

Meeting Nazionale ITACARE-P 2025

La Cardiologia Riabilitativa e Preventiva
come snodo fondamentale
della cura della persona con cardiopatia



CENTRO CONGRESSI FRENTANI
Roma, 21-22 novembre 2025



**Esercizio fisico in ambito cardiovascolare e internistico:
quello che i documenti dicono... e quello che non dicono**

Moderatori: Alessandro Biffi, Francesco Dentali, Giampiero Patrizi

Training fisico nella riabilitazione cardio-oncologica: principi e modelli organizzativi



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No COI to disclose relevant to this topic

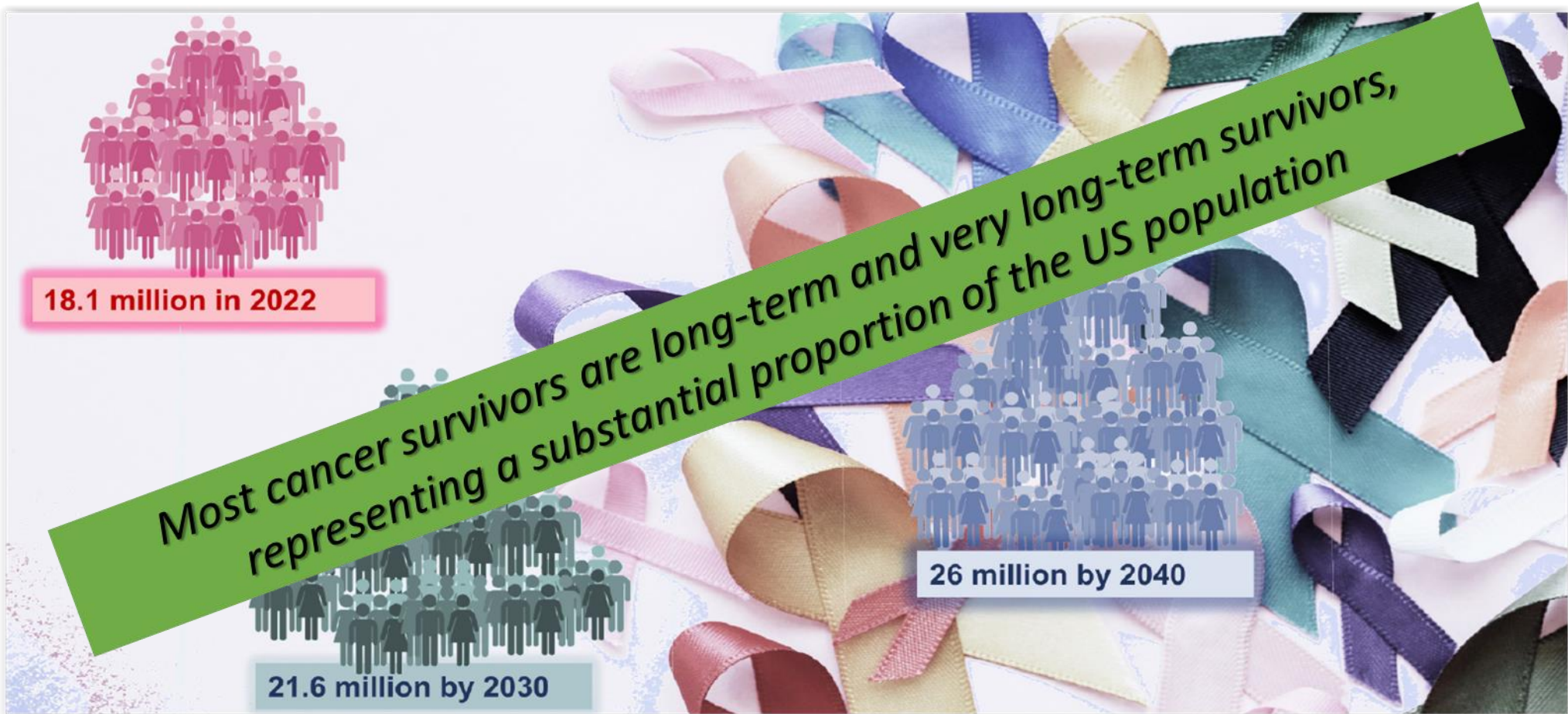


Outline

- **Una richiesta in rapida crescita**
- Da dove nasce l'idea
- Efficacia della CORE: dalla fisiopatologia alla clinica
- Proposta di CORE nella Azienda UsI Toscana Nord Ovest



Prevalence of cancer survivors in the United States

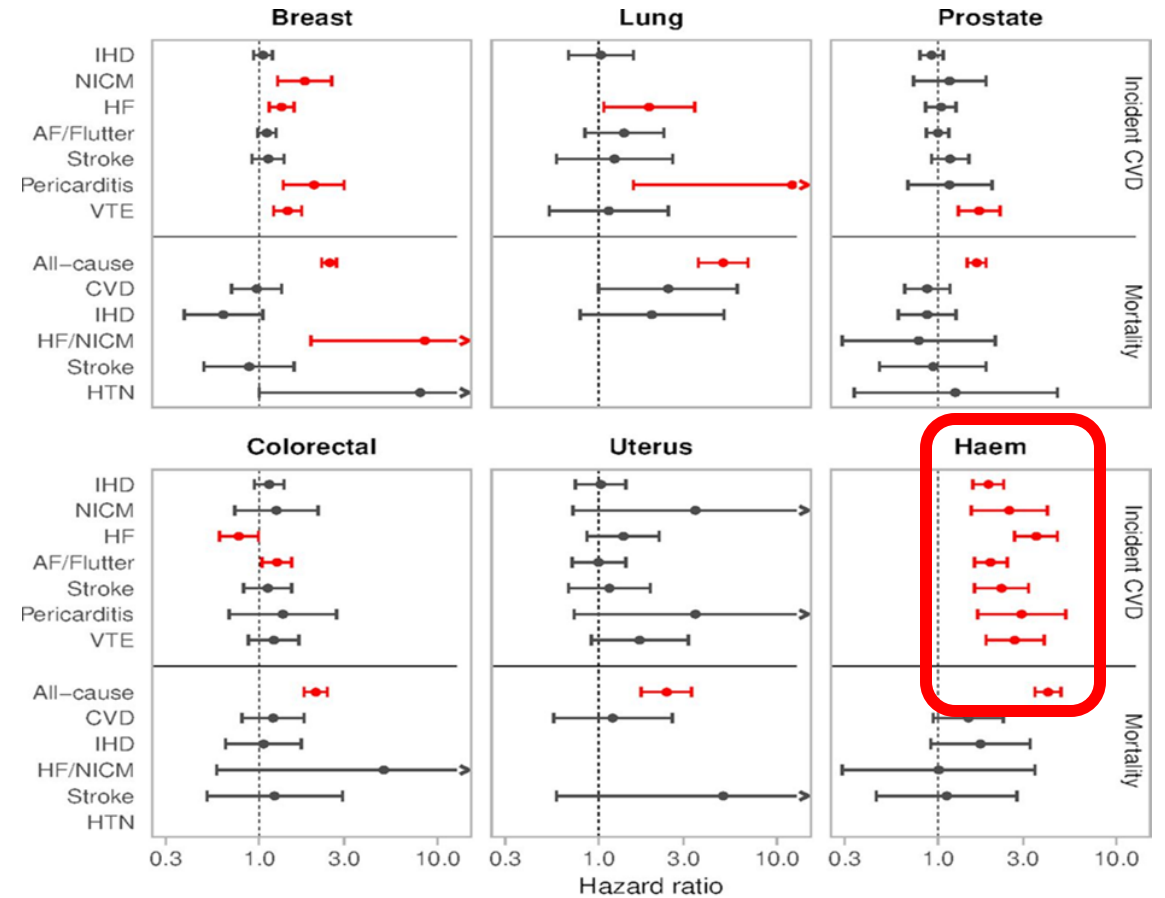


(Tonorezos E et al. *J Natl Cancer Inst.* 2024)



A population at extreme Cardiovascular Risk

- Cancer history is linked to increased risk of incident CVDs and adverse cardiac remodeling independent of shared CRF.
- The heightened CVR persist several years after initial cancer diagnosis.
- This study highlights the specific cardiovascular care needs of patients with cancer.

