Segrate, 13 maggio 2025

ATTIVITA’ FISICA IN ONCOLOGIA

Federico Bozzetti

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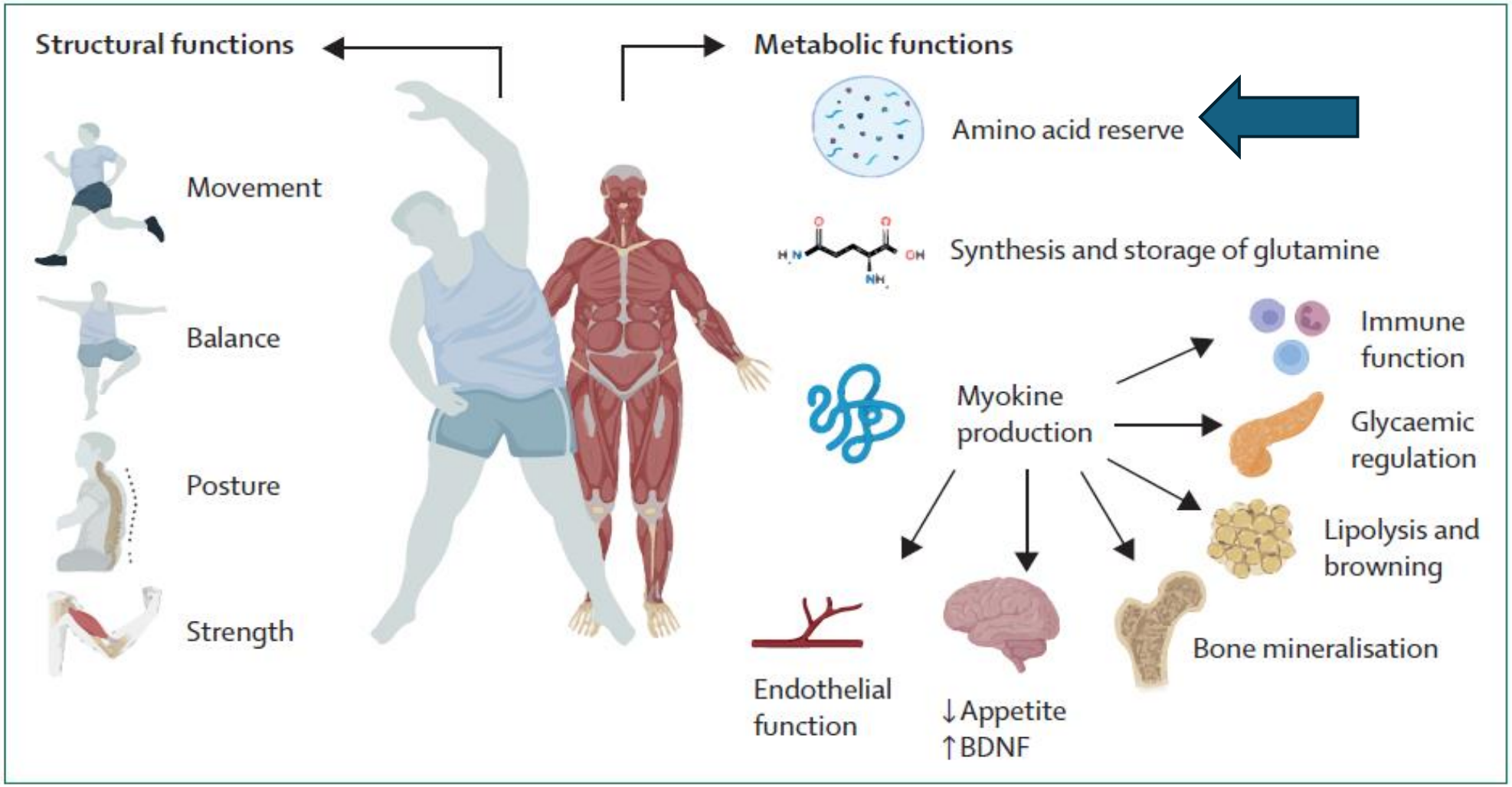
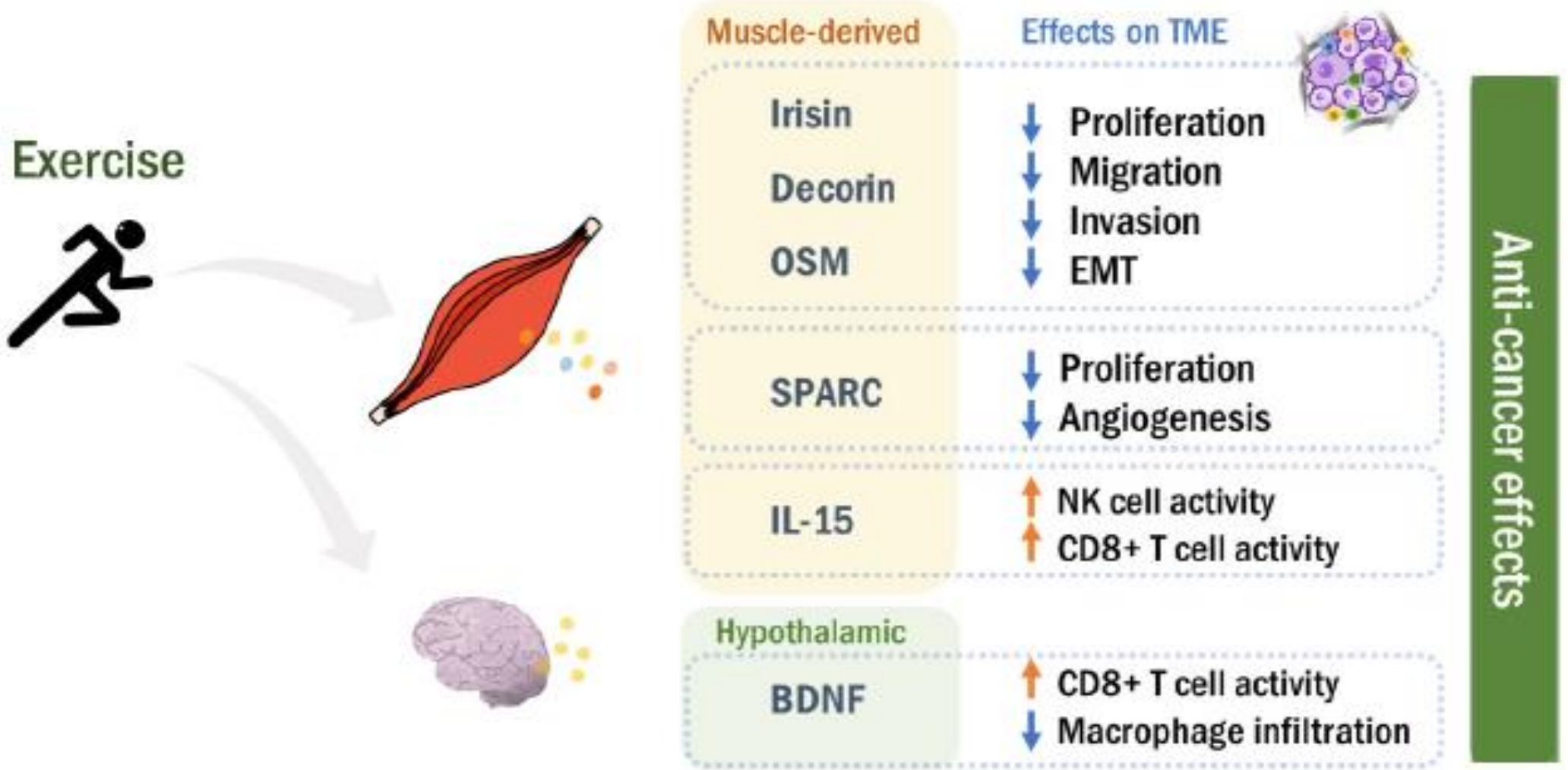
IL MUSCOLO NON E' SOLO UN ORGANO CONTRATTILE MA UN ORGANO ENDOCRINO E METABOLICO



