Multi-domain Rehabilitation for Older Patients with Myocardial Infarction

The PIpELINe trial

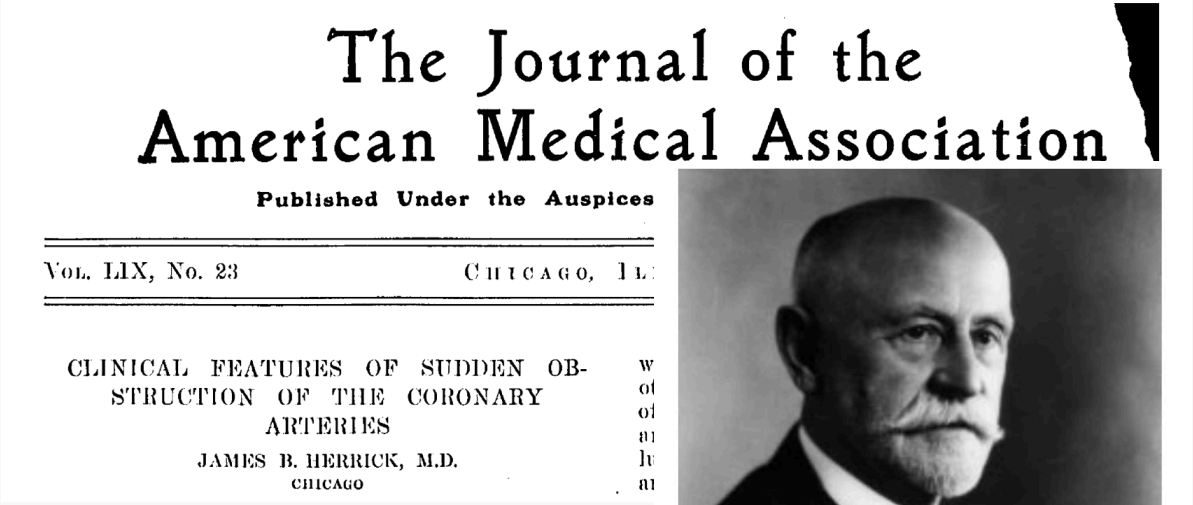
- **Elisabetta Tonet, MD**
- On behalf of the PIpELINe investigators
- University Hospital of Ferrara

elementrials.org

Evolution

Contemporary myocardial infarction MANAGEMENT has evolved dramatically in the XX century

Origins – physical inactivity



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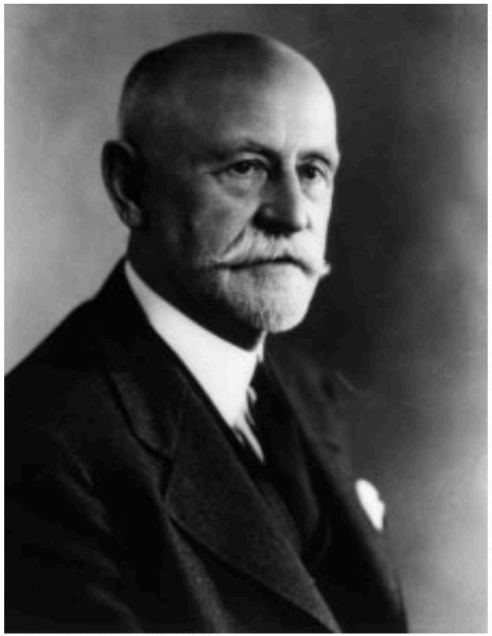
CLINICAL FEATURES OF SUDDEN OBSTRUCTION OF THE CORONARY ARTERIES

JAMES B. HERRICK, M.D.
CHICAGO



National Library of Medicine

James B Herrick (1861–1954)
"The importance of absolute rest in bed for several days is clear."

1910s

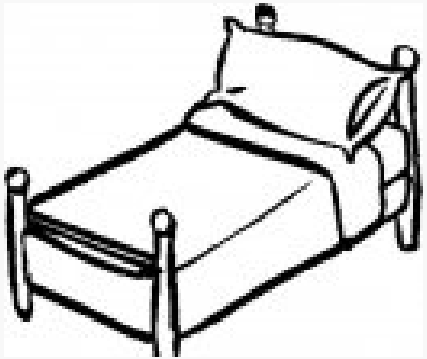
«The importance of absolute rest in bed for several days is clear»

Origins – physical inactivity

1920s

CARDIAC INFARCTION AND CORONARY THROMBOSIS.

By JOHN PARKINSON, M.D., F.R.C.P. Lond.,
PHYSICIAN (WITH CHARGE OF OUT-PATIENTS) AND PHYSICIAN IN CHARGE OF THE CARDIOGRAPHIC DEPARTMENT, LONDON HOSPITAL · PHYSICIAN TO THE NATIONAL HOSPITAL FOR DISEASES OF THE HEART;
AND
D. EVAN BEDFORD, M.D., M.R.C.P. Lond.,
ASSISTANT PHYSICIAN TO THE MIDDLESEX HOSPITAL.*



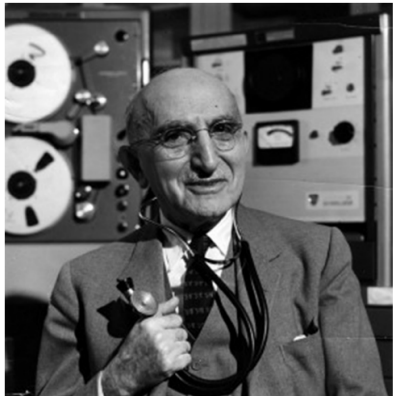
Absolute rest in bed for not less than a month is imperative to allow healing of the infarct and to reduce the risk of embolism. The subsequent management will be that of a patient known to be arteriosclerotic and prone to anginal pain, though the probability of another cardiac infarction is not great. Convalescence will therefore be prolonged and the return to ordinary life postponed as long as possible. If exertion is restricted to less than that which induces pain greater capacity may ultimately be obtained.

The Turning point

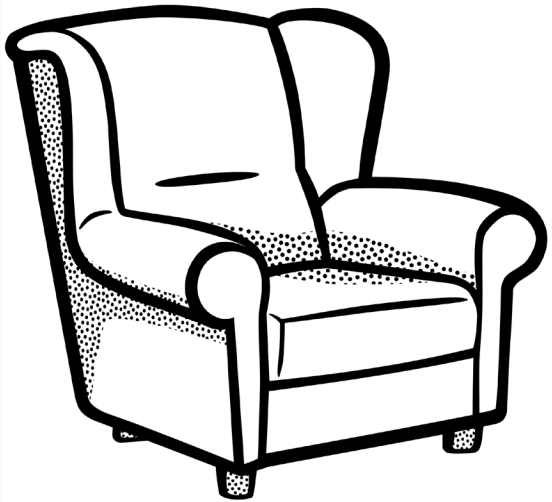
THE EVIL SEQUELAE OF COMPLETE BED REST

WILLIAM DOCK, M.D.

LOS ANGELES



1950s



The Turning point

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"ARMCHAIR" TREATMENT OF ACUTE CORONARY THROMBOSIS

Samuel A. Levine, M.D.
and
Bernard Lown, M.D., Boston

1. Physiological as well as clinical studies adduce evidence to support the view that strict rest in bed is injurious to the patient with congestive heart failure.

2. The sitting position in a chair with the feet dependent obviates some of the harm of strict bedrest.

3. This principle has been applied in the treatment of 81 patients with acute coronary thrombosis. These patients were kept in a chair varying and increasing portions of the day, beginning not later than the first week of the attack.