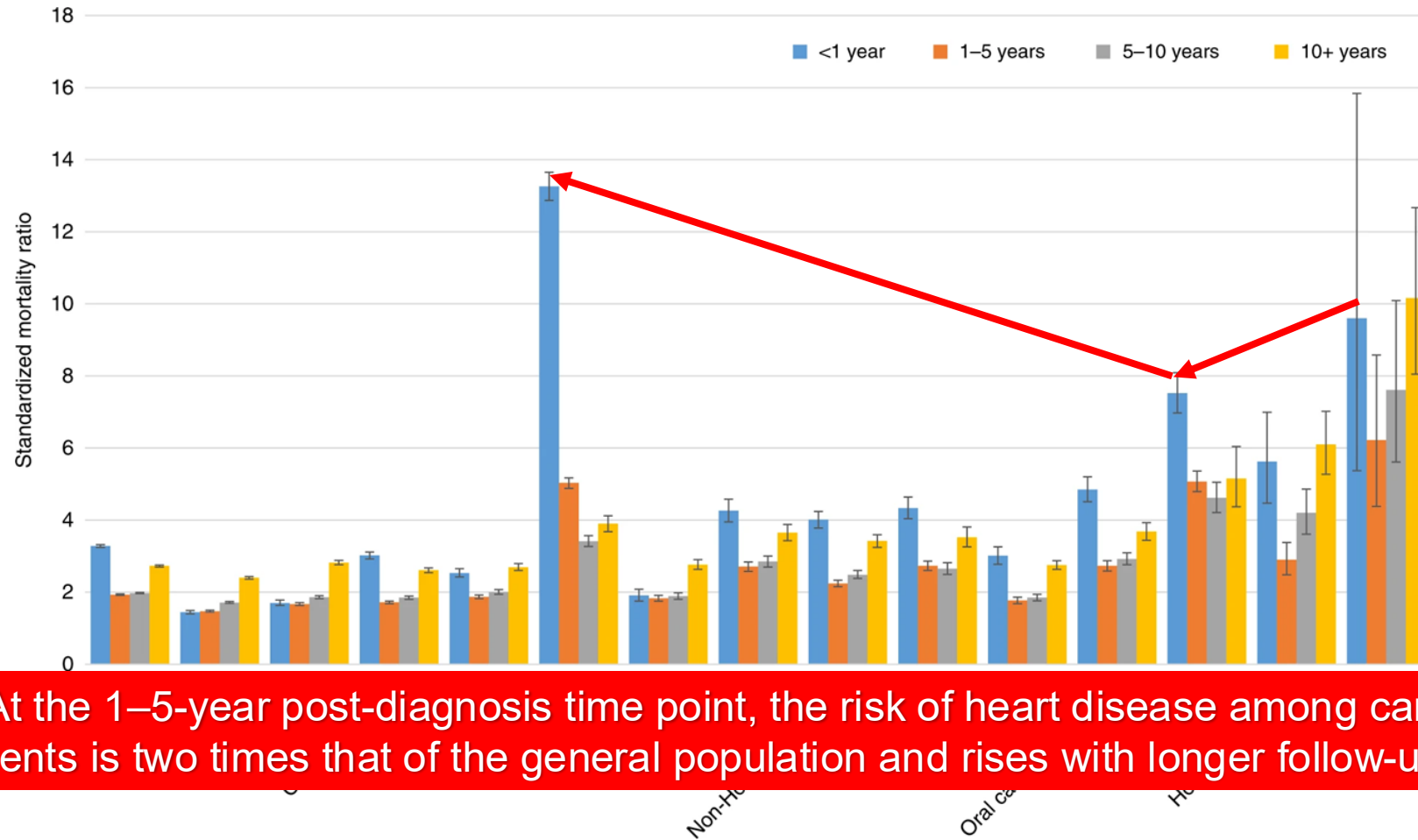


X-axis is cropped to 15, intervals with upper limits above 15 are marked with an arrow

(Raisi-Estabragh Z et al. *Heart* 2023)



Fatal heart disease among cancer patients by cancer subsite



At the 1–5-year post-diagnosis time point, the risk of heart disease among cancer patients is two times that of the general population and rises with longer follow-up time.

(Stoltzfus KC et al. *Nat Commun.* 2020)



Outline

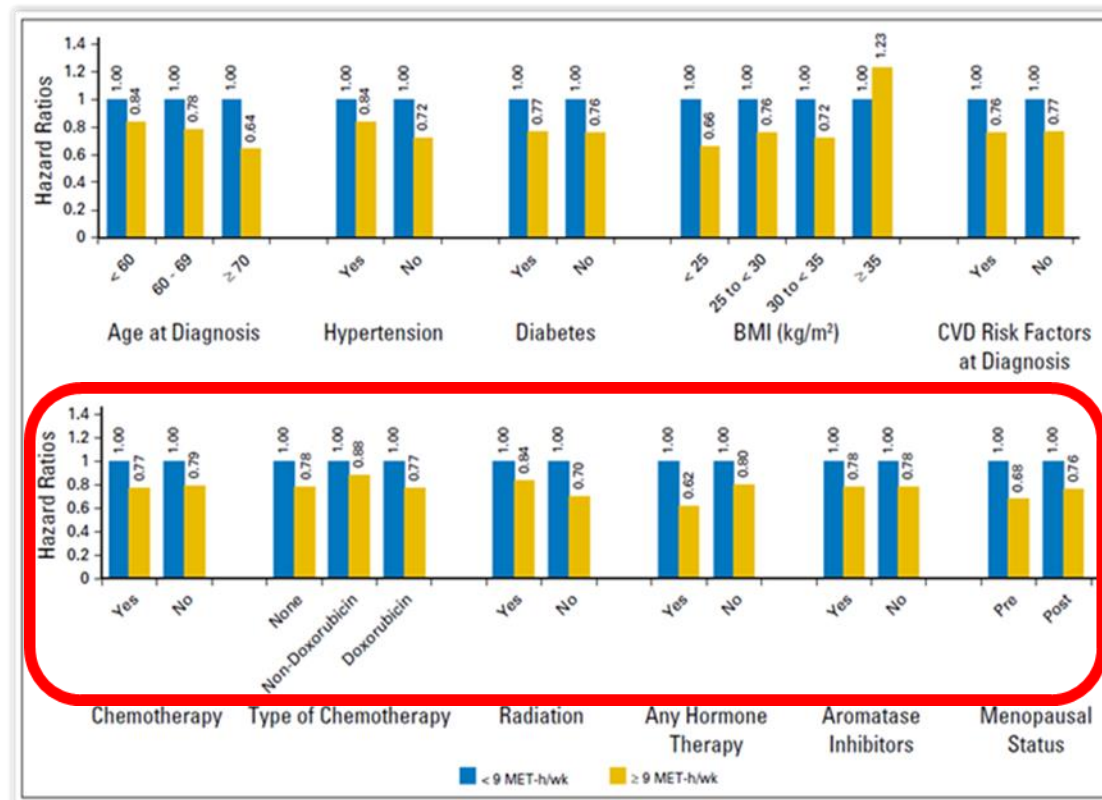
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Physical activity : a tool to fight CV events and the damage of CT/RT

- Adherence exercise GL for adult patients with cancer, ≥ 9 MET-h/wk, was associated with an adjusted 23% reduction in the risk of CVEs.
- The association with exercise did not differ according to age, CVD RF, menopausal status, or anticancer treatment.
- Limit: leisure-time recreational physical activity was assessed with questionnaire.

Adjusted RR for CV events according to dichotomized exercise exposure (9 MET-h/wk) in subgroups

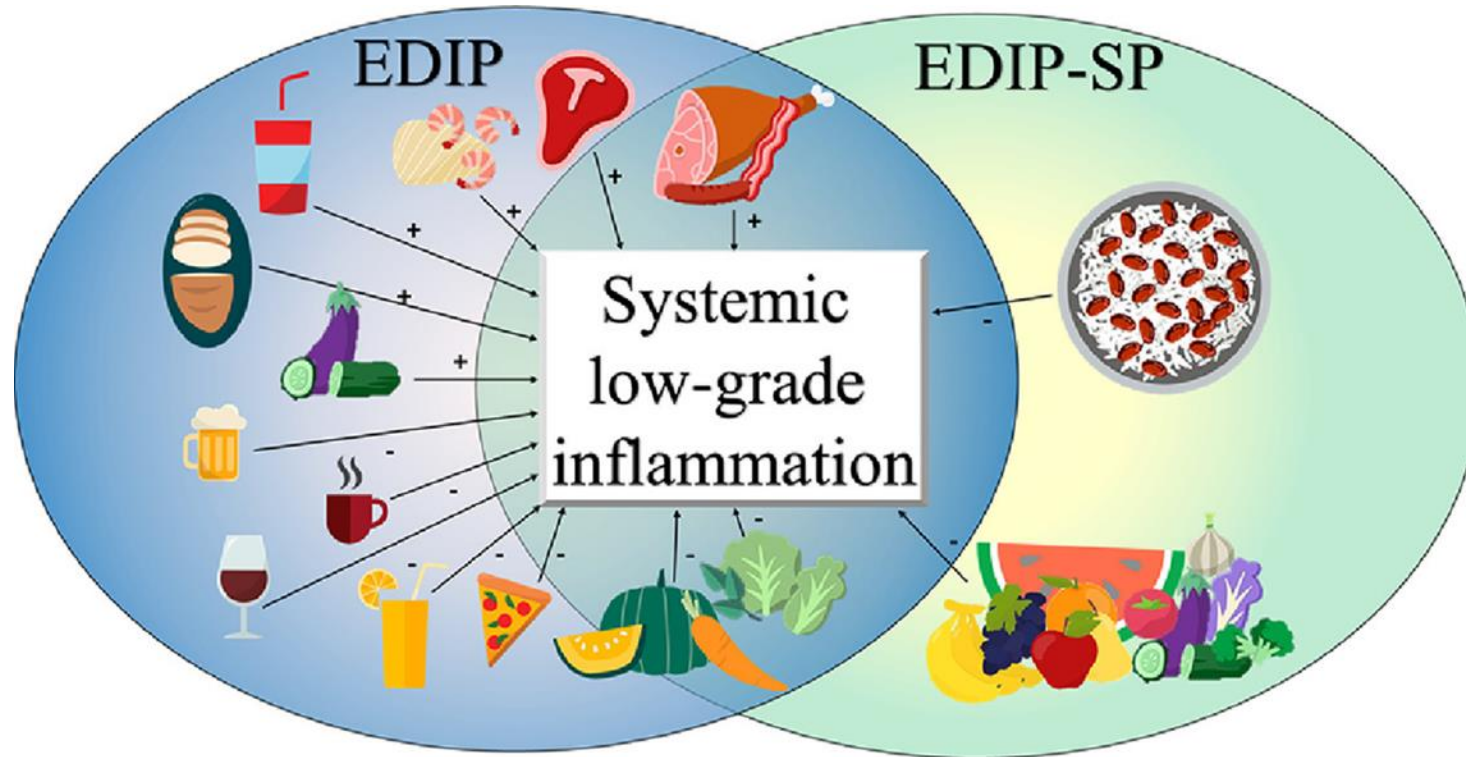


(Jones LW et al. *J Clin Oncol.* 2016)



Best survival outcomes: higher PA levels less proinflammatory diets

EDIP: empirical dietary inflammatory pattern



1,625 ps with resected stage III colon cancer.