Il muscolo sottrae il 60-80% del glucosio circolante in risposta alla insulina

Park SY et al. The role of myokines in cancer: crosstalk between skeletal muscle and tumor. BMB Rep. 2023 Jul;56(7):365-373



ATTIVITA’ FISICA IN ONCOLOGIA

- **AF nella prevenzione primaria**
- **AF nella terapia oncologica**
- **AF nella prevenzione terziaria**

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Moore et al. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. JAMA Intern Med. 2016 Jun 1;176(6):816-25

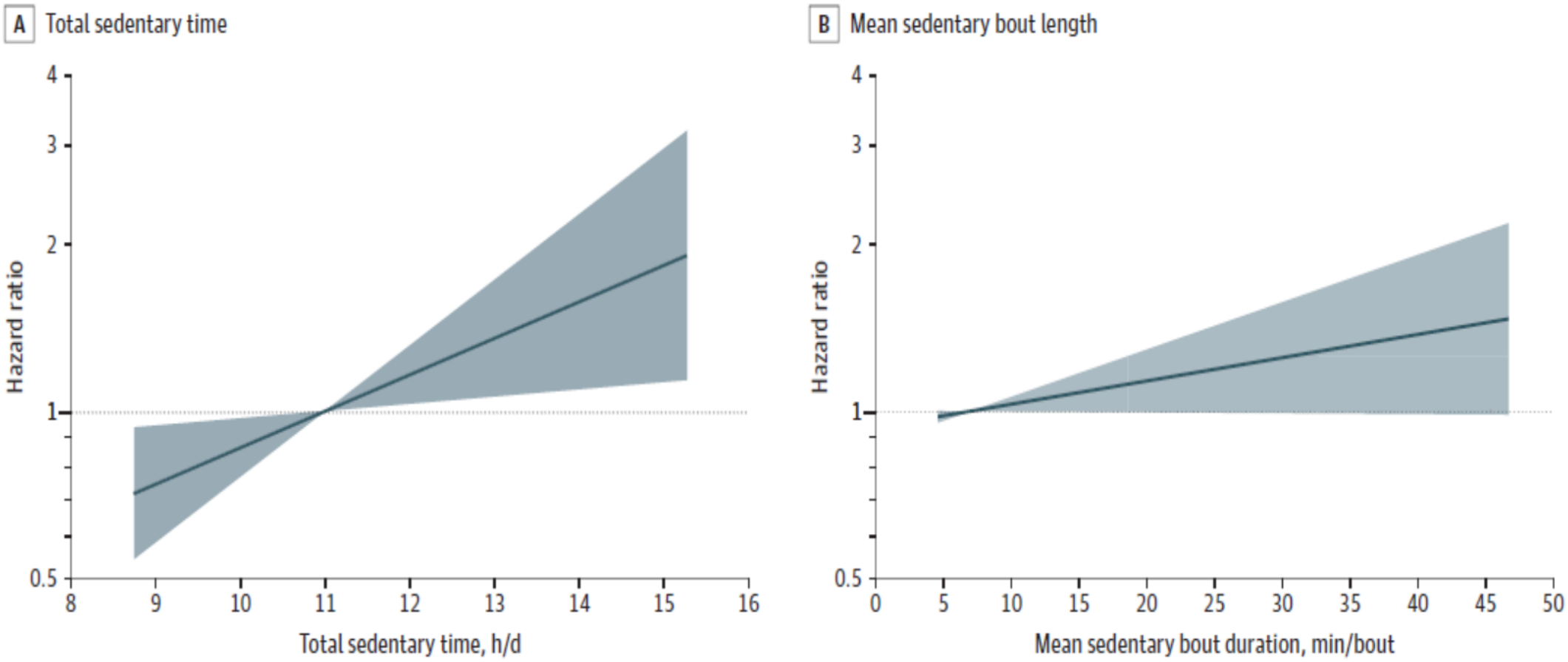
Follow up mediano 13,8 anni

- Esofago (adenocarcinoma) (HR=0.58)
- Fegato (HR=0.73)
- Colon (HR=0.84)
- Polmone(HR=0.74)
- Rene (HR=0.77)
- Stomaco (cardias) (HR=0.78)
- Endometrio (HR=0.79)
- Leucemia mieloide (HR=0.80),
- Mieloma (HR=0.83)
- Testa e collo (HR=0.85)
- Retto (HR=0.87)
- Vescica bladder (HR=0.87)
- Mammella (HR=0.90).
- Melanoma (HR=1.27)
- Prostate (HR=1.05).

Gilchrist et al. Association of Sedentary Behavior With Cancer Mortality in Middle-aged and Older US Adults. JAMA Oncol. 2020; 6(8):1210-1217.