4. There were eight deaths, an over-all mortality of 9.9%. All other methods of treatment usually employed in coronary thrombosis were used. If only the patients who received anticoagulants are considered (72 patients), the mortality was only 8.3%. There were no complications attributable to the "armchair" treatment. The prompt improvement shown by some of those desperately ill with congestive heart failure after being placed in a chair was particularly impressive.

5. This method of treatment also appeared to have beneficial effects on the psychological state of the patient and facilitated the rehabilitation process.

The Progress

The first early ambulation program in the world (1962)

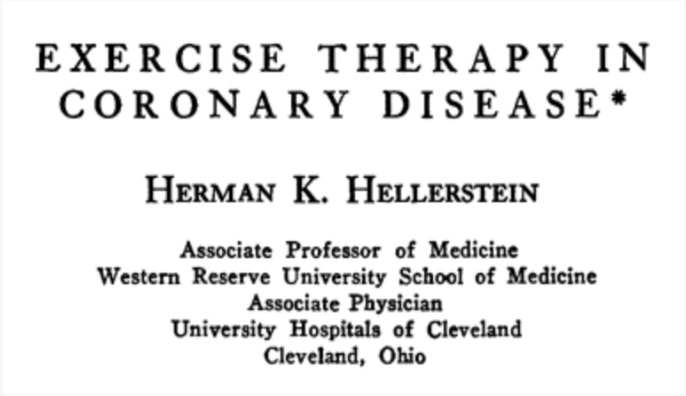
1960s

Dr Nanette Wenger

- 14-step program with a progressive step each day
- Discharge by day 18
- Patients were up and walking around their beds in the first couple of days while still attached to the monitor.

The Birth of Cardiac rehabilitation

1970s



EXERCISE THERAPY IN CORONARY DISEASE*

HERMAN K. HELLERSTEIN

Associate Professor of Medicine
Western Reserve University School of Medicine
Associate Physician
University Hospitals of Cleveland
Cleveland, Ohio

Cardiac rehabilitation concept

-Inpatient model to outpatient programs

-Focus on physical activity

3 phases - 3 issues

1980-90s

1

inpatient mobilization

2

outpatient hospital-based program 6–12 weeks

3

maintenance phase 4–6 months

1

30–50% of those eligible are referred

2

10% actually attend structured programs

3

<5% complete a full program

The diffusion of traditional programs

2000s

Features of programs	No. of programs
Model of care[†]	
Education and counselling with supervised exercise	260 (70%)
Education and counselling without supervised exercise	67 (18%)
Exercise only	18 (5%)
Setting[‡]	
Hospital	190 (51%)
Home	15 (4%)
Community	91 (25%)
Flexible	64 (17%)
Time-limited	267 (72%)
Group-based	288 (78%)
Maintenance offered	125 (34%)
Heart failure management program offered	64 (17%)

Low enrollment of older adults

High number of sessions

Late onset after MI

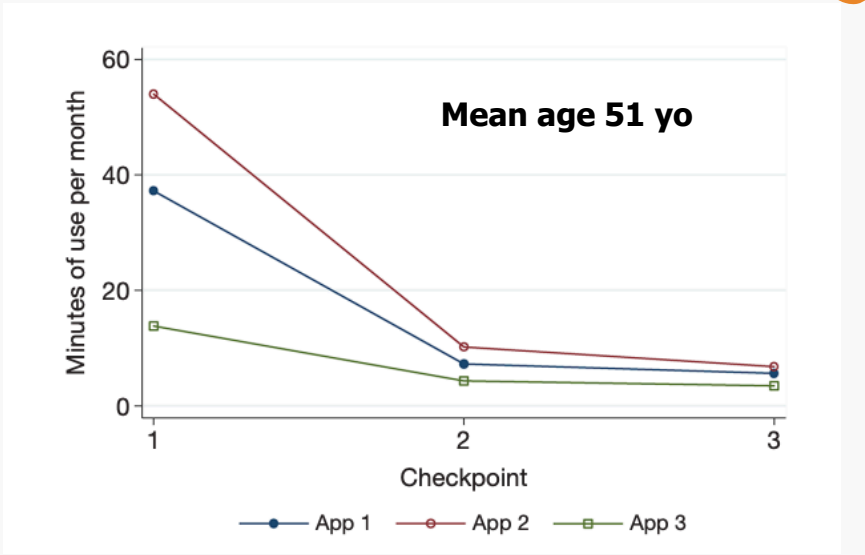
Mainly physical exercises

Standardized activities

No long-term maintenance

The modern attempt

2010-20s



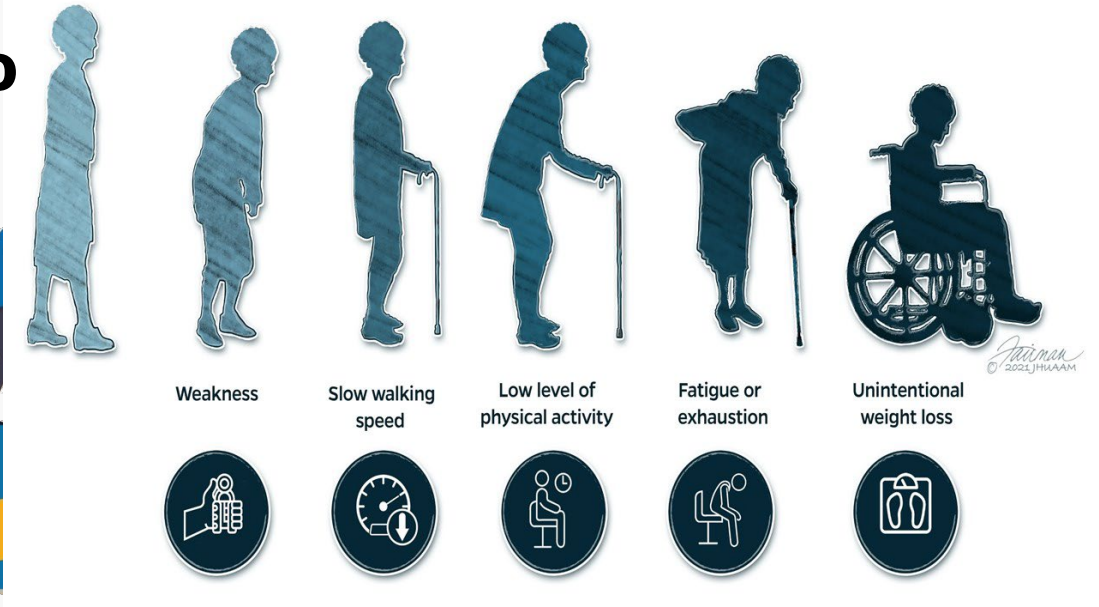
- **>50%** of users stopped wearing them within six months
- **<20%** keep using them after six months
- No multi-domain

