

DIET-EXERCISE IN PREVENTION AND TREATMENT OF METABOLIC SYNDROME



Faculty/Presenter Disclosure

- *Consultant: Abbot Inc.*
- *Consultant: Seaford Inc .*
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- *Research Support : Abbot Inc.*



Disclosure of Commercial Support

- This program has received NO Commercial support
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 - Not Applicable

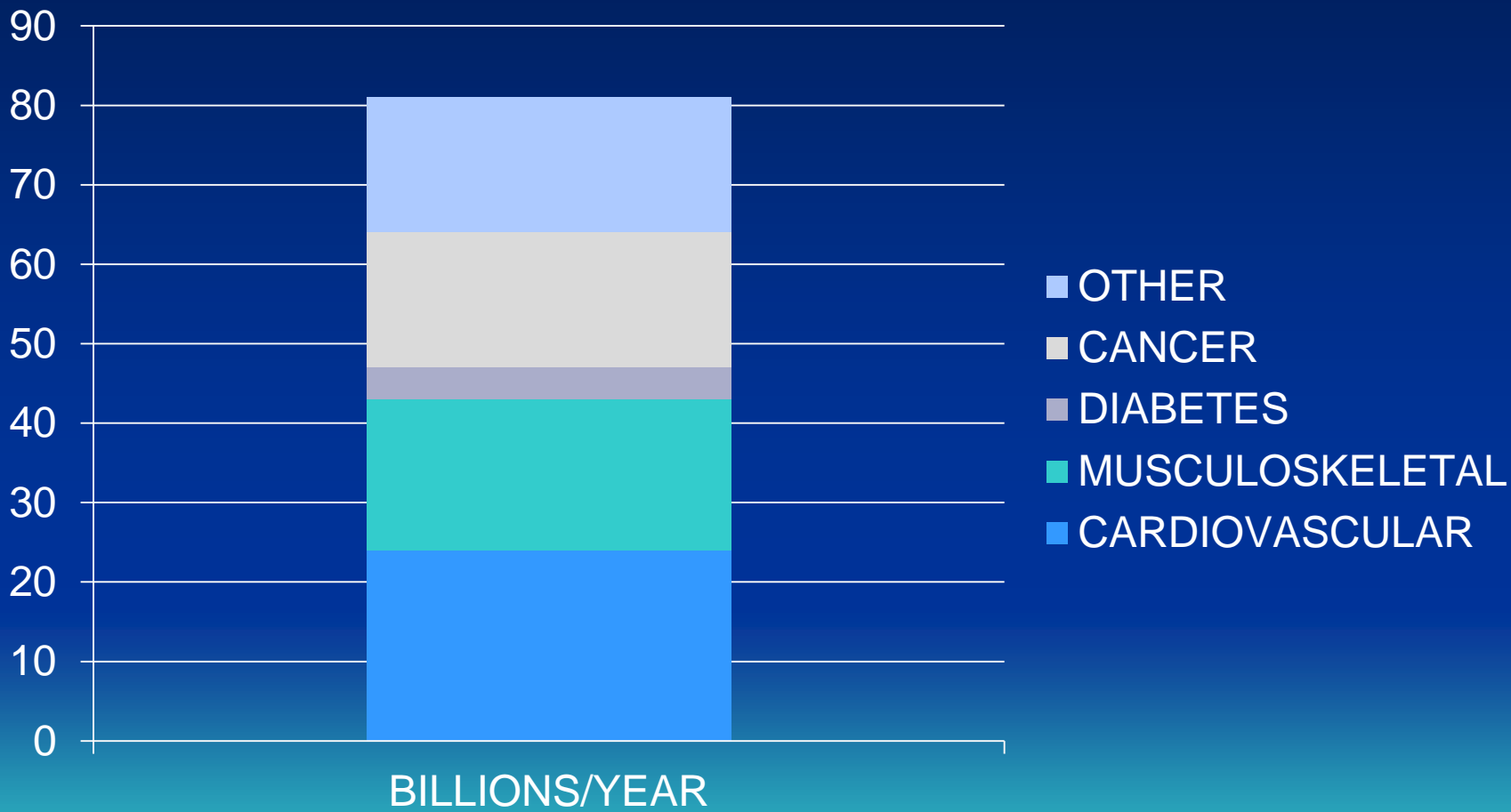


Mitigating Potential Bias

- Not Applicable



WHAT SHOULD WE PREVENT?



HOW AGING AFFECTS BELT HEIGHT...