A study of 8002 subjects with a follow-up of 5.3 years

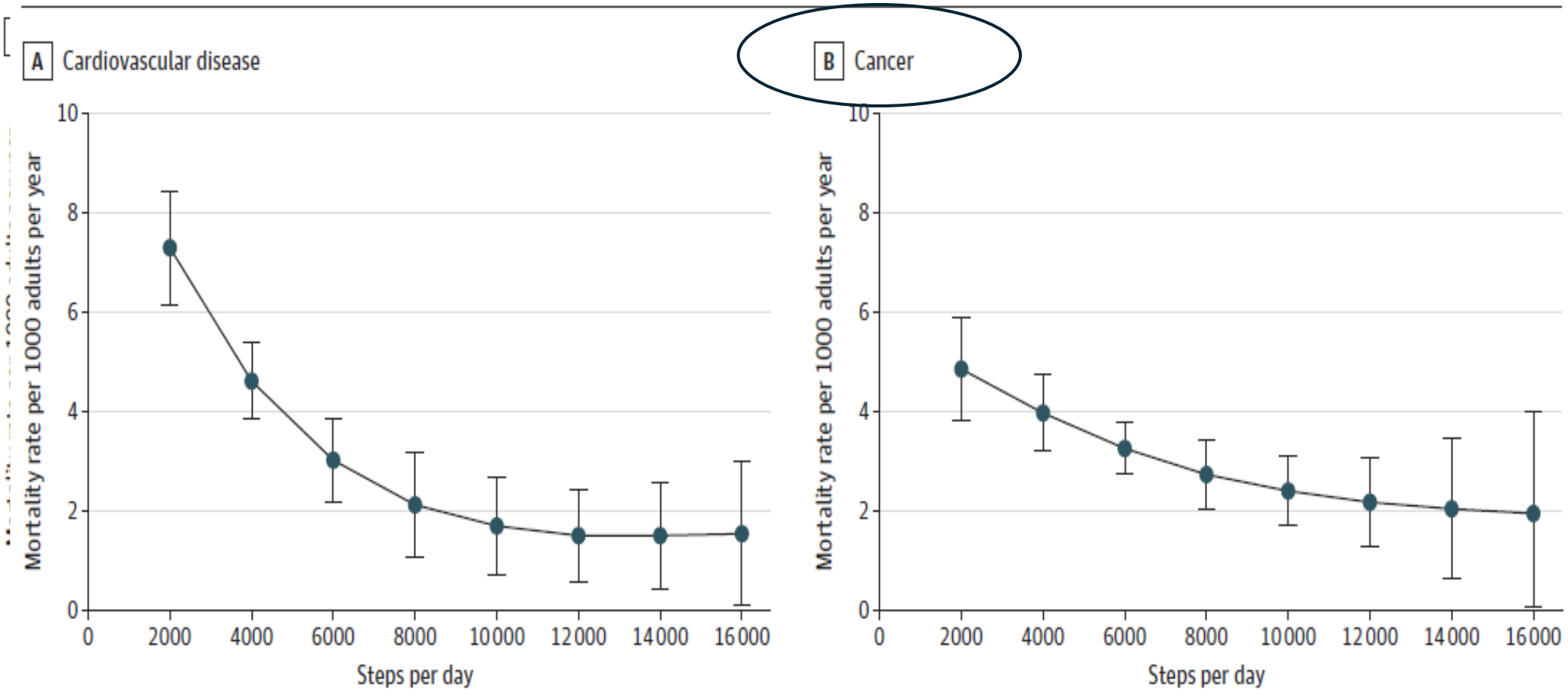
Figure 2. Dose-Response Association Between Cancer Mortality and Total Sedentary Time and Mean Sedentary Bout Length



Saint-Maurice et al. Association of Daily Step Count and Step Intensity With Mortality Among US Adults. JAMA. 2020 Mar 24;323(12):1151-1160

49.143 soggetti consecutivi seguiti per 7,7 anni (mediana)

Figure 4. Steps per Day and Mortality From Cardiovascular Disease (CVD) and Cancer in a Study of the Association of Daily Step Count and Step Intensity With Mortality Among US Adults Aged at Least 40 Years



La attività fisica protegge da molte malattie gravi

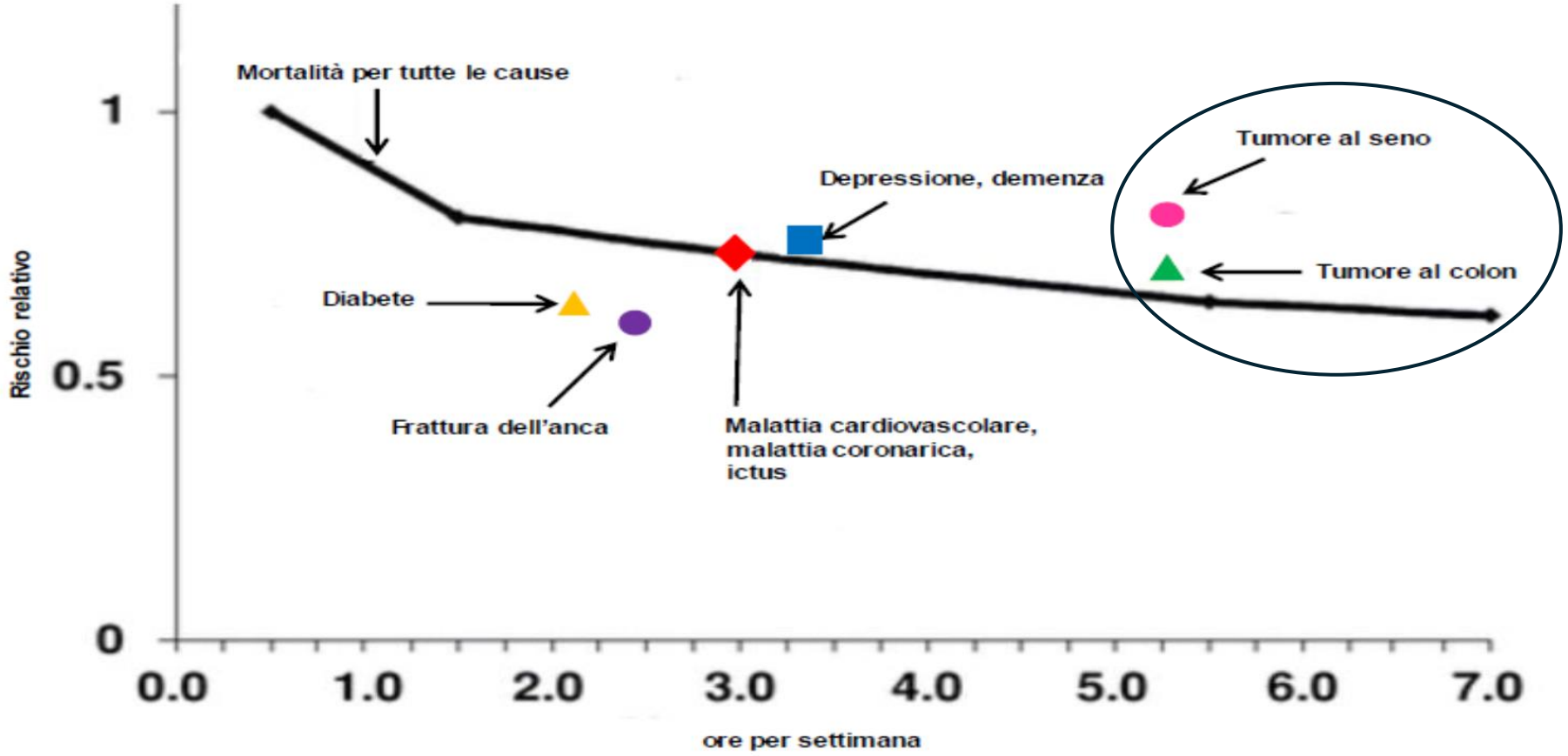


Figura 4.1. Associazione tra attività fisica moderata-intensa con eventi chiave di salute, inclusa la mortalità per tutte le cause

Ahmadi et al. Vigorous physical activity, incident heart disease, and cancer: how little is enough? Eur Heart J. 2022 Dec 7;43(46):4801-4814

Studio su 71 893 adulti seguiti per un periodo medio di 5.9 anni

Table 2 Mortality and disease incidence event rates per 1000 person-years[a]