Herrmann LK, Mhealth 2017
Lee BC, Int J Environ Res Public Health 2020; 17: 10

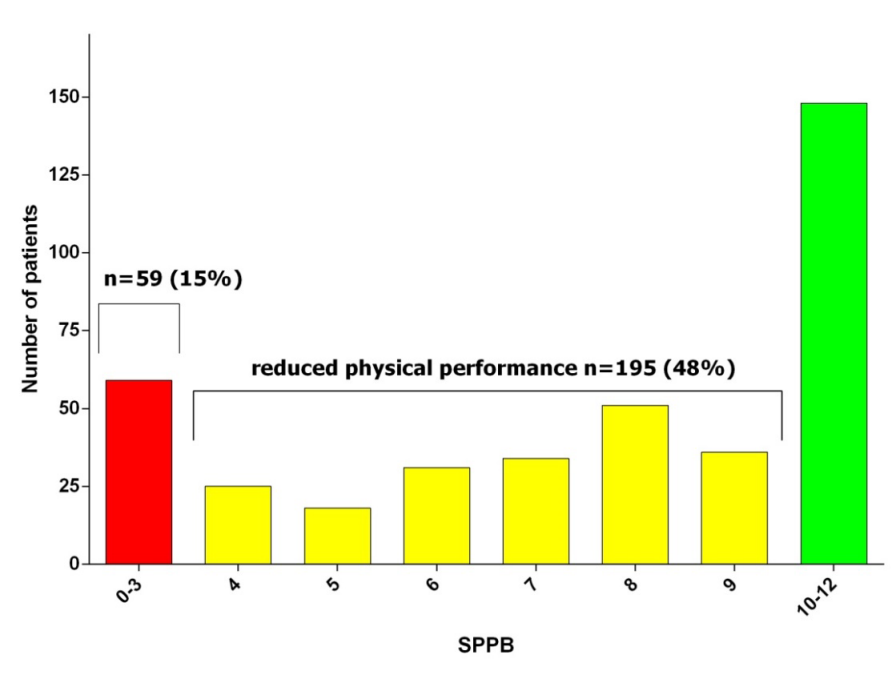
Evolution

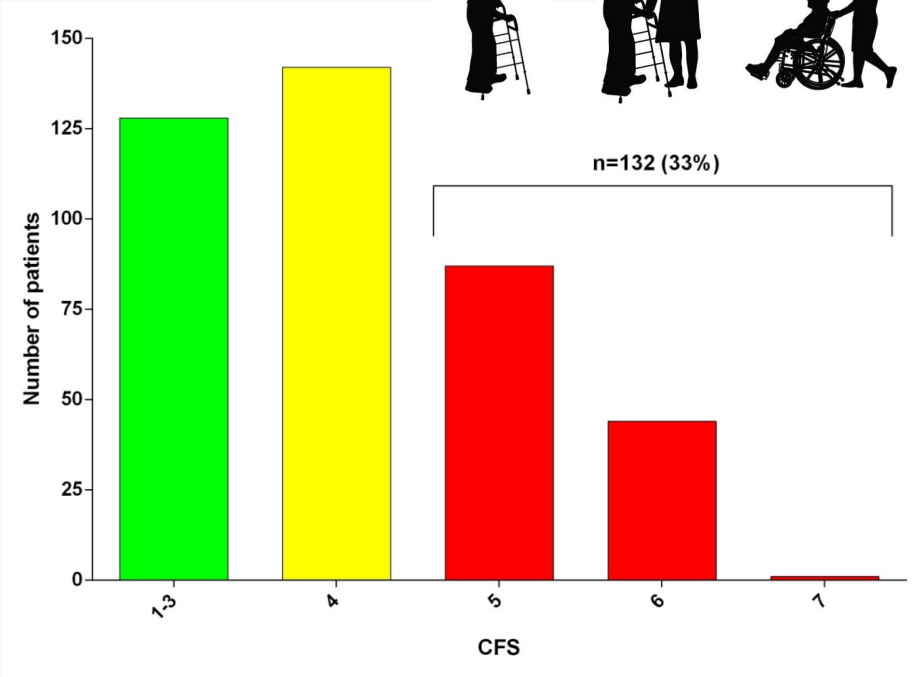
Contemporary myocardial infarction PATIENT has evolved significantly in the XX century

2/3 MI patients >65 yo



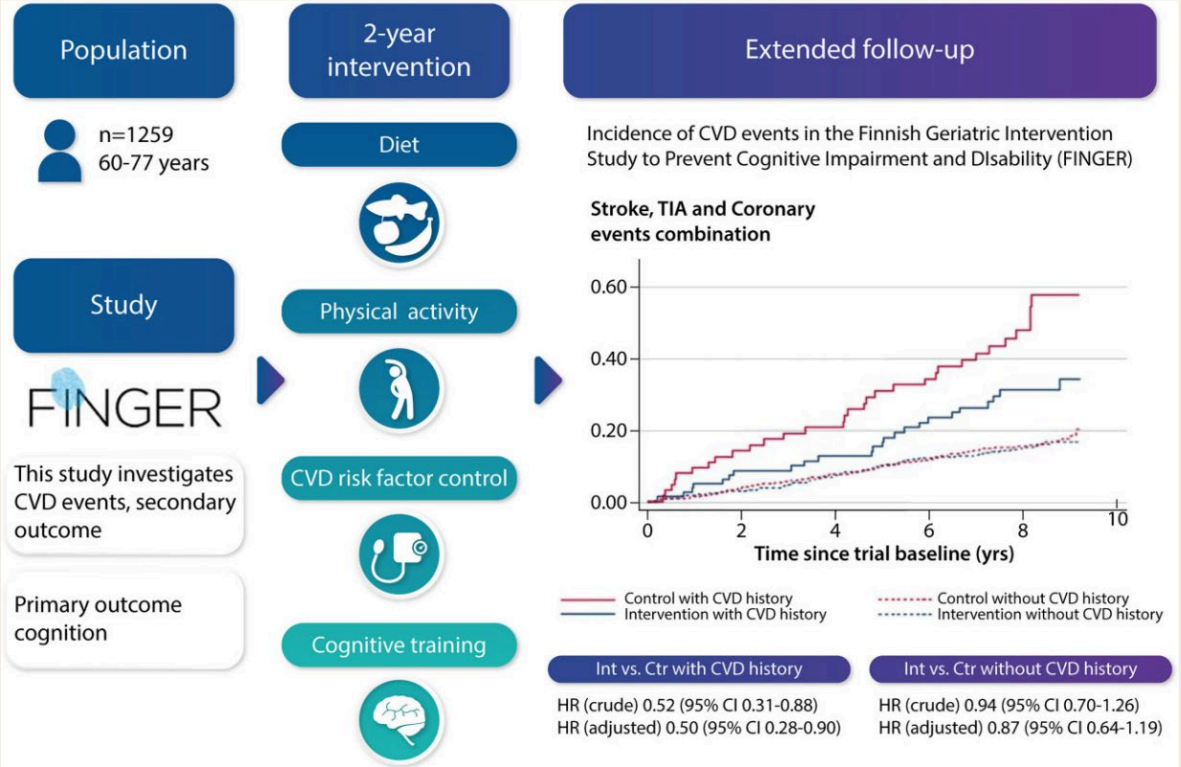
Peculiarity





Campo G J et al, J Gerontol A Biol Sci Med 2020

Multi-dimensionality



Lehtisalo J et al, Eur Heart J 2022

Identikit

Multi-dimensional

Early

Supervised sessions

Home-based program

Tailored

The HULK pilot study

Prospective, Multicentre, Randomized

235 patients with ACS, aged ≥ 70 y, SPPB 4-9

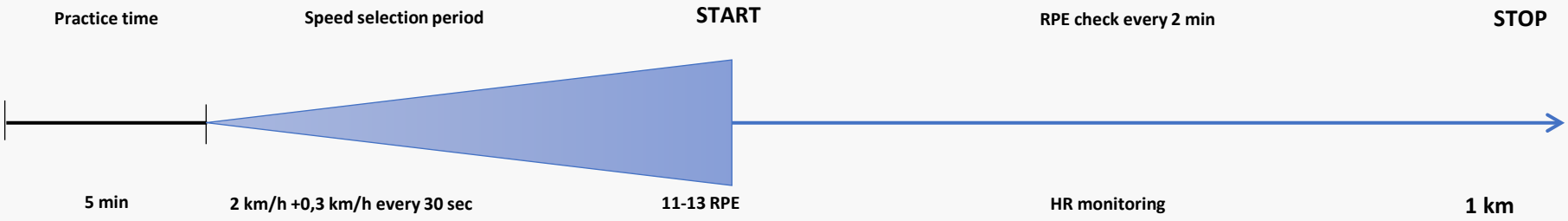
Primary Endpoint: SPPB value 6 months after ACS

