

Exercise as Therapy for Older Patients with Heart Failure with Preserved Ejection Fraction

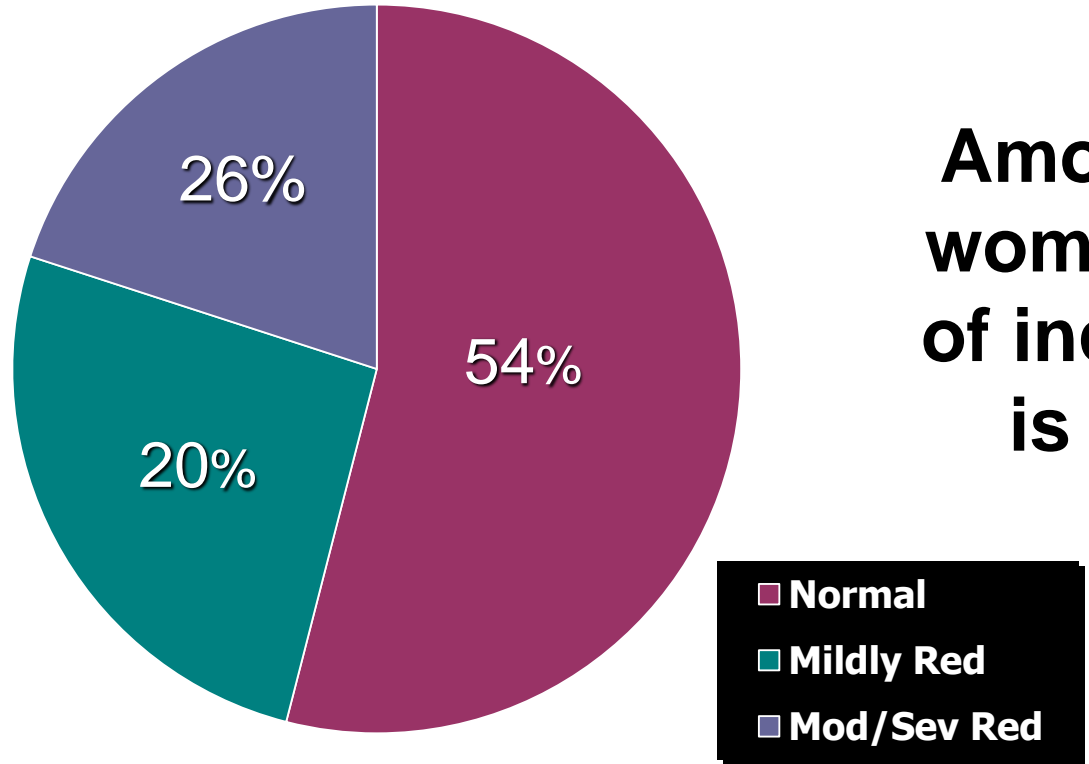
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**How to Succeed in Aging Research
Despite Countless Setbacks:
A Journey**

Heart Failure with Preserved EF (HFpEF): The Most Common Form of HF in Community-Dwelling Older Persons: The Cardiovascular Health Study

Confirmed in
Framingham
and 4 other NIH-
funded
population
studies



Among older
women, **>90%**
of incident HF
is HFpEF

Kitzman et al, Am. J. Cardiol 2001
Aurigemma et al, JACC 2001

Despite the high prevalence and poor prognosis, there are few proven drug treatments for HFpEF!



- **>20 negative medication trials**
- **The most common cardiovascular disorder for which optimal pharmacological treatment is unknown**

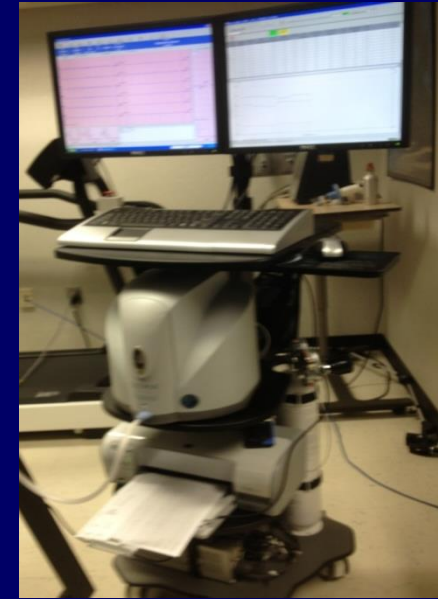
Older Patients with HFpEF Have Marked Physical Dysfunction



- **Severe exertional dyspnea and profound fatigue**
- **High rates of physical frailty (up to 90%)**
- **Major contributor to their severely reduced quality of life**
- **Strong predictor of death, hospitalization, and nursing home placement**