	Events	Vigorous physical activity (min/week)[b]				
		None	>0 to <10	≥10 to <30	≥30 to <60	≥60
All-cause mortality	1927	13.4 (11.7, 15.4)	5.5 (5.1, 5.9)	3.8 (3.6, 4.1)	2.6 (2.3, 3.0)	1.8 (1.4, 2.1)
CVD mortality	602	4.4 (3.4, 5.6)	1.9 (1.7, 2.2)	1.2 (1.0, 1.4)	0.7 (0.5, 0.9)	0.3 (0.2, 0.5)
Cancer mortality	1150	5.5 (4.4, 6.9)	2.6 (2.3, 2.9)	1.9 (1.7, 2.1)	1.4 (1.2, 1.7)	1.0 (0.8, 1.4)
CVD incidence	4567	22.5 (20.1, 25.1)	14.5 (13.9, 15.2)	10.8 (10.3, 11.3)	8.8 (8.2, 9.4)	7.4 (6.7, 8.1)
Cancer incidence	2854	13.2 (11.4, 15.2)	8.0 (7.5, 8.5)	6.1 (5.8, 6.5)	5.2 (4.7, 5.7)	3.9 (3.4, 4.5)

Attività fisica di moderata intensità (Circa 3-6 METs)	Attività fisica di Vigorosa intensità (Circa >6 METs)
Richiede una moderata quantità di sforzo e accelera notevolmente la frequenza cardiaca.	Richiede un grande sforzo e provoca una respirazione rapida e un aumento sostanziale della frequenza cardiaca.
Esempi di esercizi a intensità moderata includono: • Camminata svelta • Danza • Giardinaggio • Lavori domestici e faccende domestiche • Coinvolgimento attivo in giochi e sport con bambini / portare a spasso il cane • Lavori leggeri di costruzione (ad es. verniciatura) • Trasporto / spostamento di carichi moderati (<20 kg)	Esempi di esercizio di vigorosa intensità includono: • Corsa • Camminare / arrampicarsi rapidamente su una collina • Ciclismo veloce • Ginnastica aerobica • Nuoto veloce • Sport competitivi e giochi sportivi (ad es. calcio, pallavolo, hockey, pallacanestro) • Spalare la neve o scavare fossati • Trasporto / spostamento di carichi pesanti (> 20 kg)

Gli equivalenti metabolici (MET) sono comunemente usati per esprimere l'intensità delle attività fisiche. Il MET è il rapporto tra il tasso metabolico di lavoro di una persona e il suo tasso metabolico a riposo.

Attività aerobica

- Sforzo moderato per un periodo di tempo prolungato (si attiva dopo 3-4 minuti e si stabilizza dopo 20 minuti)
- Migliora il sistema cardiovascolare e il sistema cardipolmonare
- Aumenta il metabolismo ossidativo dei grassi

Attività anaerobica

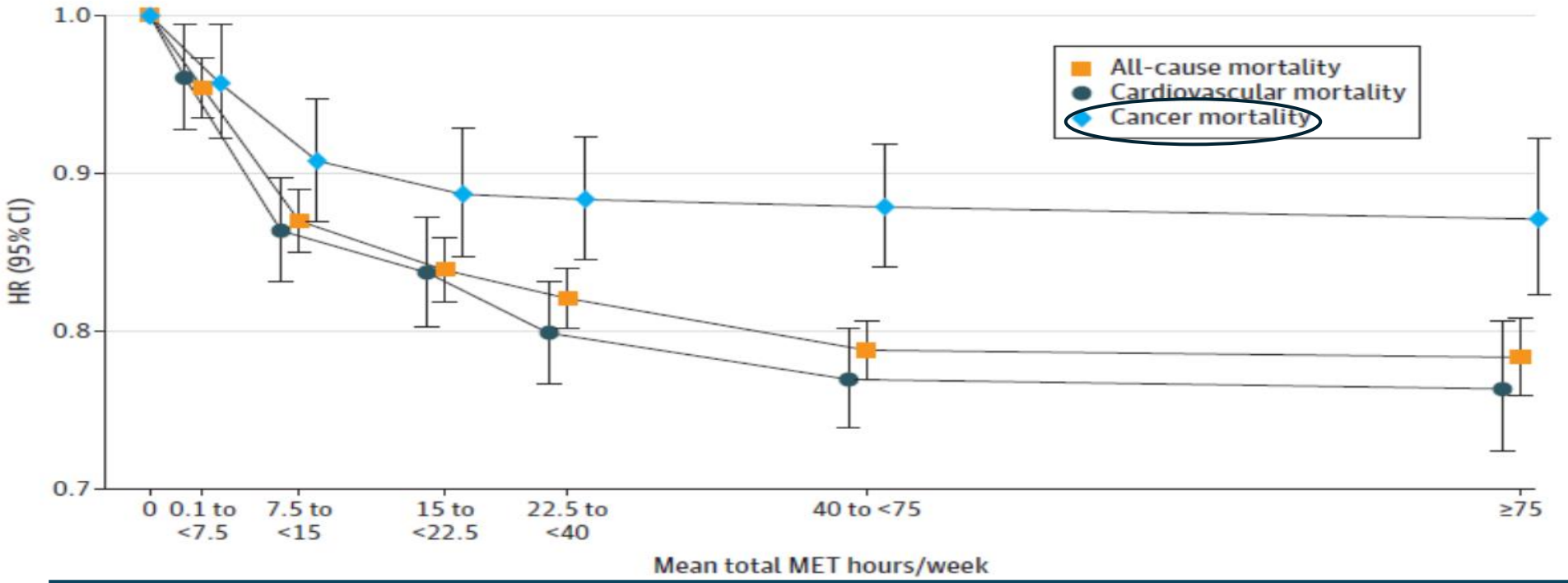
- Sforzi intensi ma di breve durata
- Favorisce l'aumento della forza e della potenza muscolare e l'aumento della massa magra

1 MET = 1Kcal/Kg/ora = 0,2L ossigeno/Kg/ora (24Kcal/kg/die)

Watts et al. Association of Leisure Time Physical Activity Types and Risks of All-Cause, Cardiovascular, and Cancer Mortality Among Older Adults. JAMA Netw Open. 2022 Aug 1;5(8):e2228510. doi: 10.1001/jamanetworkopen.2022.28510

Uno studio su 272 550 soggetti che facevano varie attività sportive aerobiche, seguiti per 12,4 anni

Figure 1. Associations of Mean Total Sum Metabolic Equivalent of Task (MET) Hours per Week of the 7 Activities With All-Cause, Cardiovascular, and Cancer Mortality



Vi e' una associazione significativa tra MET/ora/settimana e mortalita' per tumore

Zhao et al.
Recommended physical activity and all cause and cause specific mortality in US adults: prospective cohort study
BMJ 2020;370:m2031