YOUTH

ADULT

**MIDDLE-
AGE**

**OLD
AGE**

Reynolds

**The Cause of Disease and Death
in the Western World:
The Metabolic Syndrome and infirmity**

BASIS of the Metabolic Syndrome

Epigenetic Trait

Environmentally acquired then heritable

Insulin resistance

Basis of Infirmity

Sarcopenia

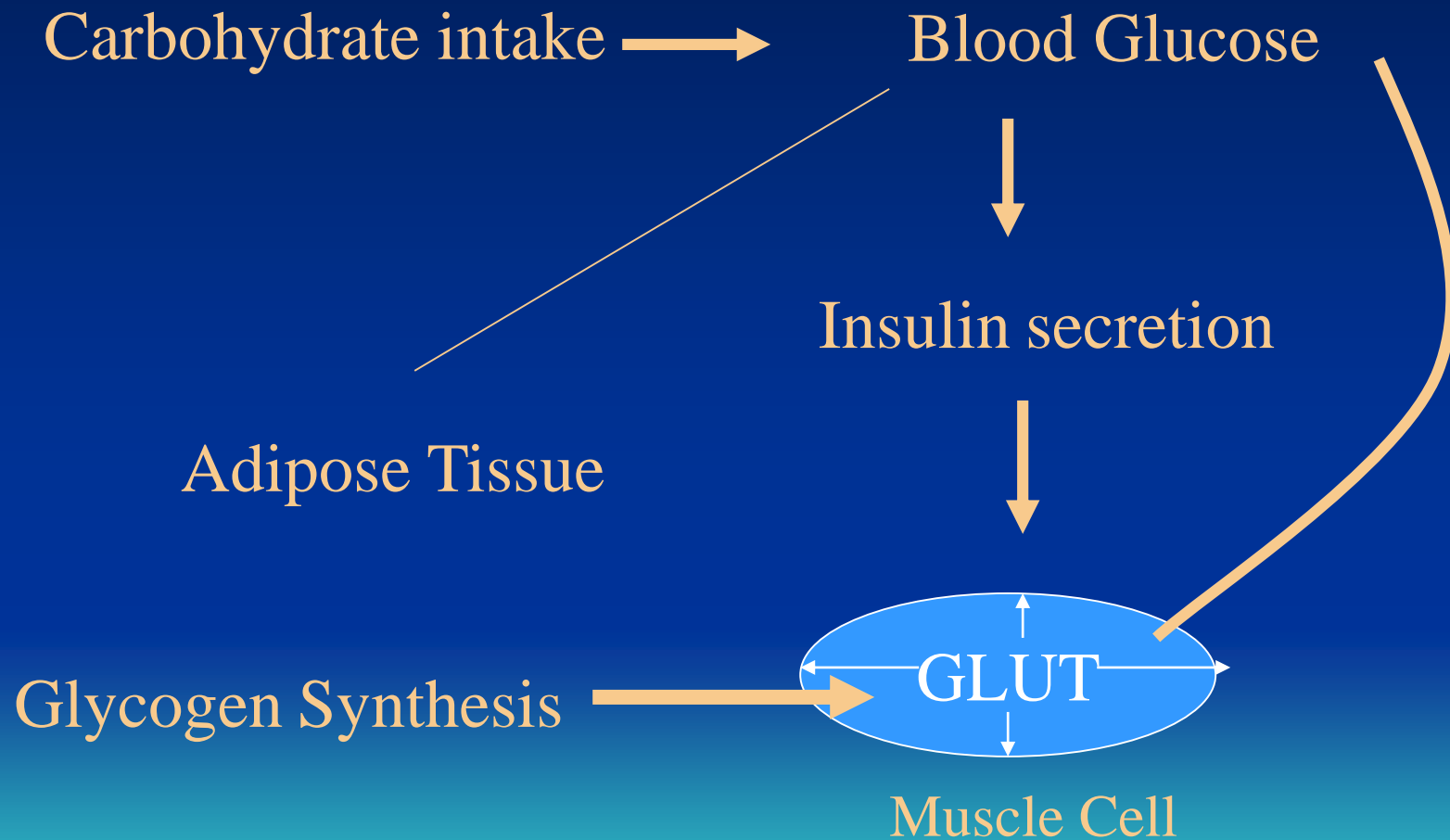


Insulin Resistance

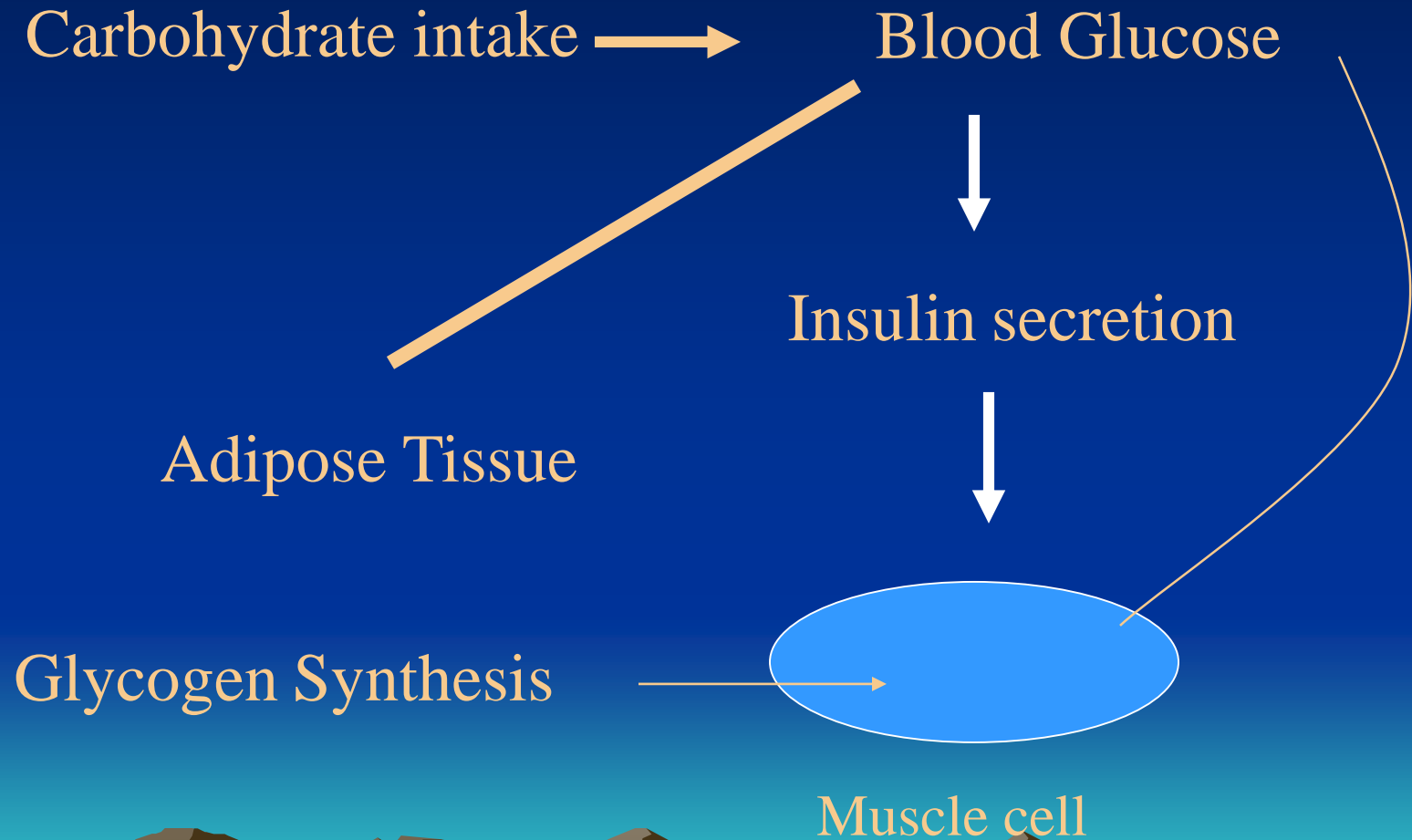
- Protects against malnutrition and death during Famine
- During times of Plentiful Food Results in :
 - Obesity
 - Hyperglycemia
 - Hyperlipidemia
 - Hypertension
 - inflammation



Insulin Sensitive State




Insulin Resistant State



EFFECT OF INSULIN RESISTANCE

- INCREASED BODY FAT (OBESITY)
- DEPLETED MUSCLE GLYCOGEN (FATIGUE)
- INCREASED OXIDATIVE STRESS (INFLAMMATION)



#	CHARACTERISTICS OF THE METABOLIC SYNDROME
1	Fasting Blood Glucose ≥ 5.6 mmol/L or receiving pharmacotherapy
2	Blood Pressure of $\geq 130/85$ mm Hg or receiving pharmacotherapy.
3	Triglyceride of ≥ 1.7 mmol/L or receiving pharmacotherapy
4	HDL-C < 1.0 mmol/L Males and < 1.3 mmol/L females
5	<p>Abdominal circumference as determined by a pre-specified technique:</p> <ul style="list-style-type: none"> • Europids, Whites, sub-Saharan Africans, Mediterranean, middle east (Arab) ≥ 94 cm Males, 80 cm Female. • Asian and South Central Americans ≥ 90 cm males and 80 cm females • US and Canadian Whites ≥ 102 cm males, 88 cm females. 

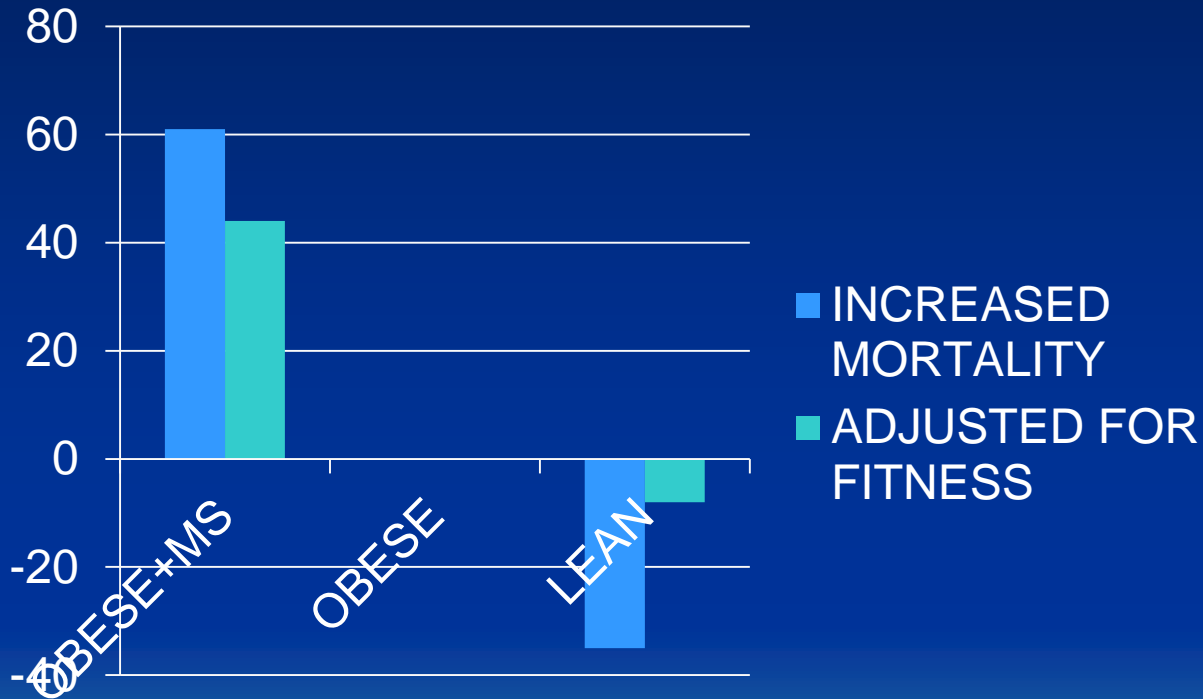
WHAT ABOUT OBESITY ??

FB. Ortega, D-c Lee, PT. Katzmarzyk, JR. Ruiz
The intriguing metabolically healthy but obese phenotype:
cardiovascular prognosis and role of fitness.
European Heart J Sept 4 (epub ahead of print).

Sharma AM, Kushner RF. A proposed clinical staging system for obesity.
Int J Obes (Lond) 2009;33:289–295



WHAT ABOUT OBESITY ??



WHAT ABOUT OBESITY ??

Once fitness is duly accounted for

:

The metabolically healthy but obese person has a benign condition.

The metabolically abnormal obese person has a 30-50% increased mortality.

No difference in the prognosis is observed between metabolically healthy but obese individuals and metabolically healthy normal-fat individual once fitness is accounted for.

