Heart Failure and Exercise

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Disclosure

Research – NIH

DSMB – Abbott (ARIES and Momentum)

Consultant – Medtronic

Site PI – HEART-FID, METEORIC, Pfizer ATTR-CM study (B3461087)

Used to have support – Under Armour

Outline

Exercise physiology in heart failure patients

Current medical therapy for heart failure patients and how it effects exercise capacity

Benefit of exercise in heart failure/LVAD/transplant

Unique aspects to watch for in LVAD/transplant patients

Case presentation

Mrs. S (she sent me this picture and tells me to use it)

74 yo

Hx L breast Ca and received Adriamycin/trastuzumab 2001

I met in 2017 when referred for new EF 20

Cath with normal cors

Started meds and she did well

Rides 10 miles/day in 55 minutes

Case presentation cont.

Mar 2018 – comes to clinic complaining that her 10 mile ride now takes over an hour

Nov 2018 – now has to walk up the hill on her ride

CPX – 12/3/18 – Peak VO2 7.3 (41% predicted), Ve/VCO2 slope 57.6

Undergoes implantation of LVAD 1/7/19

Recovers well, enjoyed cardiac rehab

Wanted to start riding again but worried with having to handle two batteries and controller and on warfarin

Case presentation

Spring 2019 - S Russell made the mistake of telling wife that on ride ended up in the ditch while trying to avoid 3 deer running across the road and then later on same ride dinged by a wide mirror on a truck

Father's Day 2019 – S Russell gets Peloton and threats to cut my bike up if I ever rode on the road again

July 2019 – Tells Ms. S his story and she buys a Peloton

Nov 2019 – "Why can't I increase my output on the Peloton?"

New, cool data

Circulation

ORIGINAL RESEARCH ARTICLE

Long-Term Leisure-Time Physical Activity Intensity and All-Cause and Cause-Specific Mortality: A Prospective Cohort of US Adults

Dong Hoon Lee, ScD; Leandro F.M. Rezende, ScD; Hee-Kyung Joh, MD, PhD; NaNa Keum, ScD; Gerson Ferrari, PhD; Juan Pablo Rey-Lopez, PhD; Eric B. Rimm, ScD; Fred K. Tabung, PhD; Edward L. Giovannucci, MD, ScD

Circulation 2022;146:523

Physical activity and mortality

116,221 adults from Nurses Health Study and Health Professional f/u Study

1988-2018

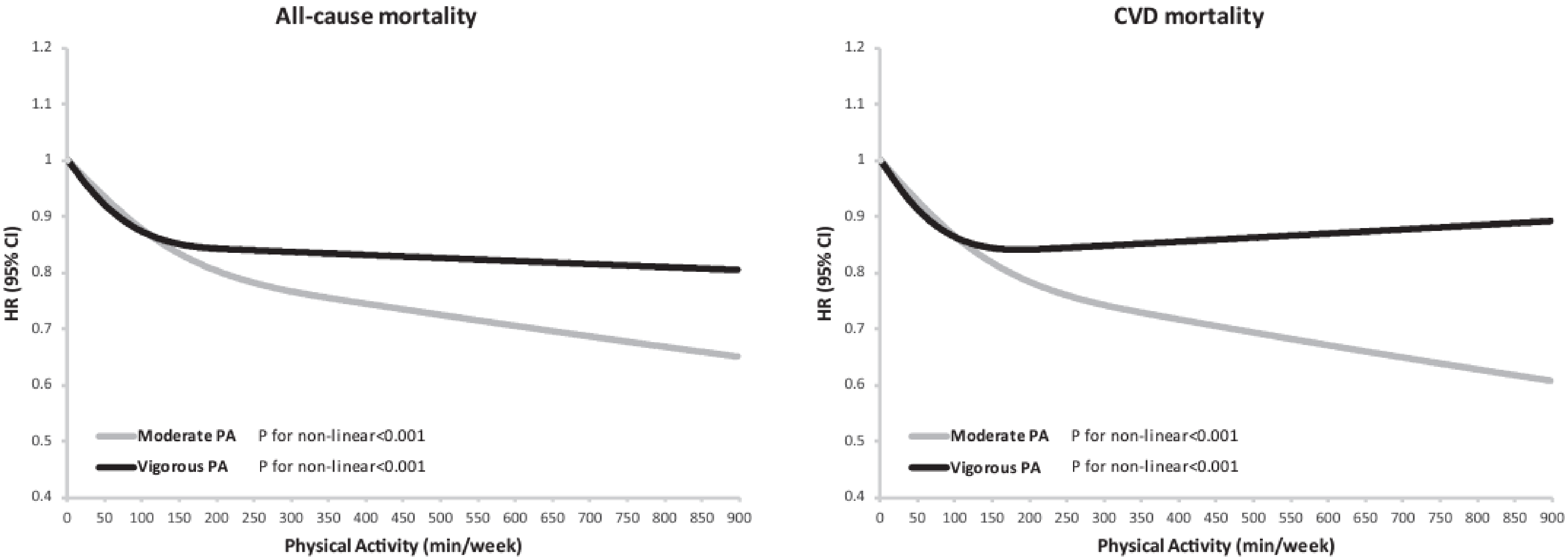
Detailed self-reported leisure time activity logs

Repeated 15 times

Over 30 years of f/u, 47,596 deaths

Circulation 2022;146:523

Physical activity and mortality



150 min/wk moderate
75-150 min/wk vigorous

Circulation 2022;146:523

Examples of exercise intensity

2020 WHO Physical Activity Guidelines for Aerobic Exercise	Activity[a]	Duration (min/wk)
150-300 min moderate-intensity aerobic exercise per week	Walking (2.5 miles/h, moderate pace)	150-300
	Ballroom dancing (slow pace)	150-300
	Gardening and yardwork	113-225
	Bicycling (light, <10 mph)	113-225
	Brisk walking (3.5 miles/h, fast pace)	105-209
75-150 min vigorous-intensity aerobic exercise per week	Jogging (4.0 miles/h)	75-150
	Swimming (leisure)	75-150
	Hiking	75-150
	Bicycling (moderate, 12-14 miles/h)	56-113
	Running (6 miles/h)	46-92

JACC 2022;80:1091-1106

Circulation

ORIGINAL RESEARCH ARTICLE

Association Between Device-Measured Physical Activity and Incident Heart Failure: A Prospective Cohort Study of 94 739 UK Biobank Participants

Frederick K. Ho, PhD*; Ziyi Zhou, MPH*; Fanny Petermann-Rocha, PhD; Solange Para-Soto, MSc; Jirapitcha Boonpor, MSc; Paul Welsh, PhD; Jason M.R. Gill, PhD; Stuart R. Gray, PhD; Naveed Sattar, MD; Jill P. Pell, MD; Carlos Celis-Morales, PhD

Circulation 2022 Aug 29. doi: 10.1161/CIRCULATIONAHA.122.059663

Physical activity and heart failure

Prospective cohort study

94,739 participants

Wore a device to measure physical activity from 2013-2015

No history of heart failure or MI

Measured intensity of activity with an accelerometer

Overall incidence of HF 98.5/10,000 person years over 6.1 yrs f/u

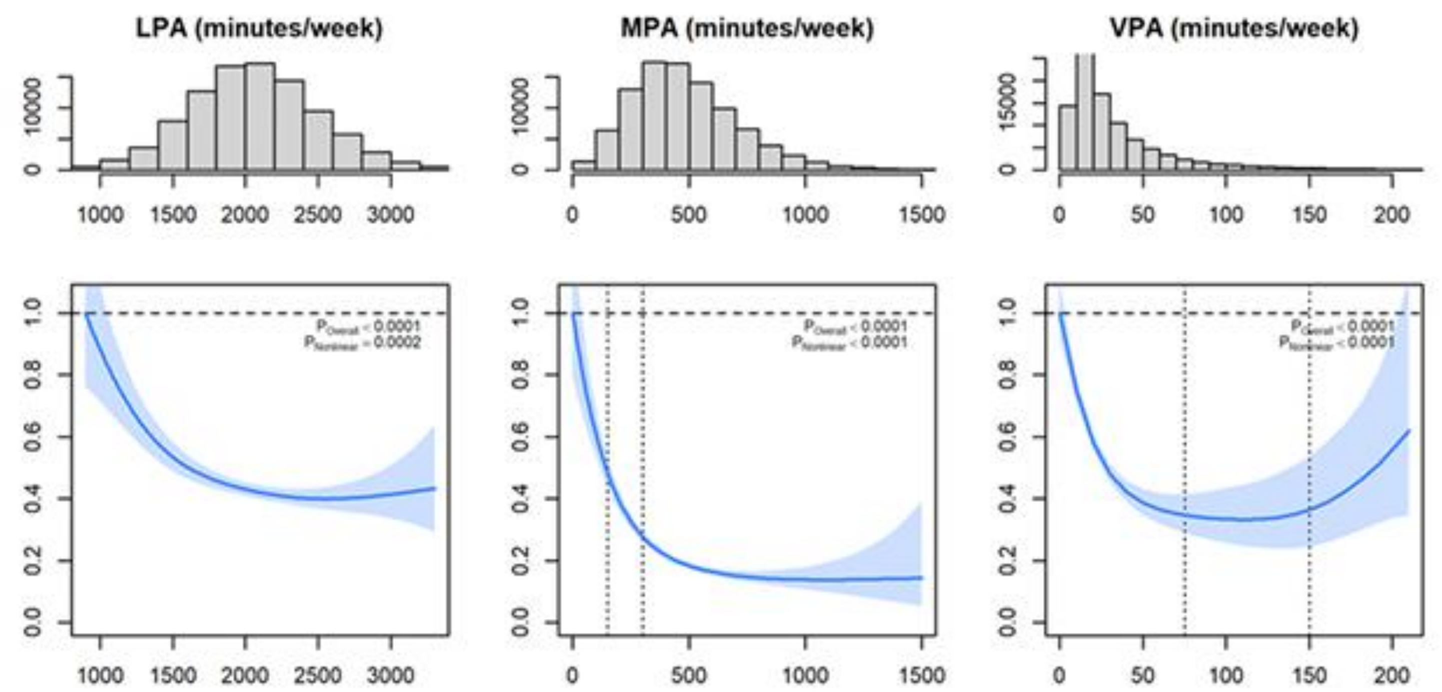
Physical activity and heart failure

Light intensity 30-125 mg

Moderate intensity 126-400 mg

Vigorous intensity > 400 mg

Measured minutes at each



How much should you do

2020 WHO Physical Activity Guidelines for Aerobic Exercise	Activity[a]	Duration (min/wk)
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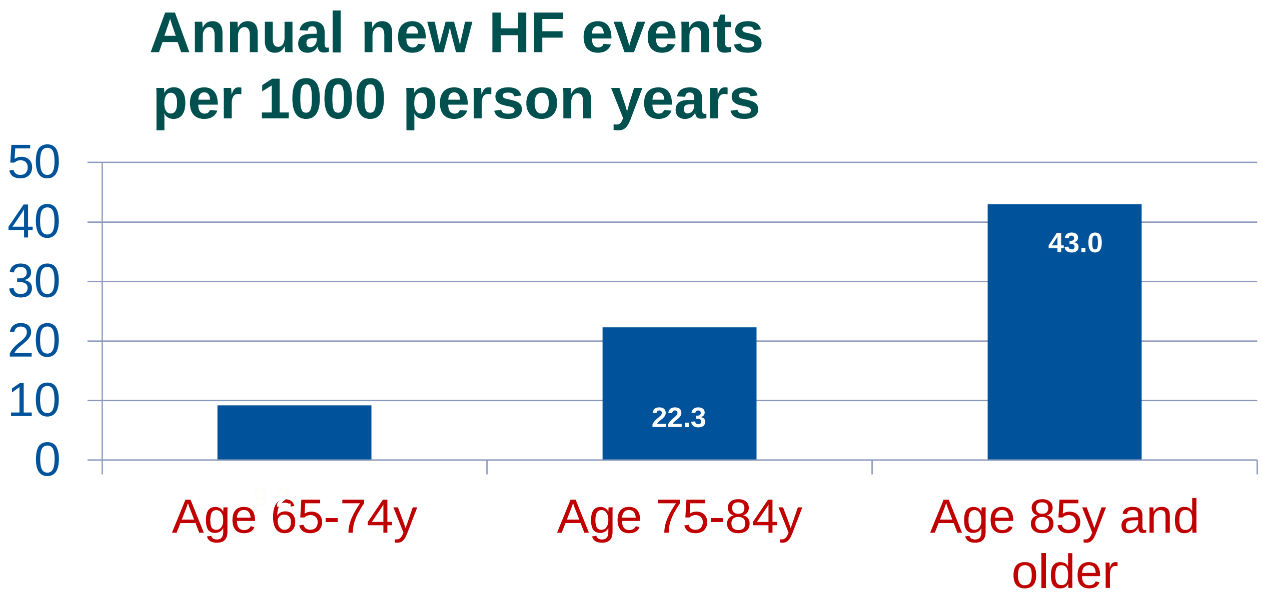
	Optimal Effects and Preferred Recommendation of Mode and Exercise Intensity		
	High-Intensity Training	Moderate-Intensity Training	Resistance Training
Chronic coronary disease without heart failure	↑↑	↑↑	↑
Peripheral artery disease	↑↑	↑	(↑)
HFrEF	↑	↑↑	↑
HFpEF	↑↑	↑↑	↑
Atrial fibrillation	↑	↑↑	↑

Scope of Heart Failure (HF)

6.5 million Americans ≥20 years of age have HF

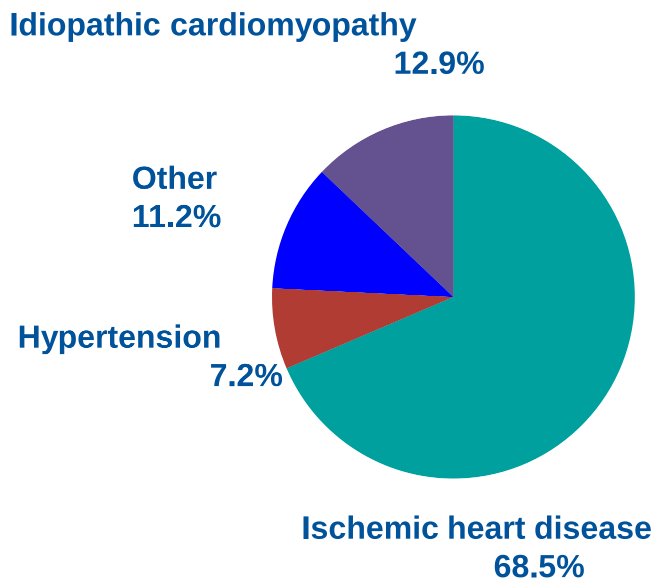
960,000 new cases of HF are diagnosed annually

5-year survival rate for HF is ~50%



Benjamin EJ, et al. *Circulation*. 2017;135(10):e146-e603.

Etiology of heart failure



Valve disease
Myocarditis
Drugs – adriamycin 550mg/m^2
herceptin
Systemic disease
- Amyloid
- Sarcoid
- Chagas
- HIV
- Thyroid
- Hemachromatosis
- Rheumatologic
- Muscular dystrophy
- Peripartum
- Pheochromocytoma

Alcohol

JACC 1993;22:14A

ACC/AHA stages of HF

STAGE A:
At-Risk for Heart Failure

Patients at risk for HF but without current or previous symptoms/signs of HF and without structural/functional heart disease or abnormal biomarkers

Patients with hypertension, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy

STAGE B:
Pre-Heart Failure

Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:

- Structural heart disease
- Evidence of increased filling pressures
- Risk factors and
  - increased natriuretic peptide levels or
  - persistently elevated cardiac troponin

  in the absence of competing diagnoses

STAGE C:
Symptomatic Heart Failure

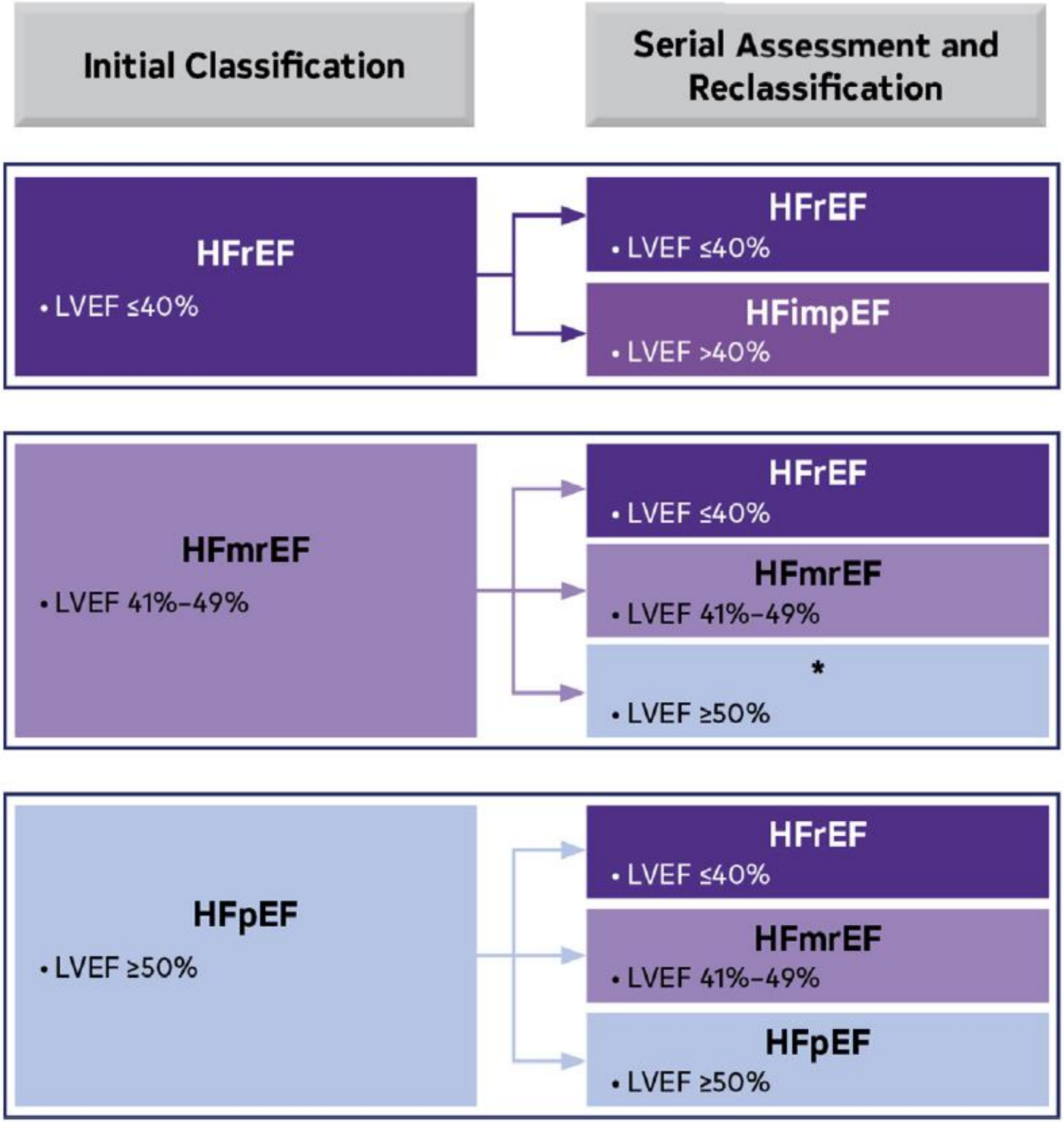
Patients with current or previous symptoms/signs of HF