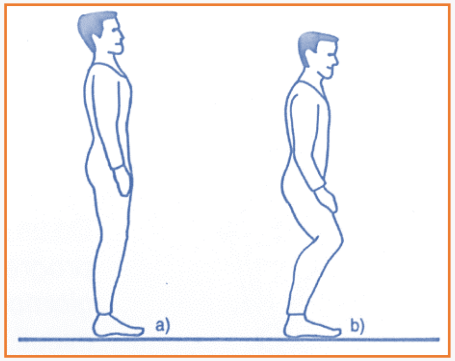
Secondary Endpoints
-Handgrip strenght
-Gait speed
-Quality of life
-aADL

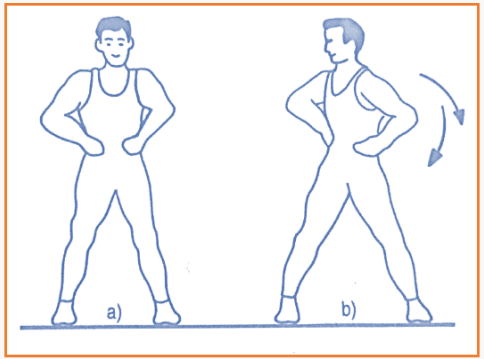
Campo G et al, JACC 2019

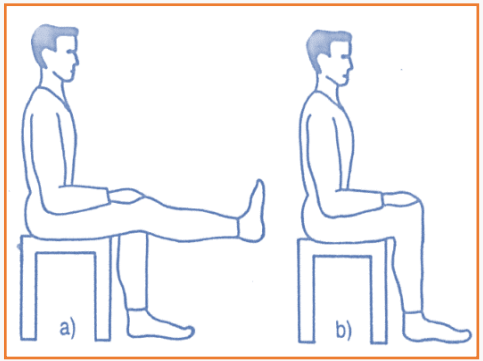
Physical activity model

1, 2, 3, 4 months after ACS



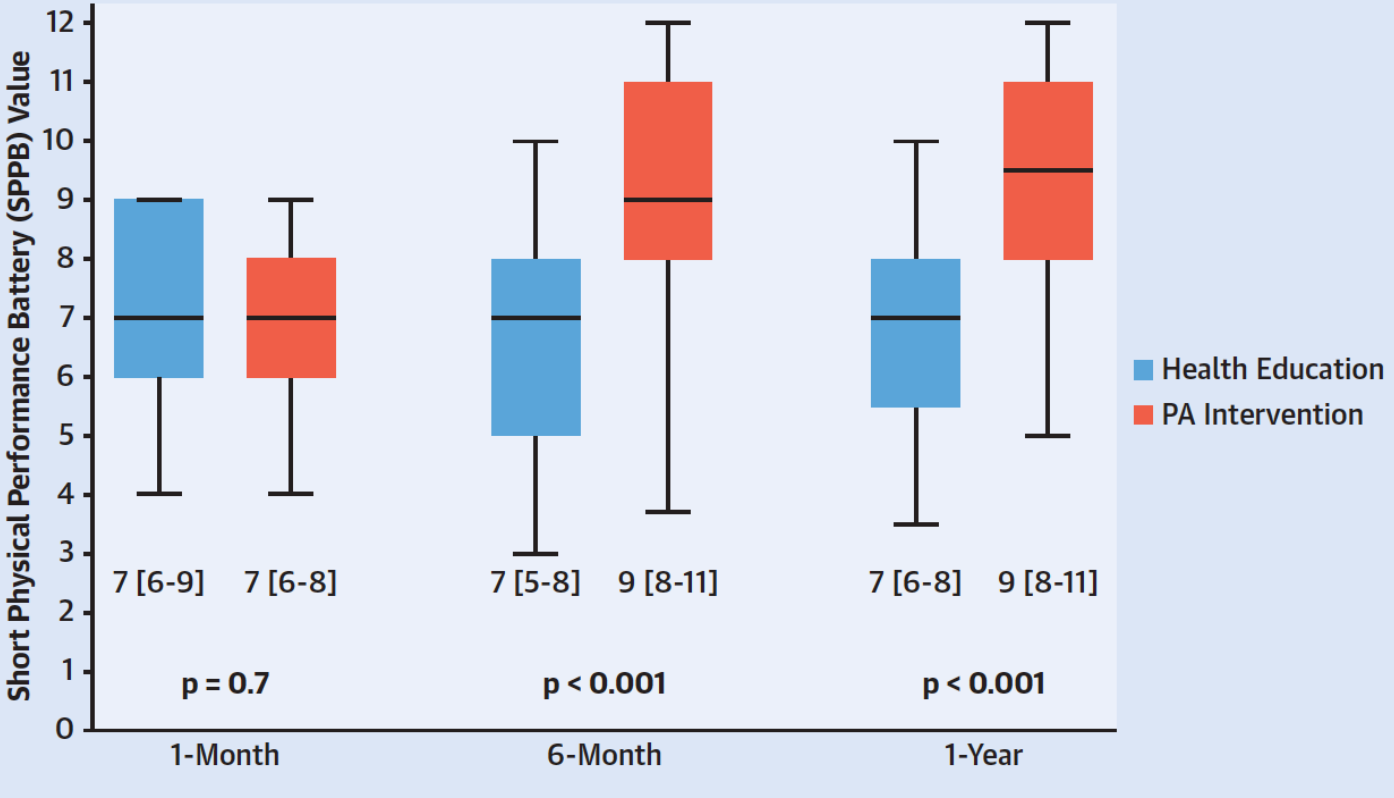






Campo G et al, JACC 2019

SPPB Value in Study Groups at Different Time Points



Campo G et al, JACC 2019

Background

- Despite advancements in acute care, older patients presenting with myocardial infarction (MI) are the highest risk population with the worst prognosis[1]
- Older adults represent the least physically active group with often experiencing functional decline, frailty and disability after MI[2]
- Traditional cardiac rehabilitation programs show several limitations such as low participation rate, early withdrawal and high costs, especially in older patients[3]

1. JACC 2018; 2. J Gerontol A Biol Sci Med Sci. 2020; 3. NEJM 2024.

Research Question

- **To evaluate whether, in older patients (65+ years old) admitted to hospital for MI and with impaired physical performance, an early, tailored, multi-domain rehabilitation intervention was superior as compared to standard of care in improving outcomes.**

Organization

Country: Italy

7 centers

Study PI: Gianluca Campo

Study Chair: Giovanni Grazzi

Executive Committee: Elisabetta Tonet, Stefano Volpato, Andrea Raisi, Gianni Mazzoni

CEC: Rita Pavasini, Paolo Cimaglia

DSMB: Simone Biscaglia, Roberta Campana

ARO: Veronica Lodolini, Chiara Manzalini, Cecilia Chiarelli, Elisa Mosele, Martina Viola, Alice Santoni

Stats: Donato Martella, Nicola Pesenti

The Physical Activity Intervention in Elderly Patients with Myocardial Infarction (PIpELINe) trial was an **investigator-initiated, multicenter, prospective, superiority, randomized trial**.