There is a key role of fitness in these associations



**IS LIFESTYLE INTERVENTION
BETTER THEN DRUGS?**



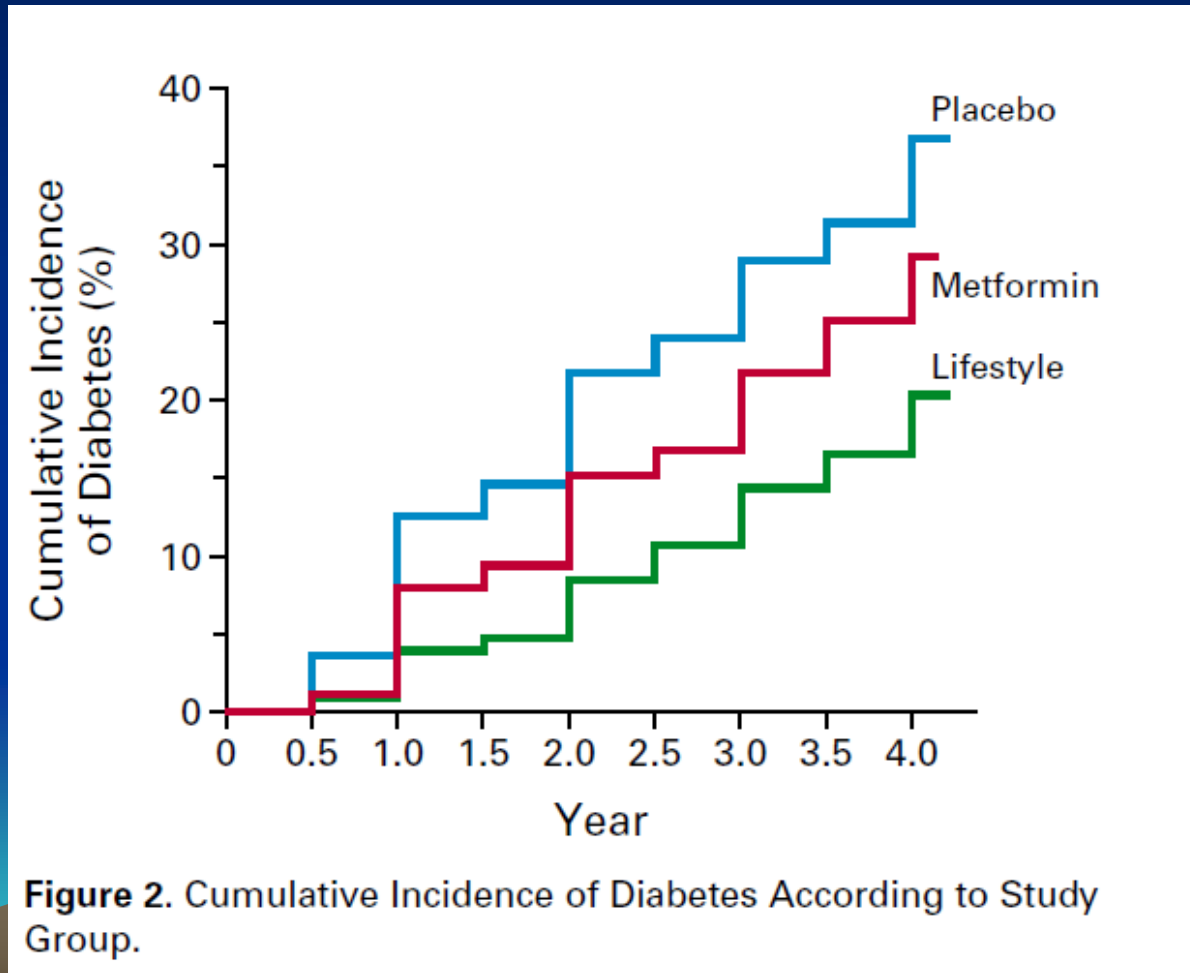
REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE

INTERVENTION OR METFORMIN : NEJM 2002;346:393-403

- 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations
- Randomized to placebo,
 - metformin (850 mg twice daily)
 - lifestyle-modification program
 - Goals of at least a 7 percent weight loss and
 - At least 150 minutes of physical activity per week.



REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN : NEJM 2002:346:393-403



**Percutaneous Coronary Angioplasty Compared With
Exercise Training in Patients With Stable Coronary
Artery Disease**

A Randomized Trial

Rainer Hambrecht, MD; Claudia Walther, MD; Sven Möbius-Winkler, MD; Stephan Gielen, MD;
Axel Linke, MD; Katrin Conradi, MD; Sandra Erbs, MD; Regine Kluge, MD; Kai Kendziorra, MD
Osama Sabri, MD; Peter Sick, MD; Gerhard Schuler, MD

***Circulation.* 2004;109:1371-1378.**

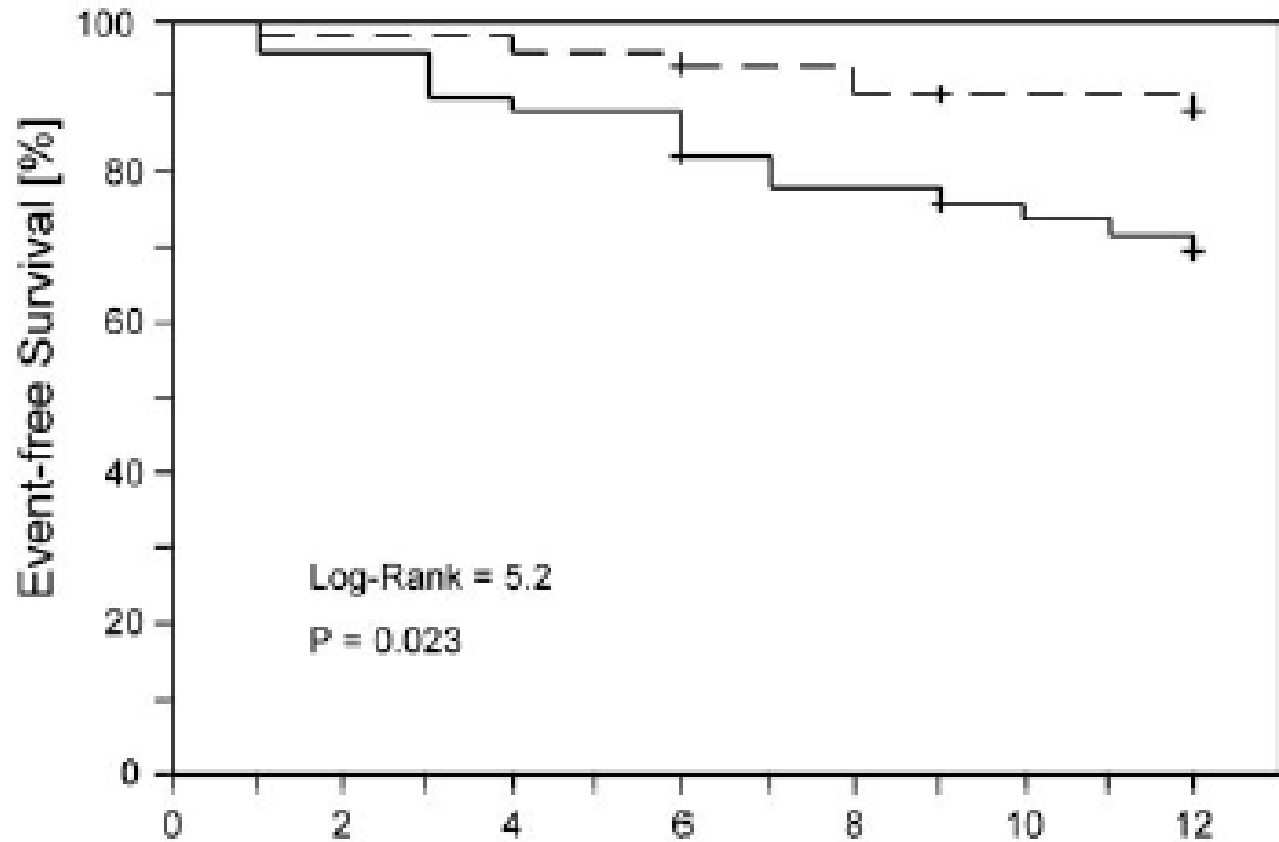
EXERCISE vs ANGIOPLASTY

Circulation 2004;109:1371-1378

- 101 Patients randomized to Angioplasty or exercise protocol
- $\geq 75\%$ stenosis with Class I-III Angina
- Demonstrated Ischemia by Stress or Nuclear Scintigraphy
- Maximal Medical therapy matched both groups
- Triple Vessel disease in 18%