Those in the lower EDIP quintiles (80% of the study population) who had higher physical activity (≥ 9 METs hours/week) experienced the best overall survival (HR: 0.37) when compared with patients in the highest EDIP quintile (20% of the study population) who had lower physical activity (< 9 METs hours/week; P interaction $< .001$).

(Sara K. Char, ASCO 2025)



The Insight: exploiting the CR model for Cardiac Oncology REhabilitation



- Is mandatory the identification of cancer patients and survivors at elevated CV risk for the direct effects of cancer therapies and the accumulation of CVRF.
- CR is a ready-to-use resource to provide structured exercise and ancillary services to cancer patients and survivors.
- Utilizing the CR network, the CORE can address the complication related to cancer, bringing this therapy accessible to larger numbers of cancer survivors.

Cardiac Rehabilitation	Oncology Rehabilitation
Exercise training	Same
Physical activity counseling	Same
Nutrition counseling	Same
Psychosocial management	Same
Weight management	Same
Coronary risk factor management: <ul style="list-style-type: none">• Management of hypertension and dyslipidemia• Diabetes management• Smoking cessation	Persistent effects after oncology therapy: <ul style="list-style-type: none">• Fatigue/sleep issues• Surgical/radiation related impairment• Pain syndromes, arthralgias• Deconditioning/weakness/balance issues

(Dittus KL et al. *J Cardiopulm Rehabil Prev.* 2015)



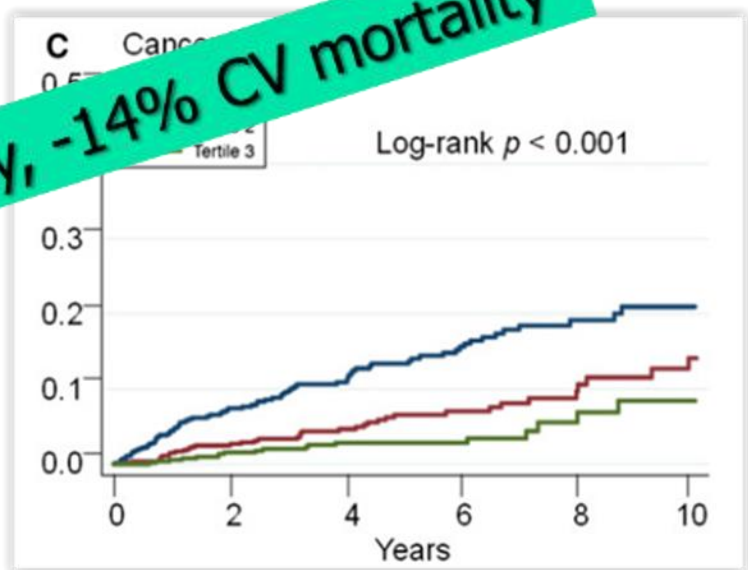
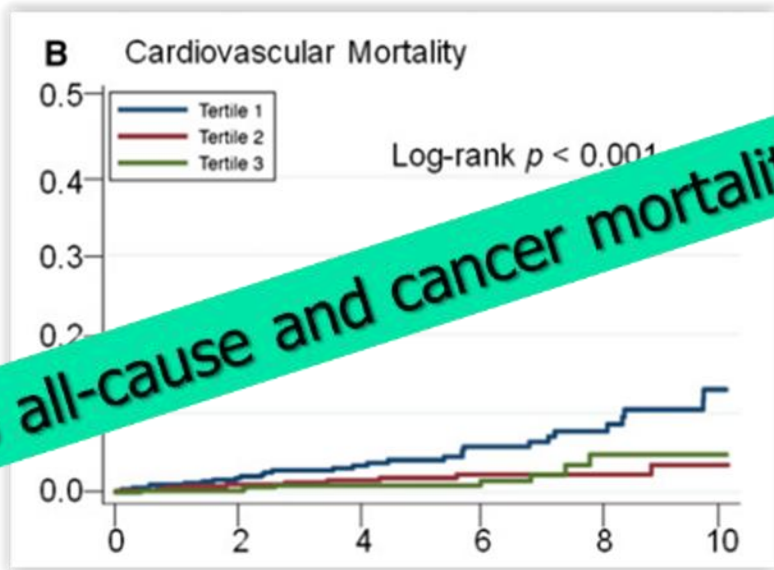
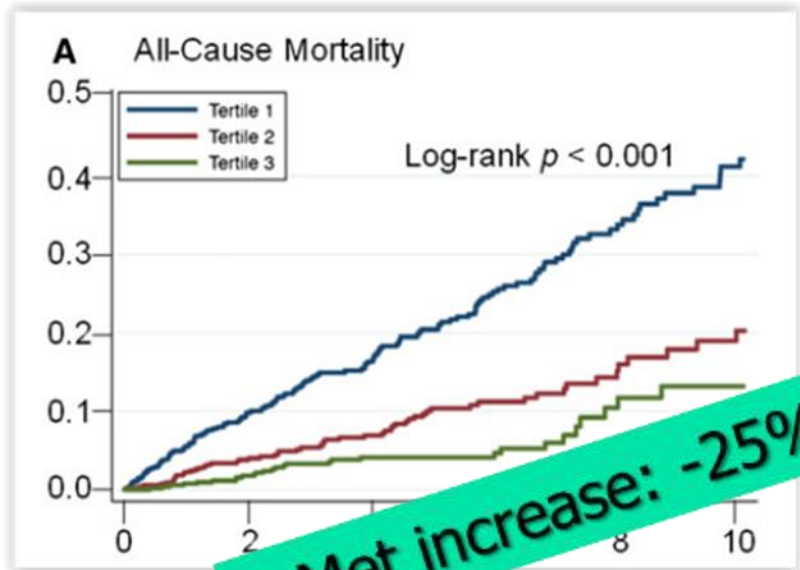
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Impact of CRF on prognosis

Probability of all-cause mortality (A), cardiovascular mortality (B), and cancer mortality (C) in cancer patients according to CRF fitness tertiles achieved during exercise treadmill testing: low CRF (blue line), intermediate CRF (red line), and high CRF (green line)



1 Met increase: -25% all-cause and cancer mortality, -14% CV mortality

(Groarke JD et al. *Eur Heart J Qual Care Clin Outcomes*. 2020)



The BReast Cancer Randomized EXercise InTervention (BREXIT)