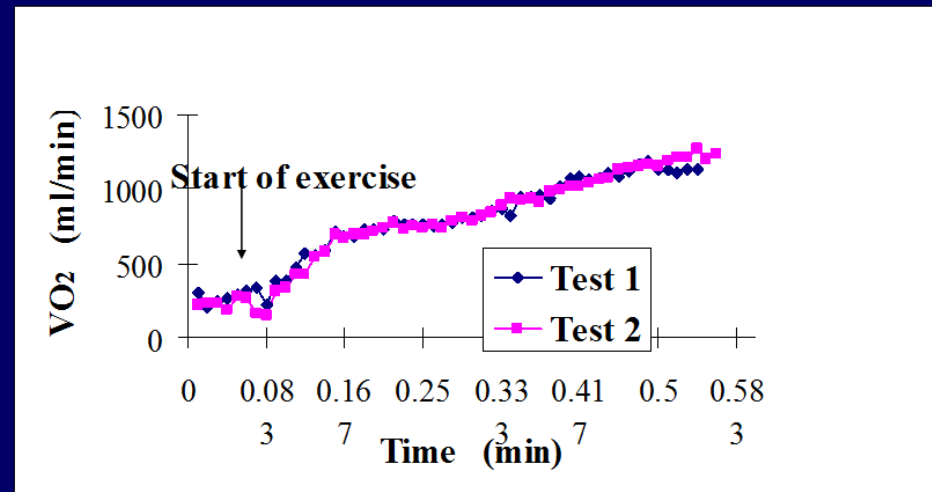
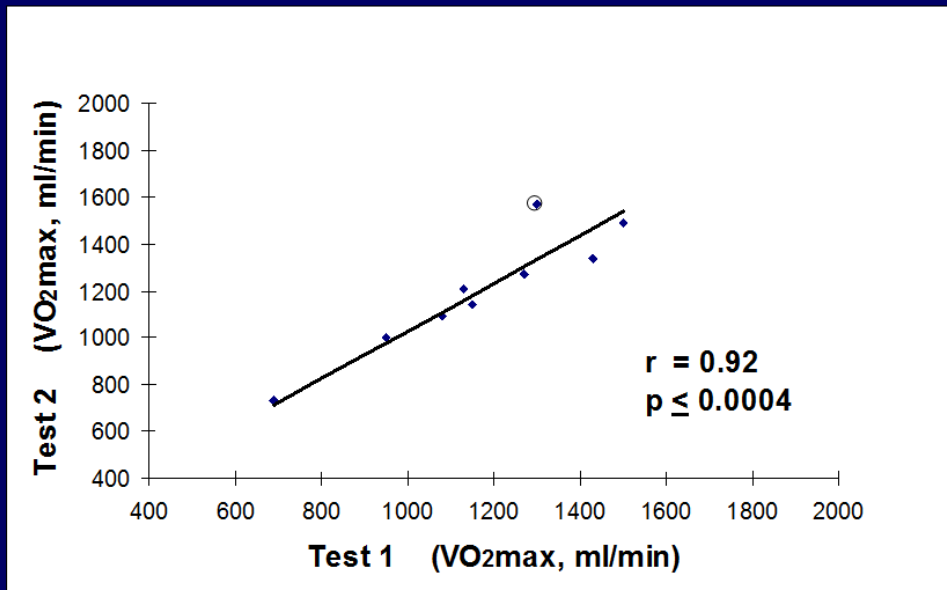
Quantifying Exercise Intolerance: Peak Oxygen Consumption (VO_2)

- Non-invasive, standardized, objective measure of exercise capacity.
- Valid and reproducible even in very old HFpEF patients (Scott, Kitzman 2012).



