

# **How to Start a Big Project: A Journey in Aging Research**

Dalane W. Kitzman, M.D.

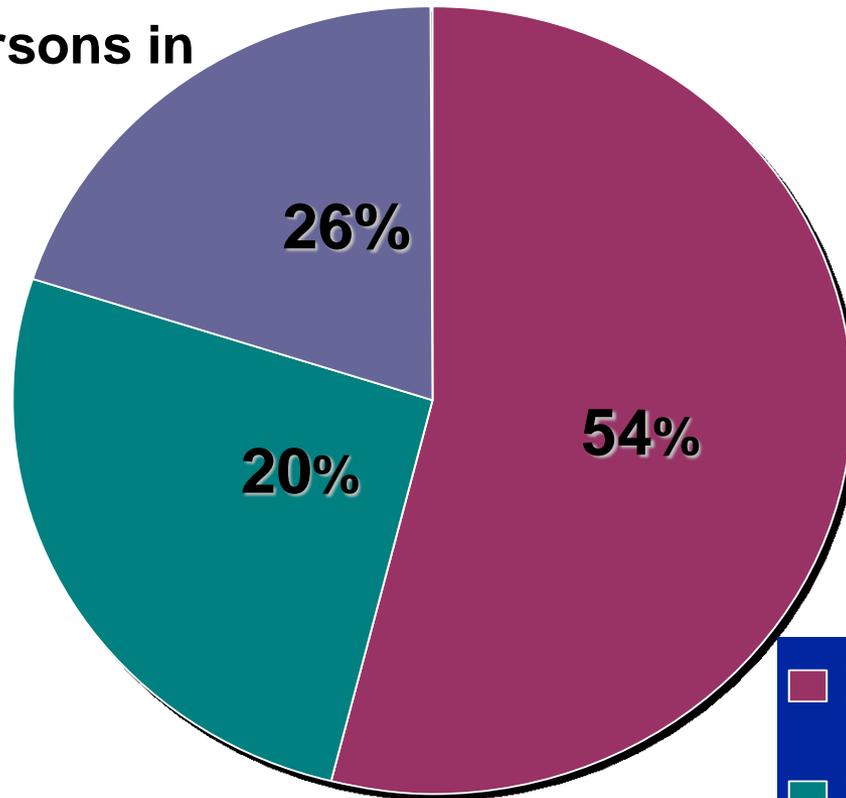
Kermit Glenn Phillips II Chair in Cardiology



# Heart Failure with Preserved EF (HFPEF): The Most Common Form of HF in Older Persons

## The Cardiovascular Health Study

2.1 million persons in  
U.S.



**Women >> Men**

**Prevalence increasing**

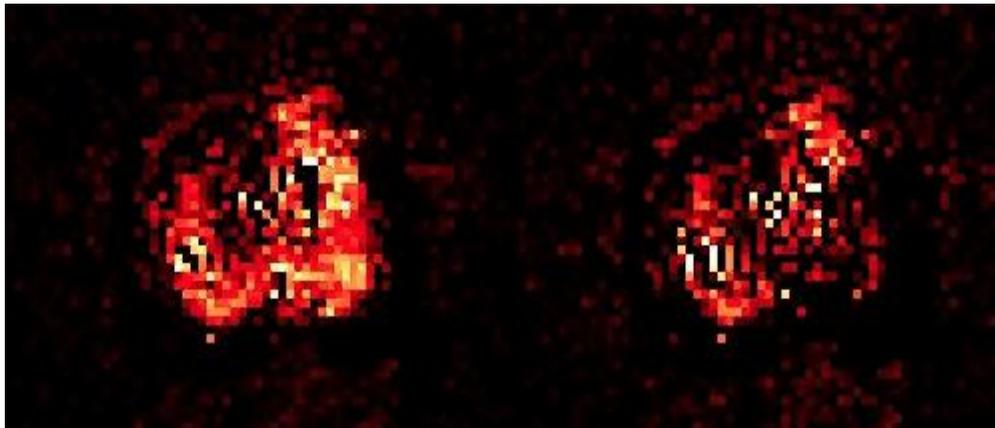
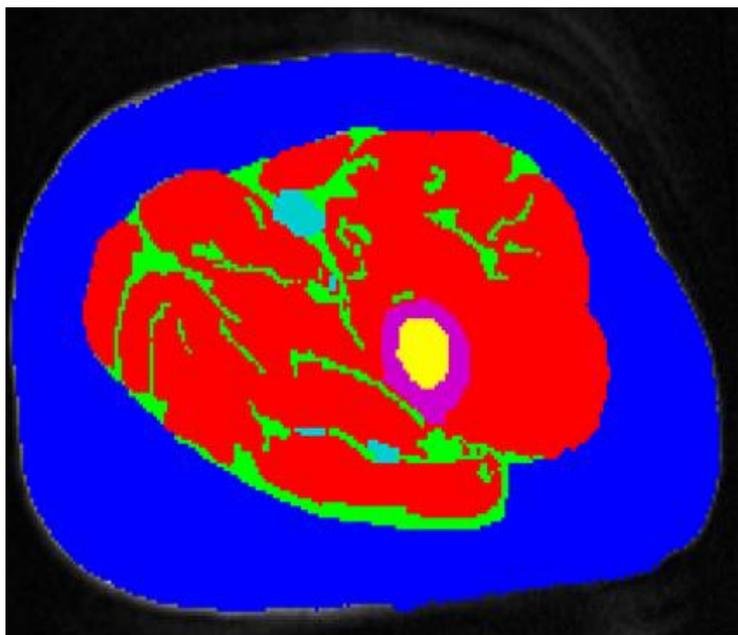
**Prognosis worsening**