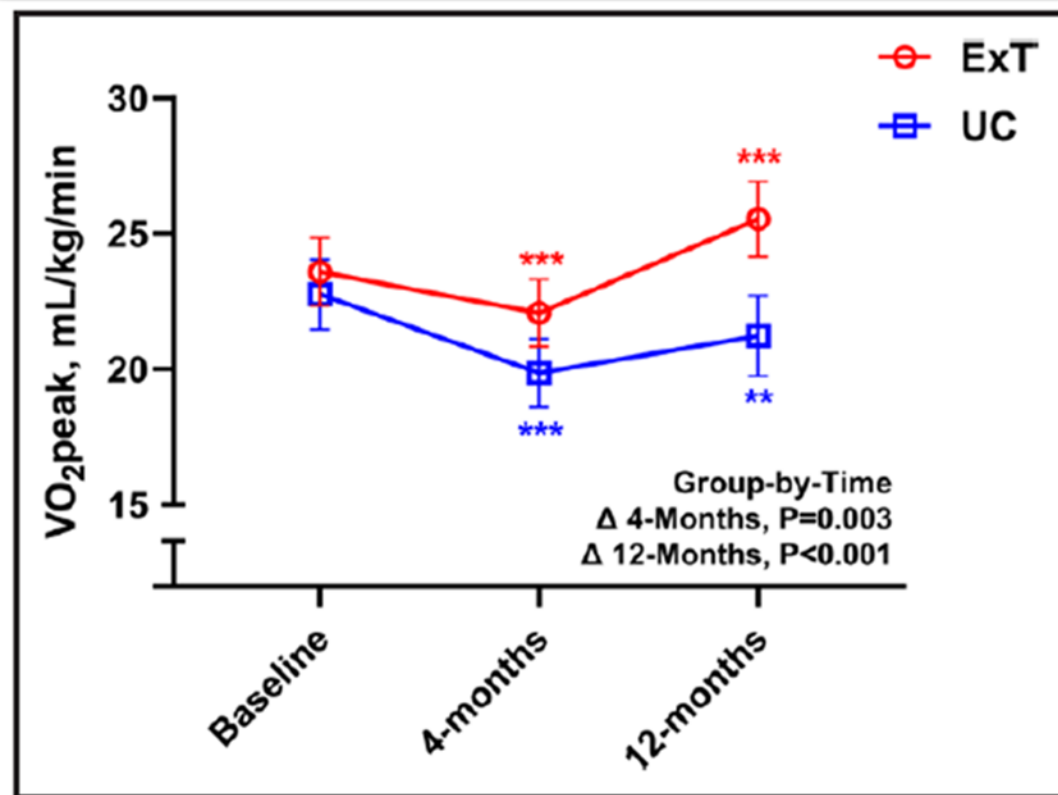
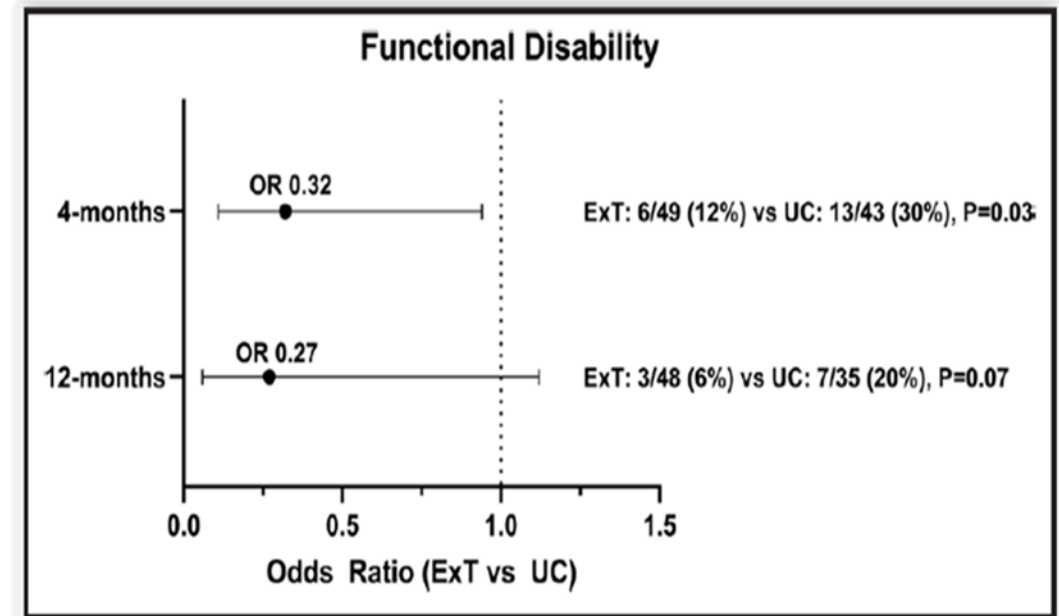


Figure 3. Changes in cardiorespiratory fitness (VO₂ peak) with ExT and UC.

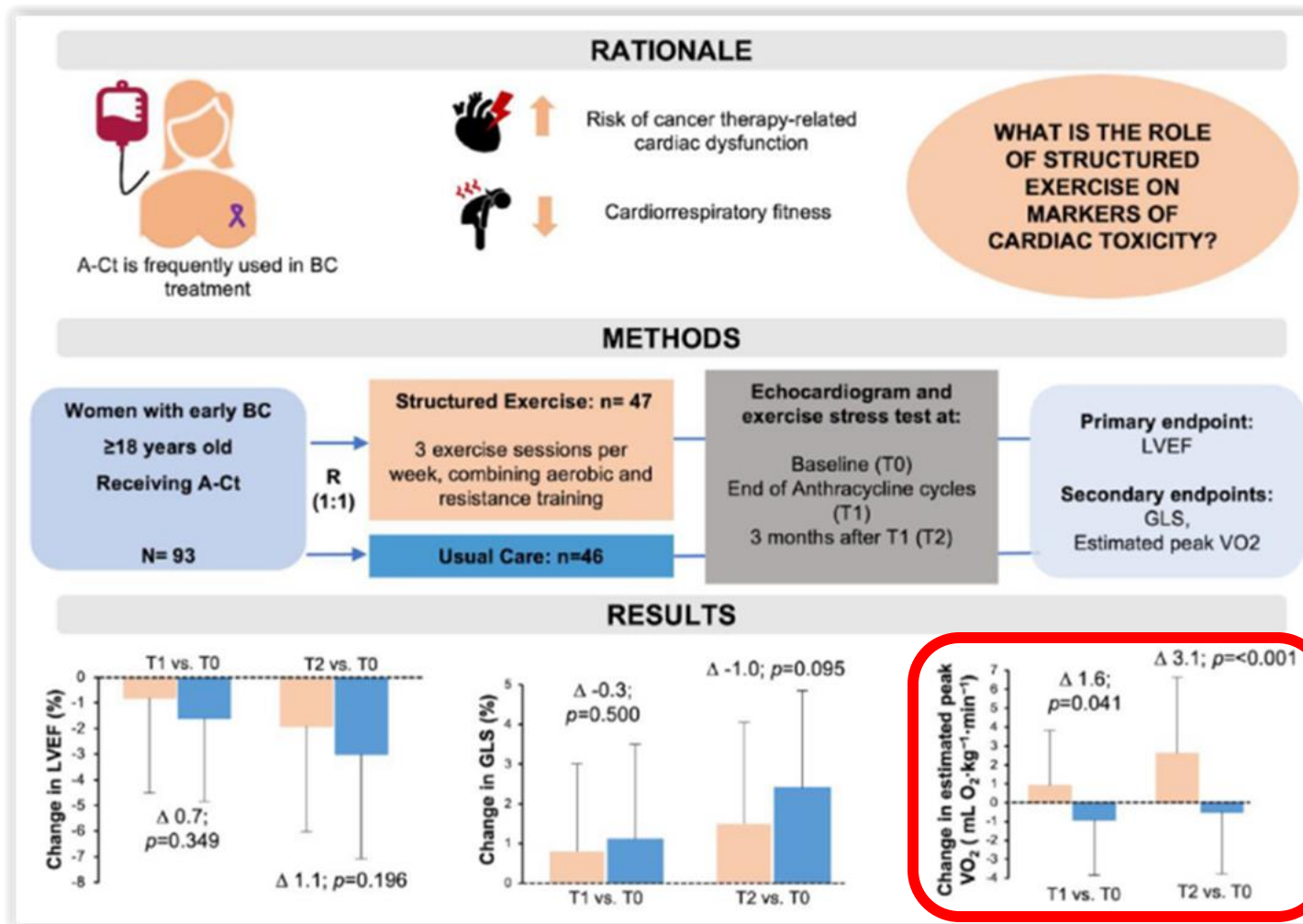


(Foulkes SJ et al. *Circulation*. 2023)

The magnitude and consistency of benefit from ExT provide the strongest evidence to date for recommending exercise to all patients with BC.



Effects of Training on toxicity markers in women with BC







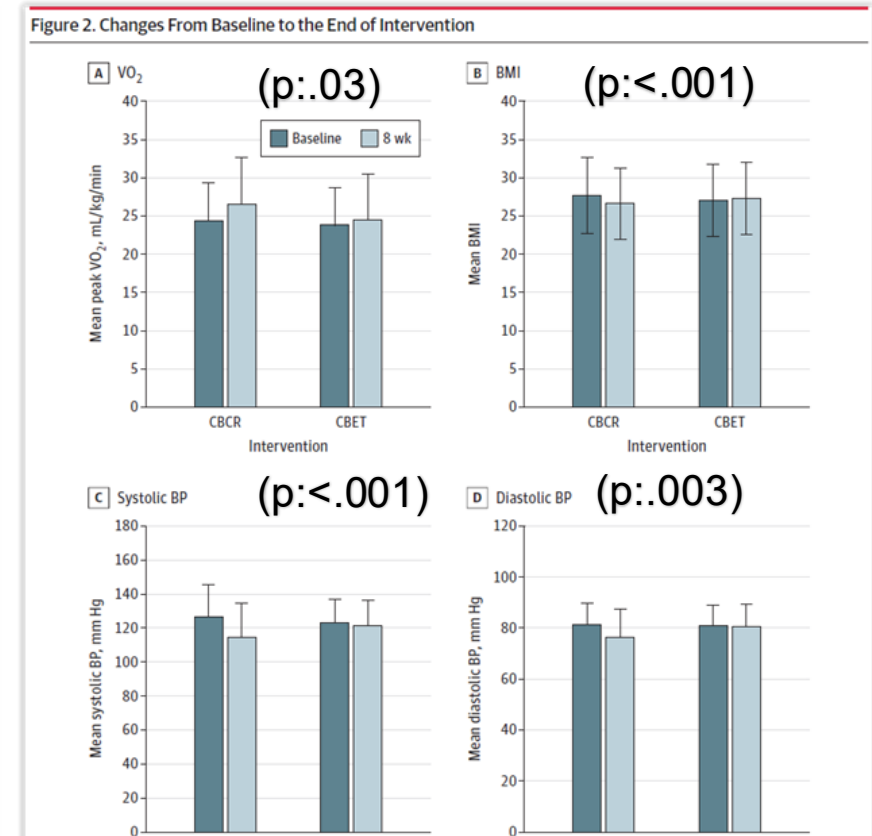
(Antunes P et al. *Eur J Prev Cardiol.* 2023 Jul)