Group data

Individual data



Activities of Daily Living as a Percent of Peak VO₂ in Older Patients with HFpEF

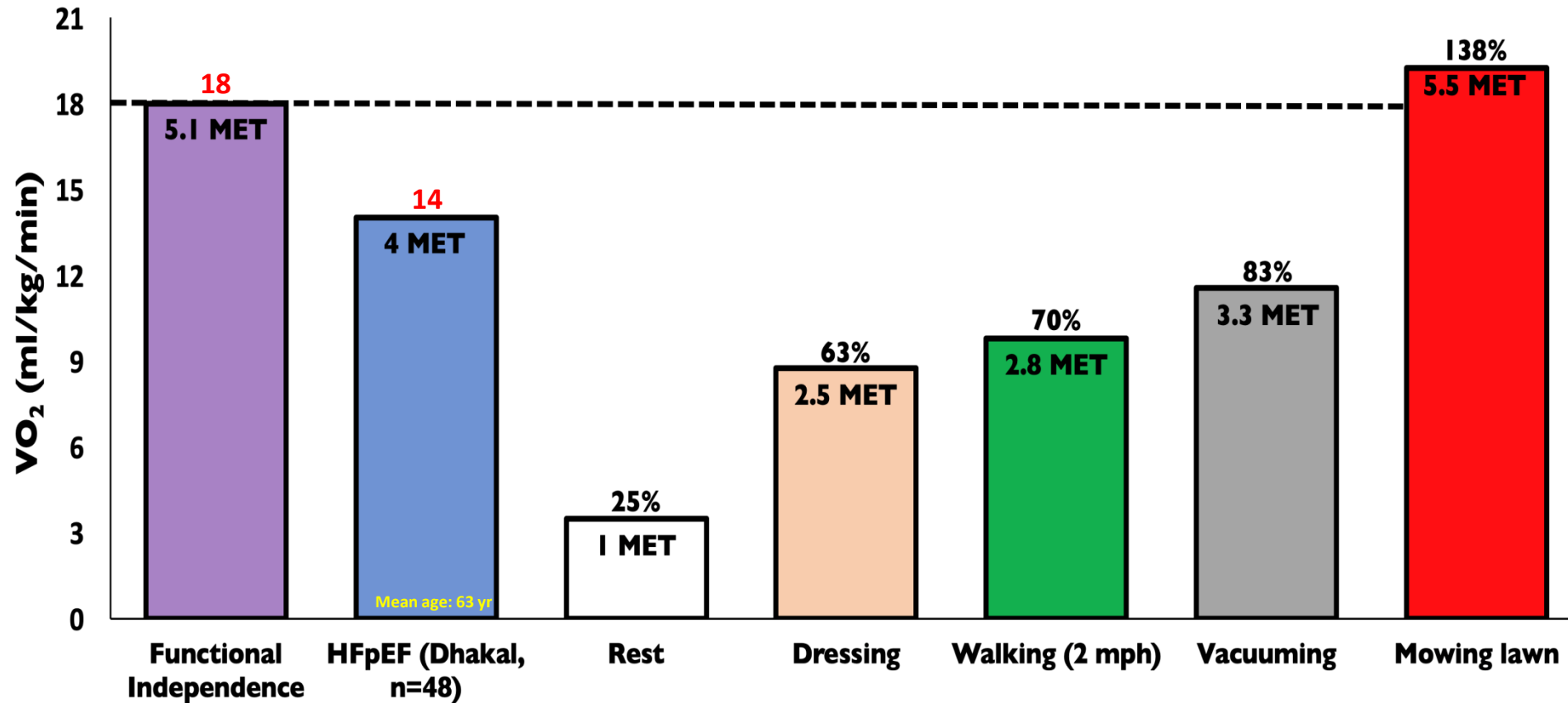