Sponsor

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara

Università degli Studi di Ferrara

Supporter

Ministero della Salute

Ricerca Finalizzata 2018

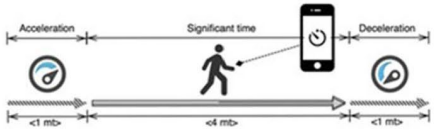
GR 2018-12367114

Inclusion and Exclusion Criteria

- 65+ years old
- MI (STE or NSTE-MI)
- Indication to invasive management
- SPPB value 4-9 at 1-month

- Planned coronary revascularization
- Life expectancy to < 1 year
- Severe aortic or mitral disease
- Ejection fraction <30%
- NYHA class III-IV
- Severe cognitive impairment
- Physical impairment

Short Physical Perfomance Battery

BALANCE TESTS	GAIT SPEED TEST	CHAIR STAND TEST
		
• **1 point**: feet together side-by side for 10 sec plus • **1 point**: heel of one foot against side of big toe of the other for 10 sec plus • **2 points**: feet aligned heel to toe for 10 sec • **1 point**: feet aligned heel to toe for 3-9.99 sec • **0 point**: feet aligned heel to toe <3 sec	Measures the time required to walk 4 meters at a normal pace (use best of times) • **4 points**: <4.82 sec • **3 points**: 4.82-6.20 sec • **2 points**: 6.21-8.70 sec • **1 point**: >8.7 sec • **0 point**: unable	Measures the time required to perform 5 rises from a chair to an upright position as fast as possible without the use of the arms • **4 points**: ≤11.19 sec • **3 points**: 11.20-13.69 sec • **2 points**: 13.70-16.69 sec • **1 point**: >16.7 sec • **0 point**: 60 sec or unable
0-4 points	0-4 points	0-4 points

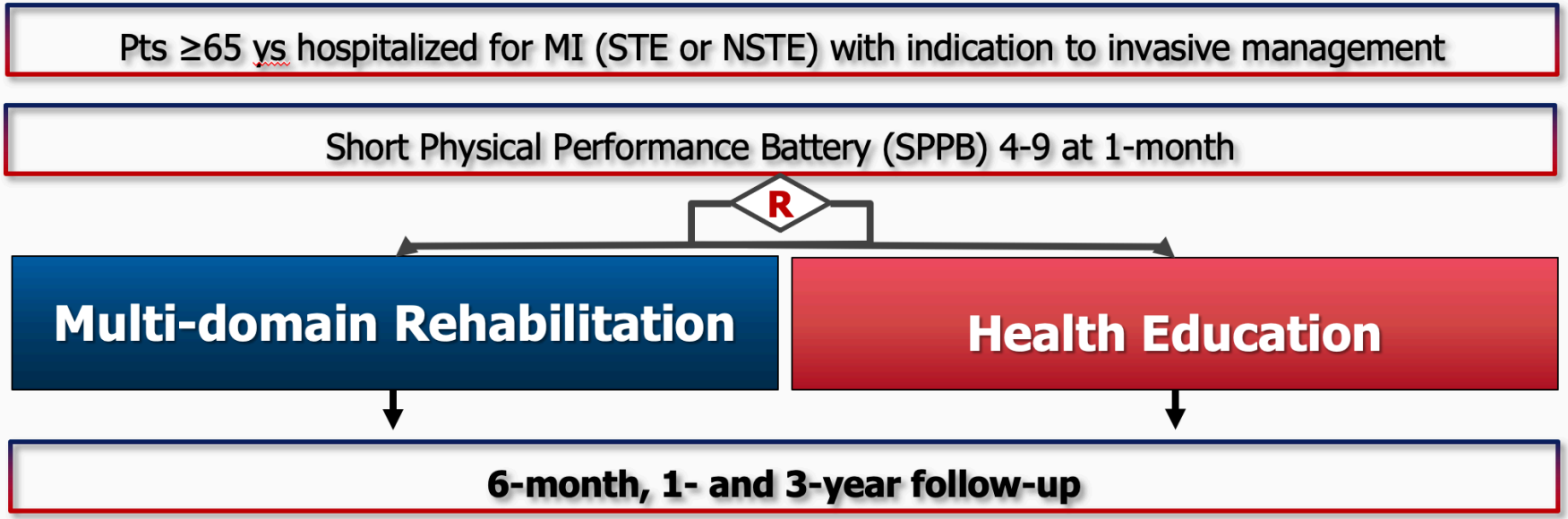
\+ \+

0-1	2	3	4	5	6	7	8	9	10	11	12

• Worst physical performance • Poor probability of recovery • Poor probability of improvement • High mortality	• Reduced physical performance • High probability of recovery • Quality of life and mortality related to physical performance improvement	• Best physical performance • Good quality of life • Very low mortality

1. J Gerontol 1994; 2. BMC Med 2016

Study Design

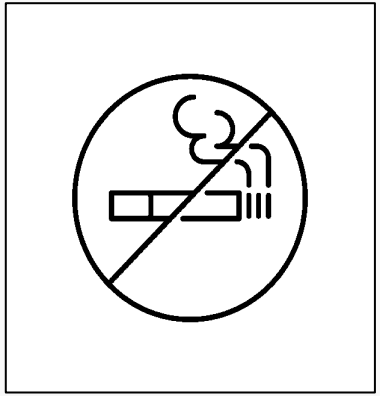


Sample Size

We assumed that 25% of patients in the control group would experience a primary-outcome event. With an anticipated relative risk reduction of at least 40% in the interventional group, we determined that enrolling at least 435 patients would provide the trial with 80% power to demonstrate the superiority of the intervention over usual care, at an alpha of 5%. To account for an anticipated 5% attrition, the final sample size was increased to at least 456 patients.

Intervention

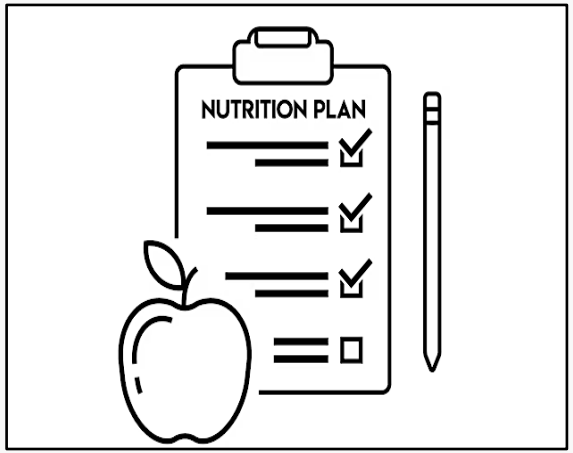
Metabolic Risk Factors Control



Risk factor management at each visit, targeting improvements in blood pressure, lipid profiles, blood glucose, and smoking cessation.