STAGE D:
Advanced Heart Failure

Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT

Circulation 2022;145

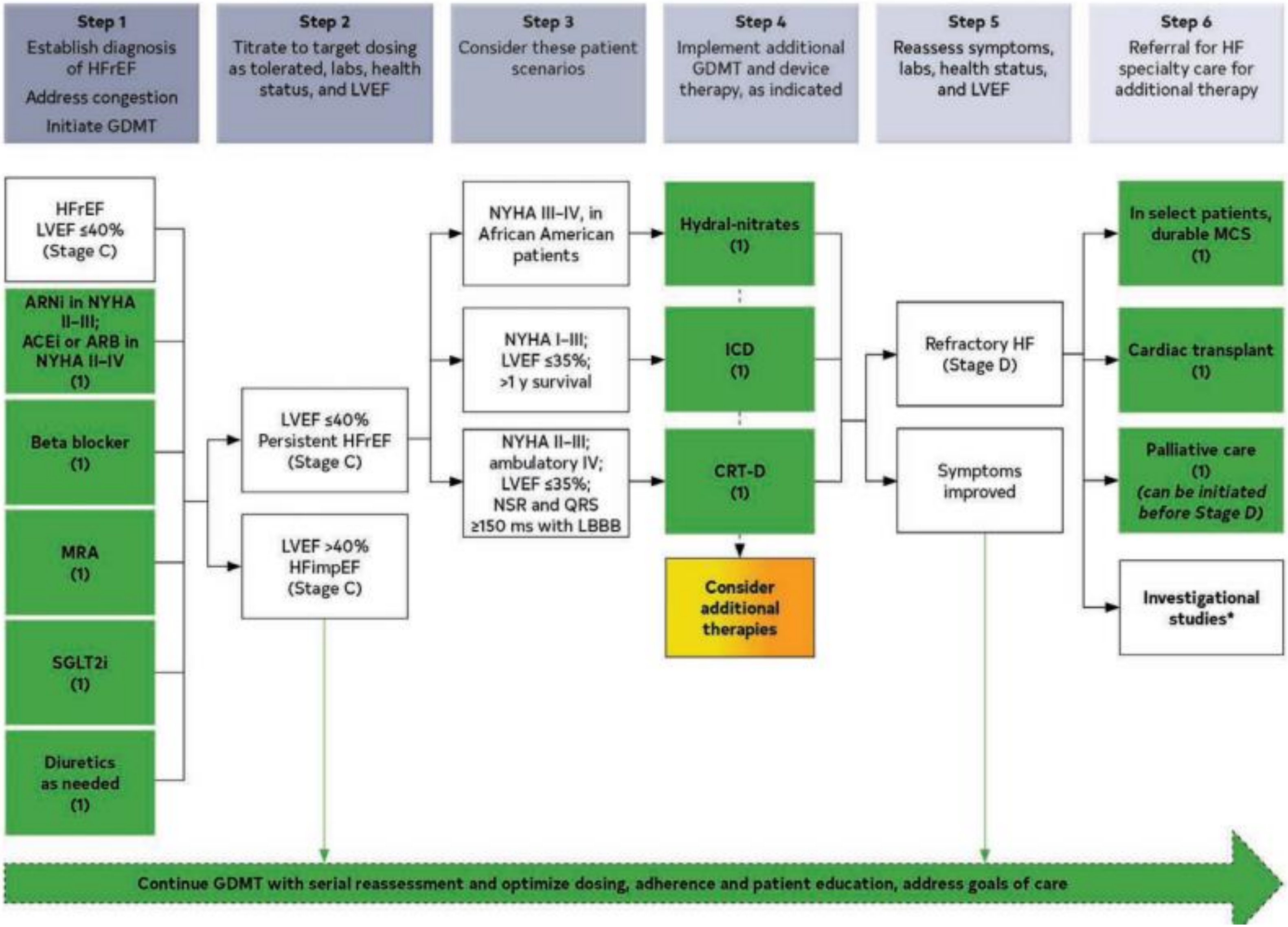
Type o[f] LVEF
HFrEF
HFimpl EF)
HFmrE duced
HFpEF EF)



Circulation 20

Lifestyle Interventions

Therapy for Stage C and D



Circulation 2022;145

What is the evidence?

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	NNT to Prevent All-Cause Mortality Over Time*	NNT for All-Cause Mortality (Standardized to 12 mo)	NNT for All- Cause Mortality (Standardized to 36 mo)
ACEi or ARB	17	22 over 42 mo	77	26
ARNi†	16	36 over 27 mo	80	27
Beta blocker	34	28 over 12 mo	28	9
Mineralocorticoid receptor antagonist	30	9 over 24 mo	18	6
SGLT2i	17	43 over 18 mo	63	22
Hydralazine or nitrate‡	43	25 over 10 mo	21	7
CRT	36	12 over 24 mo	24	8
ICD	23	14 over 60 mo	70	23

Circulation 2022;145

Cumulative Impact of HFrEF Therapies on All-Cause Mortality

	Relative Risk	2-year Mortality
None	-	35.0%
ARNI (vs. imputed placebo)	↓ 28%	25.2%
Beta-blocker	↓ 35%	16.4%
MRA	↓ 30%	11.5%
SGLT2i	↓ 17%	9.5%

Cumulative risk reduction in mortality if all GDMT are used:

RRR 73% and ARR 26%

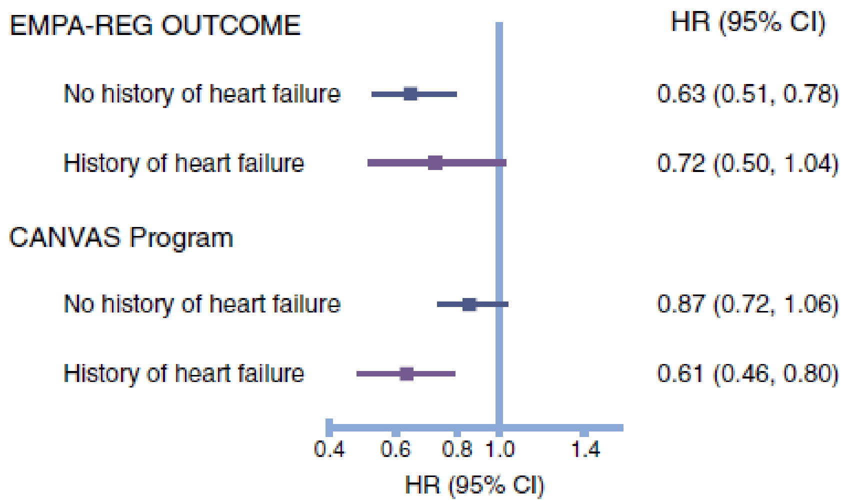
NNT = 3.9

Updated from Fonarow GC

Why diabetes drugs for heart failure?

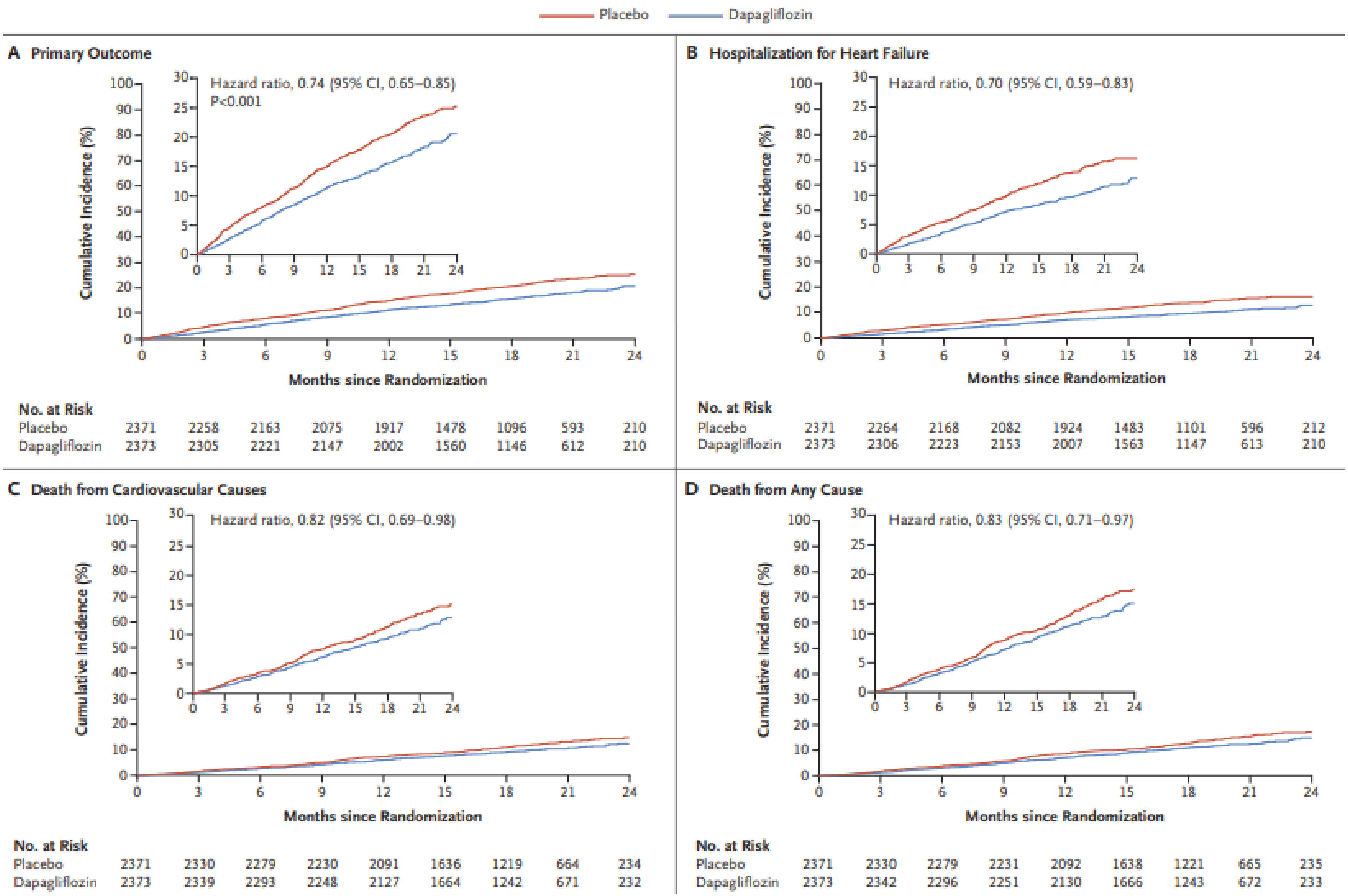
FDA mandate that all therapies being studied for patients with diabetes have cardiovascular outcome trials

CV death and HF hospitalizations



Diabetologia 2018;61:2108-17

DAPA HF



NEJM 2019;381:1995-2008

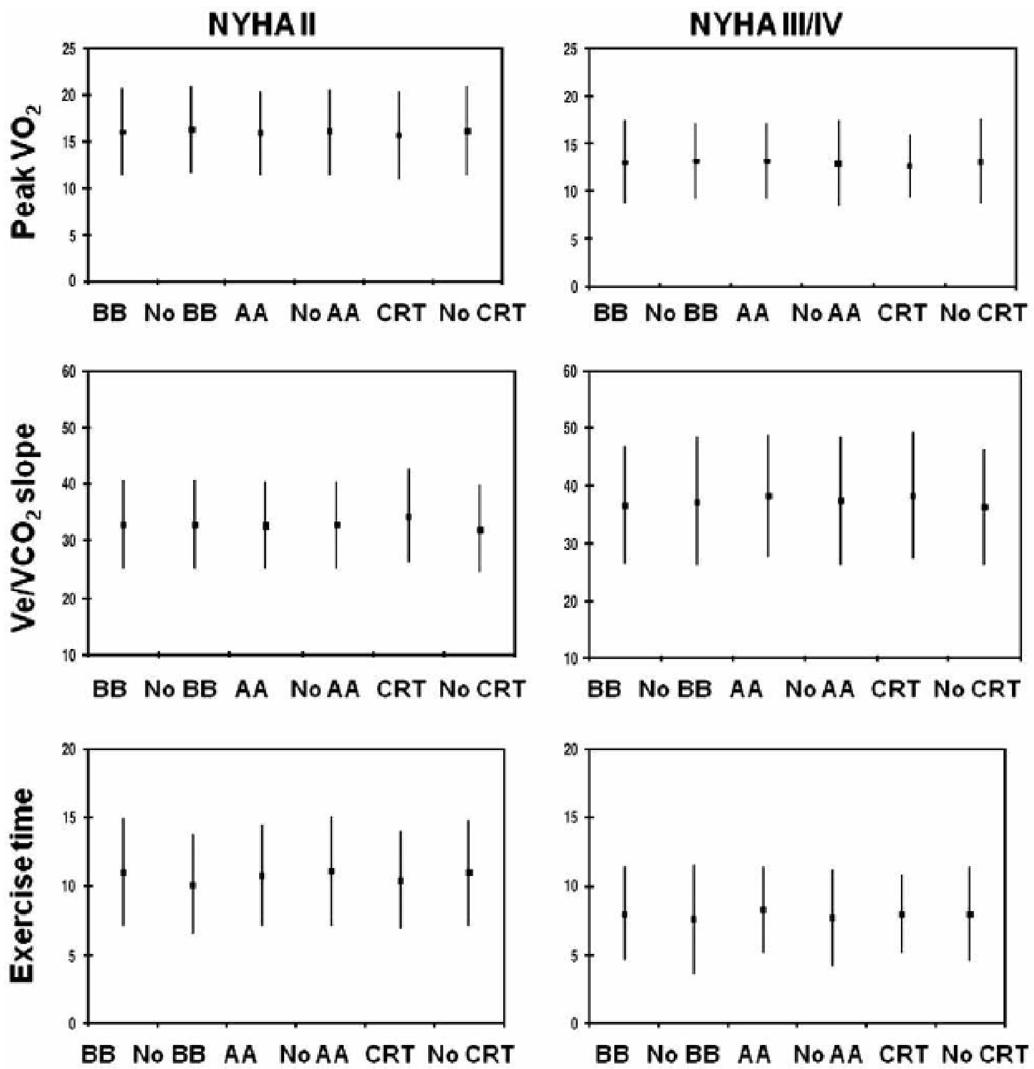
How do SGLT2 inhibitors work in HF?

1. Stimulation of natriuresis
2. Stimulation of osmotic diuresis
3. Cardiomyocyte Na^{+}/H exchanger inhibition
4. Increased myocardial energetics (via altered myocardial substrate metabolism)
5. Reduction in left ventricular mass
6. Improved systolic and diastolic function
7. Improved cardiac filling conditions secondary to reductions in preload and afterload
8. Increased circulating proangiogenic progenitor cells
9. Increased erythropoietin
10. Improved endothelial function
11. Reduction in myocardial CaM kinase II activity
12. Improved myocardial autophagy
13. Inhibition of cardiac fibrosis
14. Increased cardiac output, HR, O_2 consumption, coronary blood flow mediated by increased levels of circulating glucagon

We don't know

Lam et al JAHA 2019;8 issue 20

Effect of medical therapy and functional class on exercise capacity



AHJ 2009;158:S24

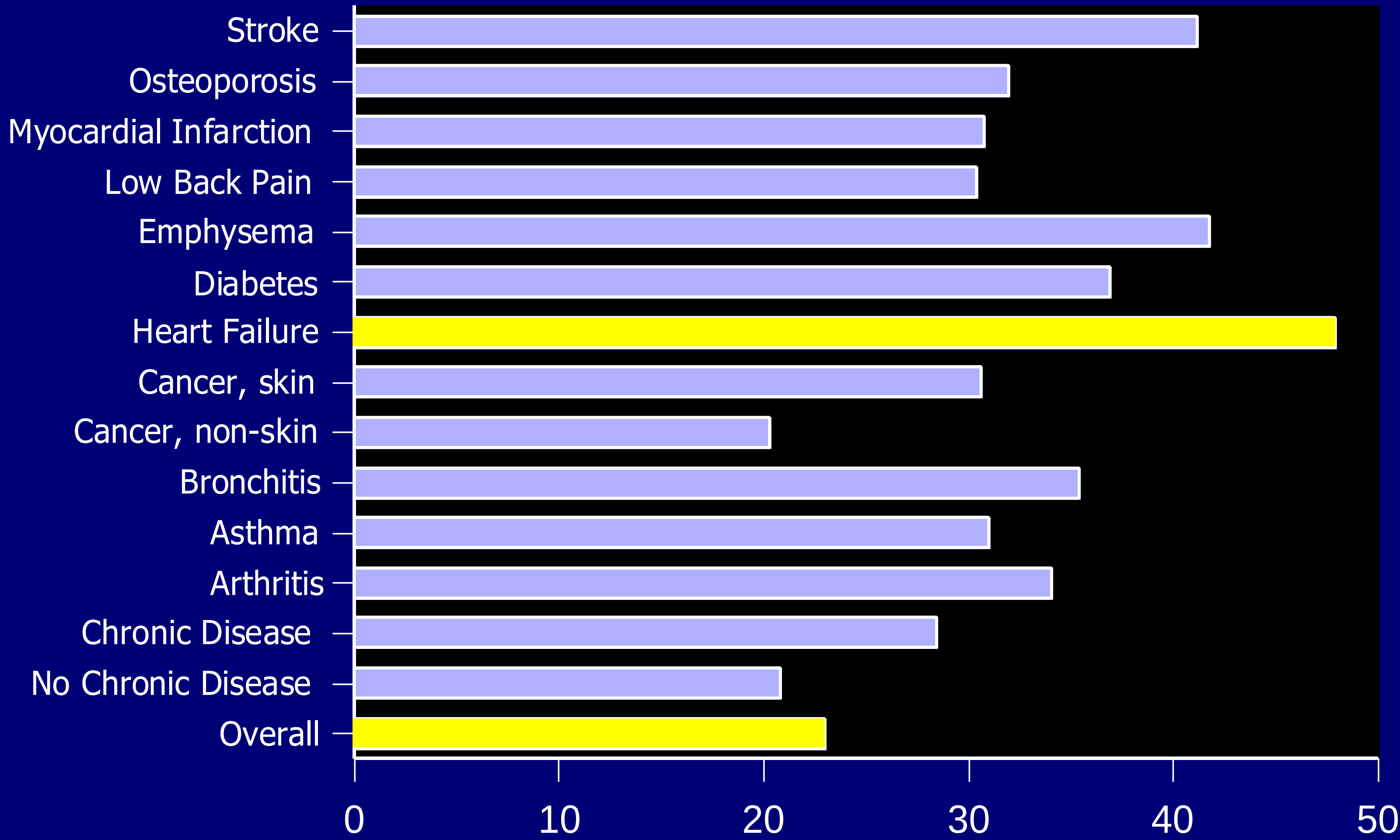
ACC/AHA Heart failure guidelines 2022

Recommendations for Management of Stage C HF: Activity, Exercise Prescription, and Cardiac Rehabilitation
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	RECOMMENDATIONS
1	A	1. For patients with HF who are able to participate, exercise training (or regular physical activity) is recommended to improve functional status, exercise performance, and QOL (1-9).
2a	B-NR	2. In patients with HF, a cardiac rehabilitation program can be useful to improve functional capacity, exercise tolerance, and health-related QOL (1,2,5,6,8).