Exercise vs Angioplasty



PTCA/Stent Group

50

41

35

Exercise Training Group

51

48

45

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

NEJM 2013;368:1279-90

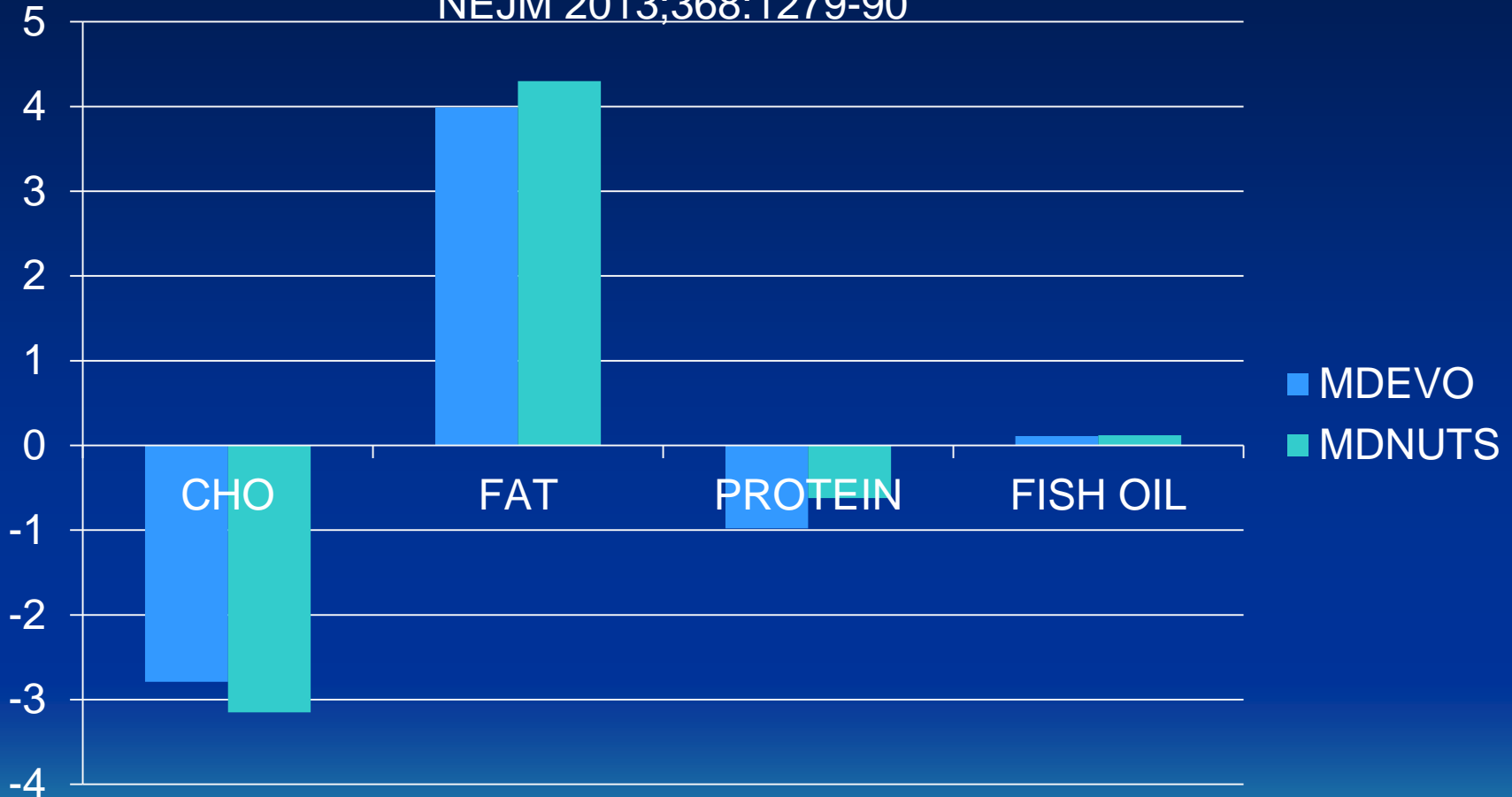
- 7447 patients randomized to:
 - Conventional Diet but reduce fats
 - Mediterranean Diet + Extra Virgin Olive Oil
 - Mediterranean Diet + Nuts
- Patients Had:
 - type 2 diabetes mellitus or at least three of the following major risk factors:
 - smoking,
 - Hypertension
 - elevated low-density lipoprotein
 - low high-density lipoprotein
 - overweight or obesity
 - family history of premature coronary heart disease.

Table 1. Summary of Dietary Recommendations to Participants in the Mediterranean-Diet Groups and the Control-Diet Group.

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day

Mediterranean Diet VS Control

NEJM 2013;368:1279-90



MDEVO = Mediterranean Diet with Extra virgin olive oil

MDNUTS = Mediterranean Diet with Nuts

ALL DATA except fishoil % difference from Controls $P < 0.001$

Fish Oil difference as g/day $p < 0.001$

Table 2. Baseline Characteristics of the Participants According to Study Group.*

Characteristic	Mediterranean Diet with EVOO (N=2543)	Mediterranean Diet with Nuts (N=2454)	Control Diet (N=2450)
Female sex — no. (%)†	1493 (58.7)	1326 (54.0)	1463 (59.7)
Age — yr†	67.0±6.2	66.7±6.1	67.3±6.3
Race or ethnic group — no. (%)			
White, from Europe	2470 (97.1)	2390 (97.4)	2375 (96.9)
Hispanic, from Central or South America	35 (1.4)	29 (1.2)	38 (1.6)
Other	38 (1.5)	35 (1.4)	37 (1.5)
Smoking status — no. (%)			
Never smoked	1572 (61.8)	1465 (59.7)	1527 (62.3)
Former smoker	618 (24.3)	634 (25.8)	584 (23.8)
Current smoker	353 (13.9)	355 (14.5)	339 (13.8)
Body-mass index†‡			
Mean	29.9±3.7	29.7±3.8	30.2±4.0
<25 — no. (%)	195 (7.7)	204 (8.3)	164 (6.7)
25–30 — no. (%)	1153 (45.3)	1163 (47.4)	1085 (44.3)
>30 — no. (%)	1195 (47.0)	1087 (44.3)	1201 (49.0)
Waist circumference — cm	100±10	100±11	101±11
Waist-to-height ratio†§	0.63±0.06	0.63±0.06	0.63±0.07
Hypertension — no. (%)¶	2088 (82.1)	2024 (82.5)	2050 (83.7)
Type 2 diabetes — no. (%)†	1282 (50.4)	1143 (46.6)	1189 (48.5)
Dyslipidemia — no. (%)**	1821 (71.6)	1799 (73.3)	1763 (72.0)
Family history of premature CHD — no. (%)††	576 (22.7)	532 (21.7)	560 (22.9)

PRIMARY END POINT: MI, Stroke, Death from CVS causes

End Point	Mediterranean Diet with EVOO (N=2543)	Mediterranean Diet with Nuts (N=2454)	Control Diet (N=2450)	P Value [‡]
				Mediterranean Diet with EVOO vs. Control Diet Mediterranean Diet with Nuts vs. Control Diet
Hazard ratio for Mediterranean diets combined vs. control (95% CI)				
Primary end point				
Unadjusted	0.70 (0.55–0.89)		1 (ref)	0.003
Multivariable-adjusted 1 [§]	0.71 (0.56–0.90)		1 (ref)	0.004
Multivariable-adjusted 2 [¶]	0.71 (0.56–0.90)		1 (ref)	0.005

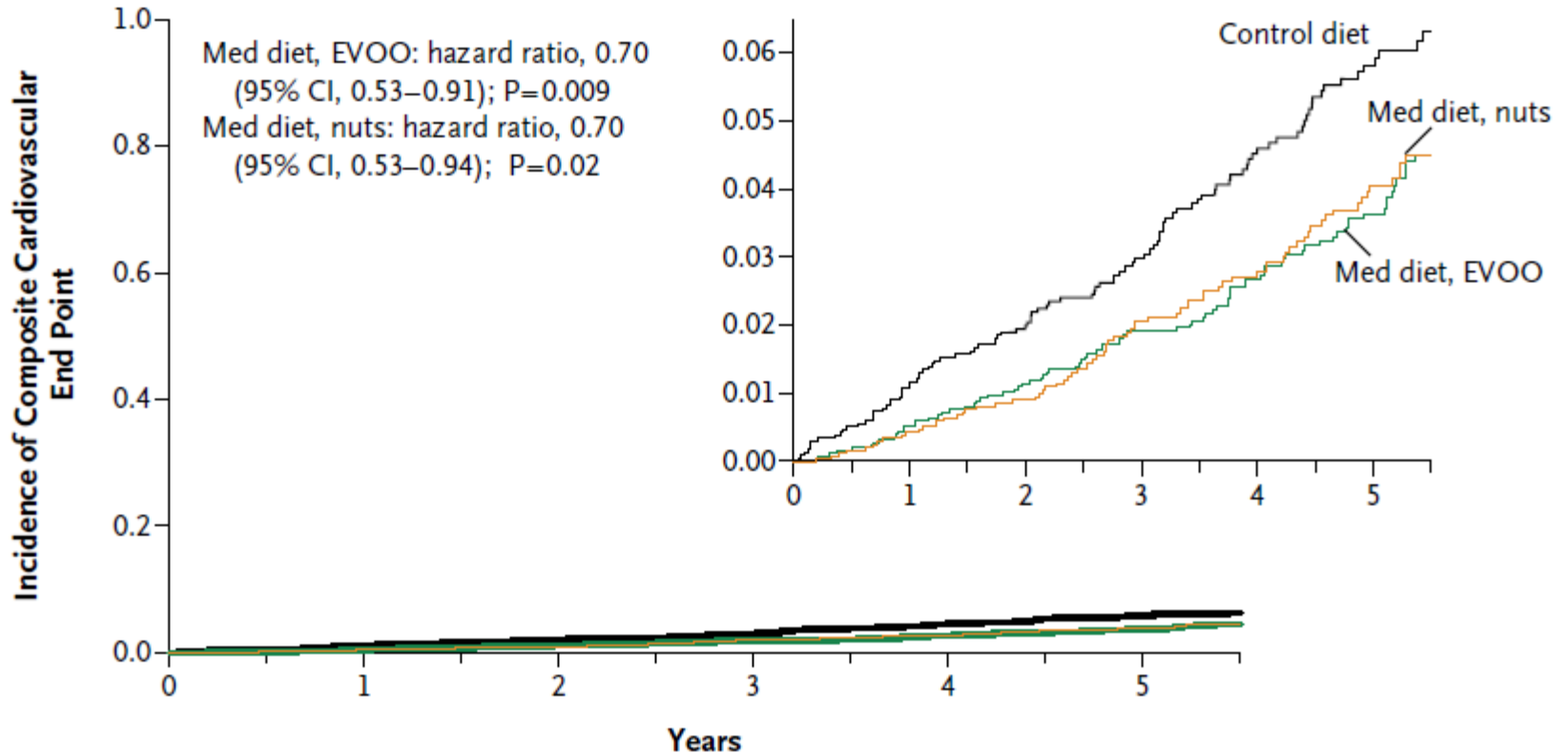
[‡] The primary end point was a composite of myocardial infarction, stroke, and death from cardiovascular causes.