CORE for cancer survivors with high CV risk



<p>POPULATION 17 Men, 58 Women</p>  <p>Adult cancer survivors after primary treatment with curative intent Mean age, 53.6 y</p>	<p>INTERVENTION 80 Participants</p>  <p>40 Center-based cardiac rehabilitation program (CBCR) Outpatient cardiac rehabilitation program delivered by a multidisciplinary rehabilitation team</p>  <p>40 Community-based exercise training program (CBET) Usual care with a community-based exercise program conducted by an exercise physiologist</p>
<p>SETTINGS / LOCATIONS</p>  <p>1 Hospital in Portugal</p>	<p>PRIMARY OUTCOME Cardiorespiratory fitness assessed by peak VO₂ change (from baseline)</p>



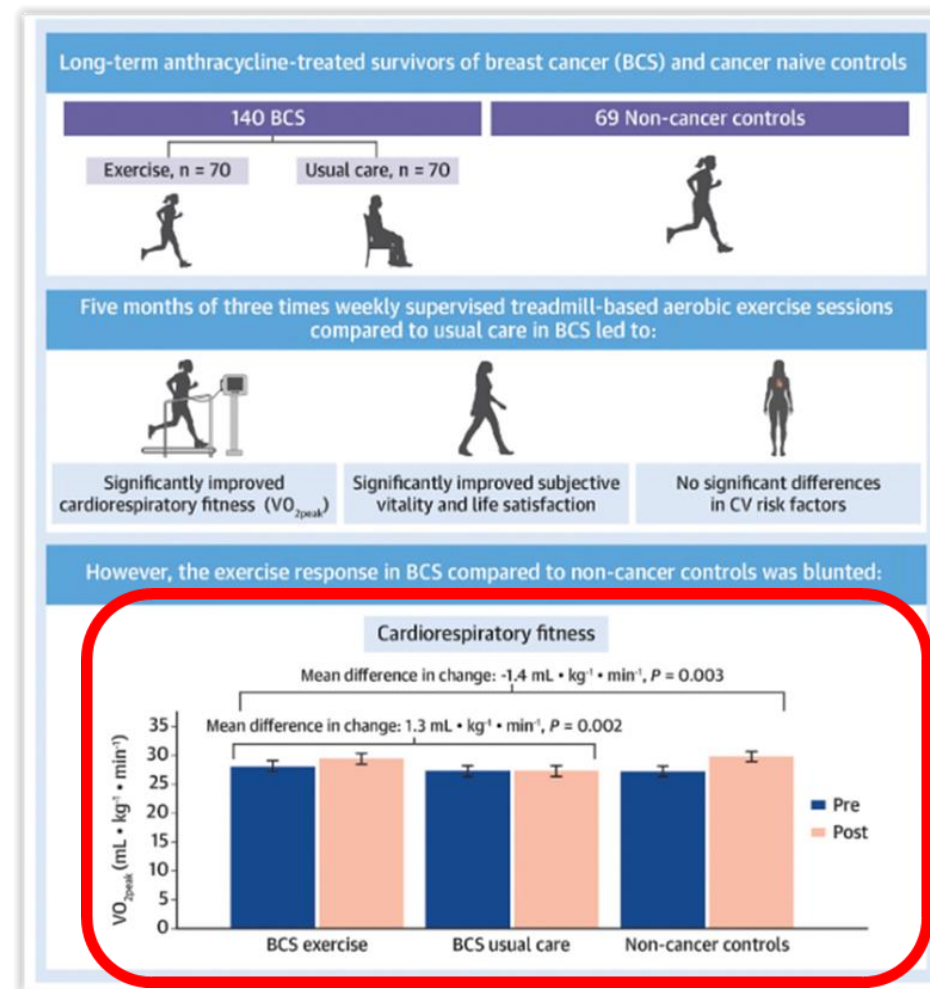
1. Exercise training benefits and successful lifestyle changes can be best optimized by a comprehensive, multidisciplinary team within the **established infrastructure of CR**.
2. **The cost per QALY was only €1,383** (the cut-off usually ranging between €5,000- €30,000); such programs can be effective.



CAUSE (CARDIOVASCULAR Survivors Exercise)



- VO_{2peak} increased by 1.2 ± 2.6 $mL \cdot kg^{-1} \cdot min^{-1}$ in the BCS exercise, by 0.01 ± 2.5 $mL \cdot kg^{-1} \cdot min^{-1}$ in the BCS usual care group: .002), and by 2.6 ± 2.5 $mL \cdot kg^{-1} \cdot min^{-1}$ in non-cancer subjects ($p = 0.003$).
- No changes in CVR, but improved subjective vitality and satisfaction with life.
- **11 ± 1 years after treatment!**



(Johansen SH et al. *JACC CardioOncol.* 2025 Jun)



Effect of HIIT on CVD risk

TABLE 6. Effects of 12 Weeks of HIIT on CVD Risk Factors in TCS

Measures	Group	No.	Baseline		Follow-Up		Between-Group Difference			
			Mean	SD	Adj Mean ^a	SE	Adj Mean ^a	SE	95% CI	P
Framingham Risk Score, %	Control	27	5.8	5.4	6.3	0.2	-0.6	0.2	-1.0 to -0.1	.011
	Exercise	35	6.9	6.1	5.7	0.2				
Vascular age, y	Control	27	42.7	12.1	43.0	0.4	-1.3	0.5	-2.3 to -0.3	.011
	Exercise	35	43.7	15.7	41.6	0.3				
MRFS (no./max 24)	Control	27	6.3	3.0	6.1	0.3	-1.4	0.4	-2.2 to -0.5	.002
	Exercise	35	7.0	3.6	4.7	0.3				

Abbreviations: 95% CI, 95% confidence interval; Adj, adjusted; CVD, cardiovascular disease; HIIT, high-intensity aerobic interval training; max, maximum; MRFS, modifiable CVD risk factor score; SD, standard deviation; SE, standard error; TCS, testicular cancer survivors.

^a Follow-up and between-group difference values were adjusted for baseline value of the outcome, age, treatment exposure, and time since treatment.

(Adams SC et al. *Cancer*. 2017)

- The training not only significantly increased CRF, but also reduced C-LDL, CRP, arterial stiffness, intima-media thickness and increased parasympathetic tone.
- The final result was a 20% reduction in modifiable CV risk factors (FRS).



Aerobic and resistance exercise reduce CVR in BC

- 100 women, stage I to III breast cancer treatment, completed within the previous 6 months, were assigned to the exercise group (n = 50) or the usual care group (n = 50).
- 55% of Hispanic ethnicity, mean age was 53.5 years.
- Supervised aerobic and resistance exercise, three times a week, for 16 weeks, reduced the risk of 10-year CV disease predicted by FRS of 11%.

Table. Comparison of FRS Variables Between Exercise and Usual Care Groups^a

Variable	Baseline, Mean (SD)	Postintervention		Postintervention Between-Group Difference	
		Mean (SD)	P Value ^b	Mean (95% CI)	P Value ^c
SBP, mm Hg					
Exercise	132.9 (13.0)	120.7 (9.5)	.001	-13.7 (-16.5 to -8.7)	.001
Usual care	133.7 (9.7)	135.9 (9.8)	.22		
FRS preset point for SBP ^d					
Exercise	0.0 (2.0)	-3.0 (2.0)	<.001	-3.0 (-5.0 to -1.0)	.002
Usual care	0.0 (2.0)	0.0 (2.0)	>.99		
HDL-C, mg/dL					
Exercise	43.1 (6.6)	64.7 (7.8)	.001	24.4 (27.9 to 17.9)	.001
Usual care	41.0 (4.3)	39.9 (4.0)	.45		
FRS preset point for HDL-C ^d					
Exercise	2.0 (1.0)	-2.0 (1.5)	<.001	4.0 (0.5 to 6.0)	<.001
Usual care	2.0 (1.0)	2.0 (2.0)	.97		
LDL-C, mg/dL					
Exercise	167.9 (19.7)	119.3 (12.1)	<.001	-48.6 (-61.2 to -27.6)	.001
Usual care	172.4 (20.3)	178.3 (21.7)	.59		
FRS preset point for LDL-C ^d					
Exercise	2.0 (1.0)	0 (1.0)	.002	-2.0 (-4.5 to -0.5)	.001
Usual care	2.0 (1.0)	2 (1.0)	.98		
Diagnosis of diabetes, No. (%)					
Exercise	20 (40)	10 (20)	<.001	-10.0 (-18.2 to -6.4)	<.001
Usual care	22 (44)	24 (53)	.45		
FRS preset point for diabetes ^d					
Exercise	2.0 (1.5)	1.0 (0.5)	.001	-1.0 (-2.5 to -0.5)	.003
Usual care	2.0 (1.0)	3.0 (1.0)	.21		
Total FRS					
Exercise	12.0 (2.0)	2.0 (1.5)	<.001	-9.5 (-13.0 to -6.0)	<.001
Usual care	12.0 (2.0)	13.0 (3.0)	.67		
FRS-predicted 10-y risk, %					
Exercise	13.0 (3.0)	2.0 (0.5)	<.001	-11.0 (-15.0 to -5.0)	<.001
Usual care	13.0 (3.0)	13.0 (3.0)	.97		