Circulation 2022;145

Prevalence of No Leisure Time Physical Activity (LTPA) Among Adults in the United States



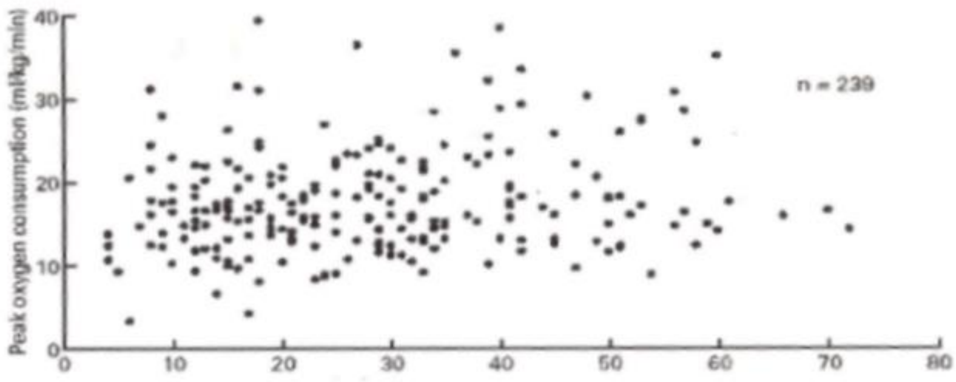
Crespo, et al. <u>Clinical Exercise Physiology</u>, 1999


STAREMASTER
WOW! 3½ HOURS!

Apparent Disconnects Between Cardiac Function and Exercise Performance

- **Left ventricular ejection fraction does not correlate with exercise performance**
- **Acute increase in cardiac output do not translate into increase in exercise performance**
- **Chronic increases in cardiac function may not increase exercise performance**

Relationship Between Exercise Capacity and Resting LVEF



Wilson, JR et al Acute Inotropes AJC 83:1305, 1984

Wilson, JR et al Acute Vasodilators Circulation 72:72, 1985

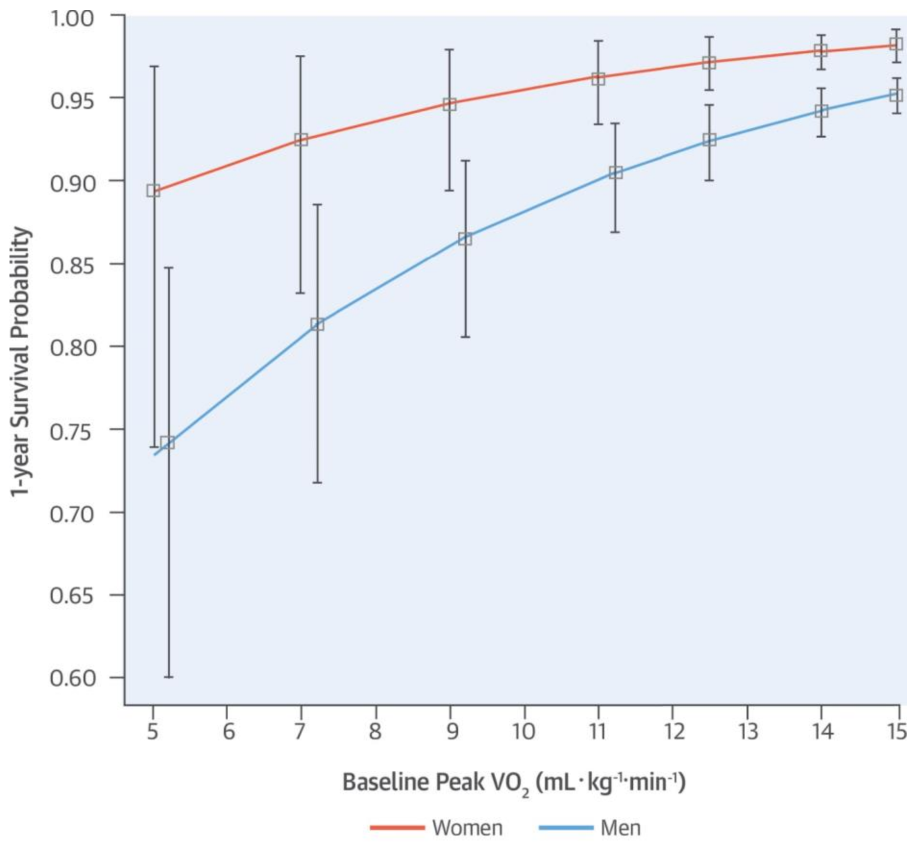
Regulation of Stroke Volume During Sub-maximal and Maximal Upright Exercise in Normal and HF patients

	Normal	Heart failure
$V0_2$ increase	8 x	3.5 x
Increase in cardiac output	3.2 x	2.0 x
Increase in $AV0_2$ difference	2.5 x	2.0 x
Increase in CO due to		
Increase SV	1.4 x	0.3 x
Increase HR	2.5 x	1.8 x

Higginbotham, Morris, Williams, McHale, Coleman, Cobb, Circ Res 58:281, 1986

Sullivan, M., et al, Circulation 80: 769, 1989

1 Year Survival and Peak VO_2



J Am Coll Cardiol 2016; 67:780.

Leg Skeletal Muscle Biochemistry and Histology in Ambulatory Patients with Chronic Heart Failure

Muscle Biopsy

Decreased oxidative enzyme capacity
- **Succinate dehydrogenase**
- **Citrate synthetase**

Decreased enzyme of beta oxidation of fatty acids
- **3 hydroxyacyl – COA Dehydrogenase**

No change in high-energy phosphagens

Decrease in slow twitch type I fibers

Increase in fast twitch type IIb fibers

Decrease in capillaries per fiber

Changes similar to exercise deconditioning

Sullivan, Green, Cobb Circulation 81:518,1990

Biochemistry Improves with Exercise Training in Patients with Heart Failure

↑ citrate synthetase ≈25-77%

↑↔ lactate dehydrogenase

↑ cytochrome-C oxidase activity

Hambrecht, et al. Circulation, 1998.

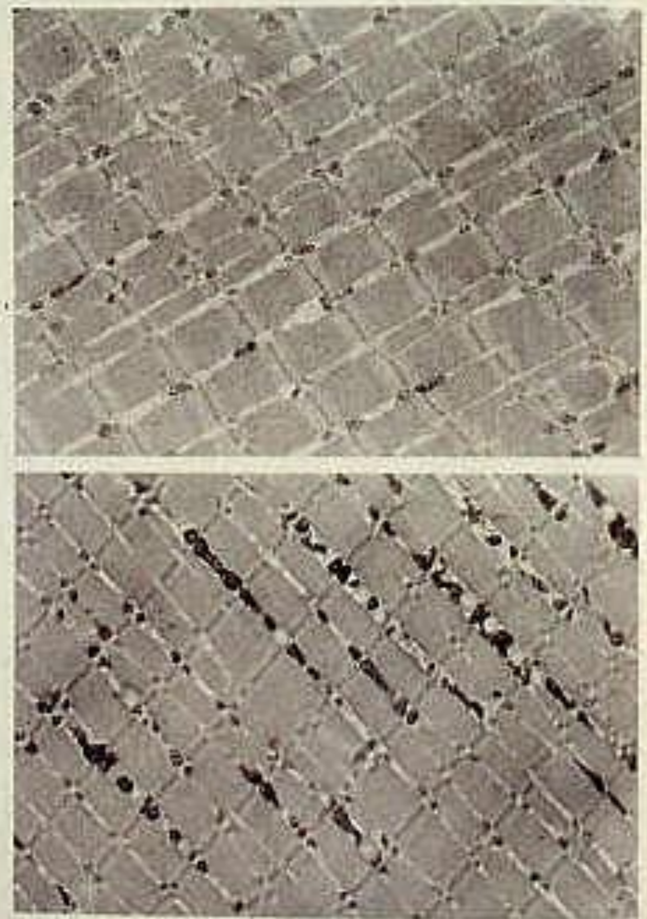


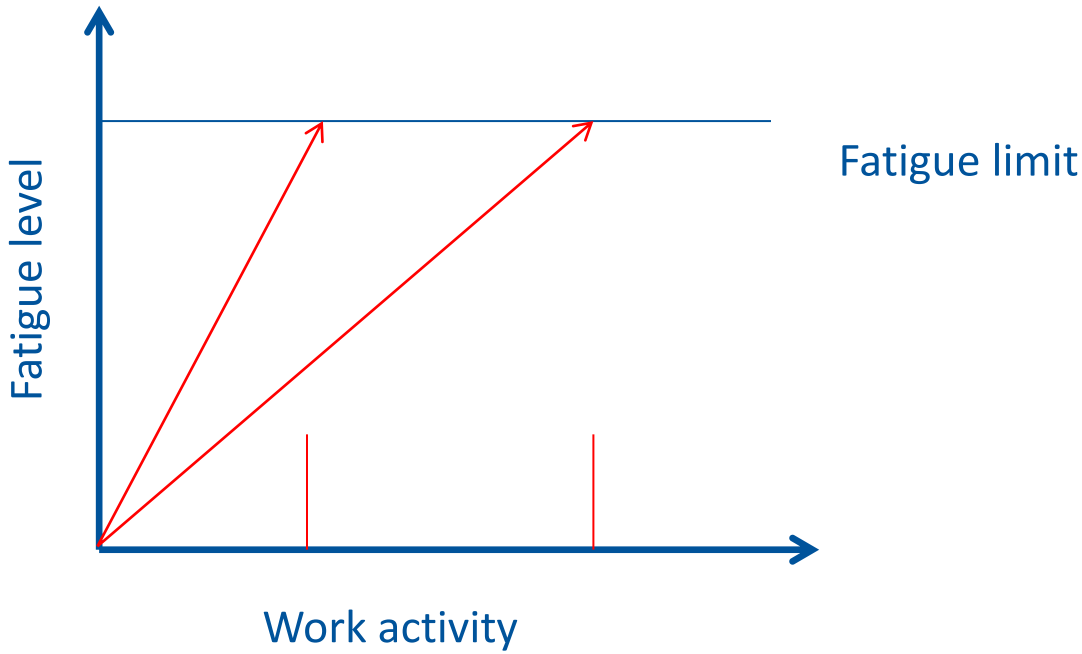
Figure 5. Electron micrographs of cytochrome c oxidase in a patient in the training group before (top) and after (bottom) 6 months of exercise training. Enzyme activity within the mitochondria (black) is increased after training.

What Limits Exercise Performance in Patients with Ambulatory Heart Failure?

Is it the heart?	**Yes**
CO, SV	
Is it the lungs?	**No**
Hyperventilation, ↑ $Ve/C0_2$	
Is it the muscles?	**Yes**
Deconditioning	
Oxidative enzyme decreased	
Muscle wasting – myopathy	
Increased ergoreceptor activity	
Is it the peripheral vasculature?	**Possibly**
Endothelial Dysfunction	
Vasoconstriction	
Reduced vasodilator capacity	
Vascular compliance changes	

Fatigability

Relates the symptom of tiredness or fatigue to the level, duration, or intensity of exercise that induces the symptom



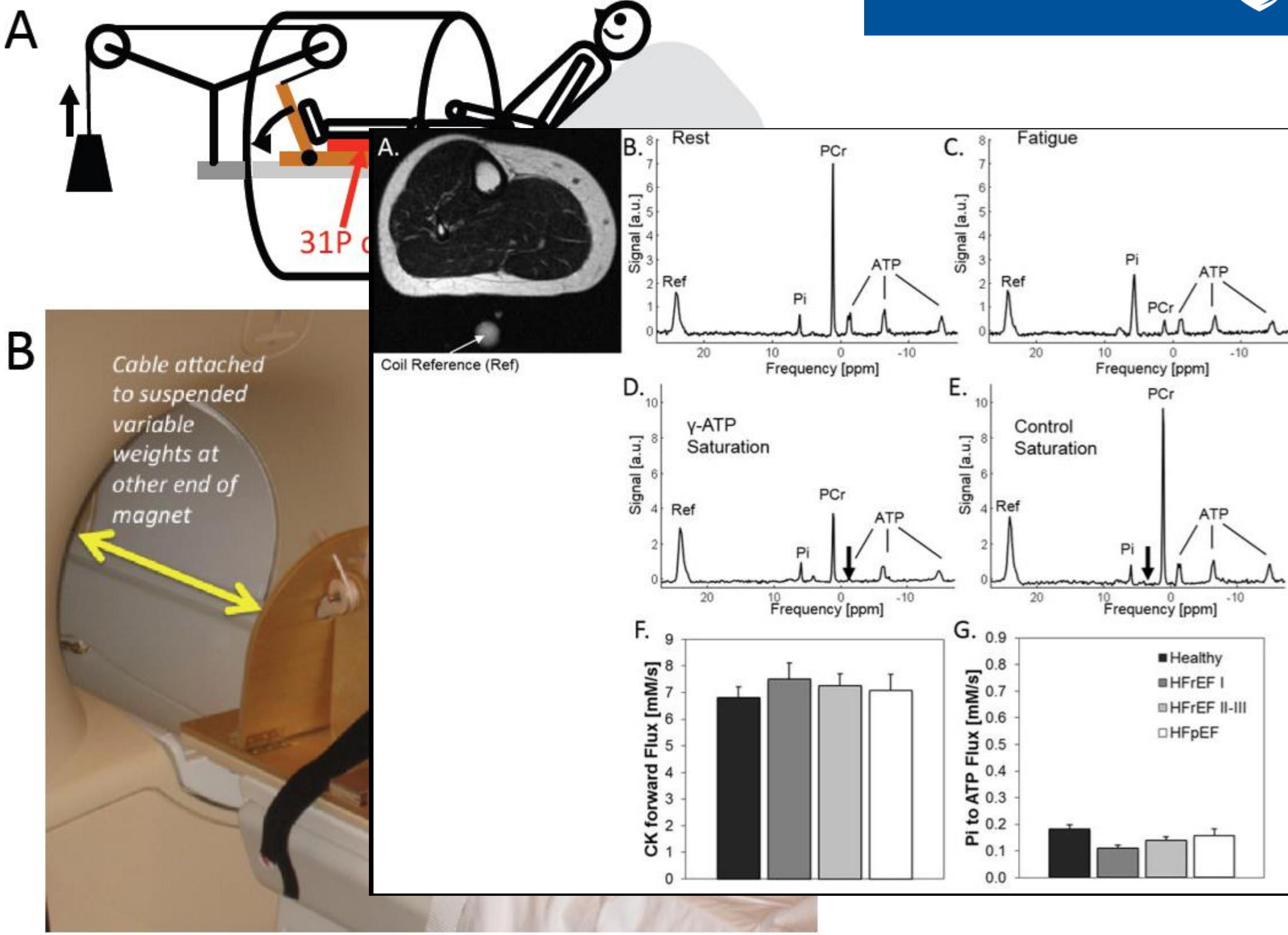
Exercise and fatigability

In isolated muscle, fatigue is associated with ..