Kitzman et al, Am. J. Cardiol 2001

# High Burden of Misery in HFPEF

- Persistent shortness of breath with exertion
- Poor quality of life
- Frequent hospitalization
- High health care costs
- Increased death rate
- No medication treatments proven effective



# 10 Major Advances by Wake Forest CV Aging Research Team

1. Among the first to describe that Heart Failure can occur with a normal left ventricular ejection fraction (HFPEF)
2. Among the first to report that HFPEF is the dominant form of heart failure in older persons, particularly women
3. First to describe how HFPEF differs from normal aging
4. First to report that medications aimed only at improving cardiac function do not improve Peak  $VO_2$  and symptoms
5. First to report that non-cardiac abnormalities are important contributors to symptoms and reduced Peak  $VO_2$  in HFPEF
6. First to report 6 specific skeletal muscle abnormalities in HFPEF and how they contribute to exercise intolerance
7. First to report that endurance exercise training improves HFPEF
8. First to report that exercise works mainly by improving skeletal muscle function rather than cardiac or vascular function
9. First to describe abnormal mitochondrial function in HFPEF
10. First to report that caloric restriction diet improves HFPEF and is additive to exercise training

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

1. The first grant I applied for as a Wake Forest faculty was not funded, even though I was the only applicant to show up at the interview at the foundation headquarters in Manhattan.  
-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. All 5 medication trials I led or helped lead were neutral, including an international trial with 4000 patients that took over 7 years  
-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. Adapt
5. Reach out to others who can help you learn new techniques
6. Learn from your 'mistakes', they may be your best clue
7. Have fun, enjoy the journey of discovery

# 16 Essential Ingredients for a Successful Medical Research Project (or Career)

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

# 16 Essential Ingredients for a Successful Medical Research Project (or Career)

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. A bit of intelligence
16. Luck

# Critical Influence of Mentors and Role Models on the Development of a Physician-Scientist

- Madelynn Roll
  - Never quit
- Barbara Shaver
  - Follow your dream
- William Edwards
  - How to write my first medical research journal article
- Michael Higginbotham
  - How to write my first grant application
- Debra Kitzman
  - Courage and support to start over after a wrong turn
- William Hazzard, Walter Ettinger, William Little
  - Seeing something in me that I wasn't sure was there

# Major Contributions from Many Key Collaborators

Peter Brubaker

Barbara Nicklas

Anthony Molina

W. Gregory Hundley

Timothy Morgan

David Herrington

Mark Haykowsky

Steve Kritchevsky

Denise Houston

Mary Lyles

Craig Hamilton

Deborah Wesley

Bharathi Upadhyia

Kathryn P. Stewart, Judy Brown, Bonita Trivette, Nancy Clay

# National Institute on Aging

Susan Ziemann  
Basil Eldadah  
Evan Hadley

R01 AG12257 (First R01)  
R37 AG18915 (MERIT Award)  
R01 AG045551 (First Multicenter Trial)  
P30 AG 12332 (Pepper Center – Program Project)

Thank you!