(Lee K et al. *JAMA Oncol.* 2019)

The ERASE Randomized Clinical Trial: from CV to Oncologic Outcomes

Open Access
Protocol

Table 2.1

Variable
Cardiopu
Peak V
HIIT
Usu
Peak V
HIIT
Usu

BMJ Open Intense Exercise for Survival among Men with Metastatic Castrate-Resistant Prostate Cancer (INTERVAL-GAP4): a multicentre, randomised, controlled phase III study protocol

Robert U Newton,^{1,2,3} Stacey A Kenfield,⁴ Nicolas H Hart,^{1,3,5} June M Chan,^{4,6} Kerry S Courneya,^{1,7} James Catto,⁸ Stephen P Finn,⁹ Rosemary Greenwood,¹⁰ Daniel C Hughes,¹¹ Lorelei Mucci,¹² Stephen R Plymate,¹³ Stephan F E Praet,^{13,14} Emer M Guinan,¹⁵ Erin L Van Blarigan,⁶ Orla Casey,¹⁵ Mark Buzza,¹⁶ Sam Gledhill,¹⁶ Li Zhang,^{6,17} Daniel A Galvão,^{1,3} Charles J Ryan,^{4,17,18} Fred Saad¹⁹

veillance

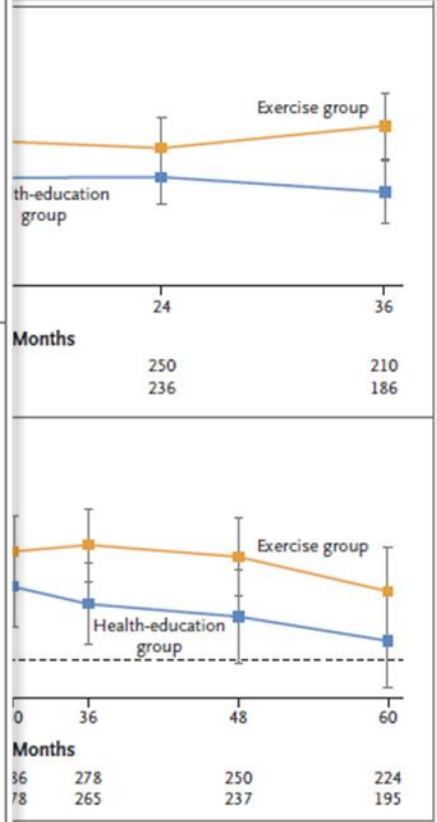
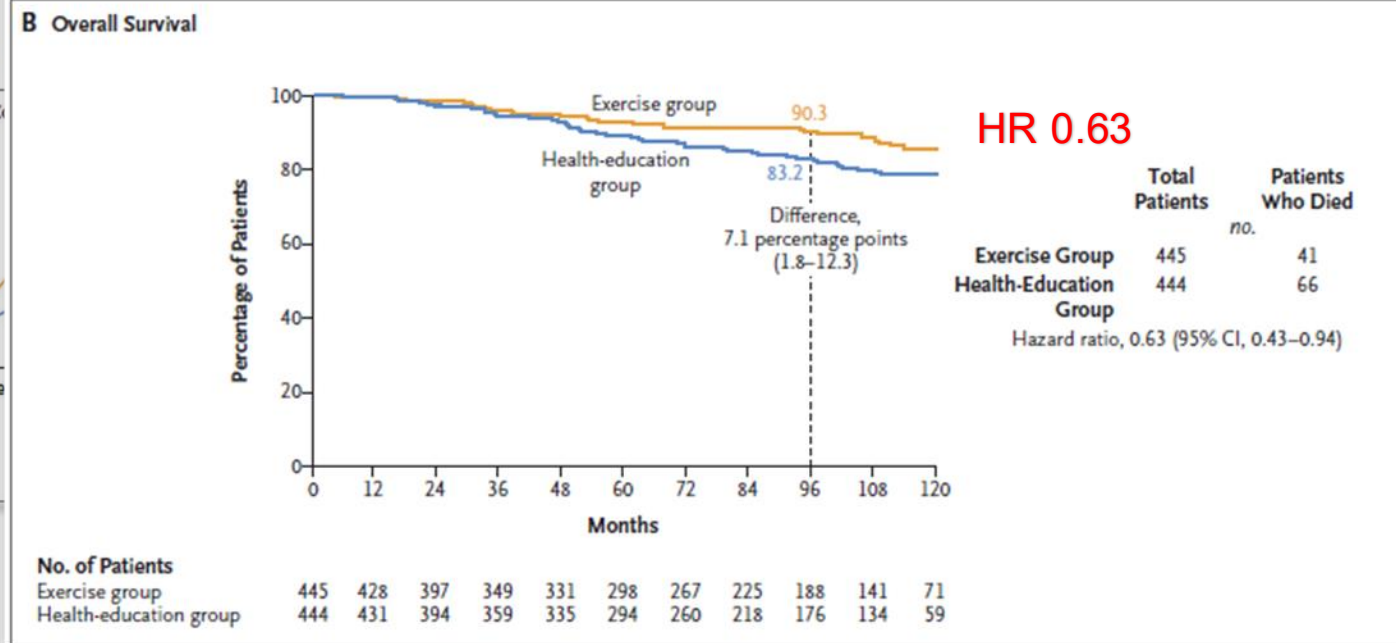
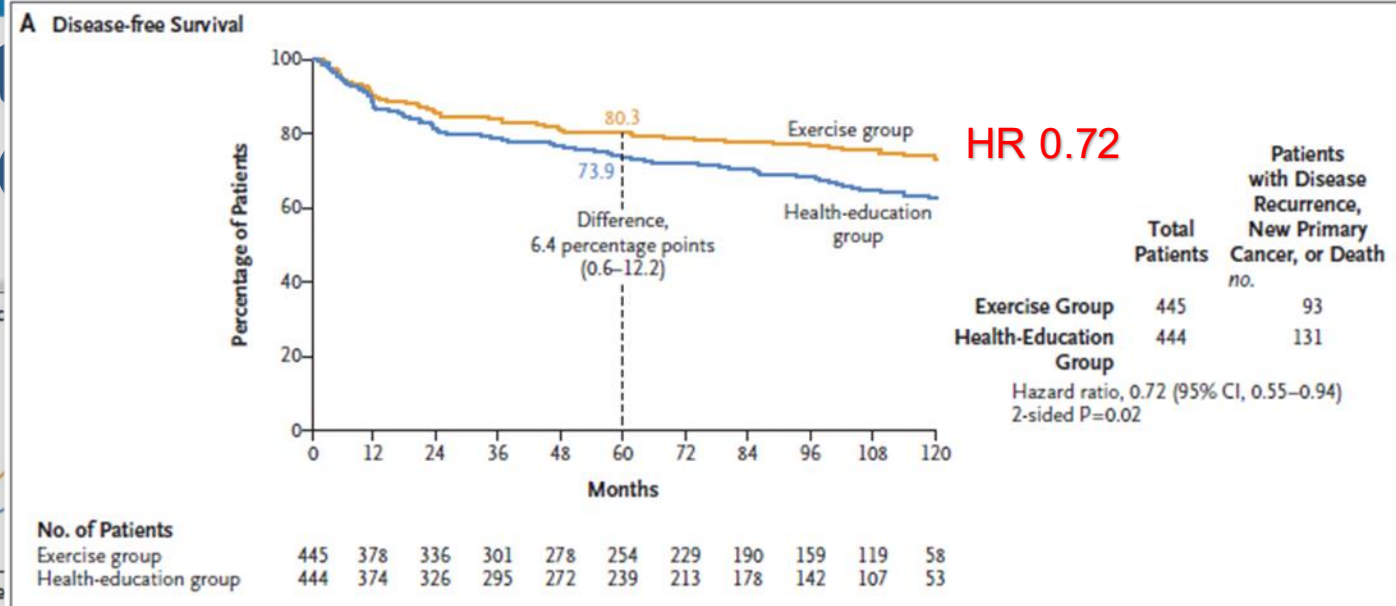
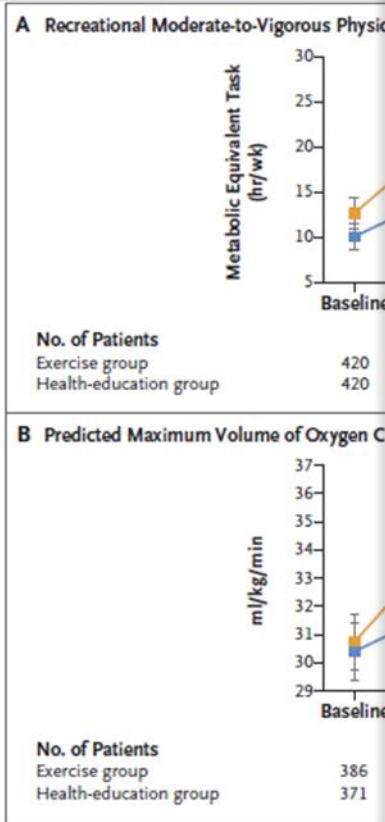
P value for adjusted between-group difference

.01

.03

AMA Oncol. 2021)

Colon Health (CHALLENGE)

