical function in 58 patients with cirrhosis through 30-minute strength training videos and a health coach or standard of care
- While safe, only 14% of participants adhered to the videos for 10-12 weeks
- Improved quality of life

Prehabilitation for Kidney Transplant Candidates

- Weekly physical therapy sessions at an outpatient rehabilitation center
  - Sessions were 40 minutes long and conducted by a PT assistant
  - 20 minutes of additional supervised, free exercise
  - At a Johns Hopkins outpatient Physical Medicine and Rehabilitation (PM&R) center
  - Goal of improving global physical functioning and performing cardiovascular exercises as well as targeting any specific concerns that a patient expressed (eg, fall risk, lower back, etc)
- Participants were asked to participate in at-home exercise between prehabilitation sessions

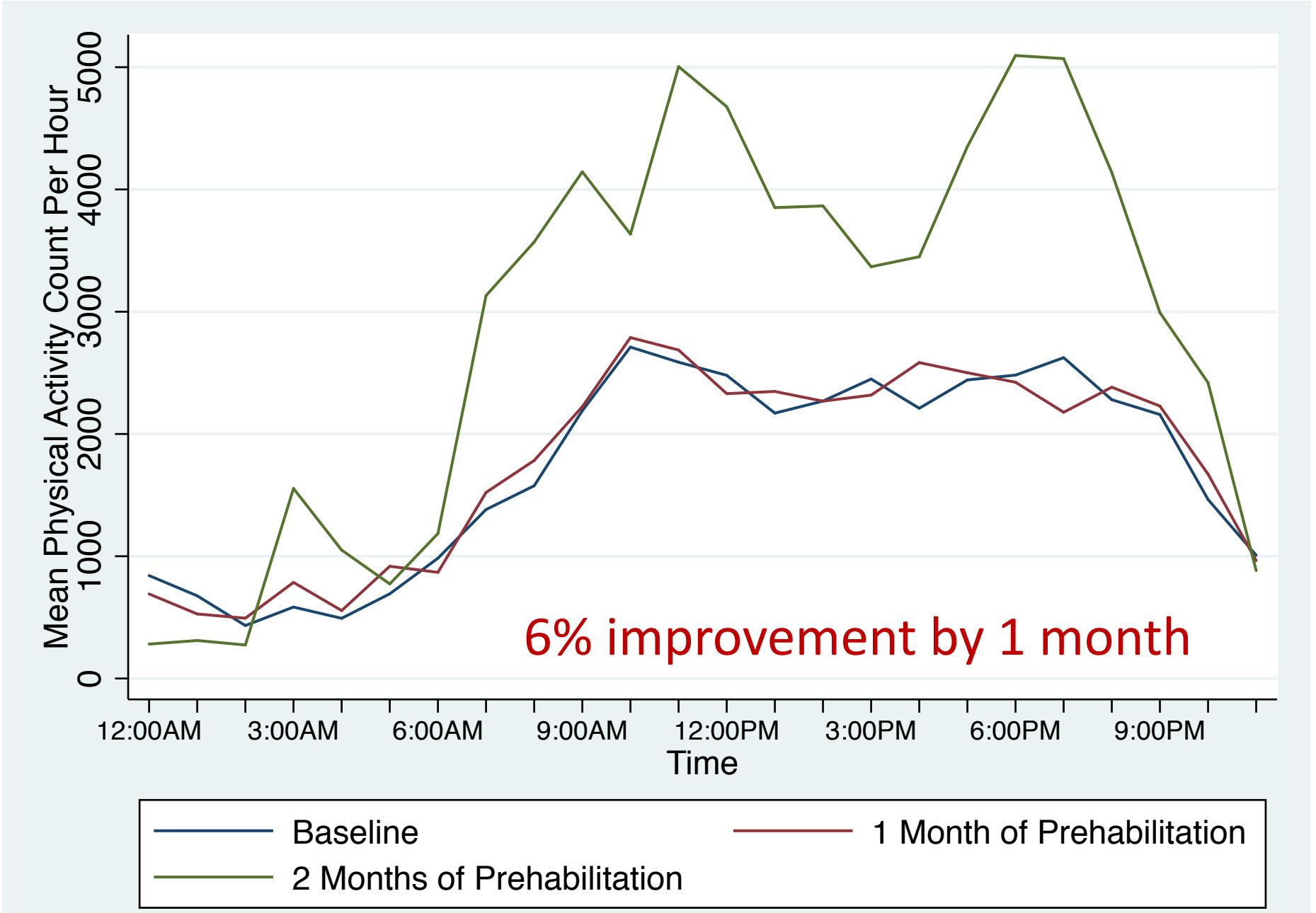
Prehabilitation Pilot Study

- Enrolled 24 kidney transplant candidates in a study on weekly prehabilitation in patients within 3-6 months of transplantation
- Participants have attended 12.6 sessions on average
  - Mean age=52 (range 34-72)
  - 72% were African American
  - 49% were female
  - 31% were frail
  - 53% had lower extremity impairment