Intervention

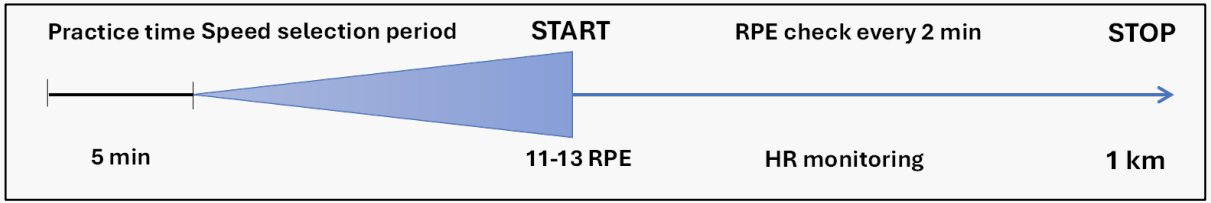
Diet Counselling



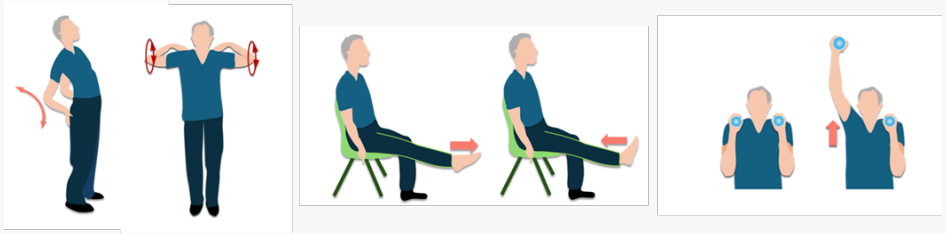
A nutritional status assessment was performed and each patient received a tailored diet plan

Intervention

Exercise Training



Supervised sessions (1-, 2-, 3-, 6-, 9-,12-month)



Tailored home-based exercises 20 minutes x3-5 days moderate walking

Exercise intensity and progression were individualized based on patient performance at each session. [1,2,3]

1. Heart 2016; JACC 2019; 3. Heart 2020

End Points (at 1-year)

Primary

CV death or unplanned hospitalization for CV causes

Secondary

Death, HF, MI, revasc, CVA, Unplanned hospitalization

Other

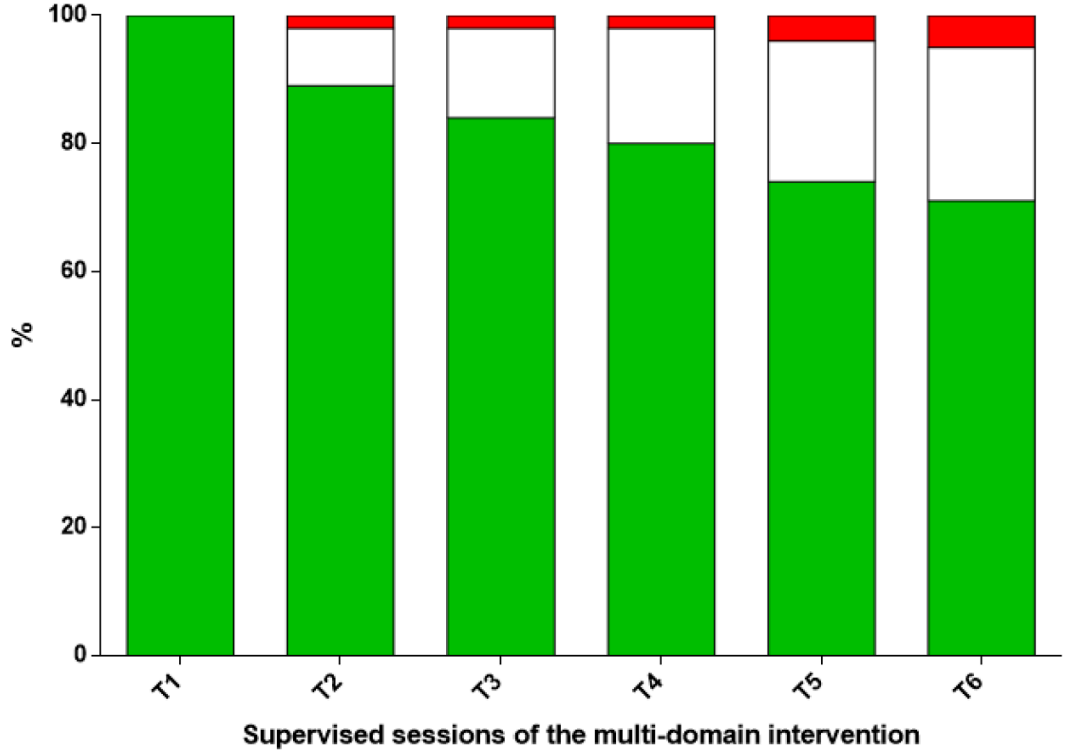
SPPB, gait speed, handgrip strength, QoL

Baseline Characteristics

Characteristic	Control (N=170)	Intervention (N=342)
Age (IQR) – yr	80 (76-83)	80 (75-84)
Female sex	65 (37.6)	122 (35.7)
Comorbidities		
Hypertension	148 (87.1)	294 (86)
Diabetes	50 (29.4)	87 (25.4)
Prior MI	45 (26.5)	81 (23.7)
eGFR <60 ml/min	33 (19.4)	56 (16.4)
PAD	35 (20.6)	74 (21.6)
Clinical presentation		
STEMI	63 (37.1)	127 (37.1)
NSTEMI	107 (62.9)	215 (62.9)

Characteristic	Control (N=170)	Intervention (N=342)
Nutritional Status		
Normal	118 (69.4)	232 (67.8)
At risk for malnutrition	47 (27.6)	96 (28.1)
Malnourished	5 (2.9)	14 (4.1)
Physical performance		
SPPB score	8 (6-9)	7 (6-9)
Gait speed	0.6 (0.5-0.8)	0.7 (0.5-0.8)
Handgrip strength		
Men	30 (22-36)	30 (25-37)
Women	21 (17-32)	20 (15-28)