479 856 soggetti seguiti per 5.9 anni

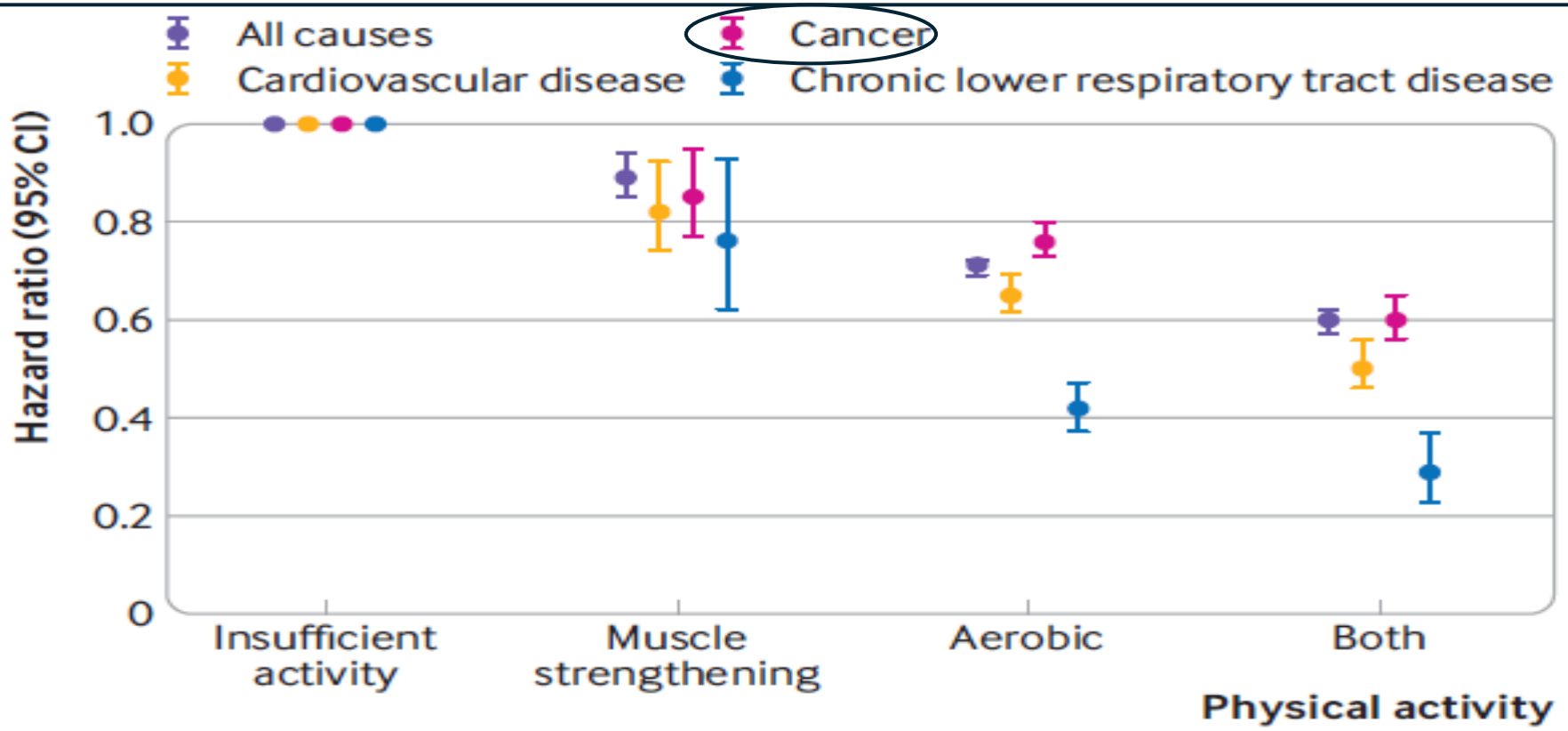
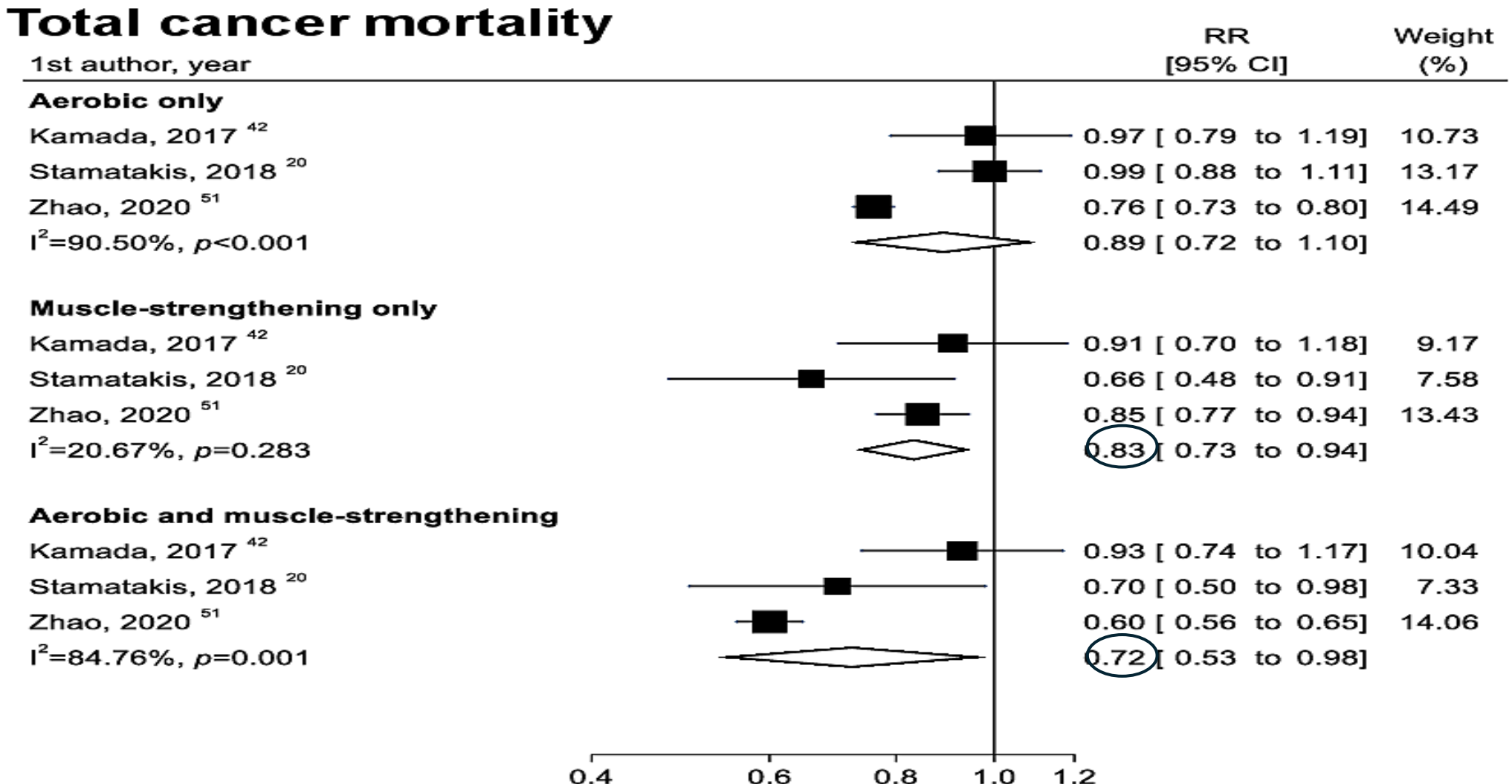


Fig 1 | Association between meeting the 2018 physical activity guidelines for Americans and all cause and cause specific mortality from three diseases. Estimates are from the fully adjusted model that includes the covariates of sex, age, race/ethnicity, education, marital status, body mass index, smoking, alcohol intake, and chronic conditions. Whiskers represent 95% confidence intervals

Momma et al. Muscle-strengthening activities are associated with lower risk and mortality in major non-communicable diseases: a systematic review and meta-analysis of cohort studies. Br J Sports Med. 2022 Jul;56(13):755-763.