- **High energy phosphate depletion**
- **Reduced ATP hydrolysis**
- **Increased inorganic phosphate**

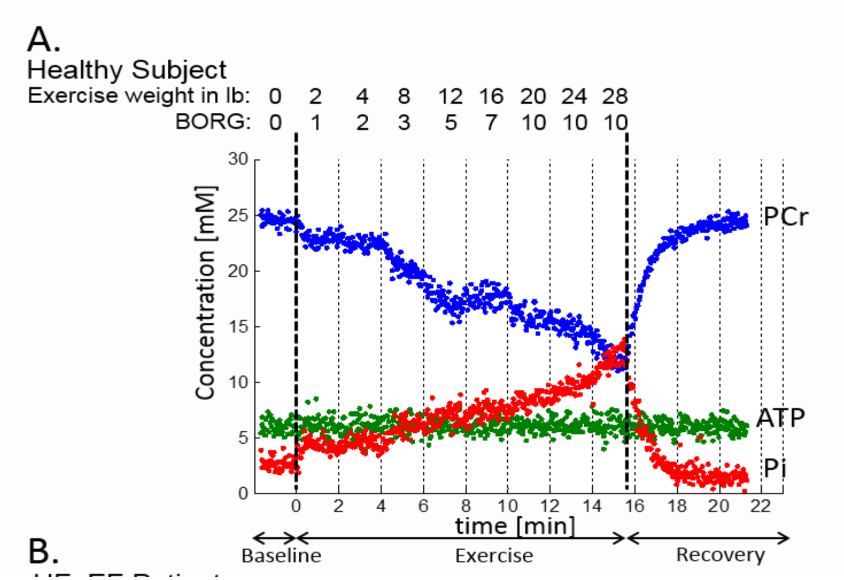
Physiol Rev 2008;88:287

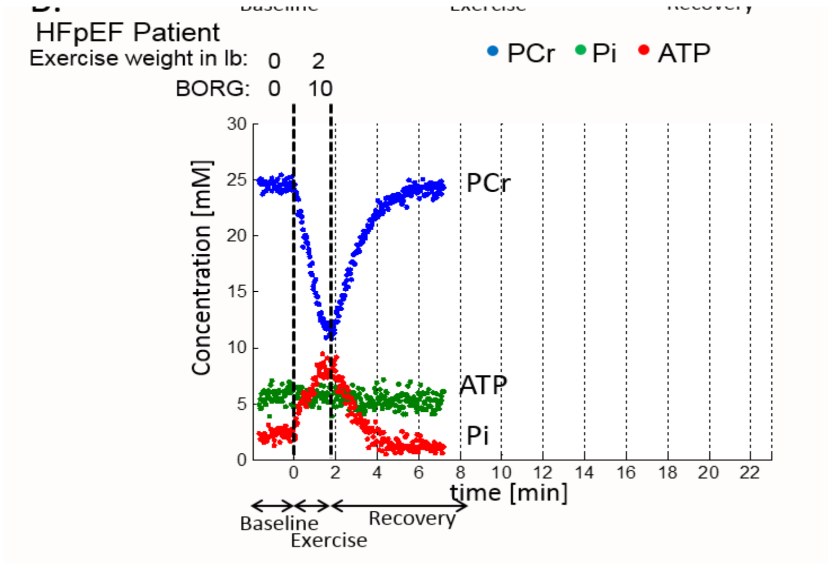
Exercise patients during MRS looking at relative and absolute concentrations of high energy phosphates and ATP synthesis rates



A
31P
B
Cable attached to suspended variable weights at other end of magnet
A.
Coil Reference (Ref)
B. Rest
Ref
Pi
PCr
ATP
Signal [a.u.]
Frequency [ppm]
C. Fatigue
Ref
Pi
PCr
ATP
Signal [a.u.]
Frequency [ppm]
D. γ-ATP Saturation
Ref
Pi
PCr
ATP
Signal [a.u.]
Frequency [ppm]
E. Control Saturation
Ref
Pi
PCr
ATP
Signal [a.u.]
Frequency [ppm]
F.
CK forward Flux [mM/s]
G.
Pi to ATP Flux [mM/s]
Healthy
HFrEF I
HFrEF II-III
HFpEF

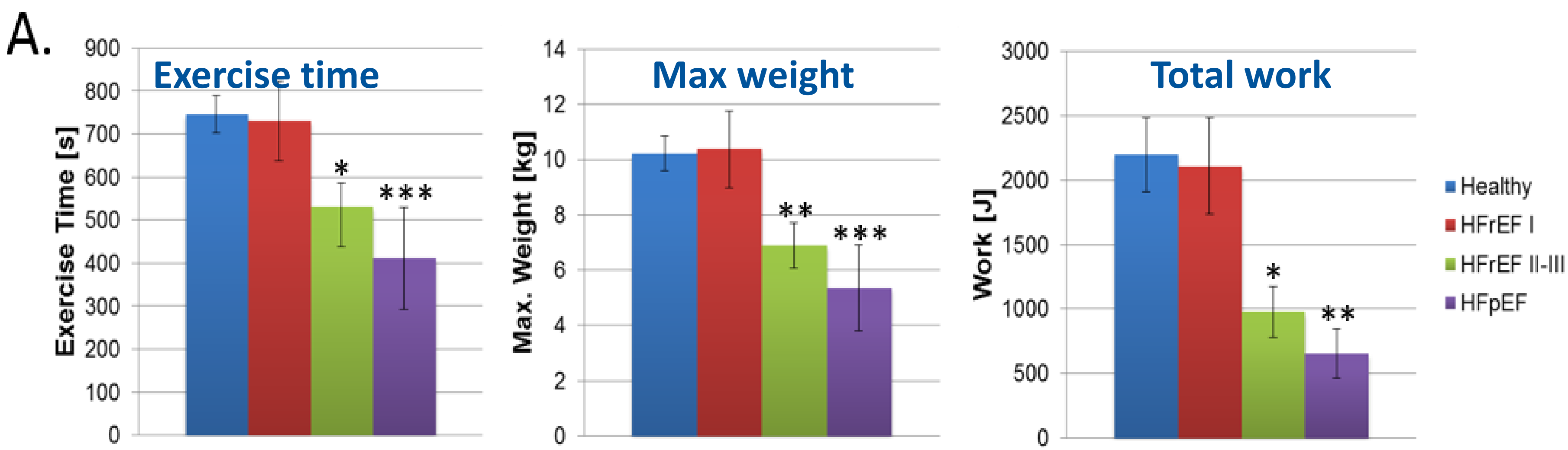
Energy characteristics



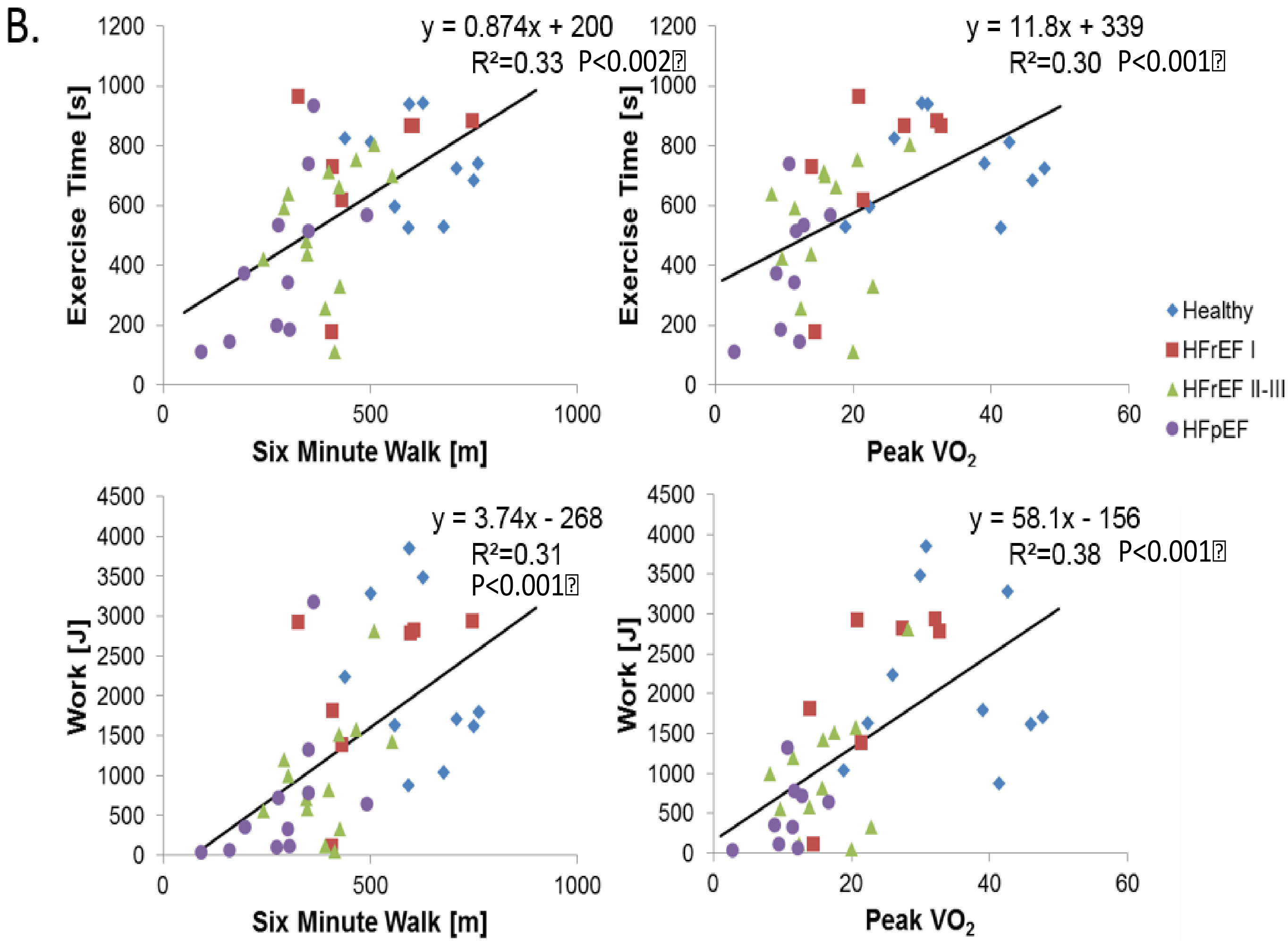


Circ HF 2017;10:e002149

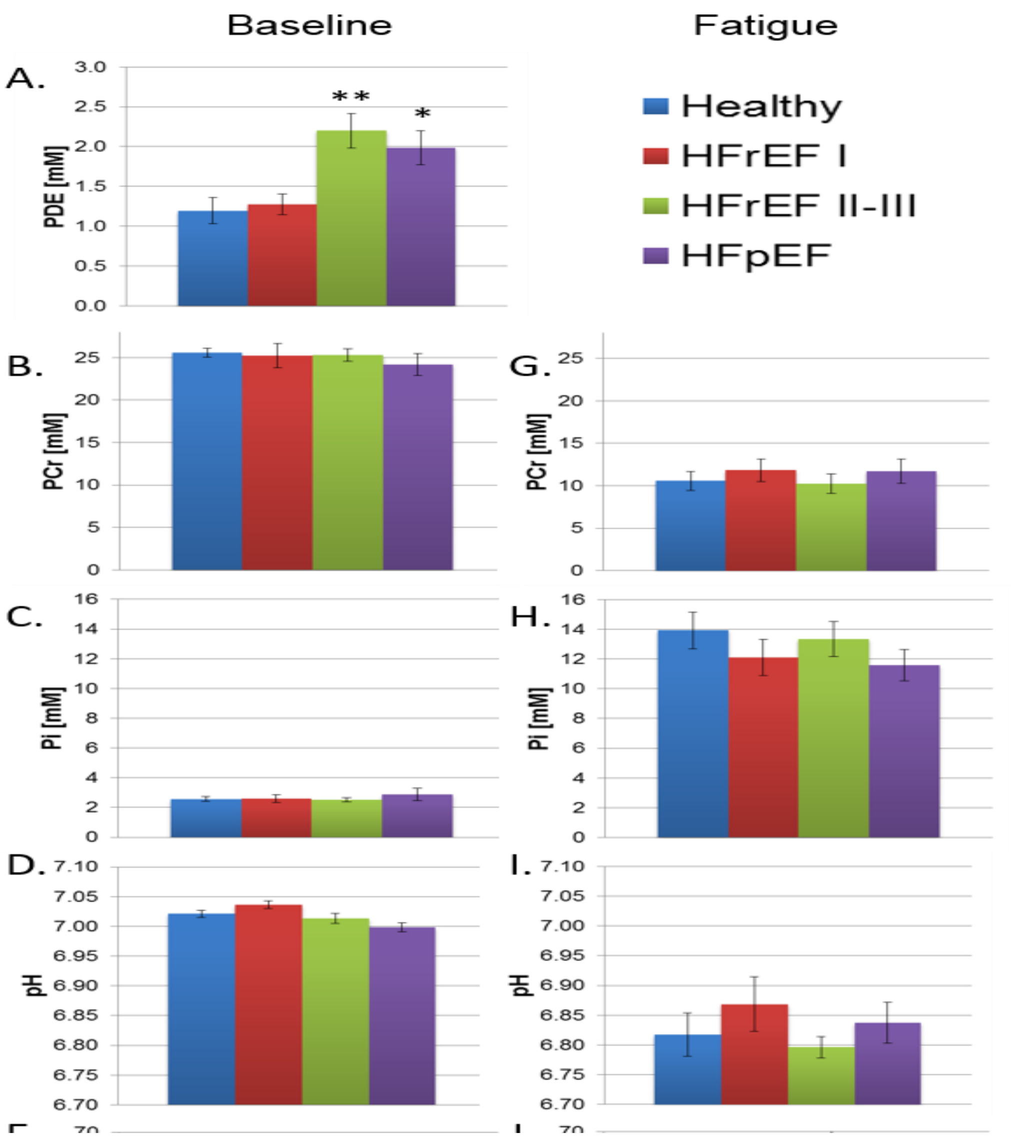
Exercise time and work



Correlation between 6MW, VO_2 and plantar flexion work



Energy and exercise



Summary

Symptomatic fatigue occurs at a common energetic limit in all. HFrEF and HFpEF patients with

EI and increased fatigability manifest early, rapid exercise-induced declines high-energy phosphates and reduced oxidative capacity

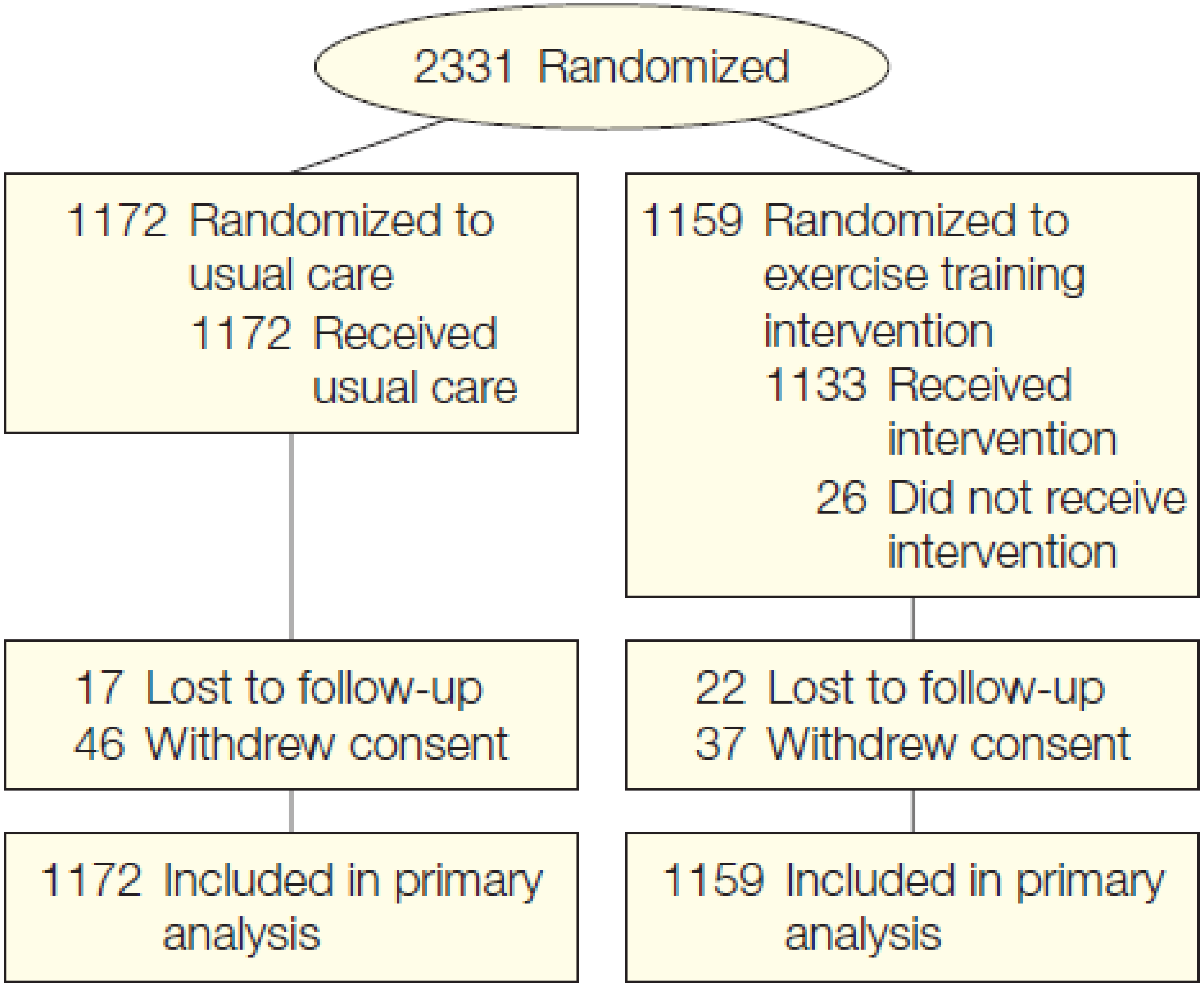
Circ HF 2017;10:e002149

Exercise Training

“An agent with lipid-lowering, antihypertensive, positive inotropic, negative chronotropic, vasodilating, diuretic, anorexigenic, weight-reducing, cathartic, hypoglycemic, tranquilizing, hypnotic and antidepressive qualities.”