[§] The primary end point was stratified according to recruiting center and adjusted for sex, age (continuous variable), family history of premature coronary heart disease (yes or no), and smoking status (never smoked, former smoker, or current smoker).

[¶] The primary end point was additionally adjusted for body-mass index (continuous variable), waist-to-height ratio (continuous variable), hypertension at baseline (yes or no), dyslipidemia at baseline (yes or no), and diabetes at baseline (yes or no).

^{||} The secondary end points were stratified according to recruiting center and adjusted for sex, age (continuous variable), family history of premature coronary heart disease (yes or no), smoking status (never smoked, former smoker, or current smoker), body-mass index (continuous variable), waist-to-height ratio (continuous variable), hypertension at baseline (yes or no), dyslipidemia at baseline (yes or no), and diabetes at baseline (yes or no).

A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)



No. at Risk

Control diet	2450	2268	2020	1583	1268	946
Med diet, EVOO	2543	2486	2320	1987	1687	1310
Med diet, nuts	2454	2343	2093	1657	1389	1031

Convert Insulin Resistant to Insulin Sensitive State



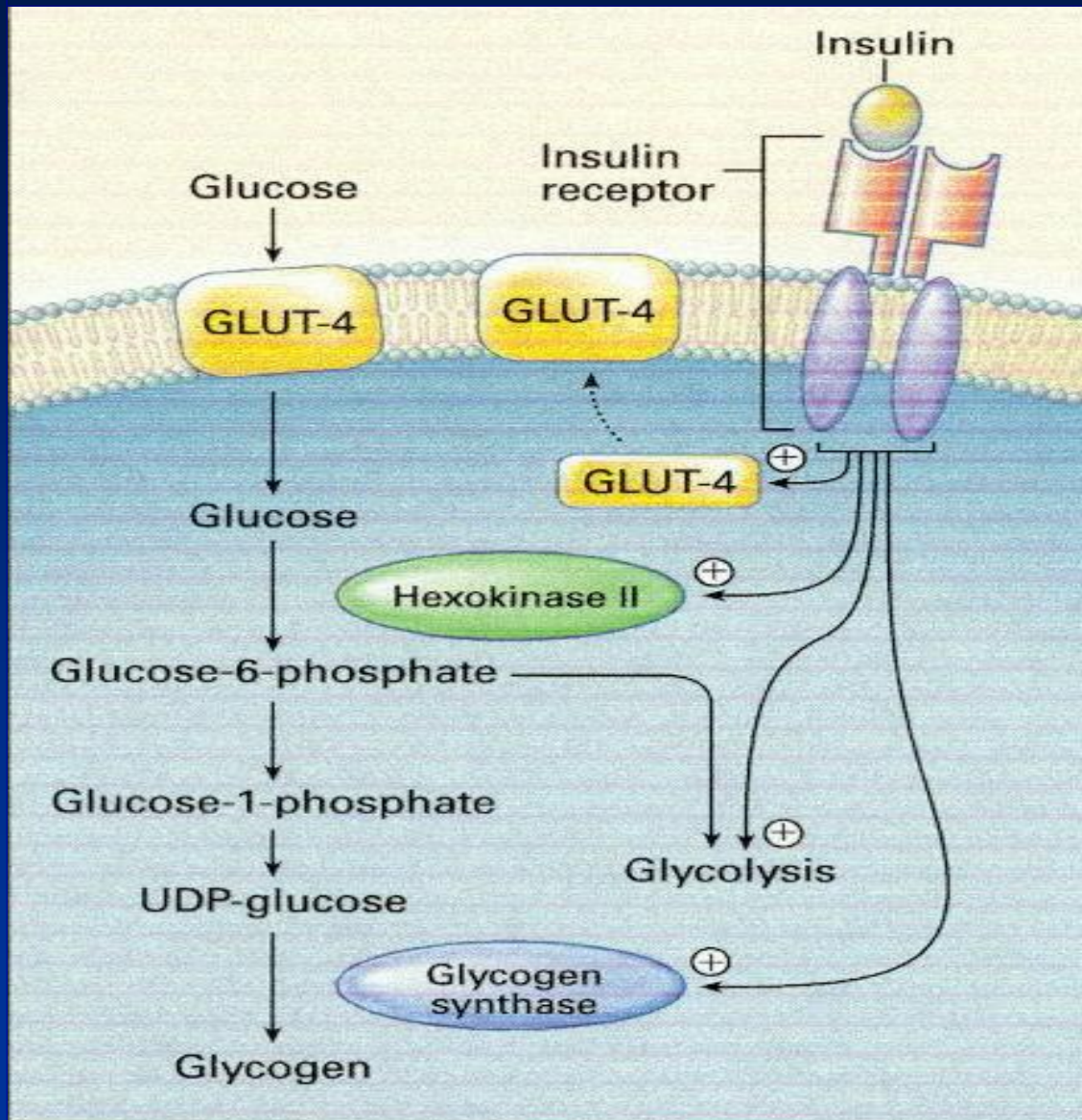
AEROBIC EXERCISE



Low glycemic index diet

Exercise and Insulin resistance

Perseghin et al N Engl J Med 335:1357-62,1996



Exercise and Insulin resistance

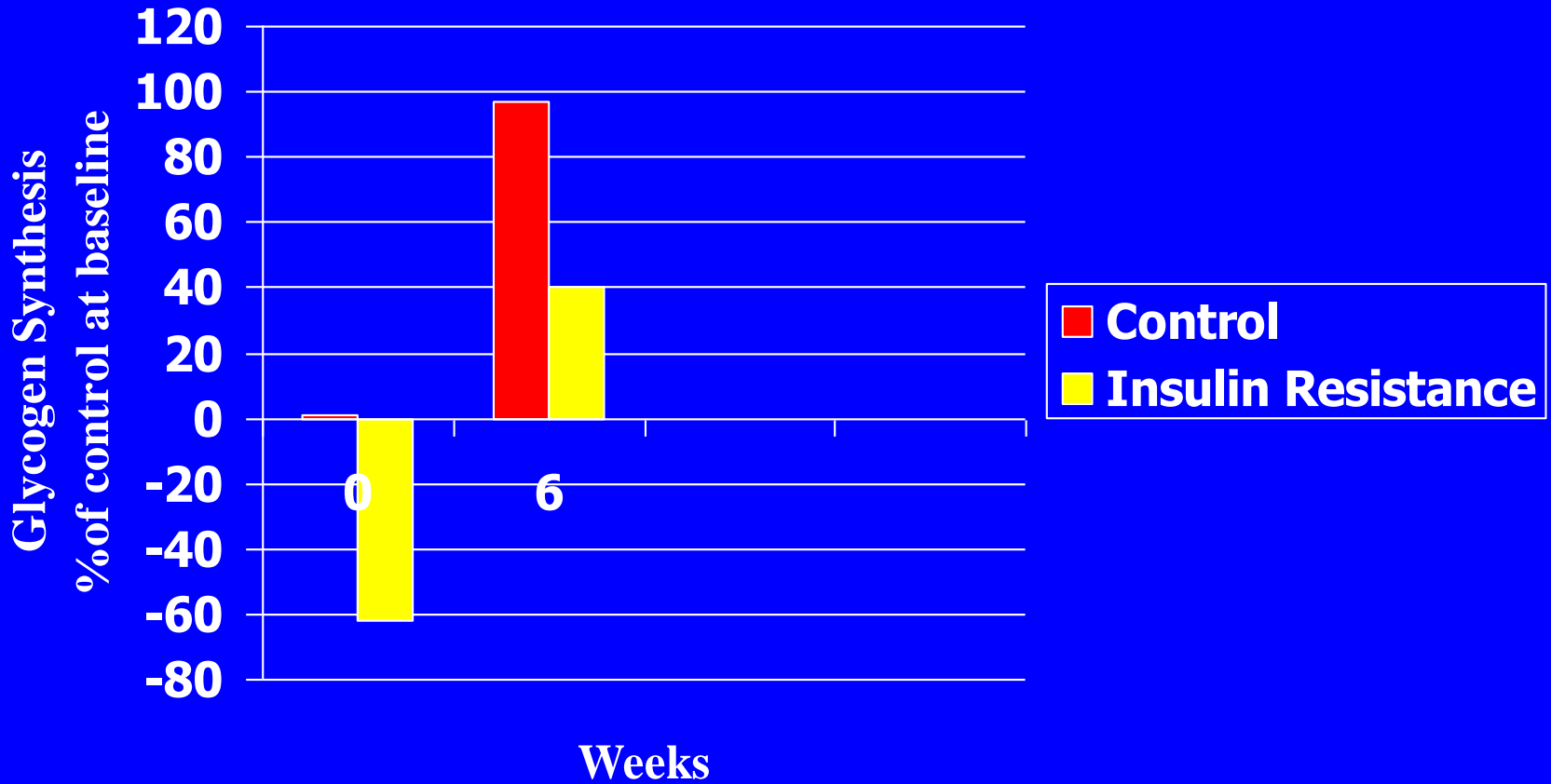
Perseghin et al N Engl J Med 335:1357-62,1996