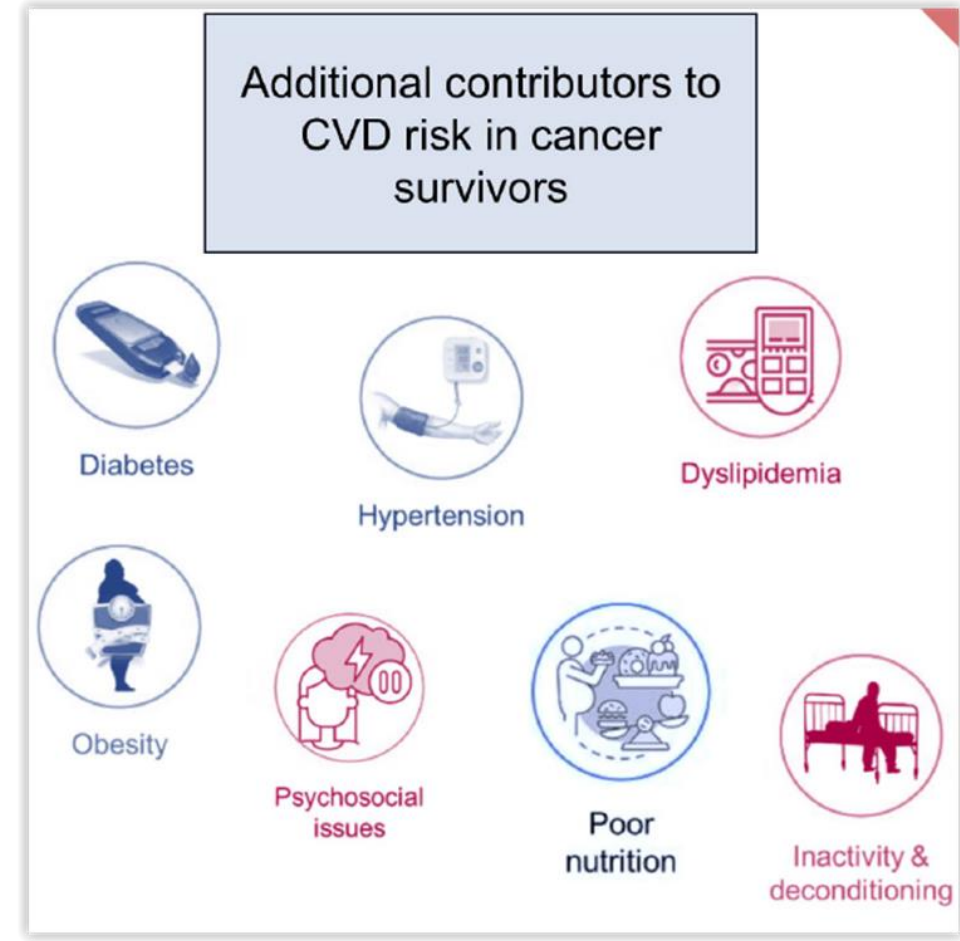
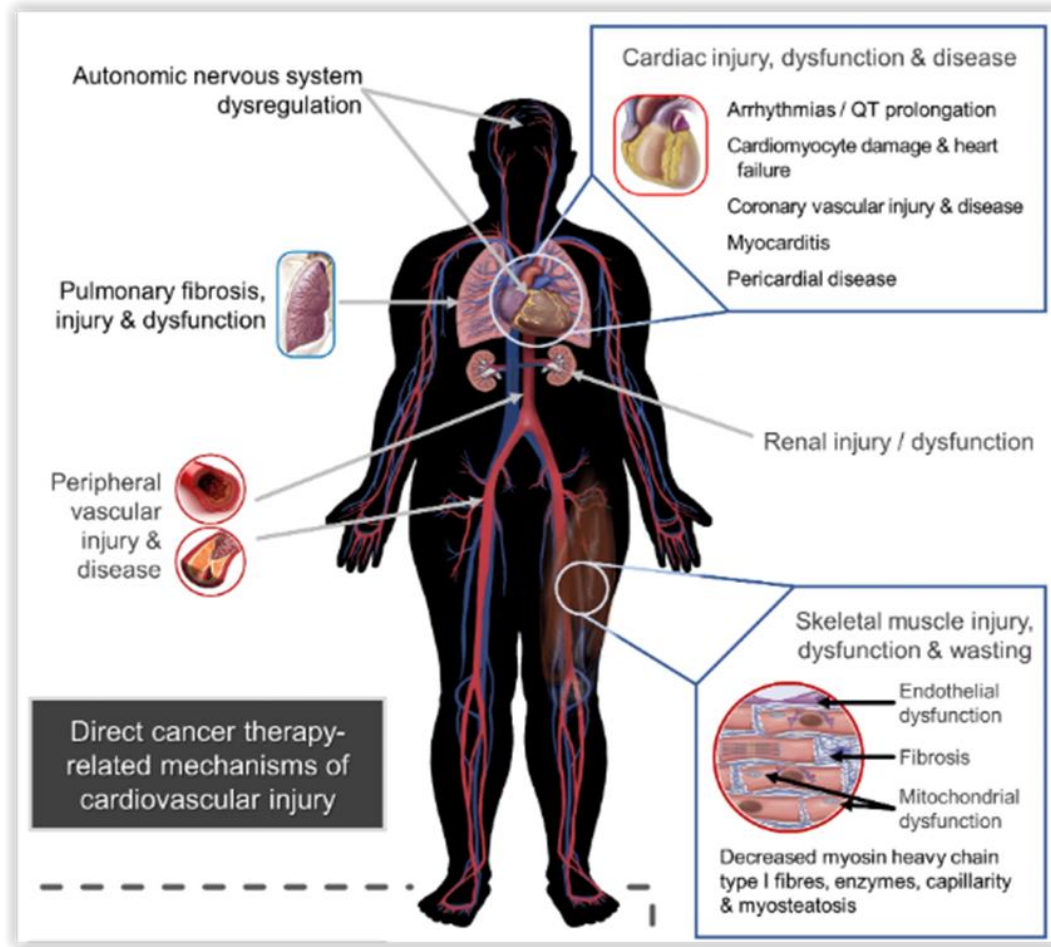


ya KS et al. *N Engl J Med.* 2025 Jul)





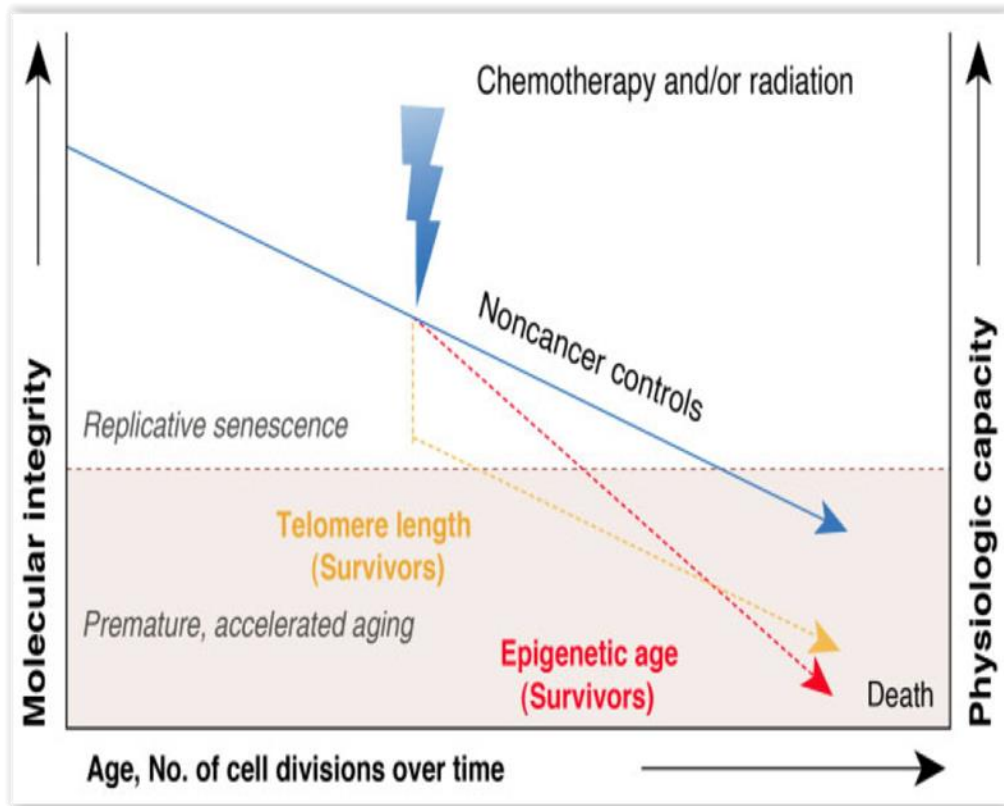
CORE: mechanisms and contributors to cancer therapy-related CVD risk