William C. Roberts, MD
Editor-in-Chief
American Journal of Cardiology 1984; 53:261

HF ACTION Study design



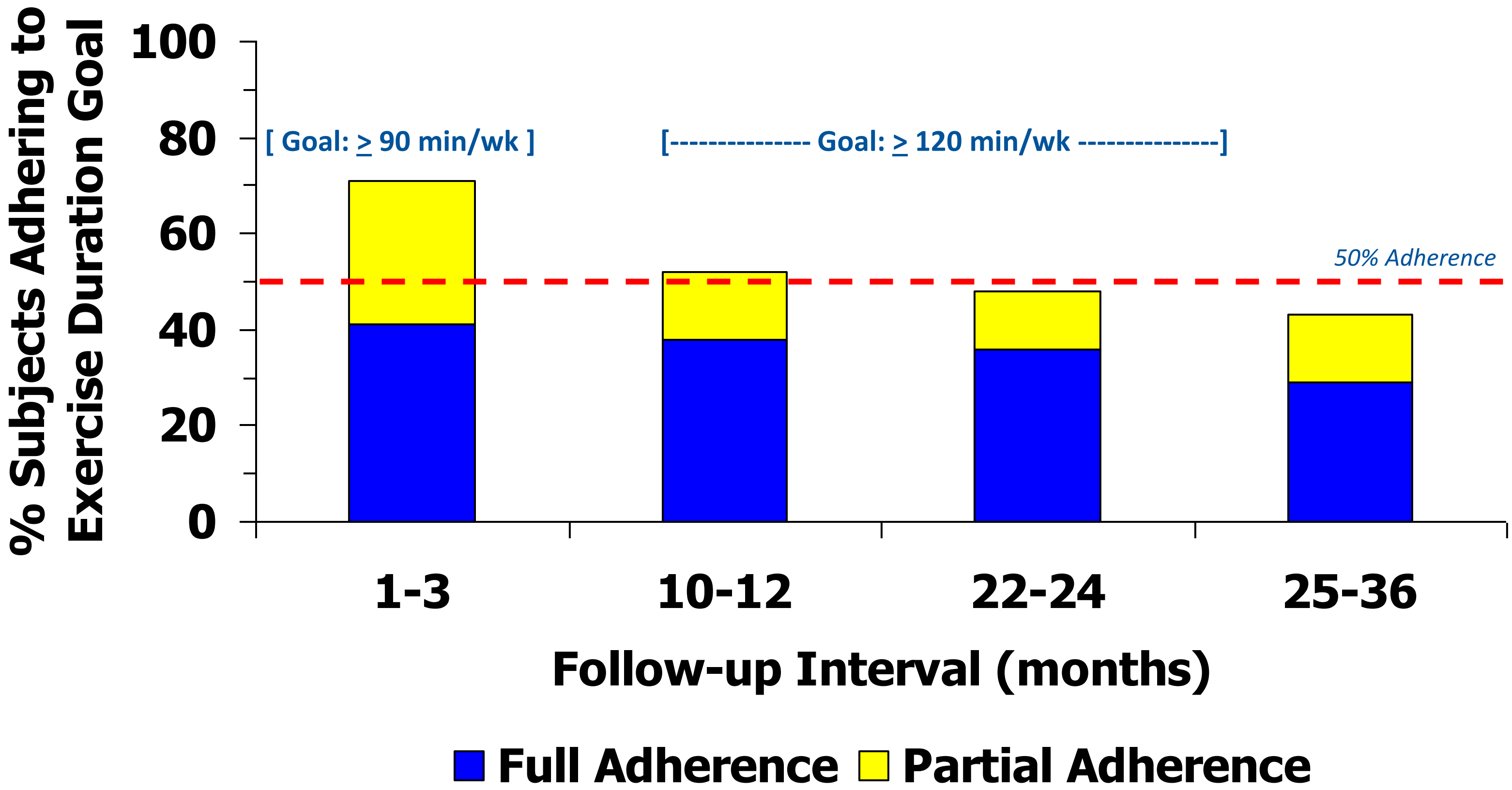
JAMA 2009;301:1439

Exercise Training Program

Training Phase	Location	Week*	Sessions / week	Aerobic minutes	Intensity (% HR reserve)	Training Mode
Initial Supervised	Clinic	1-2	3	15-30	60%	Walk/Cycle
Supervised	Clinic	3-6	3	30-35	70%	Walk/Cycle
Supervised & Home	Clinic & Home	7-12	3 & 2	30-35	70%	Walk/Cycle
Maintenance	Home	13-end	5	40	60-70%	Walk/Cycle

*Week intervals shown are goals and may vary for individual participants.

Adherence to Prescribed Exercise in HF-ACTION



Baseline Characteristics

	Usual Care N=1172	Exercise Training N=1159
Age, y *	59 (51, 68)	59 (51, 68)
Female, %	27	30
African American, %	32	33
NYHA Class, % II / III / IV	64 / 35 / 1	62 / 36 / 1
LVEF, % *	25 (20, 30)	25 (20, 30)
Ischemic etiology, %	51	52
Diabetes, %	32	33
Afib/flutter, %	21	21
History of Stroke, %	11	10
BMI, kg/m^2 *	30 (26, 35)	30 (26, 35)
Serum Creatinine, mg/dL *	1.2 (1.0, 1.5)	1.2 (1.0, 1.5)
Peak VO_2 , mL/min/kg *	14.5 (11.6, 17.8)	14.4 (11.3, 17.6)
CPX duration, minutes *	9.7 (7.0, 12.1)	9.5 (6.9, 12.0)

JAMA 2009;301:1439

Median Change in 6-Minute Walk and Cardiopulmonary Exercise (CPX) Tests

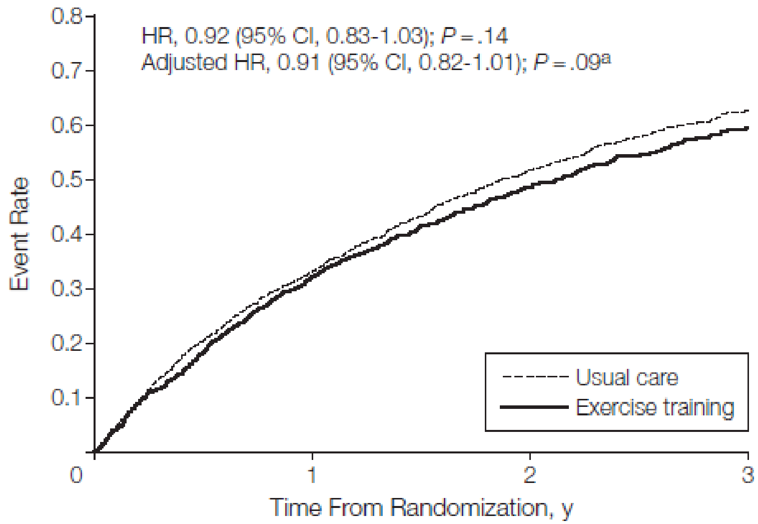
Table 4. Change in 6-Minute Walk Test and Cardiopulmonary Exercise Test Results

	Median (IQR)		
	Usual Care	Exercise Training	*P* Value
Baseline to 3 mo[a]			
Distance of 6-minute walk, m (n = 1835)	5 (−28 to 37)	20 (−15 to 57)	<.001
Cardiopulmonary exercise time, min (n = 1914)	0.3 (−0.6 to 1.4)	1.5 (0.3 to 3.0)	<.001
Peak oxygen consumption, mL/kg/min (n = 1870)	0.2 (−1.2 to 1.4)	0.6 (−0.7 to 2.3)	<.001
Baseline to 12 mo[b]			
Distance of 6-minute walk, m (n = 1444)	12 (−30 to 55)	13 (−28 to 61)	.26
Cardiopulmonary exercise time, min (n = 1476)	0.2 (−1.0 to 1.7)	1.5 (0 to 3.2)	<.001
Peak oxygen consumption, mL/kg/min (n = 1442)	0.1 (−1.5 to 1.8)	0.7 (−1.0 to 2.5)	<.001

JAMA 2009;301:1439

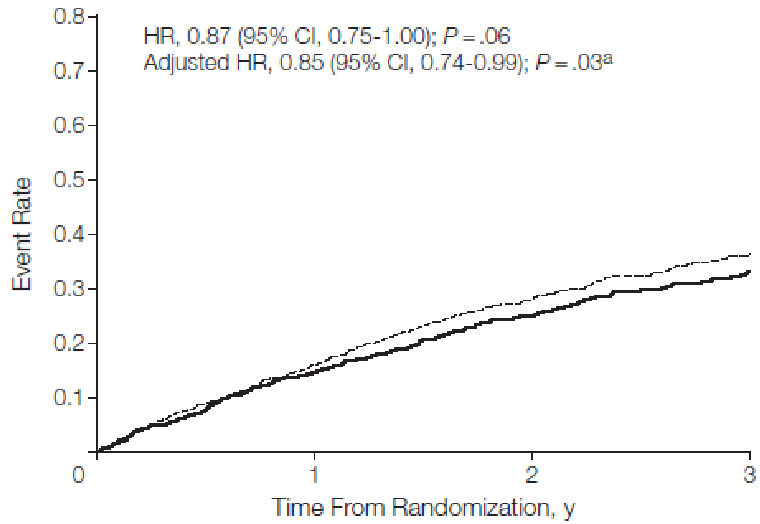
OUTCOMES – HF ACTION by risk

Cardiovascular Mortality or Cardiovascular Hospitalization



No. at risk				
Usual care	1172	753	418	202
Exercise training	1159	756	432	209

Cardiovascular Mortality or Heart Failure Hospitalization

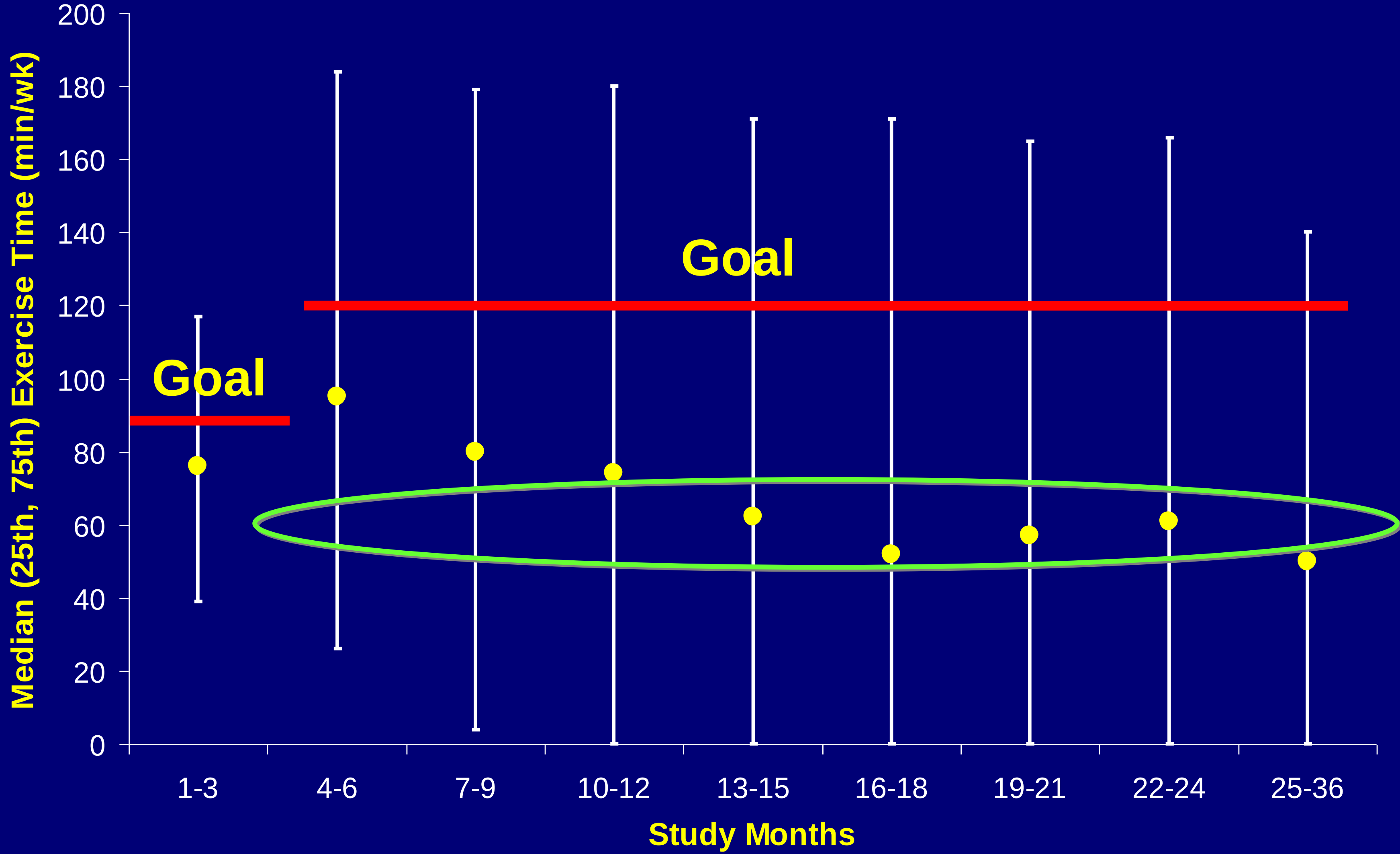


No. at risk				
Usual care	1172	937	616	342
Exercise training	1159	952	626	344

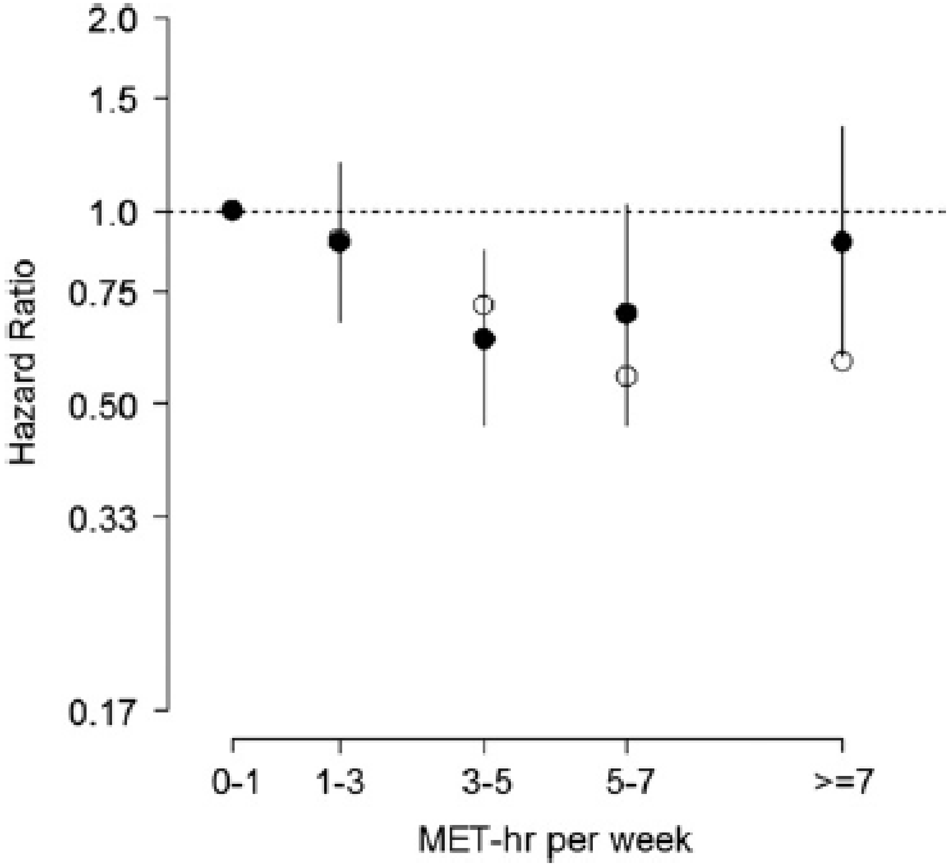
Adjustments for EF, exercise capacity, presence of a fib/CAD/depression