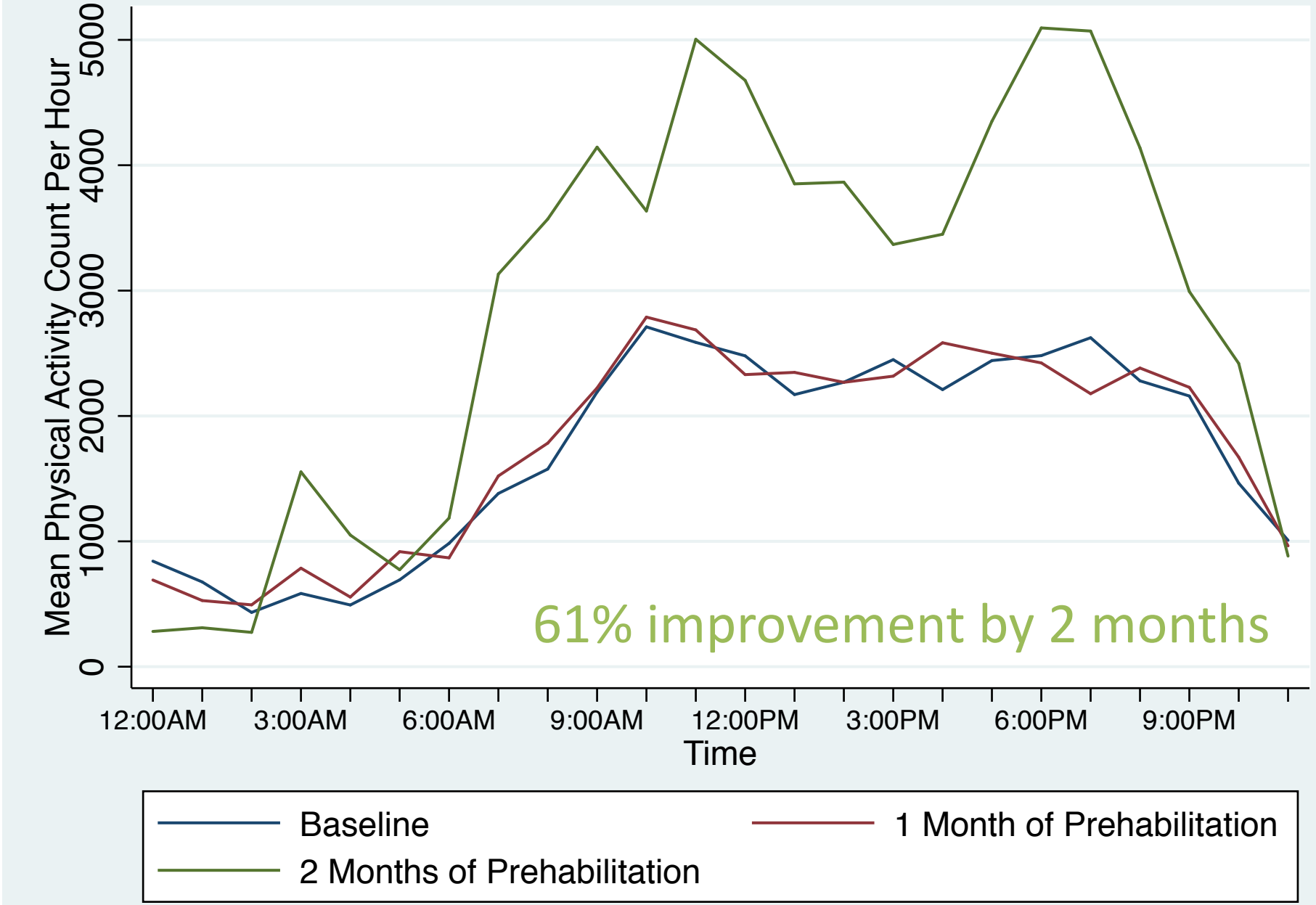
Participants were positive about prehabilitation.