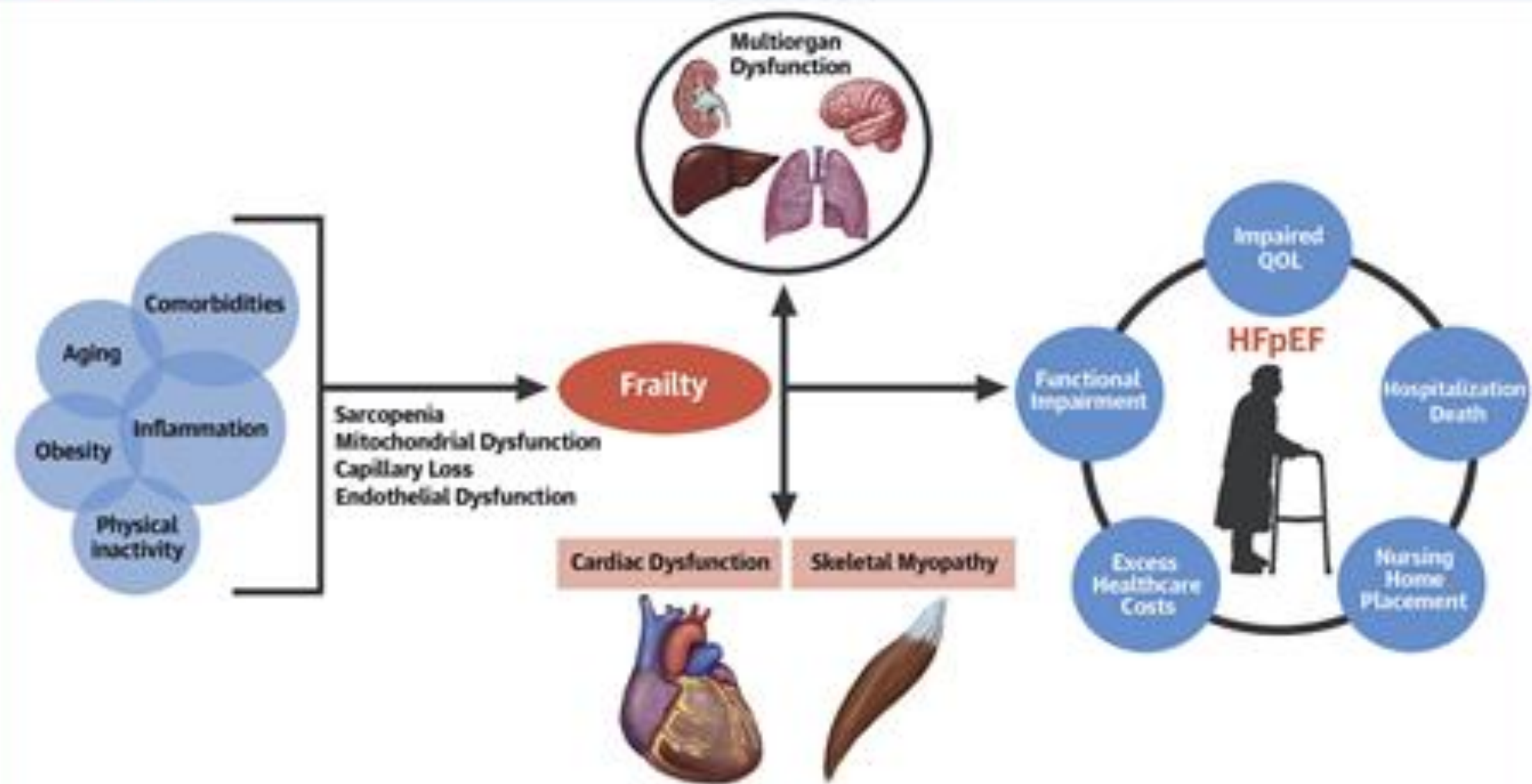
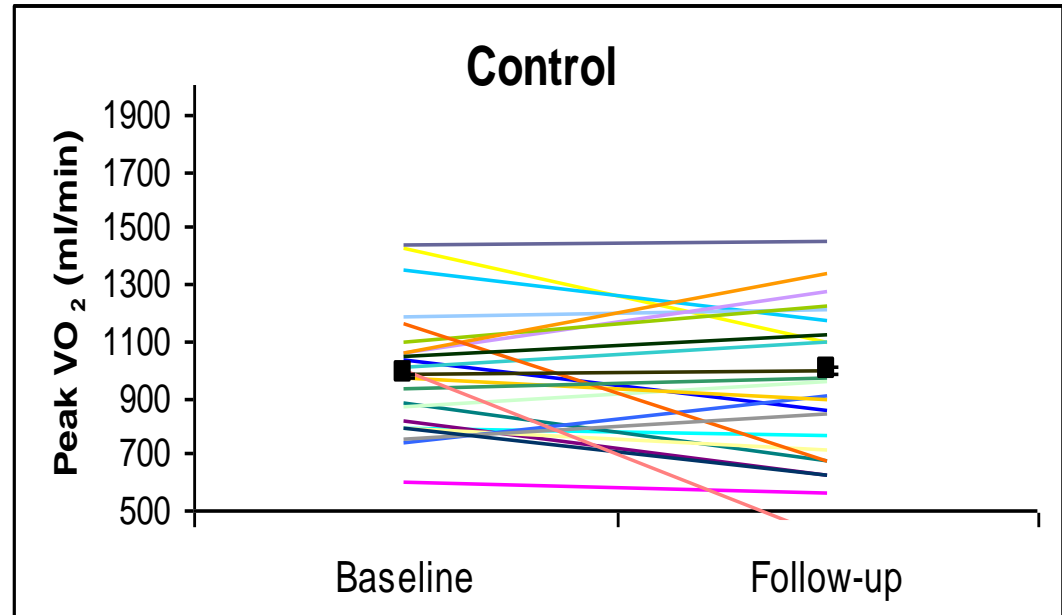
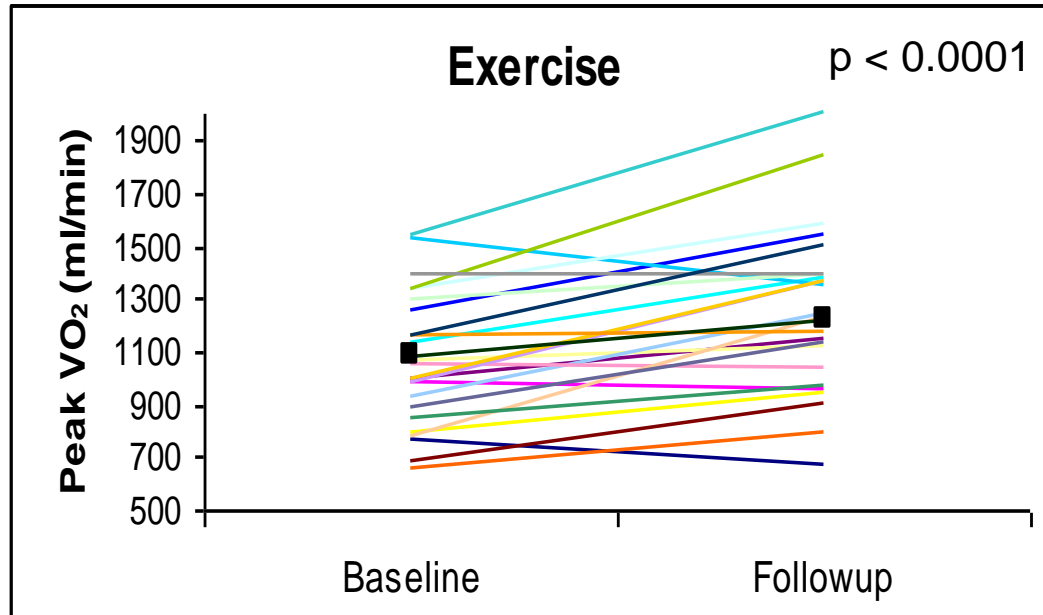