1. 10 adult children of parents with NIDDM
2. 8 normal subjects
3. 6 weeks of aerobic exercise
4. Stair Climbing (aerobic)
5. 3 sessions per week
6. 45 min /session at 65% of VO₂ Max



Exercise and Insulin resistance

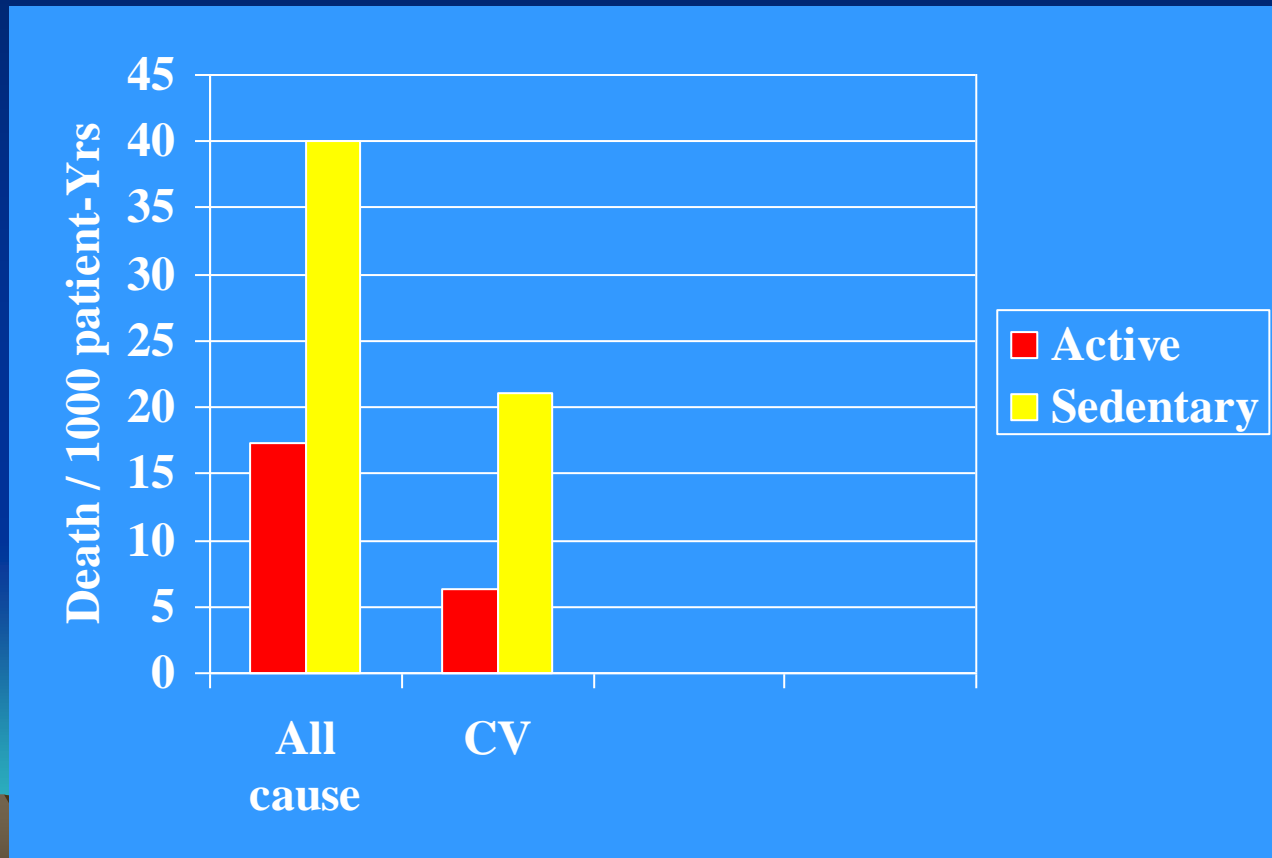
Perseghin et al N Engl J Med 335:1357-62,1996



Hypertension Exercise and Mortality

Engstrom et al. J Hypertens 17:737-42, 1999

- Cohort of 642 men followed for 25 years
- Vigorous activity 100 men BP >165/95.



TYPES OF EXERCISE

- **AEROBIC EXERCISE**
 - **SHORT TERM**
 - **ENDURANCE**
- **RESISTIVE**
 - **ISOMETRIC**
 - **ISOTONIC**



Reversal of Sarcopenic infirmity



Exercise Training and Nutrition

Fiatrone et al. N Engl J Med 330:1769-
75 1994

Age enrolled 87 ± 0.6 years.

GROUPS: Placebo, Exercise, Supplement,
Supplement + Exercise.

High intensity progressive resistance training of
hip and Knee extensors.

Frequency 3 days/wk Duration 10 weeks
Sessions 45 minutes

Supplement 360 Kcals/d 17% protein

Exercise Training and Nutrition

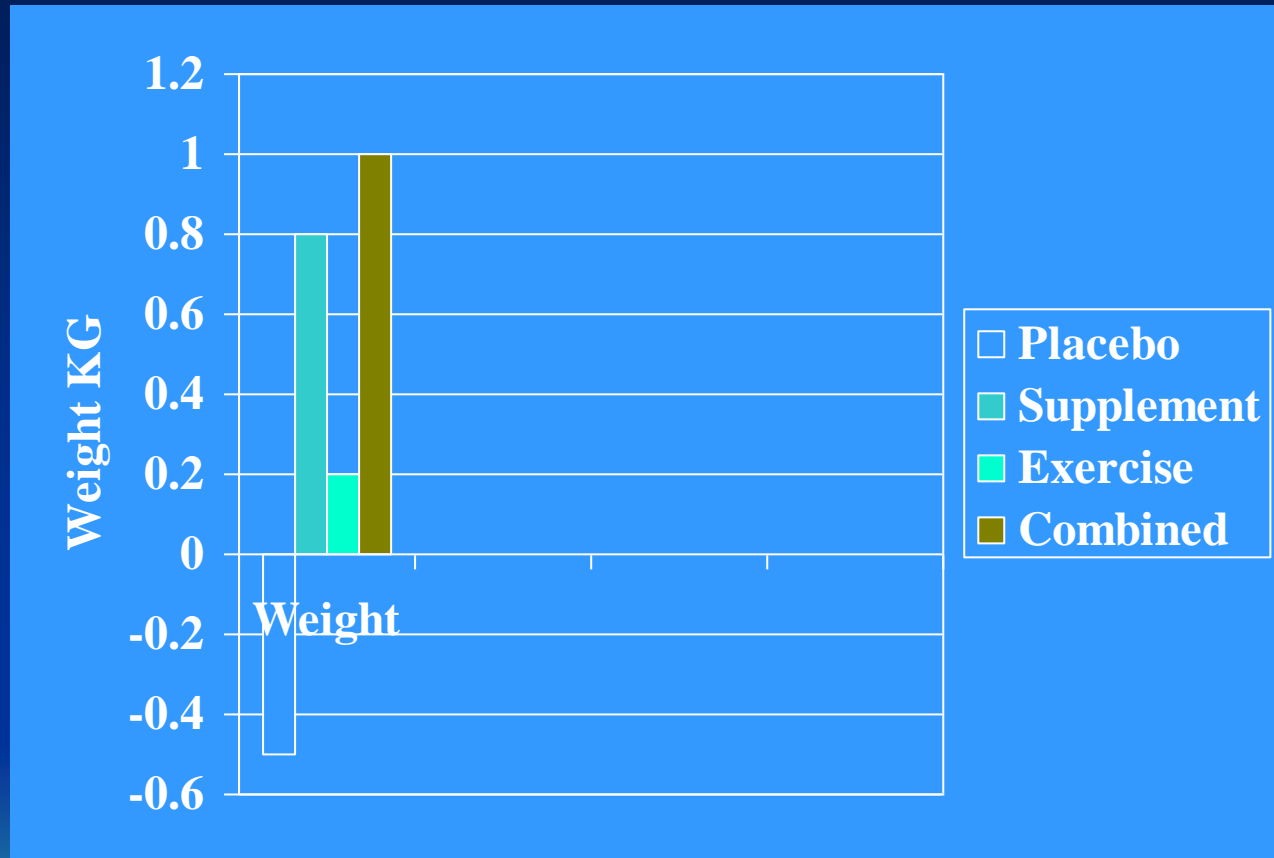
Fiatrone et al. N Engl J Med 330:1769-75,1994

Outcomes:

1. Muscle Function
2. Physical Function
3. Nutritional Intake
4. Body Composition
5. Physical Activity

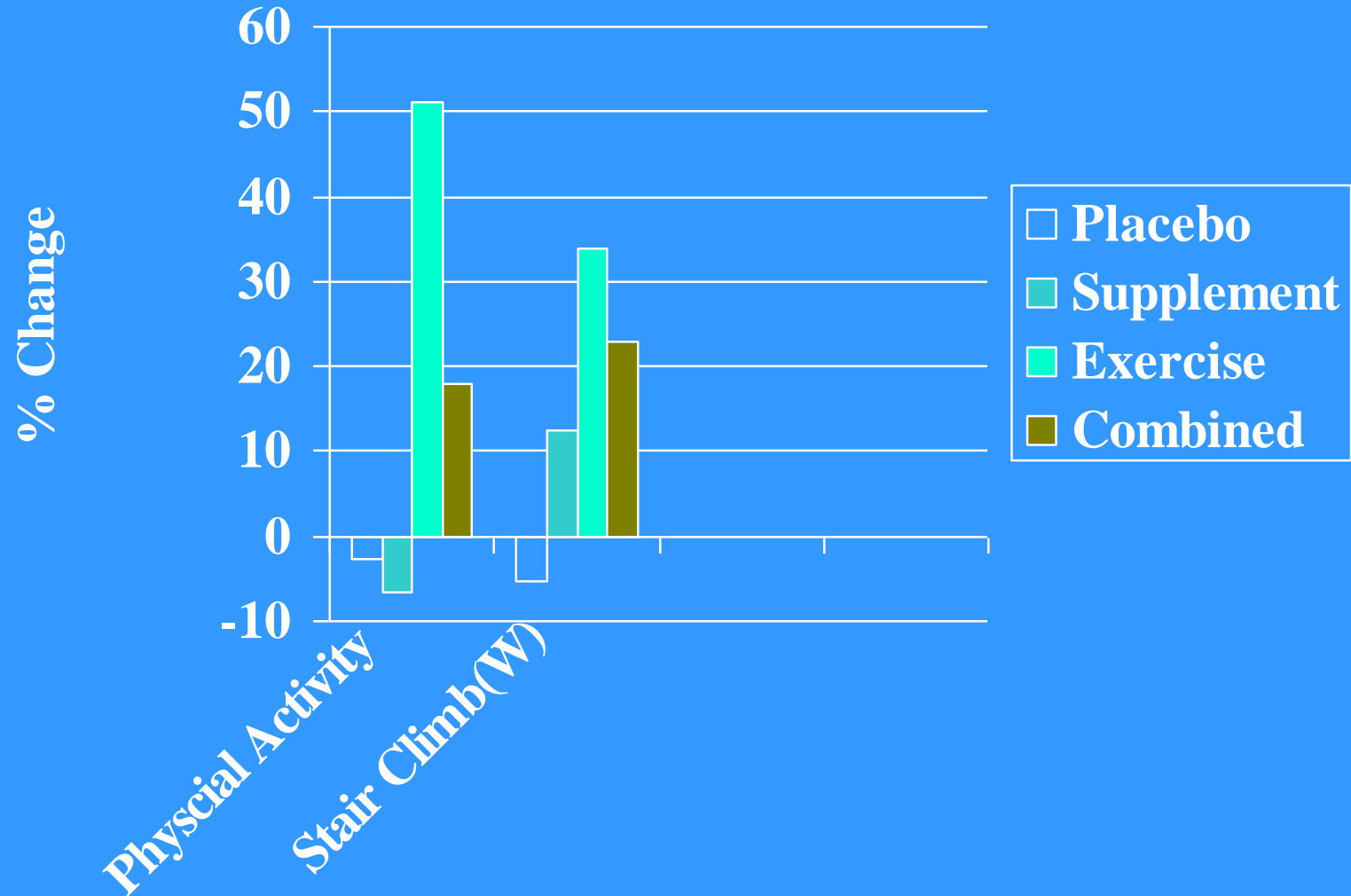
Exercise Training and Nutrition

Fiatrone et al. N Engl J Med 330:1769-75,1994



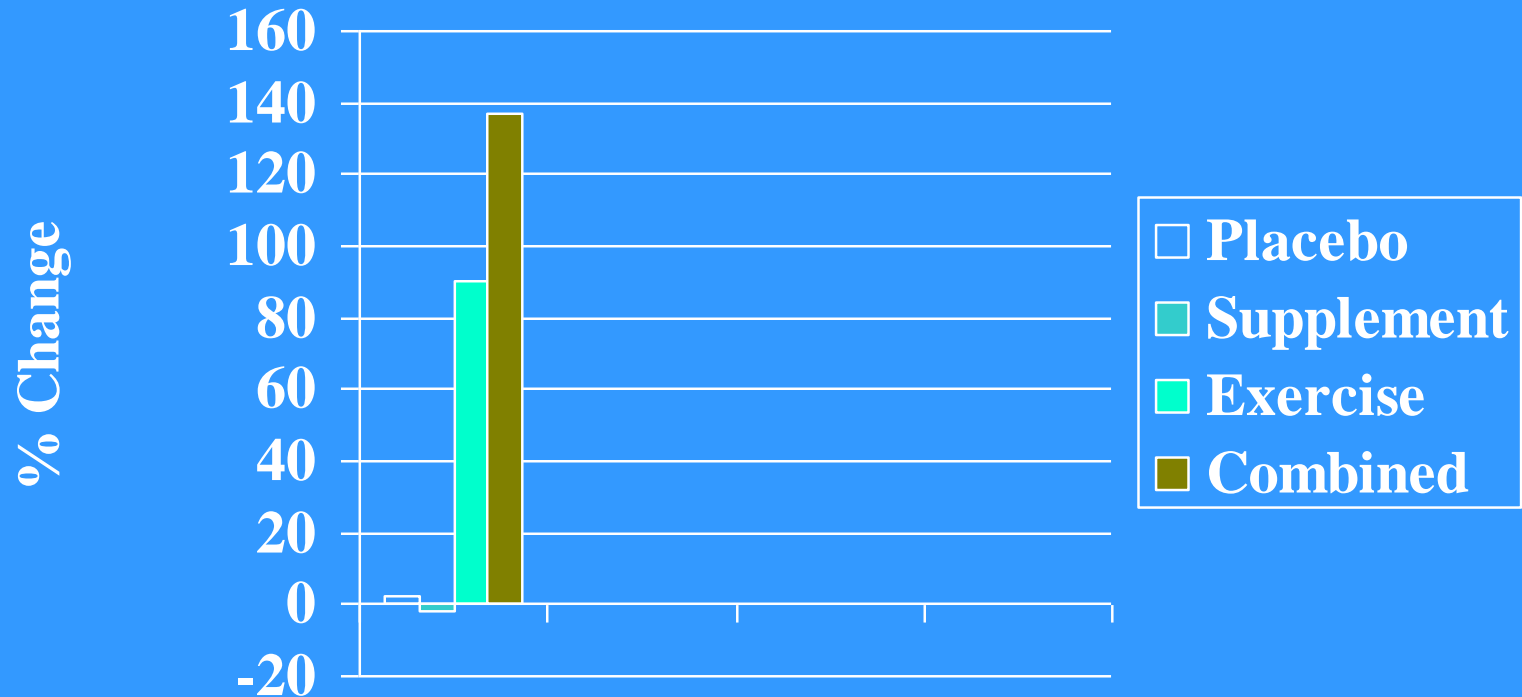
Exercise Training and Nutrition

Fiatrone et al. N Engl J Med 330:1769-75,1994



Exercise Training and Nutrition

Fiatarone et al. N Engl J Med 330:1769-75,1994



Muscle Strength

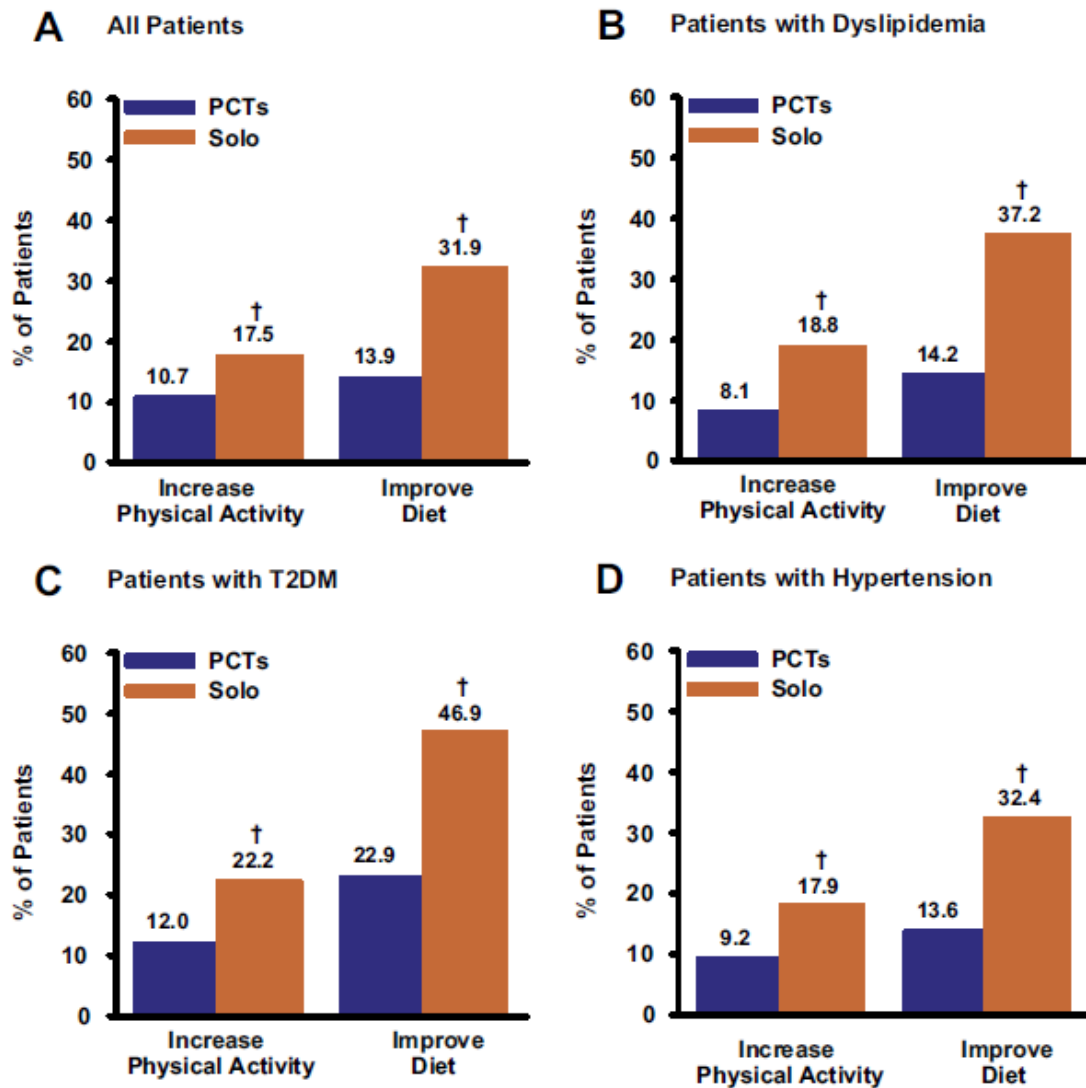


Figure 2. Breakdown of healthy behavioural changes (increase physical activity and improve diet) recommended by the physicians to (A) all of their patients, (B) patients with dyslipidemia, (C) patients with type 2 diabetes mellitus (T2DM), and (D) patients with hypertension. Solo, physicians from traditional nonteam practice. † $P < 0.0001$ vs corresponding primary care team (PCT) data.

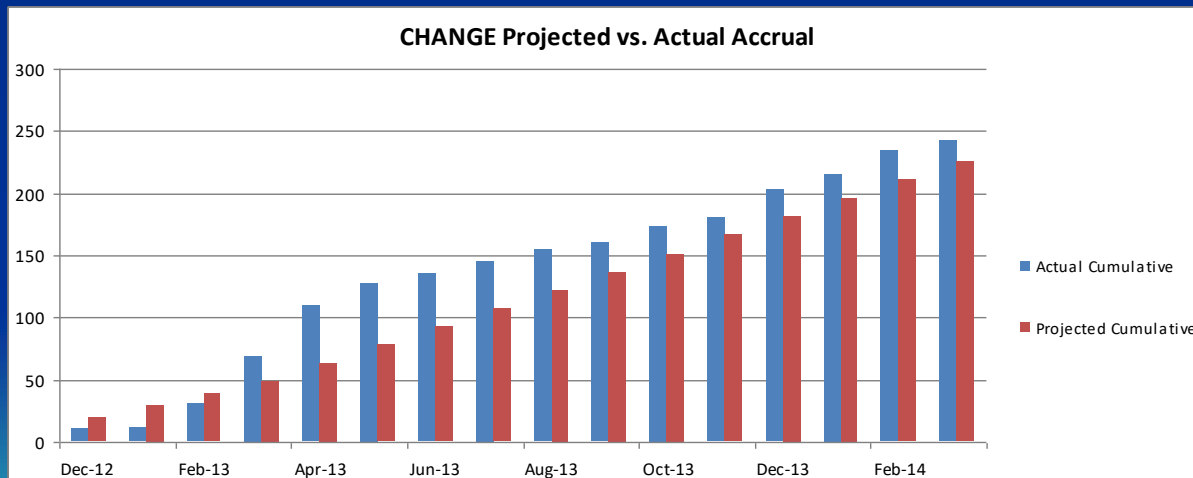