Studio su 540 543 soggetti: la combinazione rafforzamento muscolare e attività aerobica produce I risultsati migliori



RACCOMANDAZIONI OMS

ADULTI (18-64 anni)

- 150-300 min di attività fisica aerobica di intensità moderata a settimana, oppure almeno 75-150 min di attività fisica aerobica intensa. Questi obiettivi possono essere raggiunti, per es., con 5 sessioni di esercizio moderato a settimana di almeno 30-60 min oppure svolgendo almeno 25-50 min di esercizio intenso per 3 volte a settimana.
- Aggiungere attività di rafforzamento muscolare (esercizi come piegamenti, flessioni, pesi) per almeno due volte a settimana in giorni non consecutivi

Sopra i 65 anni

- **attività fisica aerobica di intensità moderata per almeno 150-300 min o attività fisica aerobica intensa per 75-150 min. A ciò andrebbero aggiunti esercizi di rafforzamento muscolare, due o più volte la settimana.**
- **Inoltre, per conservare le abilità fisiche e prevenire le cadute, occorre fare attività fisica multicomponente, cioè una combinazione di attività aerobica, rafforzamento muscolare e allenamento dell'equilibrio, almeno tre giorni a settimana.**

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Lv et al. **Efficacy of a smartphone application assisting home-based rehabilitation and symptom management for patients with lung cancer undergoing video-assisted thoracoscopic lobectomy: a prospective, single-blinded, randomised control trial (POPPER study). Int J Surg. 2025 Jan 1;111(1):597-608.**

Better recovery of the pulmonary function and decrease of symptom burden.

Hiersch et al. **Supervised, structured and individualized exercise in metastatic breast cancer: a randomized controlled trial. Nat Med. 2024 Oct;30(10):2957-2966.**

The supervised exercise has positive effects on physical fatigue and quality of life.

Schmidt et al. **Impact of exercise on sexual health, body image, and therapy-related symptoms in women with metastatic breast cancer: The randomized controlled PREFERABLE-EFFECT trial. Int J Cancer. 2025 Apr 3.**

After 9 months, women participating in the supervised, structured exercise program found that their symptoms improved, including a reduction of chemotherapy side effects.

Bozzetti F. **Potential Benefits from Physical Exercise in Advanced Cancer Patients Undergoing Systemic Therapy? A Narrative Review of the Randomized Clinical Trials. Curr Oncol. 2024 Dec 1;31(12):7631-7646.**

Compared with a control group receiving the usual care, in patients who practiced physical exercise, a benefit in some parameters of physical function and quality of life and lean body mass was reported in 61%, 47%, and 12%, respectively.

Sanft et al. Randomized Trial of Exercise and Nutrition on Chemotherapy Completion and Pathologic Complete Response in Women With Breast Cancer: The Lifestyle, Exercise, and Nutrition Early After Diagnosis Study. J Clin Oncol. 2023 Dec 1;41(34):5285-5295

GRUPPO TRATTATO: durante la chemioterapia (ciclofosfamide, paclitaxel, doxorubicina) 87 paz hanno fatto ≥150 min/sett di esercizio fisico moderato o 75 min/sett di esercizio vigoroso e 2 volte/sett esercizi di resistenza, + dieta mediterranea, per 3 mesi.
Il GRUPPO DI CONTROLLO (86 pazienti) ha continuato un trattamento standard.

Risultati Principali

RISULTATI	Gruppo Intervento	Gruppo Controllo
Risposta Patologica Completa	53%	28%
Variazione nella attività fisica (min/settimana)	+143,4 ± 119,5	+47,7 ± 99,6
Attività di resistenza durante la chemioterapia (%)	71%	7%
Cambio nel consumo di frutta/verdura (porzioni/giorno)	+0,8 ± 2,5	-0,2 ± 2,0
Cambio nell'assunzione di fibre (g/giorno)	+0,7 ± 7,7	-3,1 ± 8,1

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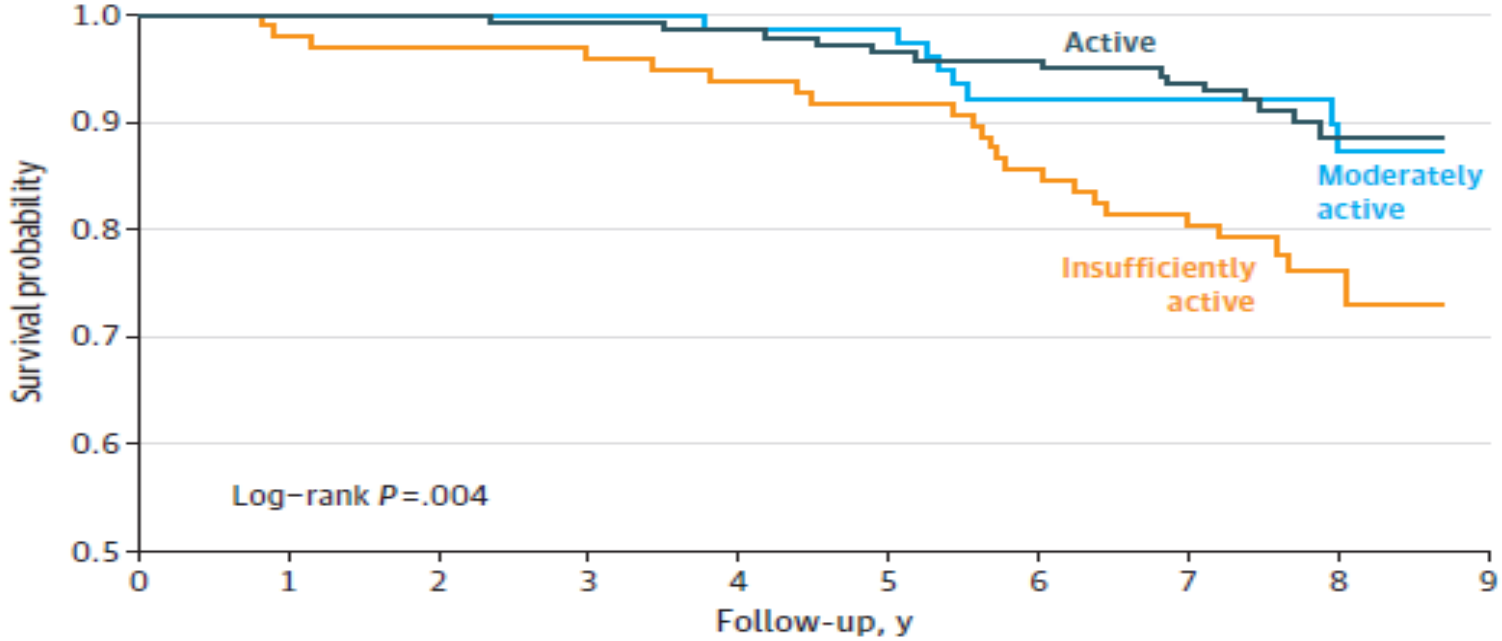
Lie Hong Chen et al. Association of Physical Activity With Risk of Mortality Among Breast Cancer Survivors. JAMA Netw Open. 2022;5(11):e2242660.