Figure 1: Pathophysiology and Outcomes in HFpEF



Effect of Exercise Training on Exercise Capacity in Older Patients with HFpEF

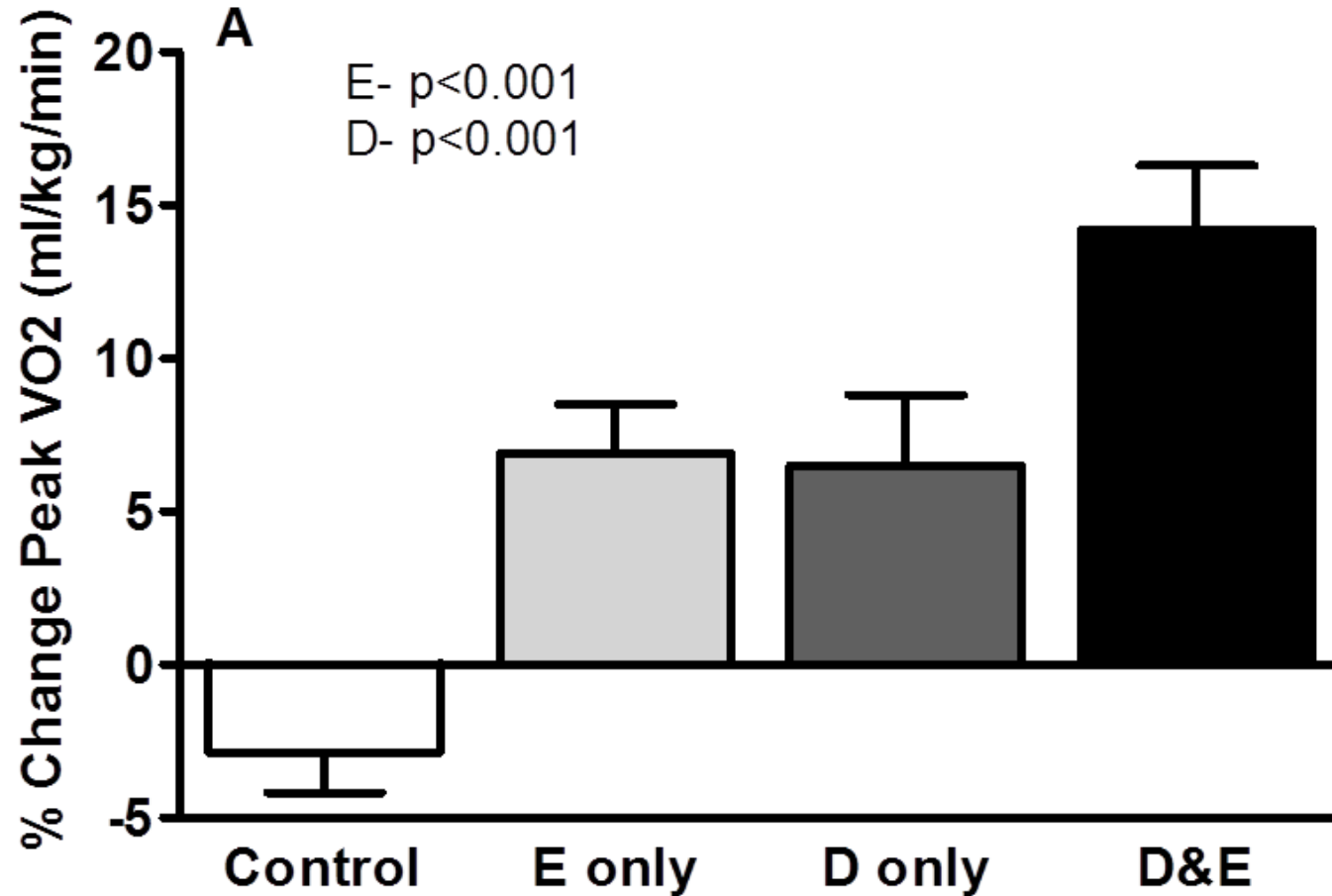


Obesity, the Elephant in the Room

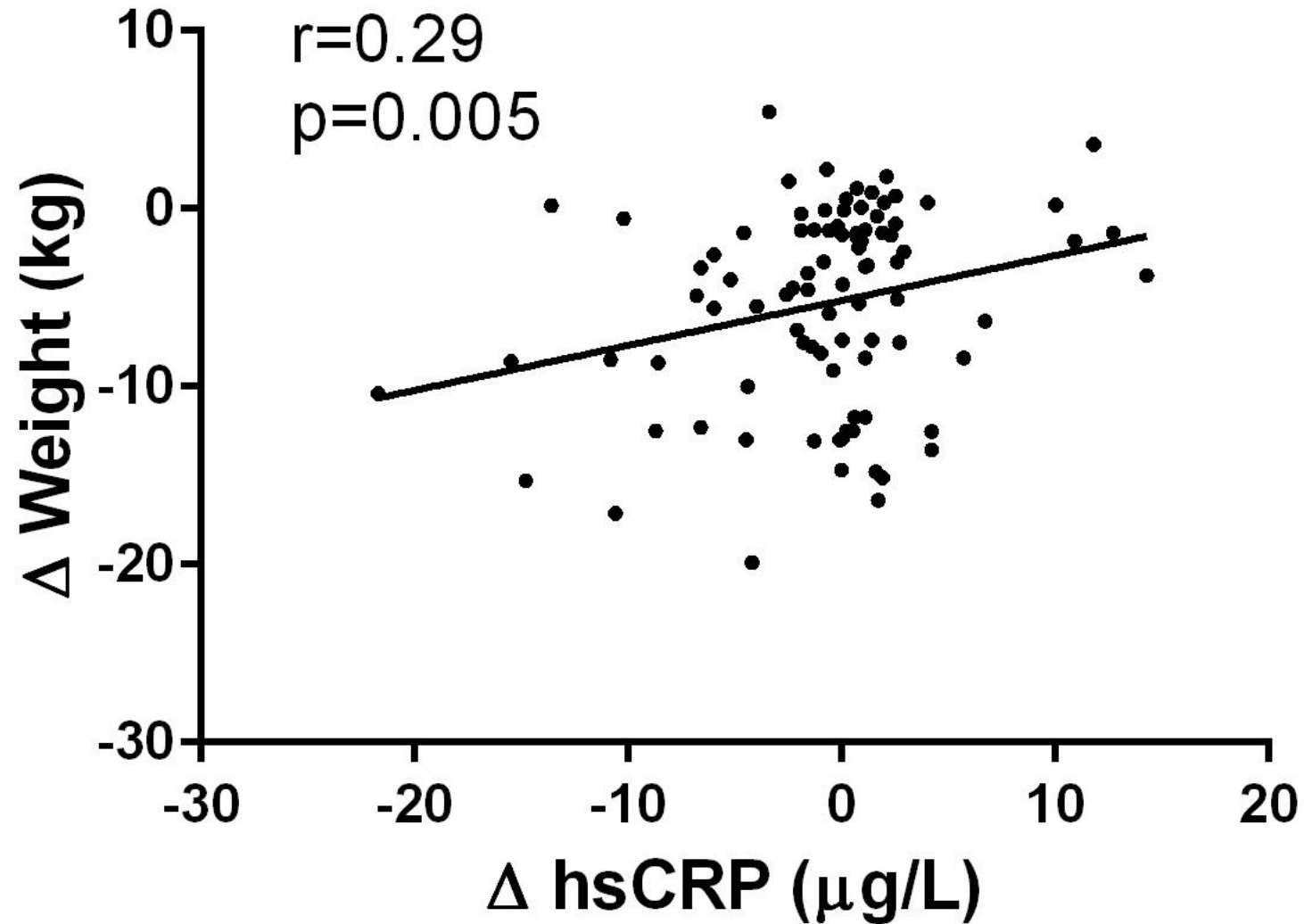


- **Obesity is the third strongest risk factor for development of HFpEF**
- **85% of HFpEF patients are overweight or obese, more than twice the general population**
- **Obesity promotes inflammation, HTN, insulin resistance, and impairs cardiac, arterial, skeletal muscle, and physical function**

SECRET Trial Primary Outcome: Peak VO₂ Improved Most with Diet + Exercise



Dietary Weight Loss in HFpEF Reduced Markers of Inflammation