CHANGE

Canadian Health Advanced By Nutrition and
Graded Exercise CHANGE Health Paradigm
IS
CENTERED ON THE FAMILY PHYSICIAN



CHANGE SITES

- PRIMARY CARE NETWORK EDMONTON
- POLYCLINIC TORONTO
- U OF LAVAL PRIMARY CARE



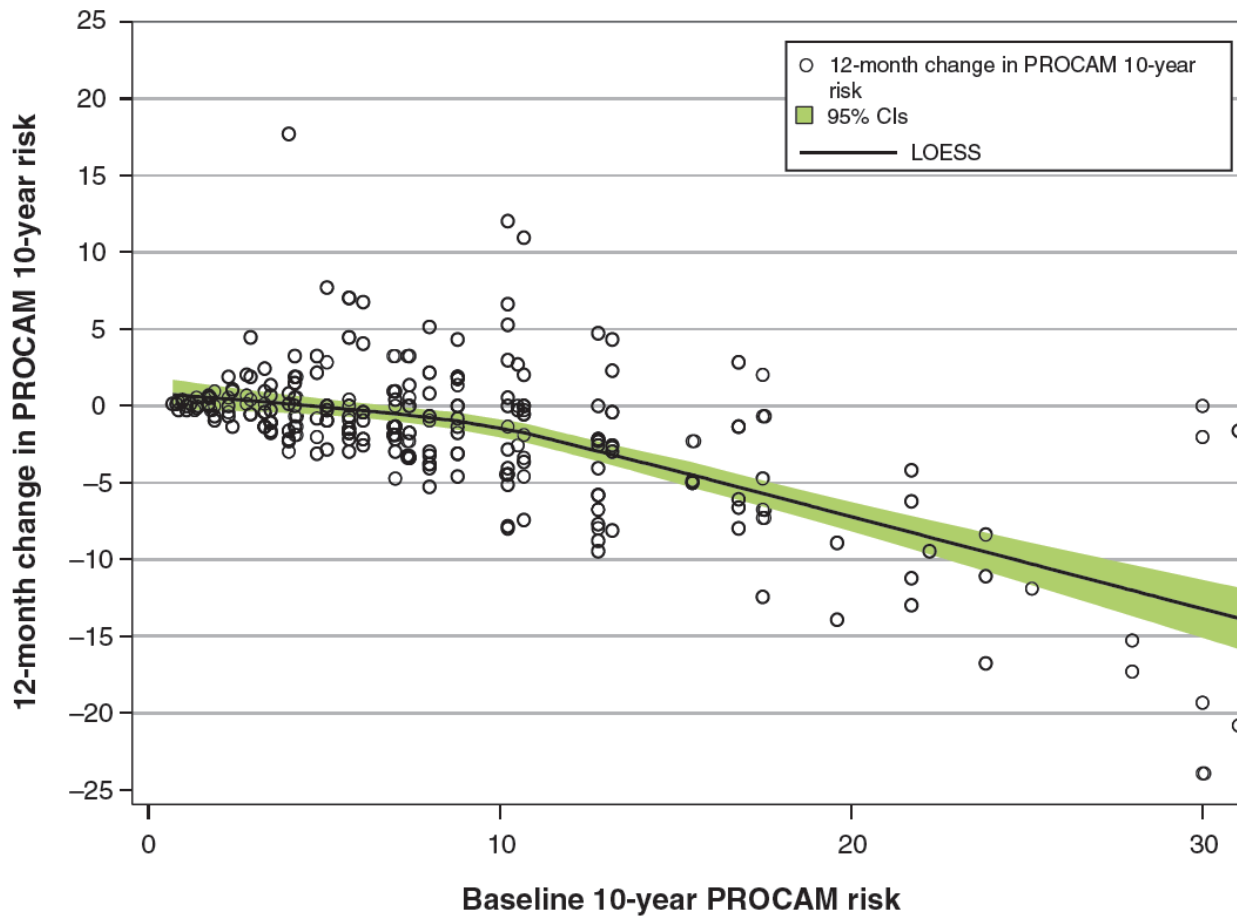


Figure 2: Change in PROCAM risk compared with baseline risk. CI = confidence interval, LOESS = locally weighted regression smoothing, PROCAM = Prospective Cardiovascular Munster.

Conclusions

- **Aerobic Exercise >3 days a week 70% VO2 Max**
 - **INSULIN SENSITIZE**
- **Resistive Exercise Target Extensor Muscles**
 - **Prevent and reduce Sarcopenia and Frailty**
- **Mediterranean Diet**
 - **Reduce risk of Cardiovascular Disease**



Conclusions

- **Totally neglected in practice except for platitudes like**
 - **“Balanced intake of all food groups”**
 - **“Go for long walks”**

**INDIVIDUALLY TAILORED
PROGRAM NEEDS TO BECOME
PART OF MEDICAL CARE**