The study included 315 participants with a follow up of 7.8 years

Figure. Risk of All-Cause Mortality Among Breast Cancer Survivors by Godin-Shephard Leisure-Time Physical Activity Questionnaire Scores at Baseline



No. at risk										
Insufficiently active	97	95	94	93	91	89	83	78	28	0
Moderately active	141	141	141	140	139	136	135	132	62	0
Active	77	77	77	77	76	76	71	71	36	0

Spei et al. Physical activity in breast cancer survivors: A systematic review and meta-analysis on overall and breast cancer survival. Breast. 2019 Apr;44:144-152. doi: 10.1016/j.breast.2019.02.001.

Study of 23,041 breast cancer survivors followed for 3,5 - 12,7 years

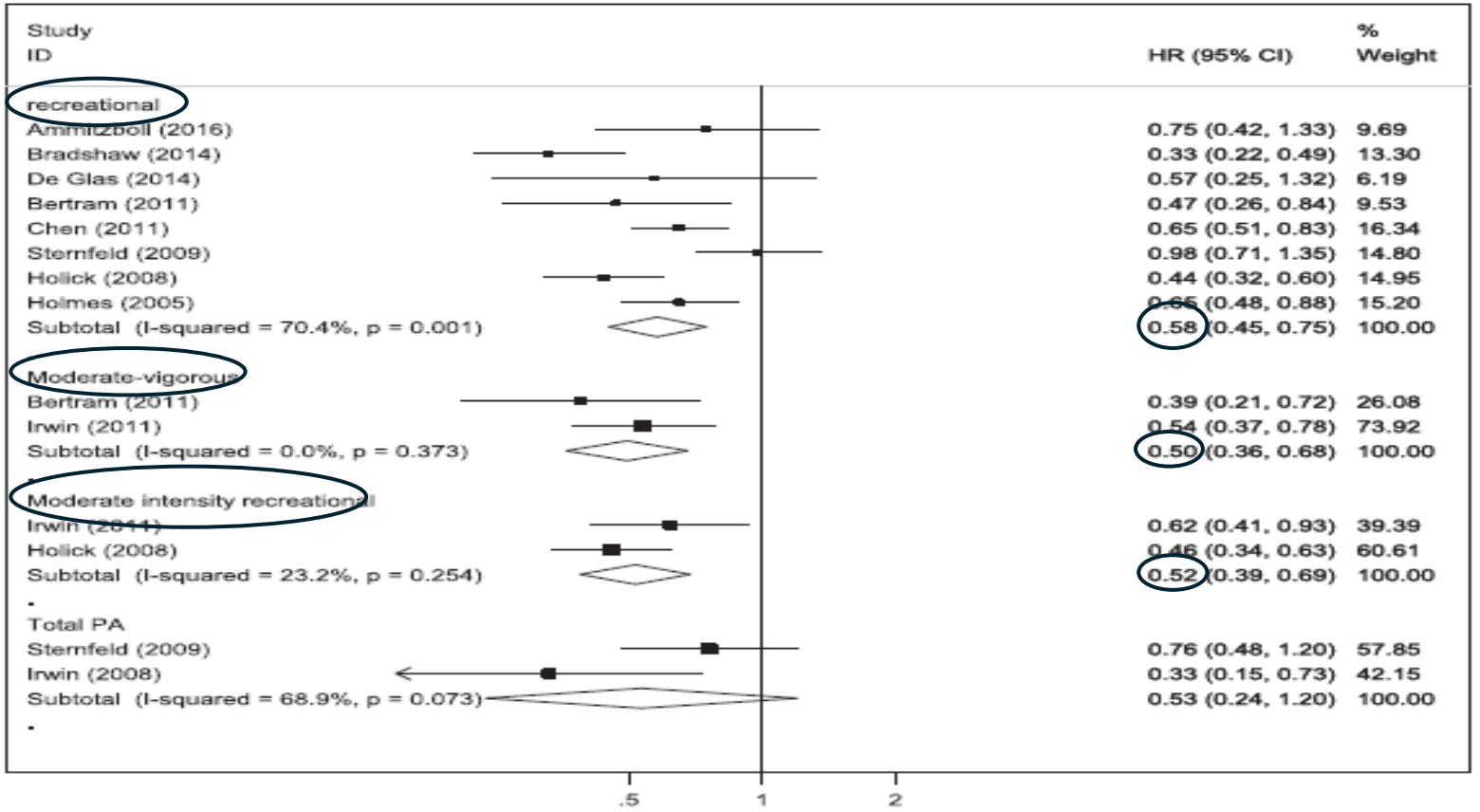


Fig. 2. Forest plot for the association between Physical activity and total mortality in breast cancer survivors. Results from random effects models. CI: Confidence Interval, HR: Hazard Ratio, PA: Physical Activity.

Spei et al. Physical activity in breast cancer survivors: A systematic review and meta-analysis on overall and breast cancer survival. Breast. 2019 Apr;44:144-152. doi: 10.1016/j.breast.2019.02.001.