- 100% of participants were “Very Satisfied” with prehabilitation

Themes	Representative quotes
Increased physical function and energy	“Can move around better” (Male, 50s) “Getting stronger” (Male, 40s) “Helped me get ‘all the kinks out of my body’ which helped me to move more than before” (Male, 40s) “It is helping [me] by regaining strength in my lower body and learning new exercises to maintain strength” (Male, 30s) “Helping to improve my mobility and daily physical functioning.” (Female, 40s)
Sustained endurance	“Giving me better endurance” (Male, 60s) “I sleep better, feel stronger, and have more endurance” (Male, 40s)
Better weight control	“It has helped me to lose the weight I need [to].” (Male, 40s) “Able to maintain…weight” (Male, 30s) “I needed to find an exercise program to help me lose the weight so I can get a transplant… the program has helped me get motivated to exercise.” (Male, 40s)
Improved attitude	“Program helps me feel a little better in life” (Male, 50s) “It helps me work and gave me a better outlook on what I'm doing and has been helpful” (Male, 40s)



McAdams-DeMarco *et al*



McAdams-DeMarco *et al*

Prehabilitation may impact kidney transplant length of stay.

- 5 candidates who participated in prehabilitation received KT
  - Compared to age-, sex-, and race-matched controls
- Length of stay was shorter for recipients who participated in prehabilitation
  - 5 days vs. 10 days, $P<0.01$
- Recipients with prehabilitation had a reduced length of stay
  - RR=0.69; 95% CI: 0.50-0.94; P=0.02

KNOWLEDGE GAPS IN PRE-TRANSPLANT INTERVENTIONS TO IMPROVE FUNCTIONING AMONG KT CANDIDATES

Conclusions

- Pre-transplant “forms an ideal window to recruit patients into self-driven efforts to modify health-related behavior, such as exercise, that pay health dividends well into the future.” (Tan *et al*)

- However, only 1 study of lung transplant candidates and 1 study of kidney transplant candidates showed that prehabilitation impacts post-transplant outcomes

Future research efforts

- To develop an optimal transplant prehabilitation intervention, we need to:
  - Identify the optimal transplant patient population to target
  - Define a standard prehabilitation regimen
  - Identify the optimal duration and timing
  - Quantify the costs of such

- Does prehabilitation improve pre- and post-transplant outcomes and prevent disability?

Epidemiology Research Group in Organ Transplantation

Dorry Segev, MD PhD, Founder and Director

Core Faculty

Andrew Cameron, MD PhD
Associate Professor of Surgery

Nadia Chu, MD
Instructor of Surgery

Christine Durand, MD
Assistant Professor of Medicine

Jacqueline Garonzik-Wang, MD PhD
Director of Training and Education
Assistant Professor of Surgery

Sommer Gentry, PhD
Professor of Mathematics (USNA)

Macey Henderson, JD PhD
Director of Policy and External Affairs
Assistant Professor of Surgery & Nursing

Allan Massie, PhD
Director of Data and Analytics
Assistant Professor of Surgery and Epidemiology

Mara McAdams-DeMarco, PhD MS
Associate Professor of Epidemiology and Surgery

Douglas Mogul, MD MPH
Assistant Professor of Pediatrics

Abimereki Muzaale, MD MPH
Instructor of Surgery

Lauren Nicholas, PhD
Assistant Professor of Health, Policy and Management

Tanjala Purnell, PhD MPH
Director of Community and Stakeholder Engagement
Assistant Professor of Surgery

Residents & Fellows

Christine Haugen
Courtenay Holscher
Kyle Jackson
Martin Kosztowski
Francisco Rivera
Sharon Weeks
Heather Wasik

Coordinators

David Helfer
Theresa Hwee
Maria (Malu) Lourdes Perez
Arthur Love
Amrita Saha
Madeleine Waldram

Collaborators

Elisa Gordon, PhD MPH
Bioethics, Northwestern University

Jayme Locke, MD
Transplant Surgery, UAB

Krista Lentine, MD PhD
Nephrology, Saint Louis University

Babak Orandi, MD PhD MSc
Transplant Surgery, UAB

Research Data Analysts

Dayawa Agoons
Mary Grace Bowring
Tanveen Ishaque
Jennifer Motter
Alvin Thomas
Zhan Shi
Sile Yu
Yifan Yu