JAMA 2009;301:1439

Exercise Training: Minutes Per Week

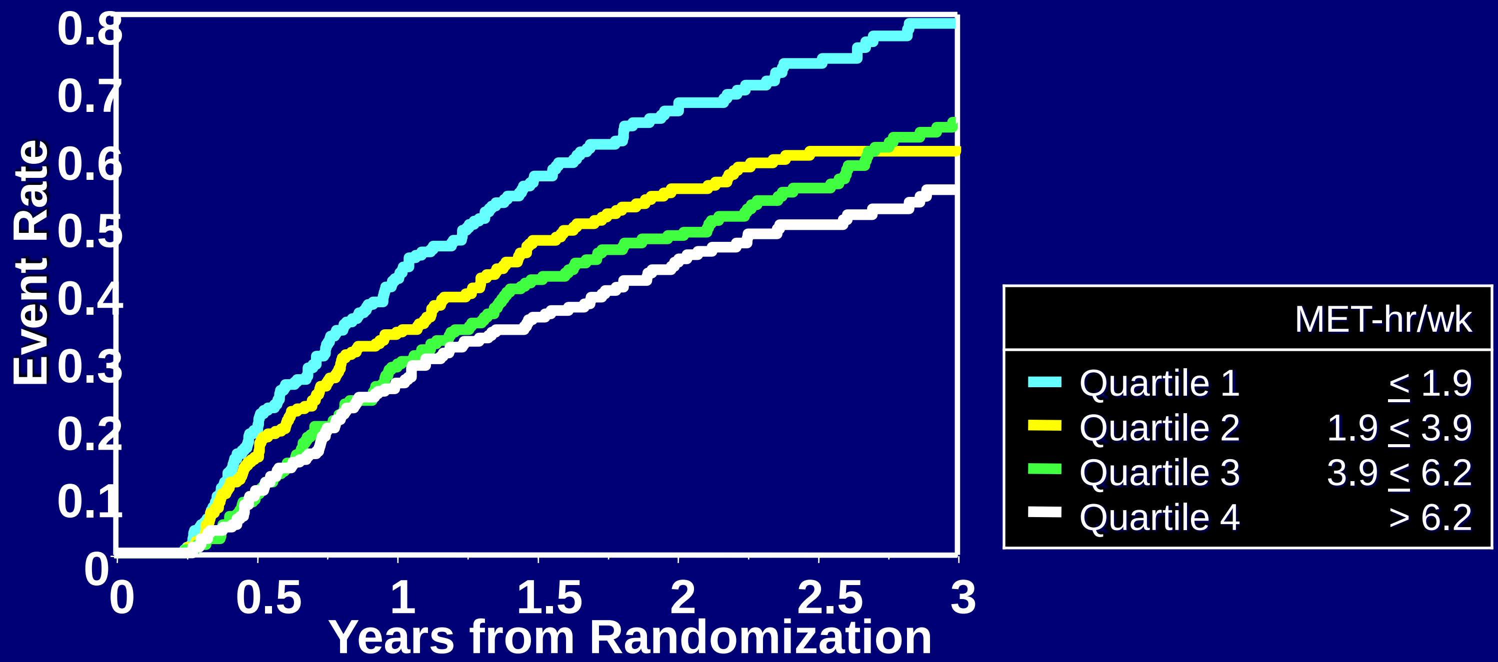


All cause mortality/hosp by amount of exercise



JACC 2012;60:1899-1905

Unadjusted Kaplan-Meier Curves of the Primary Endpoint by Quartiles of MET-hr/wk

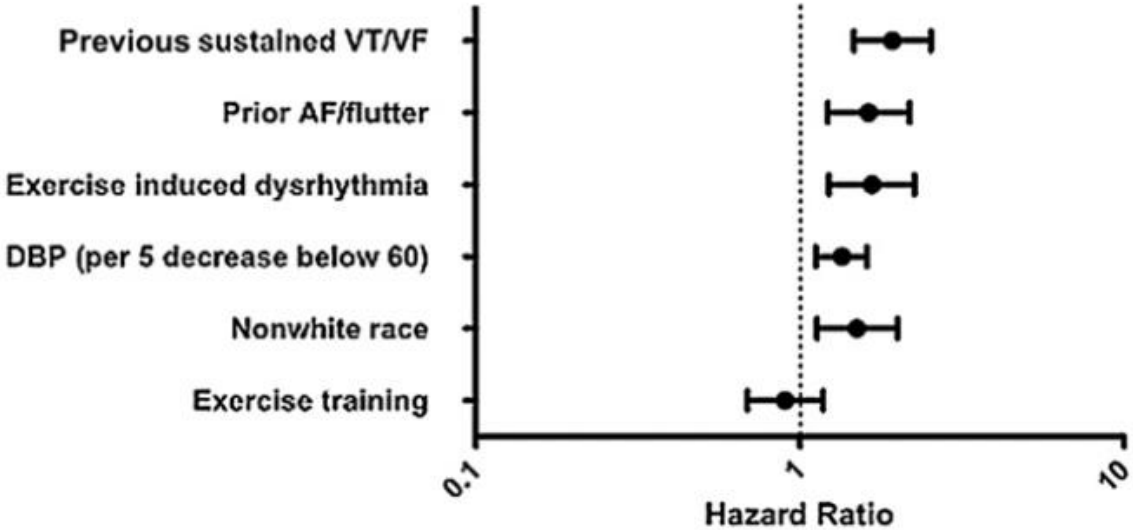


HF-ACTION
Safety of exercise

Adverse Event	No. (%) of Patients[a] Usual Care (n = 1171)[b]	Exercise Training (n = 1159)
Prespecified cardiovascular adverse events		
Worsening heart failure	340 (29.0)	303 (26.1)
Myocardial infarction	45 (3.8)	41 (3.5)
Unstable angina	88 (7.5)	86 (7.4)
Serious adverse arrhythmia[c]	164 (14.0)	167 (14.4)
Stroke	28 (2.4)	33 (2.8)
Transient ischemic attack	23 (2.0)	20 (1.7)
Any of the above events	471 (40.2)	434 (37.4)
General adverse events		
Hospitalization for fracture of the hip or pelvis	7 (0.6)	3 (0.3)
Outpatient fracture repair	20 (1.7)	13 (1.1)
ICD firing[d]	151/644 (23.4)	142/641 (22.2)
Hospitalization after exercise[e]	22 (1.9)	37 (3.2)
Died after exercise[f]	5 (0.4)	5 (0.4)

JAMA 2009;301:1439

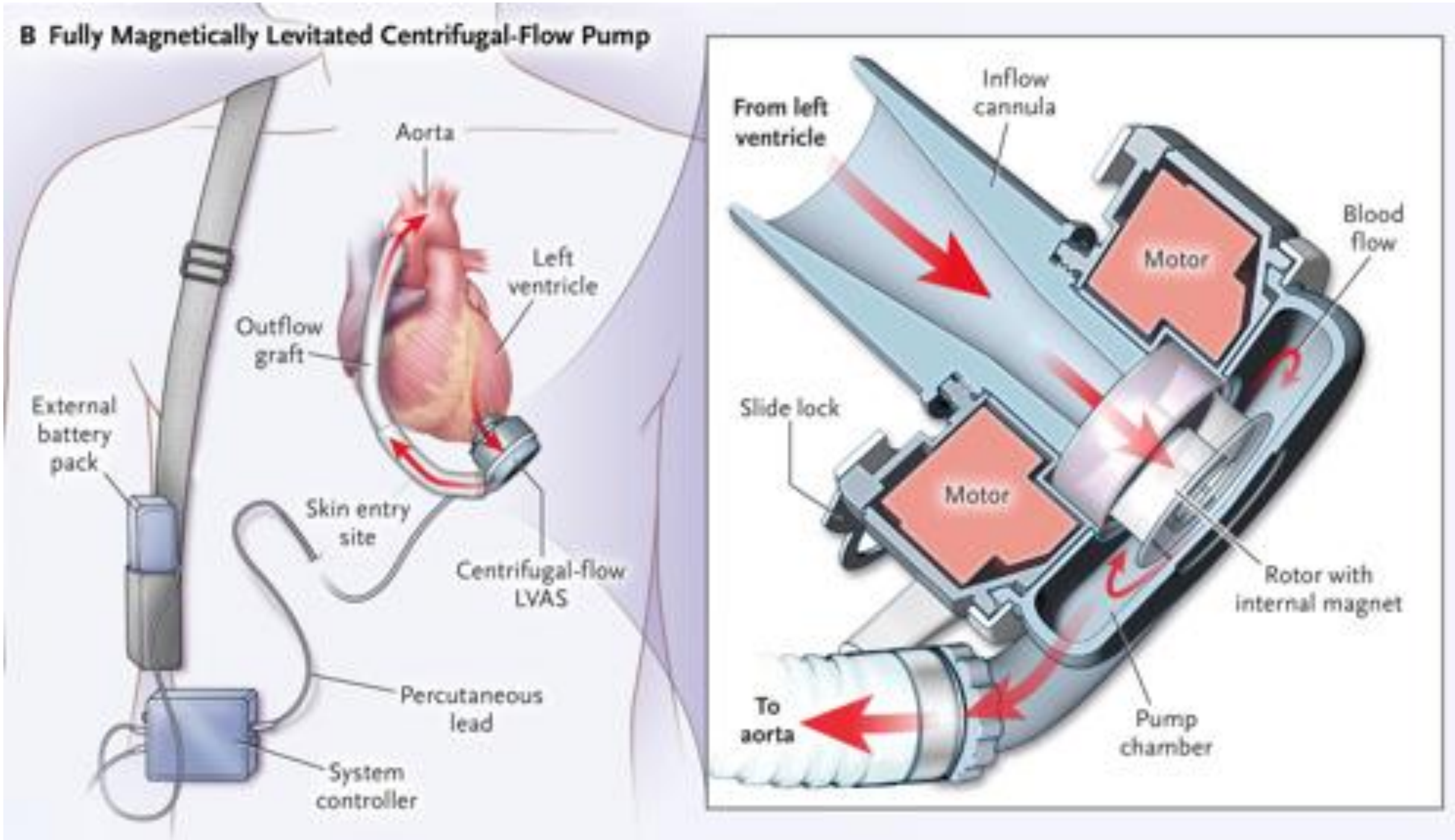
HF-ACTION
Exercise and ICD shocks



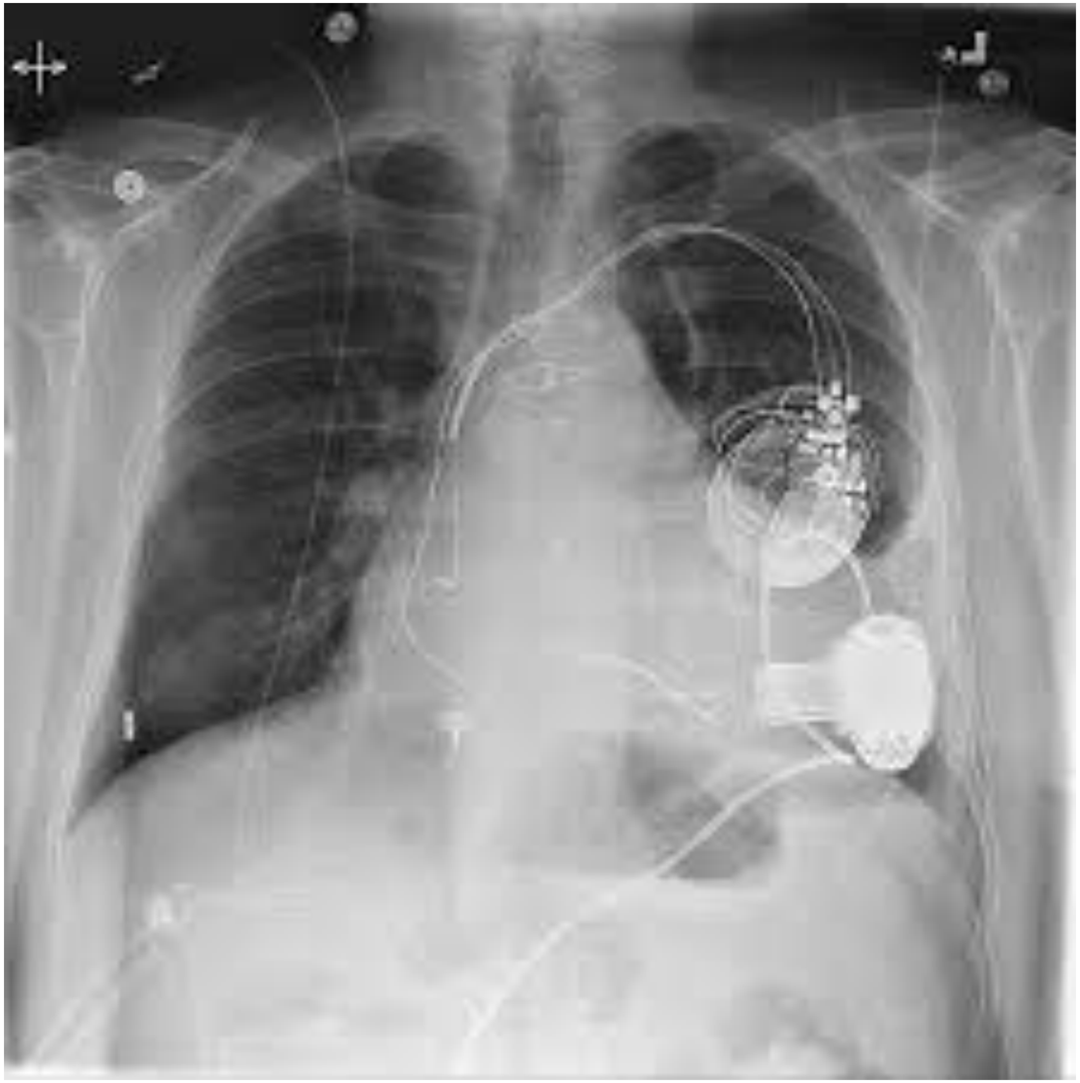
Hazard Ratio	95% CI	P-value
1.93	1.47-2.54	<.0001
1.63	1.22-2.18	0.0010
1.67	1.23-2.26	0.0011
1.35	1.12-1.61	0.0014
1.50	1.13-2.00	0.0053
0.90	0.69-1.18	0.45

JACC HF 2013;1:142-8

HeartMate III



NEJM 2017; 376:440-50



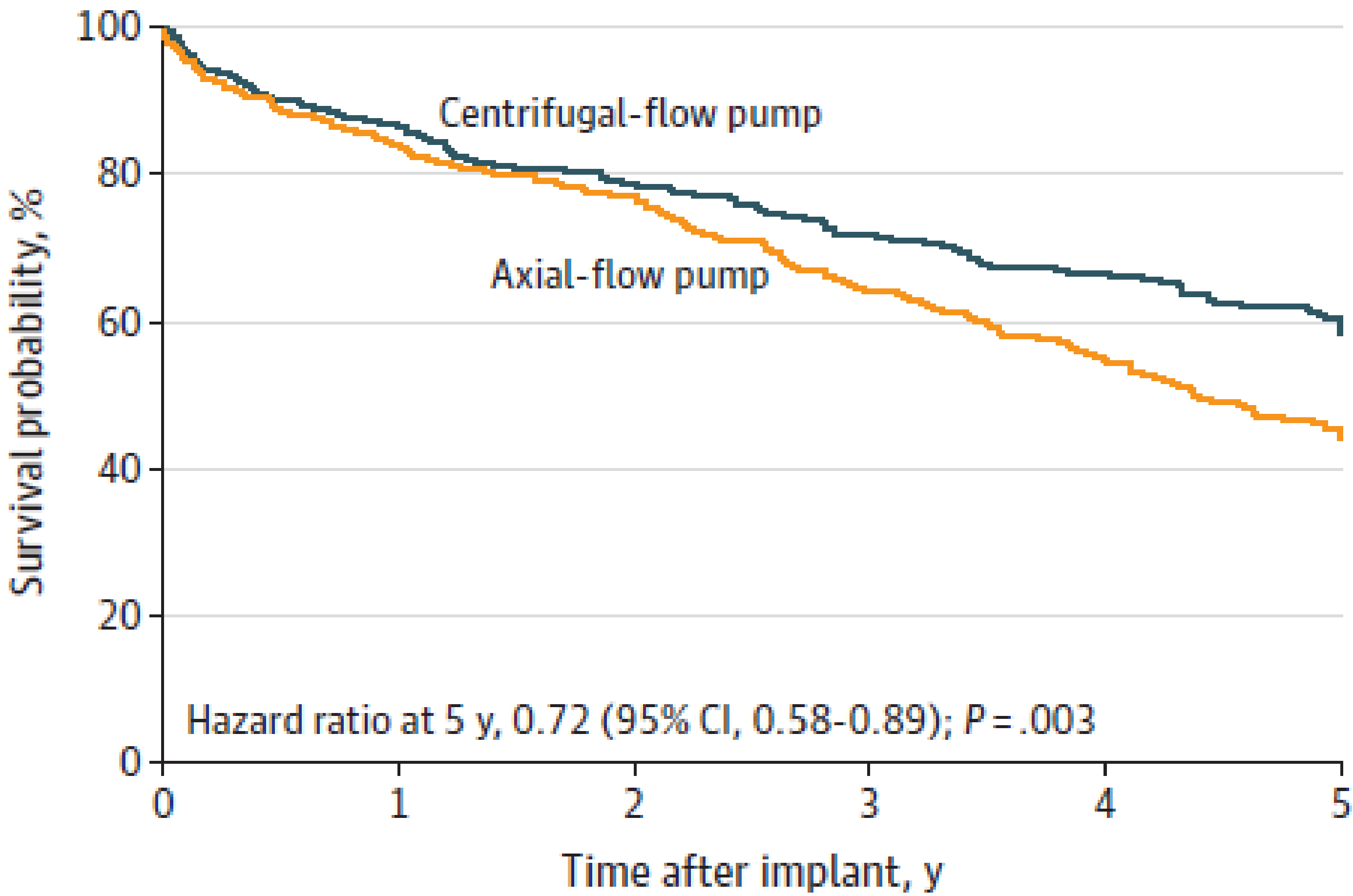
Continuous flow pumps

TABLE 1 Typical LVAD Operating Parameters

	HeartMate II	HeartMate 3	HVAD
Typical speed, rpm*	8,000-10,000	5,000-6,000	2,400-3,200
Speed adjustment increment, rpm/increment	200	100	20
Flow, l/min	4-7	4-6	4-6
Power, W	5-8	4.5-6.5	3-7
Pulsatility index (or HVAD, peak to trough)	5-8	3.5-5.5	2-4 l/min/beat

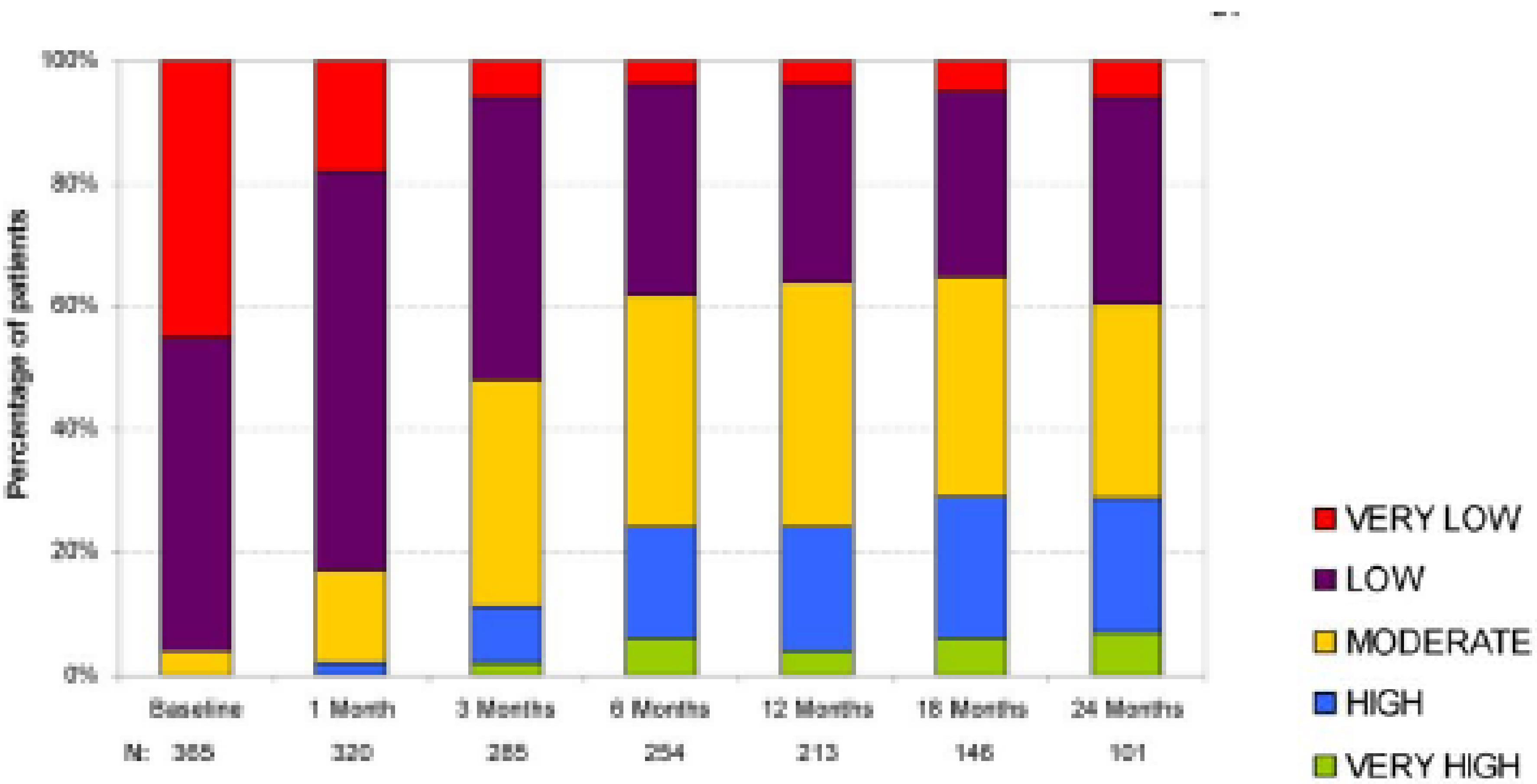
(a)