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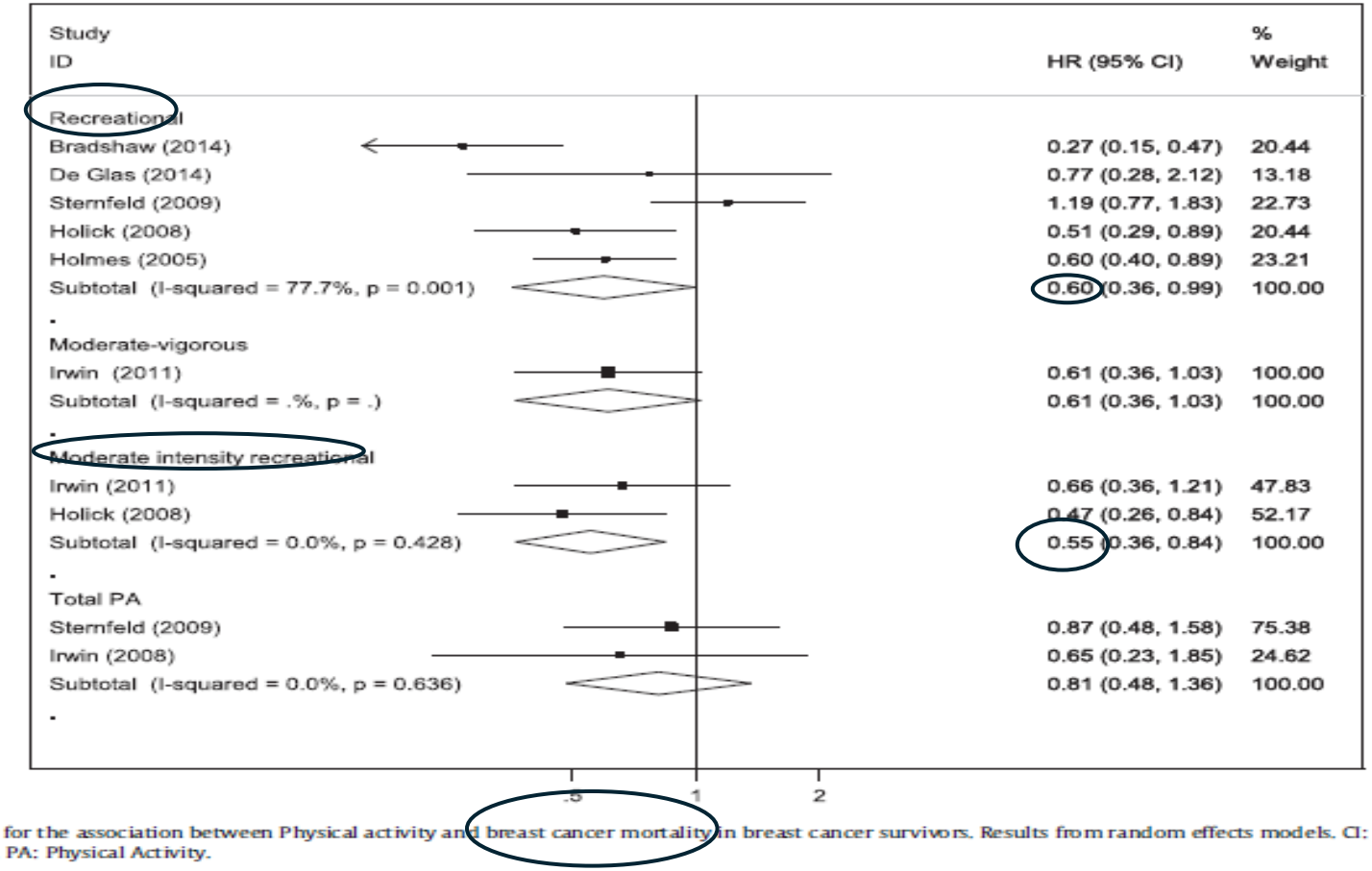

Fig. 3. Forest plot for the association between Physical activity and breast cancer mortality in breast cancer survivors. Results from random effects models. CI: Confidence Interval, HR: Hazard Ratio, PA: Physical Activity.

Brown et al. Physical Activity in Stage III Colon Cancer: CALGB/SWOG 80702 (Alliance). J Clin Oncol. 2023 Jan 10;41(2):243-254.

Studio su 1.696 pazienti seguiti per 7 anni

TABLE 2. Association of DFS and OS End Points With Category of Total Recreational Physical Activity Volume

Total Recreational Physical Activity Volume, MET-h/wk	DFS			OS		
	3-Year DFS Rate (95% CI)[a,b]	3-Year RD (95% CI)[a,c]	HR (95% CI)[a]	5-Year OS Rate (95% CI)[a,b]	5-Year RD (95% CI)[a,c]	HR (95% CI)[a]
< 3.0	76.5 (69.0 to 82.4)	0.0 (reference)	1.00 (reference)	82.6 (74.9 to 88.0)	0.0 (reference)	1.00 (reference)
3.0-8.9	82.2 (76.8 to 86.8)	5.7 (2.6 to 10.1)	0.73 (0.54 to 0.94)	88.7 (83.7 to 92.4)	6.1 (2.2 to 15.0)	0.62 (0.42 to 0.87)
9.0-17.9	86.1 (80.9 to 90.1)	9.6 (4.2 to 17.5)	0.56 (0.39 to 0.77)	91.1 (86.3 to 94.3)	8.5 (3.0 to 21.6)	0.49 (0.29 to 0.74)
≥ 18.0	87.1 (82.5 to 90.5)	10.6 (4.7 to 19.4)	0.52 (0.36 to 0.70)	91.9 (87.9 to 94.6)	9.3 (3.3 to 24.1)	0.44 (0.27 to 0.66)
P trend			< .001			< .001
PAR[d]			22%			35%

PAR fraction quantifies the percent of disease-free survival events or overall survival events that could be prevented if the target population increased their total recreational physical activity volume by m3 MET-h/wk (comparable with an additional hour of brisk walking weekly).

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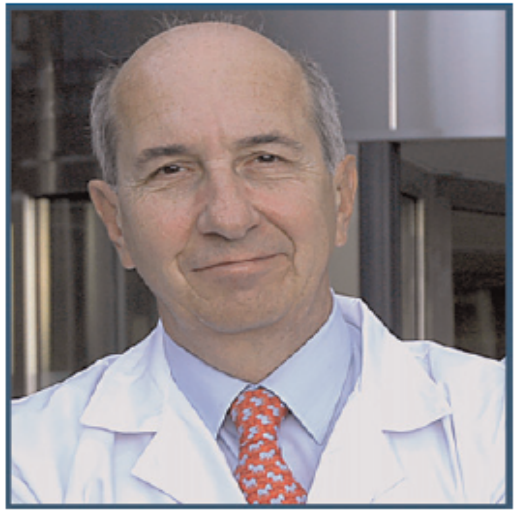
THE LAST WORD



ALFREDO CARRATO, MD, PhD

Alfredo Carrato, MD, PhD, is Professor of Medical Oncology at Alcala University, Madrid, Spain, and the Chairperson of Pancreatic Cancer Europe.

Dr. Carrato is involved in clinical and

Physical Activity is Medicine

Alfredo Carrato, MD, PhD

The frequent lack of appropriate statistical evidence regarding physical activity benefits in patients with cancer has meant that either epidemiologic or retrospective observational studies have provided the basis for our knowledge. The level of evidence for results has been weak and the basis of a controversial and not well-established issue. Scientific and clinical evidence is much more limited for less frequent and low survival cancers such as pancreatic cancer. Conducting randomized controlled trials on physical activity implementation in individuals with cancer is challenging due to the low observed adherence to trial recommendations and completion of quality-of-life questionnaires; the interference of environmental, social, and structural barriers; comorbidities as well as symptoms derived from cancer and its treatment; and the high number of patients needed, which is difficult to achieve in uncommon and deadly cancers. In the article by Neuzillet et al[1] elsewhere in this issue, we can learn from a well-designed randomized trial on the posi-