Med/Grad Students

Sunjae Bae
Jennifer Chen
Karina Covarrubias
Lindsay Dickerson
Amber Kernodle
Luckmini Liyanage
Lucy Nam
Jane Long
Hasina Maredia
Jessica Ruck
Nicholas Siegal
Ashton Shaffer*
Ashley Xu

Research Assistants

Full Time

Paul Butz
Yen Baker
Amanda DeLorenzo
Simone Goodman
Alexander Hsiao
Morgan Johnson
Sneha Kunwar
Anita Louie
Sarah Van Pilsum Rasmussen
Eileen Rosello
Estefania Velez

Part Time

Jenna Bellantoni
Shivani Bisen
Maya Flannery
Samantha Getsin
Kevin Gianaris
Esha Hase
Leyla Herbst
Kathryn Marks
Taylor Martin
Cameron Meis
Alexis Mooney
Sanjana Murthy
Aditya Patibandla
Jamilah Perkins
Prakriti Shrestha
Salma Tayel
Maisy Webster

Affiliates

Fawaz Al Ammary, MD
Nephrology

Gerald Brandacher, MD
Surgery

Dan Brennan, MD
Nephrology

Errol Bush, MD
Surgery

Josef Coresh, MD PhD
Epidemiology

Morgan Grams, MD PhD
Nephrology

Niraj Desai, MD
Surgery

Elliott Haut, MD PhD
Surgery

Lindsay Pote, PharmD
Transplant Pharmacy

Aliaksei Pustavoitau, MD
Anesthesiology

Daniel Scharfstein, ScD
Biostatistics

Kim Steele, MD PhD
Surgery

Ravi Vardhan, PhD
Biostatistics

Jason Wheatley, LCSW-C
Transplant Social Work

References

1. Duarte-Rojo A, Bloomer PM, Rogers RJ, et al. Introducing EL-FIT (Exercise and Liver FITness): A Smartphone App to Prehabilitate and Monitor Liver Transplant Candidates. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society.* 2020.
2. Florian J, Rubin A, Mattiello R, Fontoura FF, Camargo Jde J, Teixeira PJ. Impact of pulmonary rehabilitation on quality of life and functional capacity in patients on waiting lists for lung transplantation. *J Bras Pneumol.* 2013;39(3):349-356.
3. Gloeckl R, Halle M, Kenn K. Interval versus continuous training in lung transplant candidates: a randomized trial. *J Heart Lung Transplant.* 2012;31(9):934-941.
4. Kenn K, Gloeckl R, Soennichsen A, et al. Predictors of success for pulmonary rehabilitation in patients awaiting lung transplantation. *Transplantation.* 2015;99(5):1072-1077.
5. Lai JC, Dodge JL, Kappus MR, et al. A Multicenter Pilot Randomized Clinical Trial of a Home-Based Exercise Program for Patients With Cirrhosis: The Strength Training Intervention (STRIVE). *Am J Gastroenterol.* 2020;Publish Ahead of Print.
6. Li M, Mathur S, Chowdhury NA, Helm D, Singer LG. Pulmonary rehabilitation in lung transplant candidates. *J Heart Lung Transplant.* 2013;32(6):626-632.
7. McAdams-DeMarco MA, Ying H, Van Pilsum Rasmussen S, et al. Prehabilitation Prior to Kidney Transplantation: Results from a Pilot Study. *Clin Transplant.* 2018:e13450.
8. Massierer D, Bourgeois N, Rakel A, et al. Changes in 6-minute walking distance in lung transplant candidates while participating in a home-based pre-habilitation program-A retrospective chart review. *Clin Transplant.* 2020;34(10):e14045.
9. Sheshadri A, Johansen KL. Prehabilitation for the Frail Patient Approaching ESRD. *Seminars in nephrology.* 2017;37(2):159-172.
10. Singer JP, Soong A, Bruun A, et al. A mobile health technology enabled home-based intervention to treat frailty in adult lung transplant candidates: A pilot study. *Clin Transplant.* 2018;32(6):e13274.
11. Wickerson L, Rozenberg D, Gottesman C, Helm D, Mathur S, Singer LG. Pre-transplant short physical performance battery: Response to pre-habilitation and relationship to pre- and early post-lung-transplant outcomes. *Clin Transplant.* 2020;34(12):e14095.