MOMENTUM 3 five year survival



JAMA 2022;online Sept 8, 2022

Pt reported exercise ability - DT



JACC 2010;55:1826

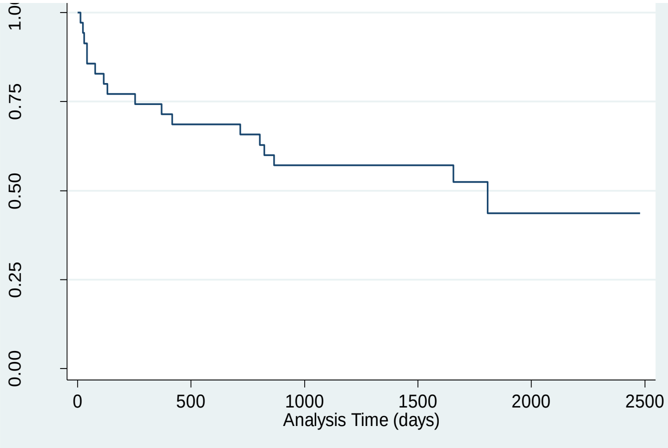
LVAD misery – Adverse events

Adverse event	Within 3 months	After 3 months
Bleeding	29.5%	23.1%
Arrhythmia	21.8%	11.3%
Device malfunction	6.0%	14.9%
Infection	28.2%	31.0%
Neuro event	10.0%	13.9%
Rehospitalization	38.2%	64.5%
Renal dysfunction	9.6%	5.5%

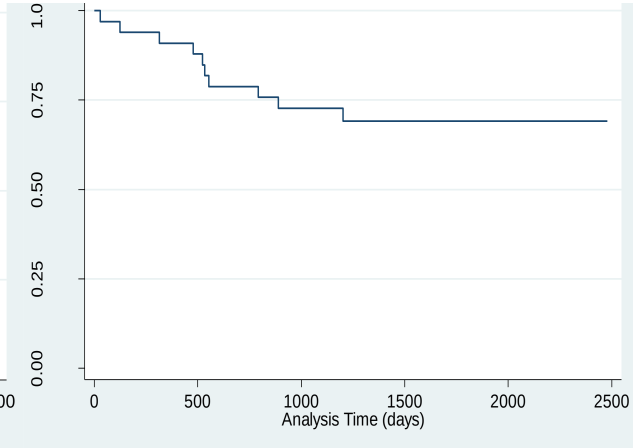
INTERMACS 2016 Annual Report

Hopkins database: 2000-2013

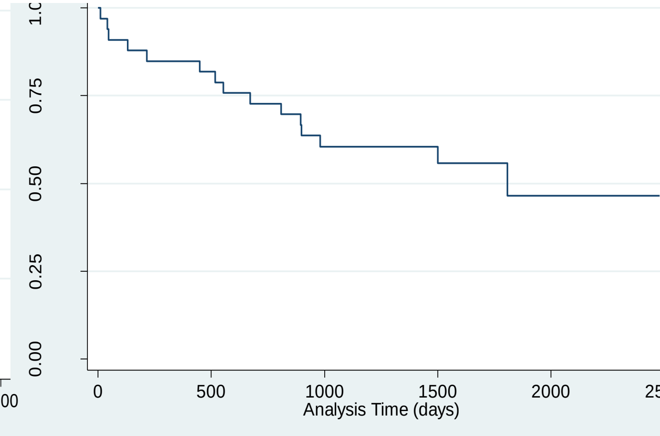
GI bleed



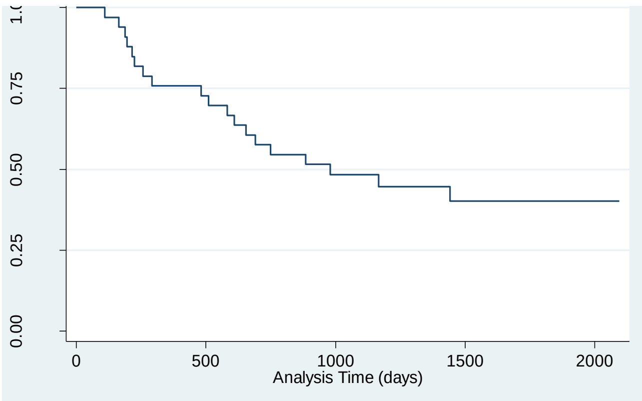
CVA



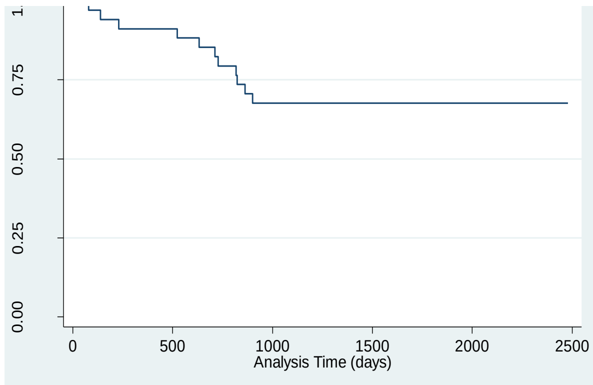
Transfusions



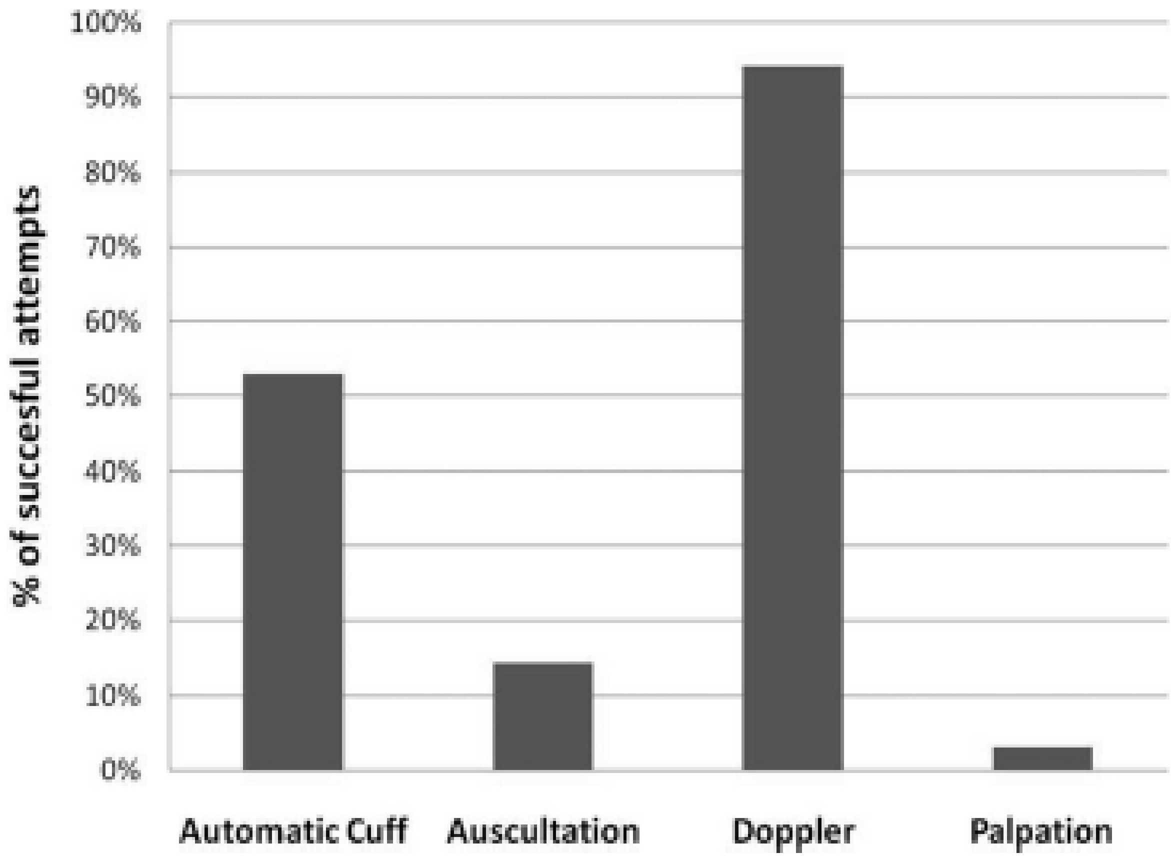
Driveline infection



Sepsis



Measuring blood pressure



Bennet M et al J Heart Lung Tx 2010;29:593

CPX with LVADs

68 LVAD patients at least a month out from implant

57 yo

Support duration 483 days

Exercise on cycle ergometer

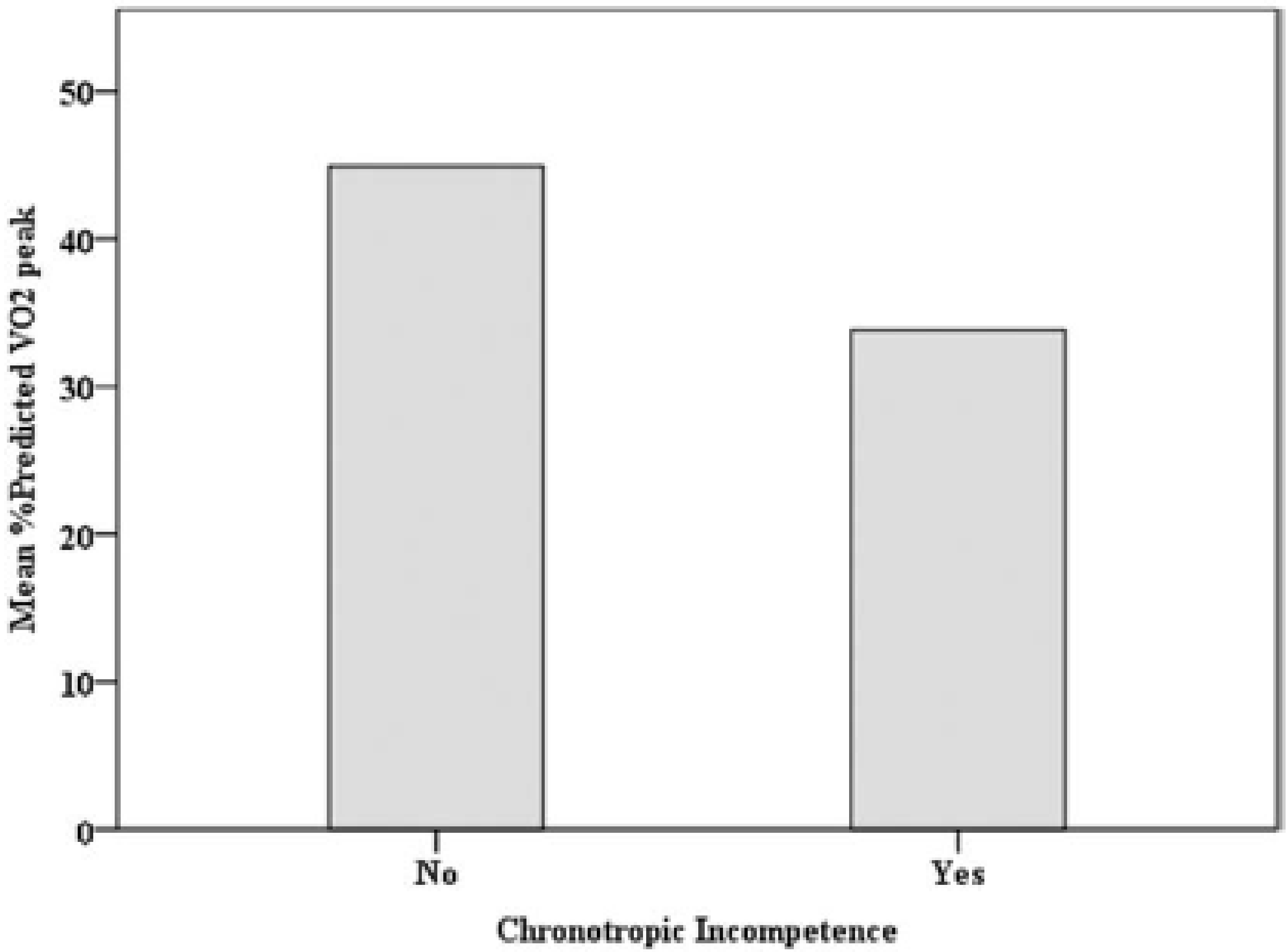
ASAIO J 2020;66:160-165

Functional capacity with LVADs

	Mean ± SD
VO_2 peak (ml/kg/min)	11.71 ± 4.06
% Predicted VO_2 peak	40 ± 13.4
Heart rate at rest (bpm)	79 ± 14
Heart rate at VO_2 peak (bpm)	123 ± 25
Heart rate reserve	59 ± 22
% Heart rate reserve	75 ± 15
Respiratory exchange ratio	1.16 ± 0.11
Load at test termination (watt), median (IQR)	75 (50–100)
Test duration (sec)	422 ± 188