Compliance to Intervention

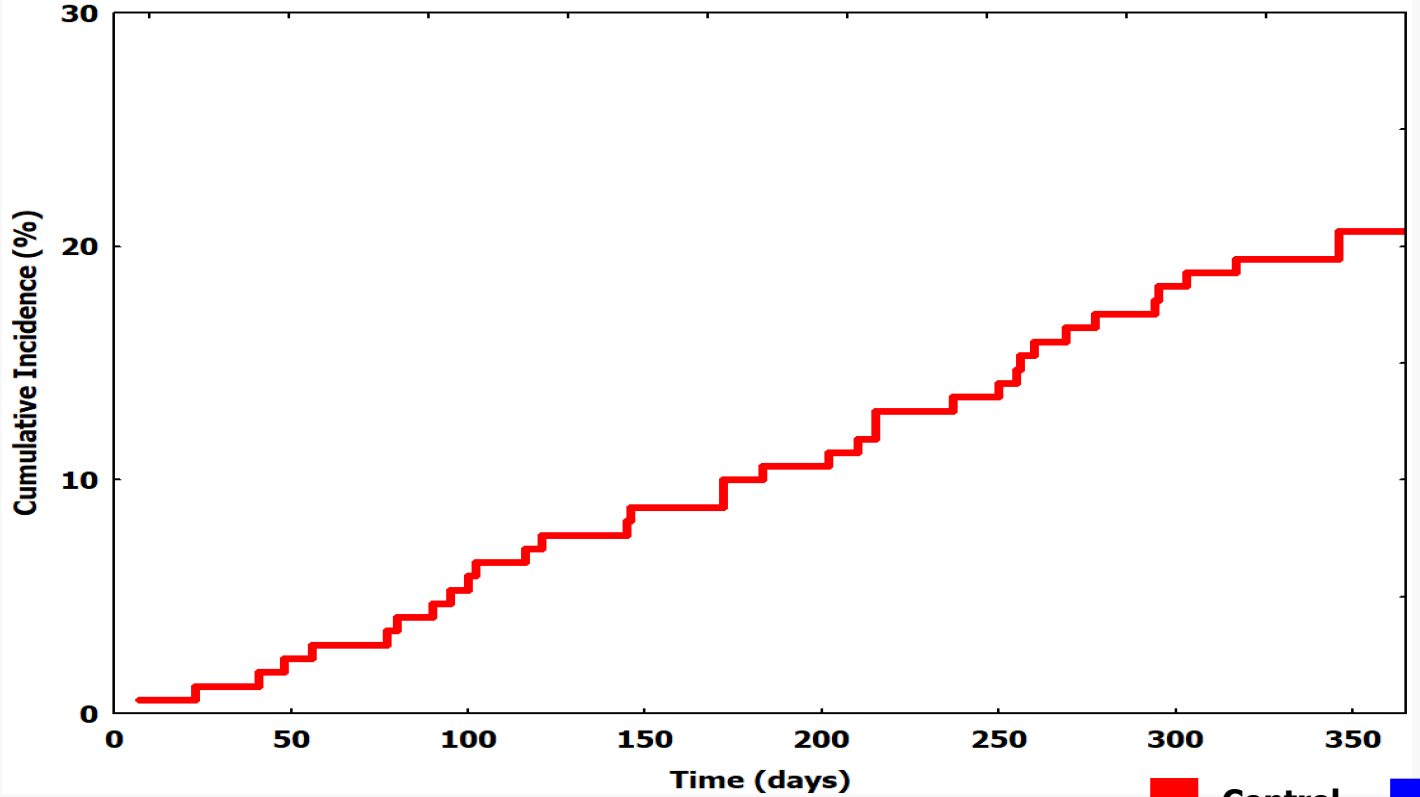


There were no serious adverse events reported during the supervised training sessions.

The overall compliance with the intervention was

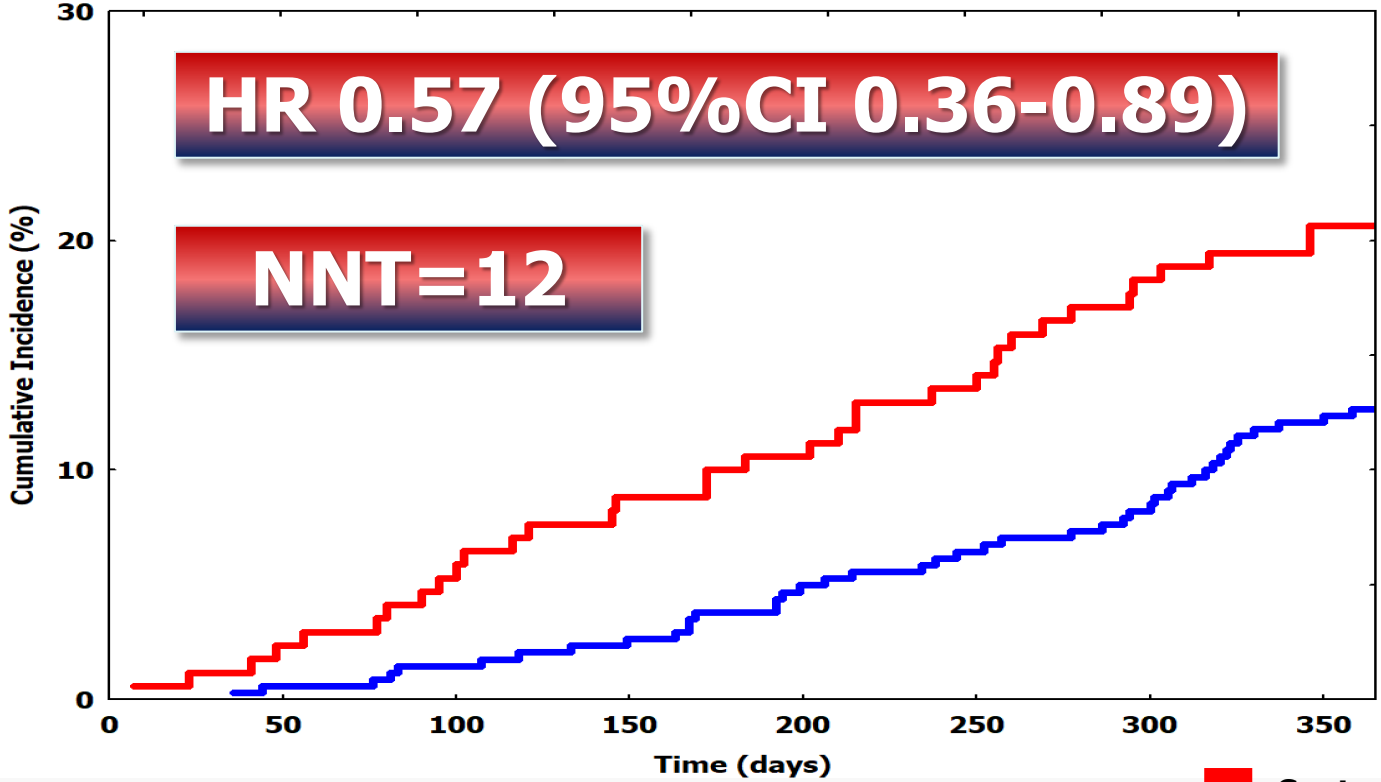
71% (95%CI 65%-75%)