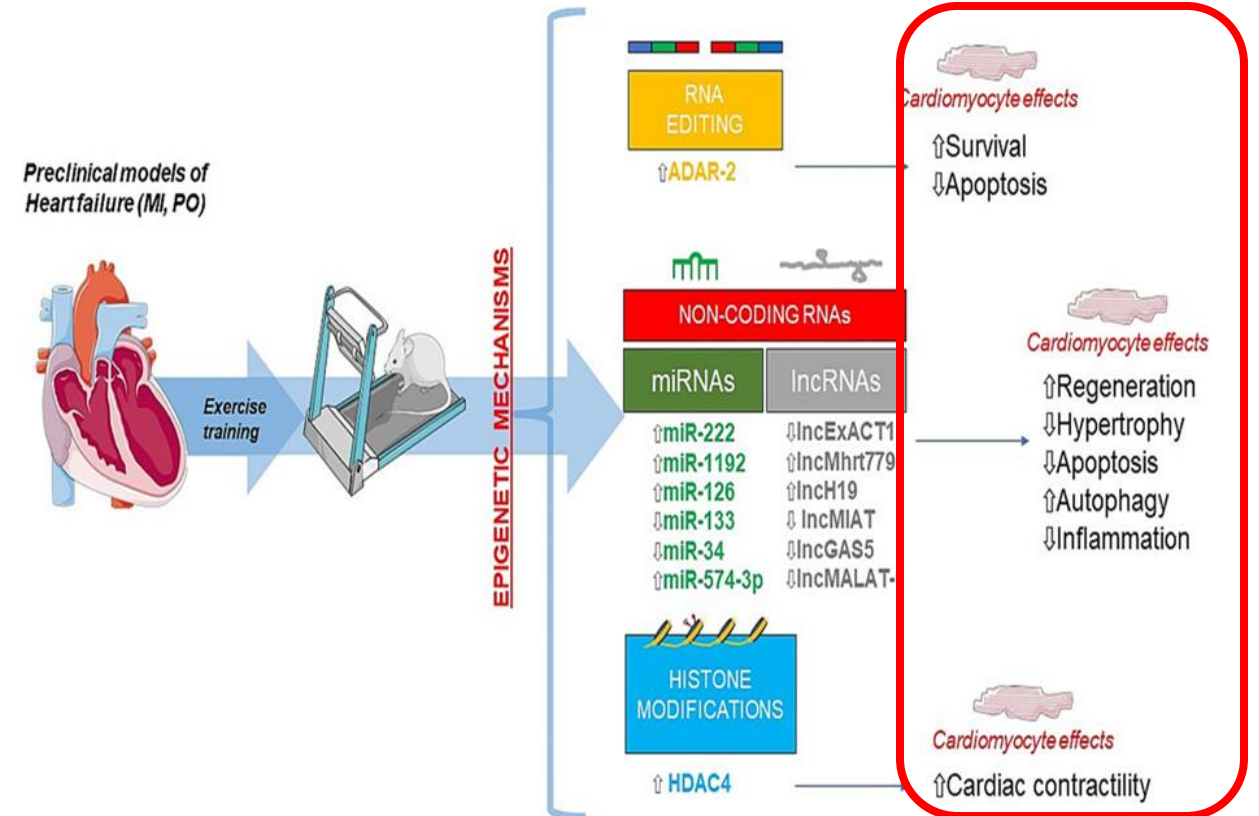
(Adams SC et al. *Eur Heart J.* 2025 Aug)



Epigenetic age acceleration and countermeasures



(Qin N et al. *J Natl Cancer Inst.* 2020)



(Visco V et al. *Int J Cardiol.* 2025 Jun)



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Referral to CORE

- Close and strong cooperation between oncologists and CORE staff, especially with the cardiologist who is the coordinator. The competence of the two professionals in evaluating the risk of treatment-related CVD is critical.
- Individuals with CVRF and/or with previous CVD, also if developed after the basal cancer diagnosis.
- Pediatric cancer survivors should be considered for CORE on the basis of prior high-risk exposures.
- Patients undergoing potentially cardio toxic CT or RT, especially if they have or develop, CVRFs (smoking, hypertension, diabetes, obesity, dyslipidemia):
 1. high-dose anthracycline (e.g., doxorubicin ≥ 250 mg / m², epirubicin ≥ 600 mg / m²) and high-dose radiotherapy ≥ 30 Gy;
 2. low dose anthracyclines + low dose radiotherapy;
 3. low dose anthracycline followed by trastuzumab.
 4. low dose anthracycline or trastuzumab +2 CVRF and age >60 y, or low LVEF and CT.

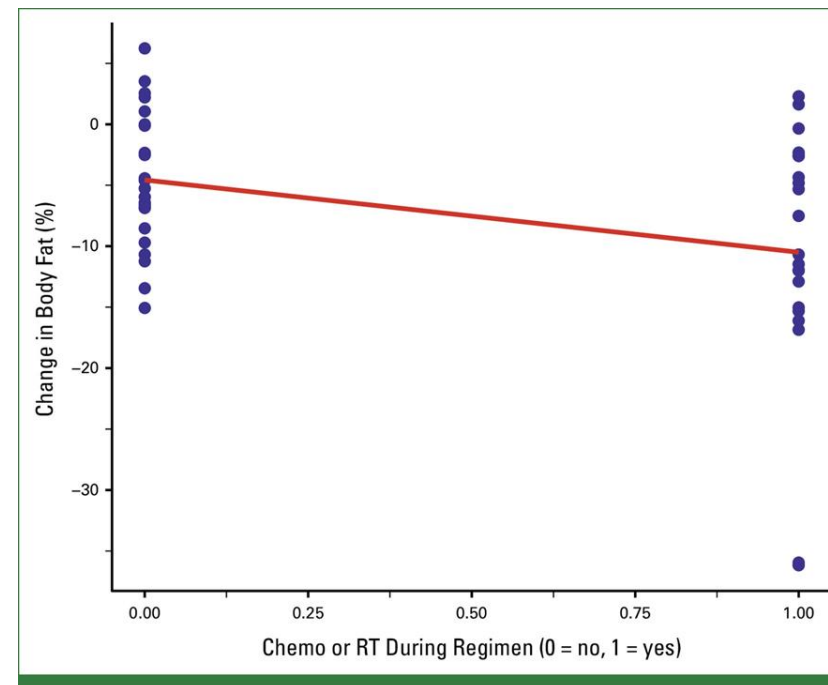
(Gilchrist SC et al. *Circulation*. 2019; Venturini E et al. *Panminerva Med*. 2021)



Obiettivi del Protocollo

1. Counselling dei FRC preesistenti o comparsi dopo la diagnosi di cancro; controllo della ipertensione arteriosa, del diabete e della dislipidemia. Stop del fumo di sigaretta.
2. Ottimizzare la terapia farmacologica, della MCV, preesistente o acquisita, e/o della compromissione asintomatica del ventricolo sinistro.
3. Ridurre il rischio di eventi CV legati alle terapie anticancro.
4. Organizzare sedute di training strutturato e supervisionato adeguate in numero e durata per aumentare la CF e ridurre i sintomi della malattia neoplastica e gli effetti collaterali delle terapie oncologiche (aumentare autonomia, indipendenza e QoL).
5. Limitare le ripercussioni psicologiche (ansia, depressione, perdita della autostima) legate alla malattia oncologica, tramite un programma strutturato di supporto psicologico e quando necessario psichiatrico. Fornire supporto psicosociale.
6. Educare il paziente ad una dieta protettiva (mediterranea). Controllo del peso, non solo valutando l'IMC, ma anche la composizione corporea per determinare la massa corporea grassa e magra, evitando la comparsa di obesità e sindrome metabolica.

Change in Body Fat



(Carpenter DJ et al. *JCO Oncol Pract.* 2025 May)



Il Protocollo ASLNO Toscana

- Oncologo compila apposito modulo condiviso (storia oncologica e le relative terapie, FRC e/o la MCV coesistente).
- Visita cardiologica con ECG sarà integrata da ecocardiogramma e da valutazione ergometrica per pianificare il training in palestra. Se HF utile valutazione ergo-spirometrica.
- Il programma ha una durata di 24 sessioni, articolate in 3 accessi settimanali di 1 ora. In casi particolari (HFrEF, severa compromissione della CRF/forza/sarcopenia) è allungato sino a 36 sessioni.
- La seduta di training al cicloergometro avviene sotto controllo telemetrico e con periodiche rilevazioni della pressione: il training (aerobico e HITT) è integrato da quello di resistenza e dagli esercizi calistenici.





Con chi iniziare? Alcune proposte (EBM)

- Carcinoma della mammella: terapia con antracicline, trastuzumab, pertuzumab, taxani, inibitori delle aromatasi e radioterapia locoregionale.
- Pazienti con cancro della prostata, del colon e linfomi e altre neoplasie ematologiche. Necessaria una consensus locale tra Oncologi e Cardiologi.
- CT e RT + almeno due FRC (fumo di sigaretta, ipertensione, dislipidemia, diabete, obesità) o età maggiore di 60aa all'inizio del trattamento, o storia di MCV.





Conclusioni

- Nei pazienti oncologici è essenziale un'attenta valutazione di base del rischio CV, l'ottimizzazione della funzione cardiaca e la prevenzione delle complicanze cardiovascolari da CT/RT
- La CORE è un approccio multidisciplinare ed efficace nel ridurre l'impatto biologico delle terapie oncologiche
- La rete di centri di riferimento è fondamentale per la gestione dei pazienti
- RCTs sono necessari per valutare l'efficacia delle strategie di prevenzione (prehabilitazione, riabilitazione cardiaca)
- **CHALLENGES**
- *The time window for cardiovascular prevention in oncology is narrow*



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