ASAIO J 2020;66:160-165

Functional capacity with LVADs



ASAIO J 2020;66:160-165

High intensity interval training LVADs

Compared high intensity versus moderate intensity training

12 weeks supervised training, 3x/week

Baseline CPX

HIIT – 80-90% of VO2 AT 4 minutes alternating with 50-60%

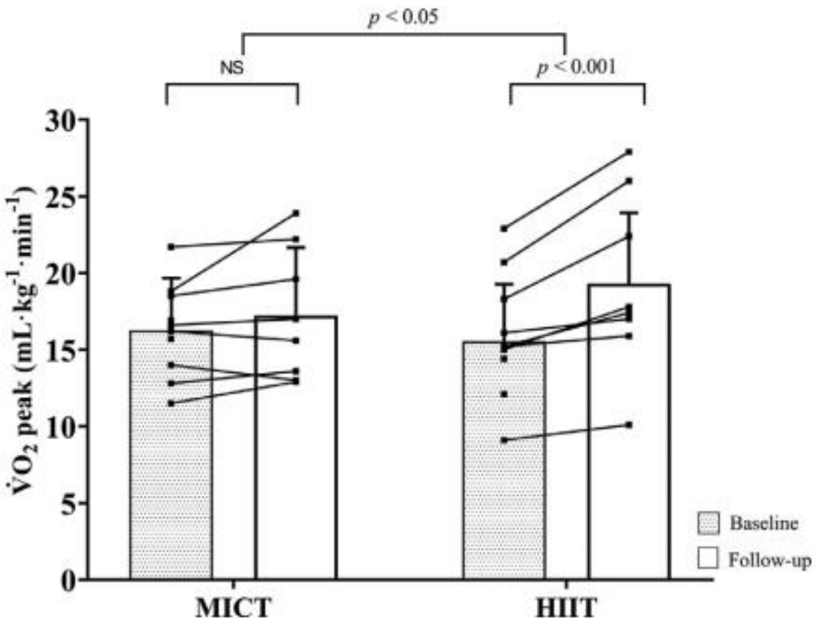
MIIT – 28 minutes 50-60%

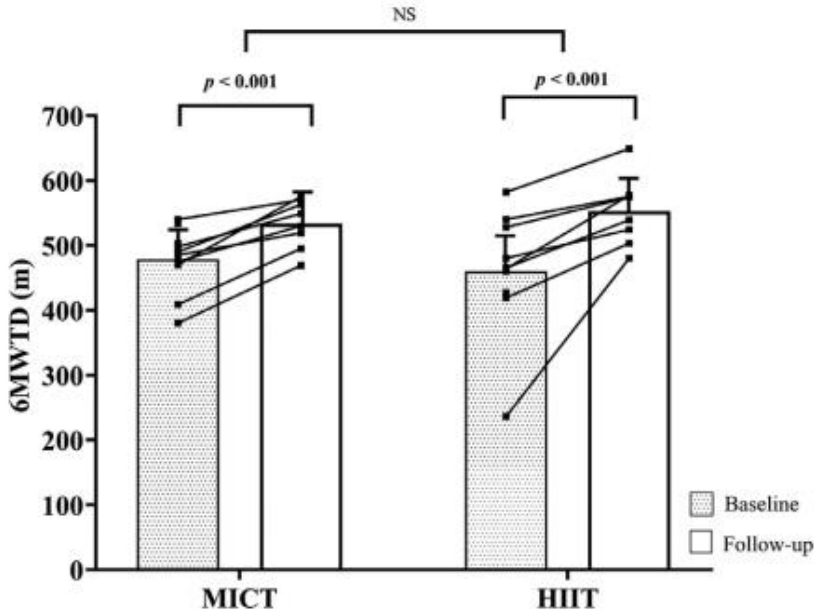
All on treadmill

21 patients

J Ht Lung Tx 2020;39:1380

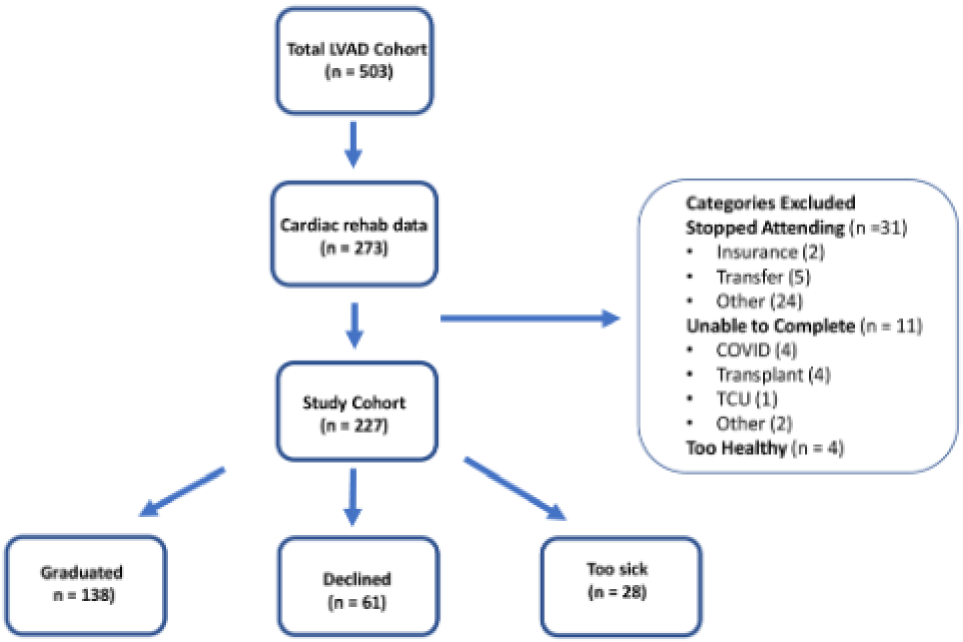
High intensity interval training LVADs

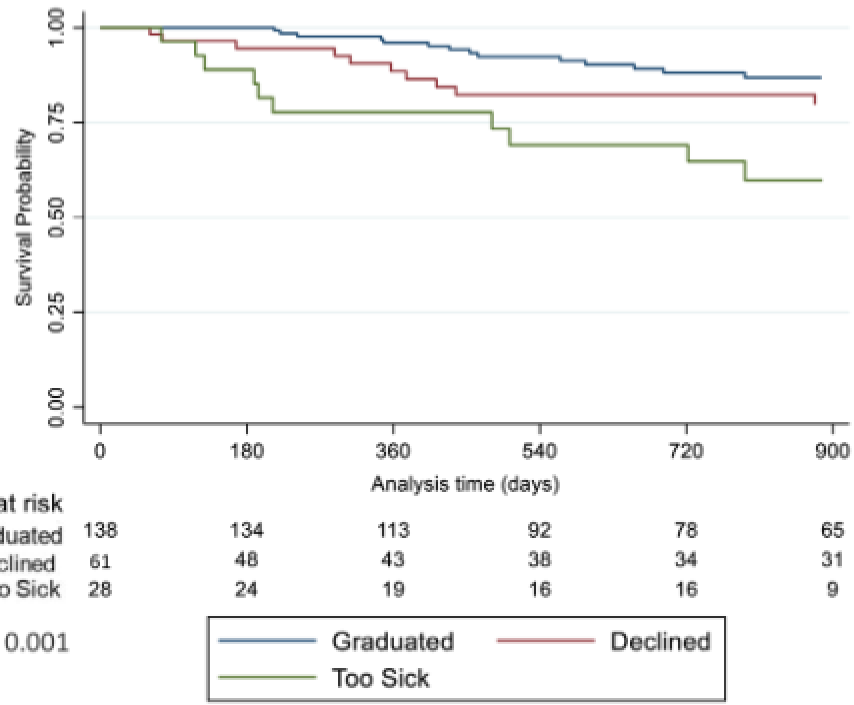




J Ht Lung Tx 2020;39:1380

Training with VADs – U Minnesota





Number at risk

	0	180	360	540	720	900
Graduated	138	134	113	92	78	65
Declined	61	48	43	38	34	31
Too Sick	28	24	19	16	16	9

ASAIO 2022;online ahead of print

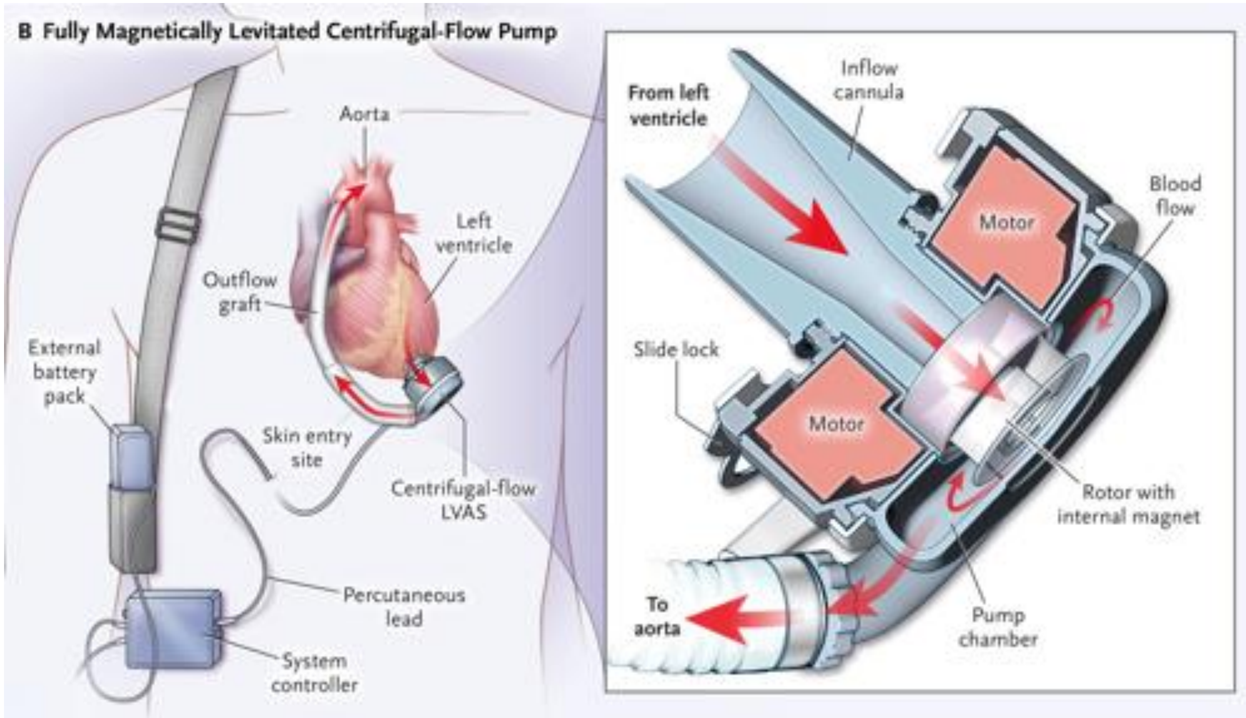
LVAD patients in rehab

Blood pressure can be hard to check

If feel different than normal, think about arrhythmias

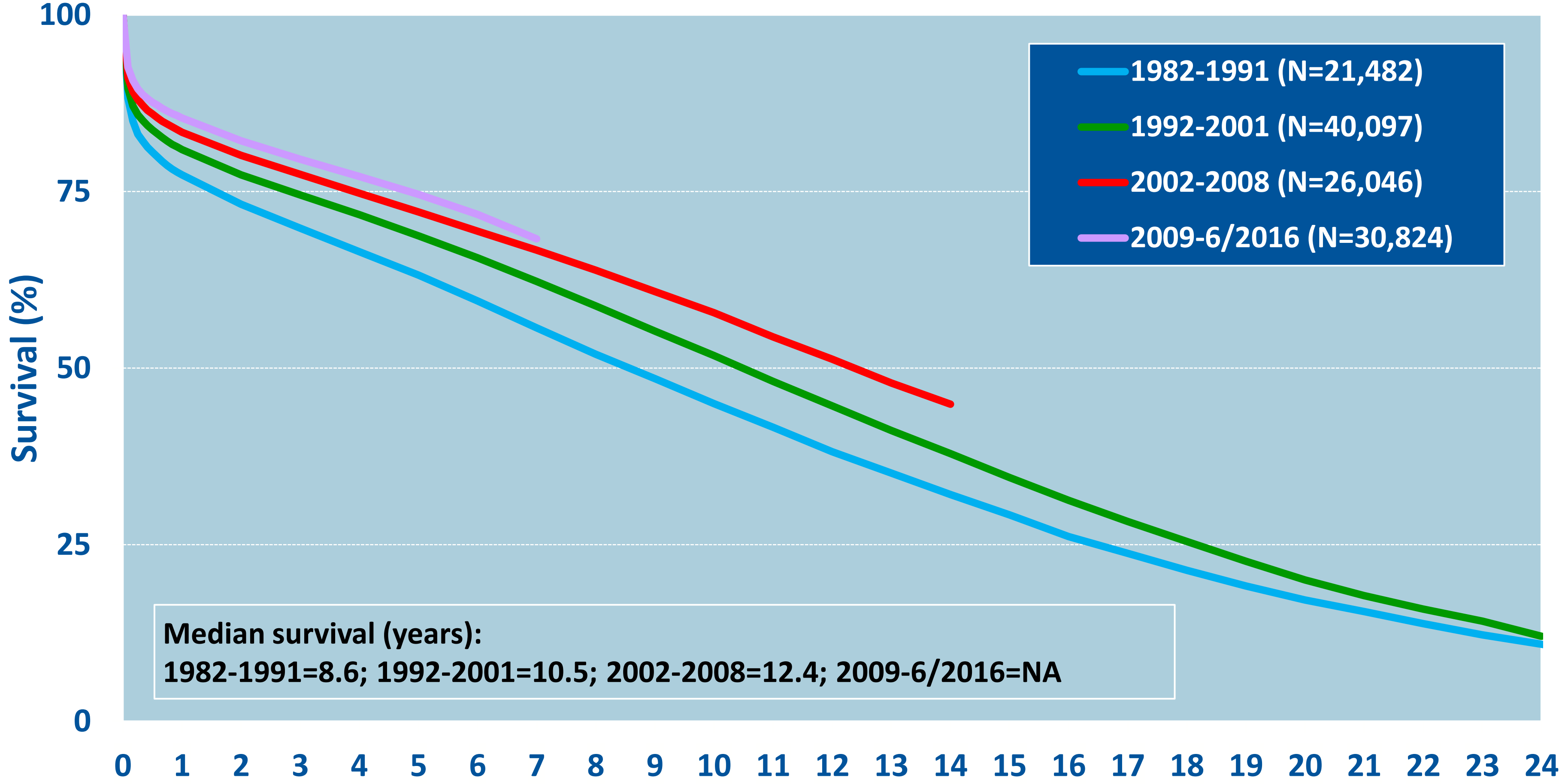
Watch the driveline

Make sure extra batteries



Adult Heart Transplants
Kaplan-Meier Survival by Era

(Transplants: January 1982 – June 2016)



Transplanted heart is denervated

No afferents or efferents

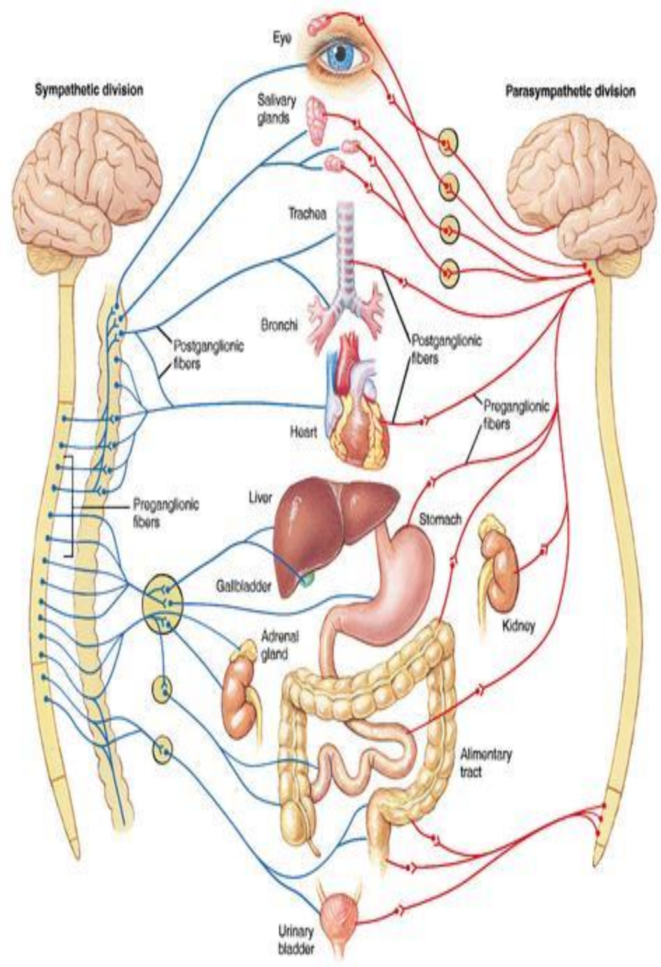
No angina

Higher resting HR

Reliance on circulating E, NE (exercise)

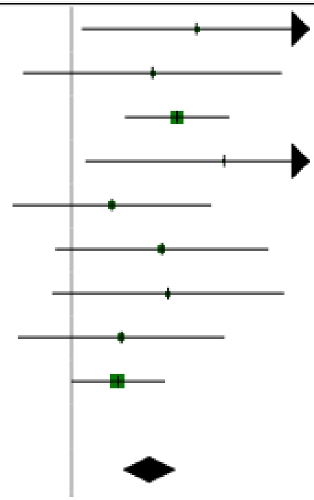
Increased receptor density → sensitivity to circulating E, NE (drugs)

Loss of feedback regulation



Training after Tx – Change in peak VO_2

Study or subgroup	Experimental (mL/kg/min)		Control (mL/kg/min)		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Bernardi 2007	13	19.6 (2.3)	11	15.6 (5.8)		5.55%	4.01[0.33,7.69]
Braith 2008	9	19.4 (5.5)	7	16.8 (2.8)		4.36%	2.6[-1.55,6.75]
Haykowsky 2009	22	3.4 (3.3)	21	0 (2.2)		26.93%	3.39[1.72,5.06]
Hermann 2011	14	28.3 (6.1)	13	23.4 (5.7)		3.79%	4.9[0.45,9.35]
Kobashigawa 1999	14	13.6 (4.8)	13	12.3 (3.7)		7.41%	1.3[-1.88,4.48]
Nytrøen 2012	24	30.9 (5.3)	24	28 (6.7)		6.43%	2.9[-0.52,6.32]
Pascoalino 2015	33	23.2 (6.7)	9	20.1 (4.5)		5.42%	3.1[-0.62,6.82]
Tegtbur 2003	8	20.1 (4.2)	12	18.5 (2.8)		6.84%	1.6[-1.71,4.91]
Wu 2008	14	1 (2.5)	23	-0.5 (1.8)		33.27%	1.5[-0,3]
Total ***	**151**		**133**			**100%**	**2.49[1.63,3.36]**



Cochrane Database Syst Rev 2017;4:CD012264

Training after Tx

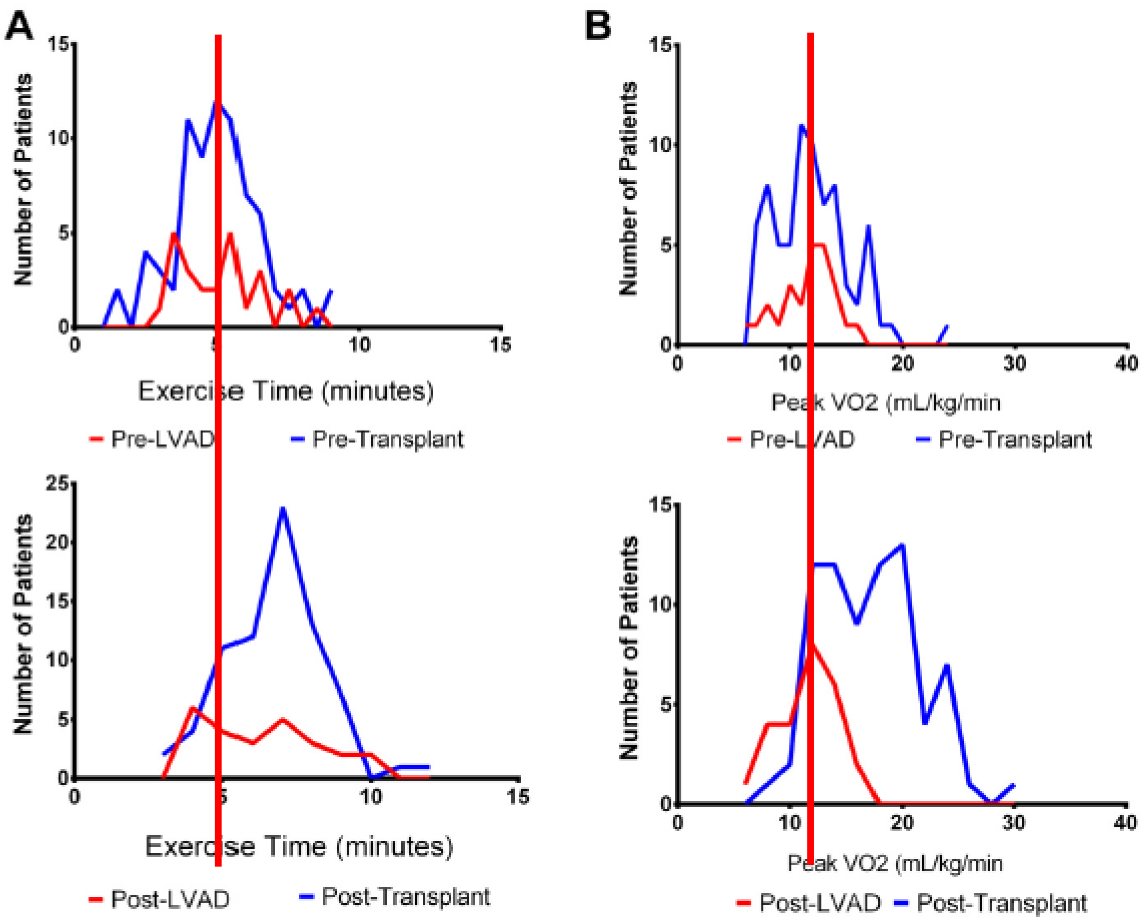
Need a longer warmup and warm down

Tend to be more hypertensive

Infectious risk is low (especially now since everyone more careful with COVID

Tend to get better improvement than LVAD patients over time

Exercise time and VO_2 pre/post VAD and transplant



J Cardiac Failure 2014;20:548

Conclusion

Heart failure patients have reduced exercise capacity related to reduced cardiac function and secondary muscle changes and energy changes

All (HF/LVAD/Tx) benefit from cardiac rehab

Watch for the unique differences between groups