Primary End Point



20.6%

Primary End Point



20.6%

12.6%

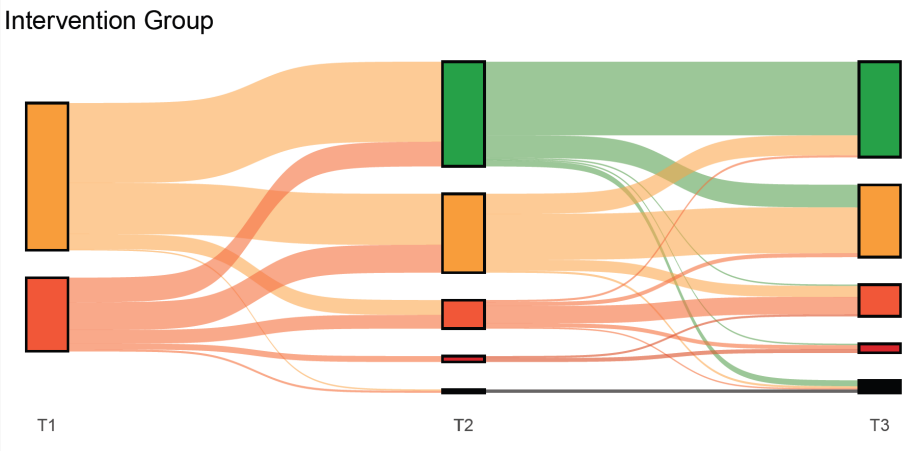
p=0.013

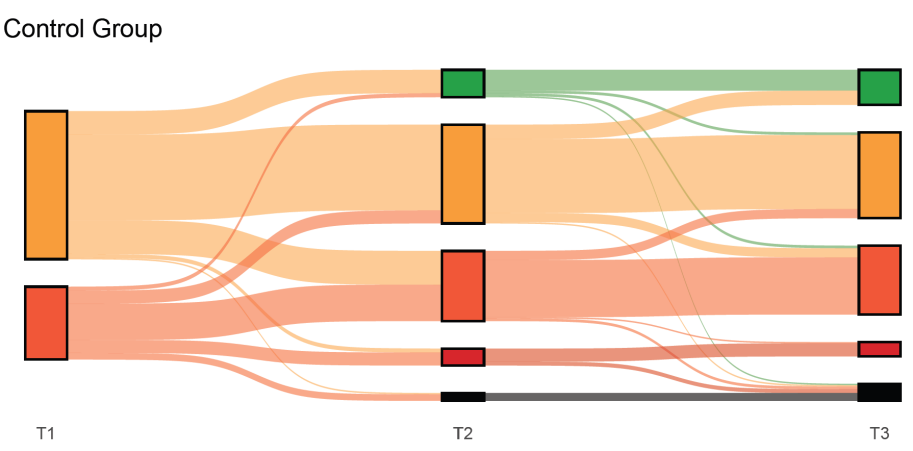
Secondary End Points

Outcome	Control (n=170) no. (%)	Intervention (n=342) no. (%)	Hazard Risk (95% CI)	P
Death	13 (7.6)	19 (5.6)	0.72 (0.35-1.45)	0.36
Cardiovascular death	10 (5.9)	14 (4.1)	0.69 (0.31-1.55)	0.37
Unplanned CV hospitalization	30 (17.6)	31 (9.1)	**0.48 (0.29-0.79)**	**0.004**
- Heart failure	12 (7.1)	5 (1.5)	**0.20 (0.07-0.56)**	**0.002**
- Myocardial infarction	10 (5.9)	13 (3.8)	0.63 (0.28-1.44)	0.26
- Revascularization	8 (4.7)	13 (3.8)	0.80 (0.33-1.93)	0.62
- Stroke	2 (1.2)	3 (0.9)	0.74 (0.12-4.43)	0.74
Unplanned hospitalization for any cause	39 (22.9)	56 (16.4)	0.67 (0.44-1.01)	0.06
Unplanned non-CV hospitalization	13 (7.6)	28 (8.2)	1.06 (0.55-2.02)	0.86

Other End Points

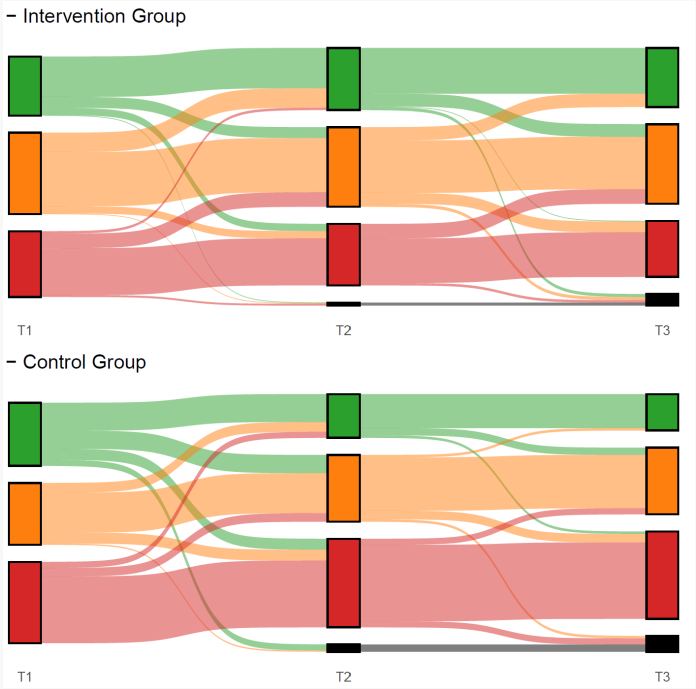
SPPB



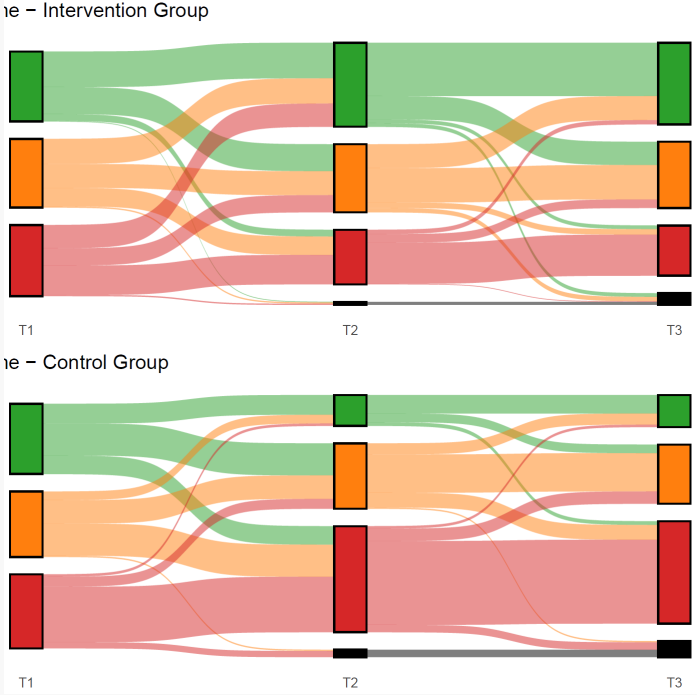


Other End Points

Handgrip

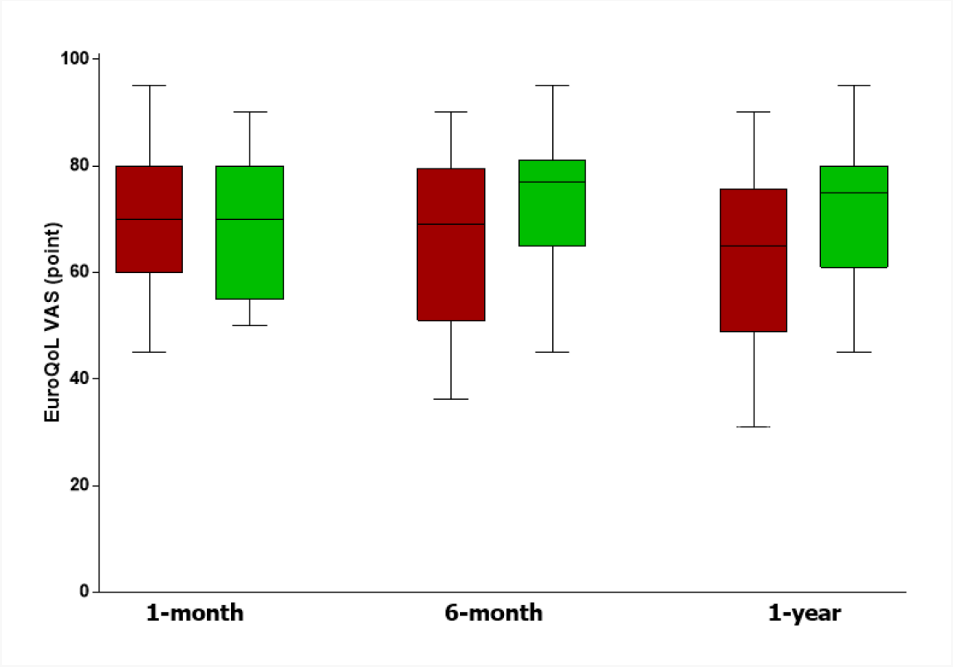


Gait Speed



Other End Points

Quality of Life



Limitations

- Open-label design
- Selection bias (1-month survivors)
- Multi-domain rehabilitation (impact each component)
- Supervised vs. home-based sessions
- Preserved cognitive function
- Longer-term follow-up is needed

Conclusions

- **A multi-domain rehabilitation reduces CV death or unplanned hospitalization for CV causes in older MI patients with impaired physical performance**
- **CV care in older MI patients is now based on RCT data!**

Strategy **Revascularization** **Rehabilitation**

1. NEJM 2024; 2. NEJM 2023

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multidomain Rehabilitation for Older Patients with Myocardial Infarction

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