Can we extend the benefits of physical exercise to Frail Older Patients Hospitalized with Acute Heart Failure (ADHF)?

- **ADHF is the most common hospital discharge diagnosis in older persons**
- **Poor QOL, frequent rehospitalization, high mortality, loss of independence, and high nursing home admission**
- **Excluded from prior exercise trials**
- **Pilot study showed marked impairments in all domains of physical function: balance, mobility, strength, endurance; >90% were frail/pre-frail**
- **Developed innovative, multi-domain, tailored physical function intervention**

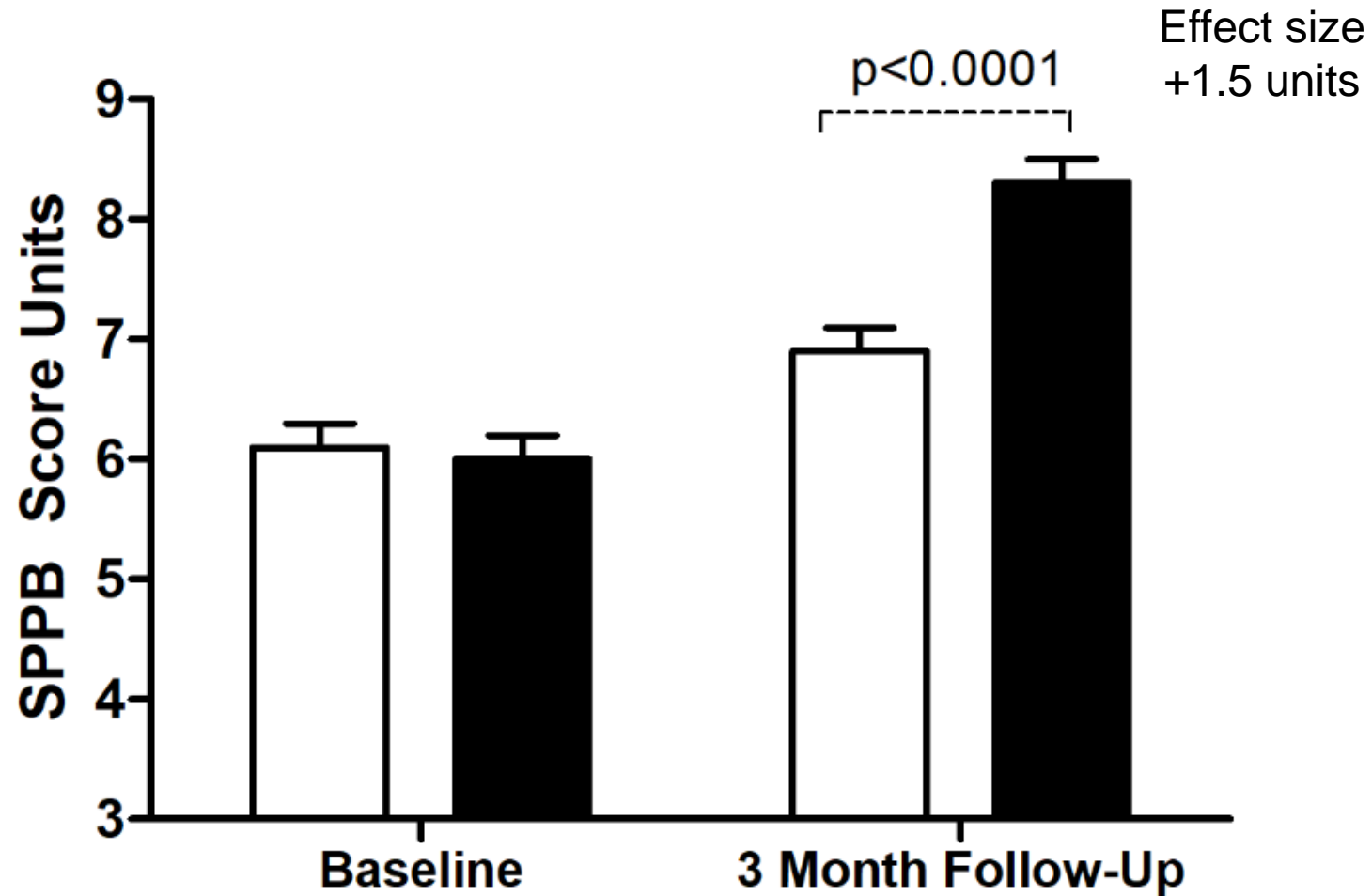
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Kitzman DW, et al. NEJM July 15 2021

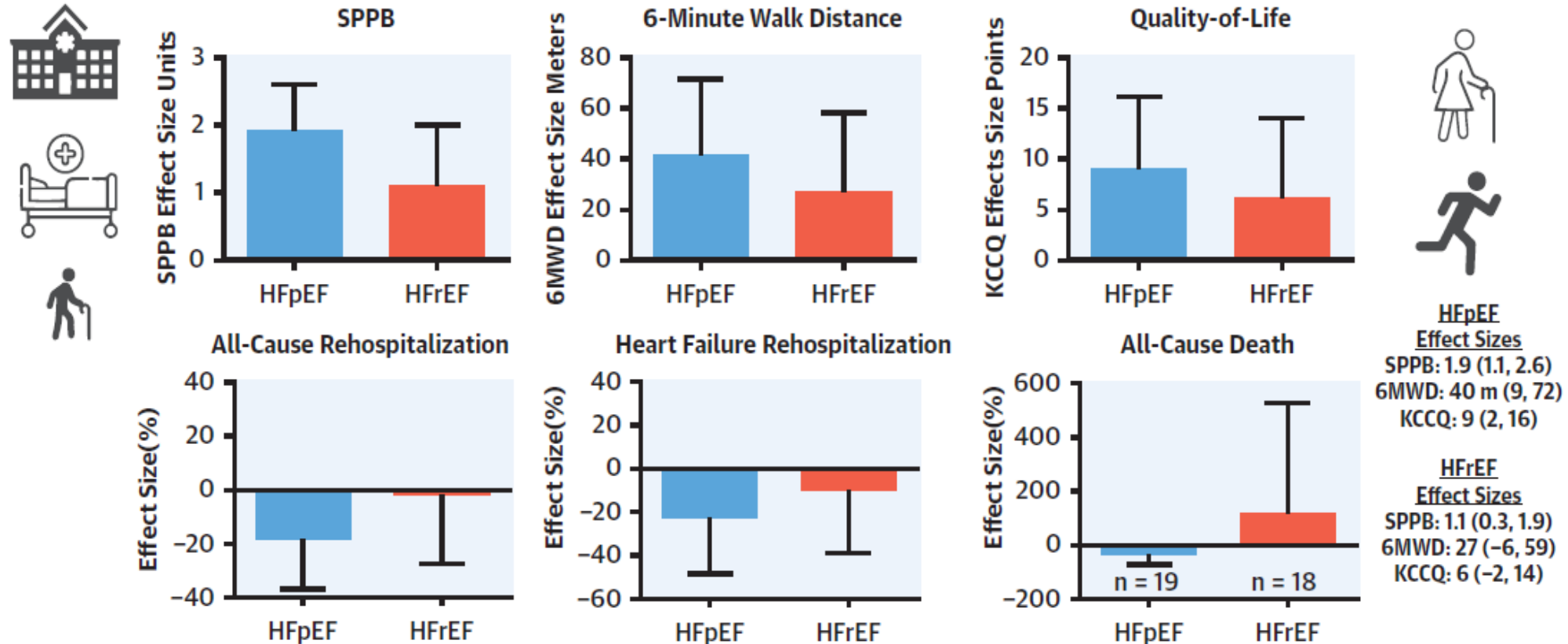
*Physical Rehabilitation for Older Patients
Hospitalized for Heart Failure*

REHAB-HF Trial Primary Outcome: SPPB at 3-Months



Clinically meaningful change is 0.5 units

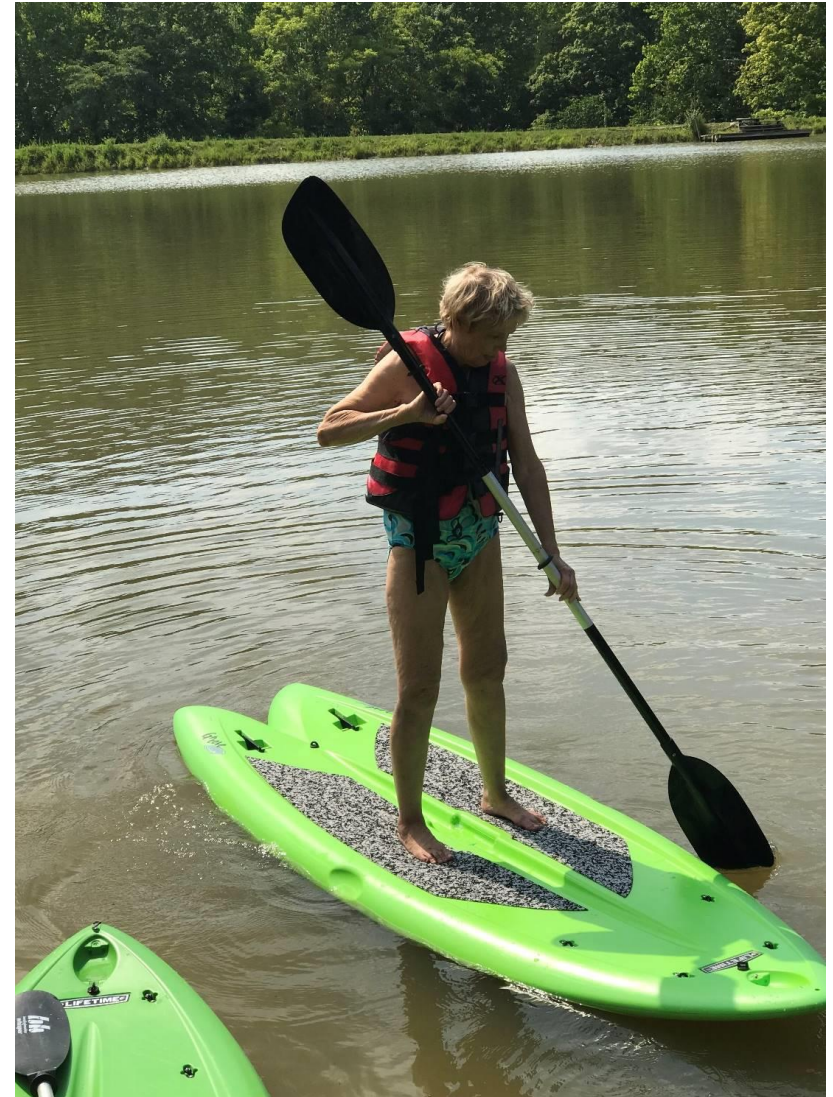
Patients with HFpEF Appeared to Have Much Greater Improvements from the novel REHAB-HF Intervention



Compared to patients with HFrEF, those with HFpEF may derive greater benefit from the intervention.

The difference that applying the right intervention to the right patient at the right time can make:

From being house-bound after her hospital discharge, to paddle-boarding with grandchildren!



Was My Research Career A Carefully Planned, Straight Pathway to Success?

- Many seminal discoveries regarding HFpEF**
- Nearly 500 publications: JAMA, Lancet, NEJM**
- External funding since first year as faculty**
- Many leadership positions and awards**

It Was a Journey, Not a Straight, Sure Path!

1. The first grant I applied for as a faculty was not funded, even though I was the only applicant who showed up at the mandatory interview
 - start over
2. The mechanistic hypothesis of my first R01 was disproven by the study results
 - start over
3. The primary hypothesis of my second R01 was disproven
 - start over
4. The primary and mechanistic hypothesis of my third R01 were disproven
 - start over
5. The first 12 (!) medication trials I led or helped lead were neutral
 - start over, and over, and over

What I Learned Along the Way

1. Never give up on your dream
2. Select an important question, and the answer will be important no matter the results
3. Relentlessly pursue the truth, regardless of where it leads you
4. Reach out to others who can help you learn new techniques
5. Build and foster a multi-disciplinary team
6. Adapt; learn from your 'mistakes', they may be your best clue
7. Have fun, enjoy the journey of discovery

17 Essential Ingredients for Success in Medical Research

1. Good training
2. Good environment
3. Important question
4. Preliminary data
5. Good mentors
6. A broad, diverse team
7. Supportive program officer
8. Supportive family

17 Essential Ingredients for Success in Medical Research

9. Affability

10. Writing skills

11. Lots and lots of really hard work and very long hours

12. True passion for the subject matter

13. Fear of failure

14. A lot of curiosity

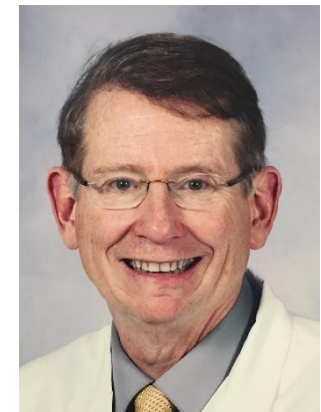
15. Perseverance

16. A bit of intelligence

17. Some luck

Mentors Who Made a Difference

- **Madelynn Roll**
 - Taught me to never quit
 - Showed me the devastation of HFpEF
- **Barbara Shaver**
 - Taught me to follow your dream
- **William Edwards**
 - Taught me how to write my first journal article
- **Michael Higginbotham**
 - Taught me how to write my first grant application
- **Debra Kitzman**
 - Gave me courage and support to start over after a wrong turn
- **William Hazzard, Walter Ettinger, William Little**
 - Saw something in me that I wasn't sure was there



Key Collaborators Who Made Critical Contributions

**Peter Brubaker
Barbara Nicklas
Anthony Molina
Denise Houston
Henry Miller
Lenny Kaminsky
Steve Kritchevsky
Steve Keteyian
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Kathryn Stewart
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Russ Newland
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David Herrington
David Zhao
Pamela Duncan
Amy Pastva
Robert Mentz
Gordon Reeves
Chris O'Conner
David Whellan
Gordon Reeves
Shelby Reed
Many more...**

Funding agencies that took a chance on my ideas

**National Institute on Aging
National Heart Lung and Blood Institute
American Federation for Aging Research
Hartford Foundation
American Heart Association**

Participants

1,526 participants who trusted me and volunteered to partner with me on a quest to discover new knowledge to improve the lives of older persons

