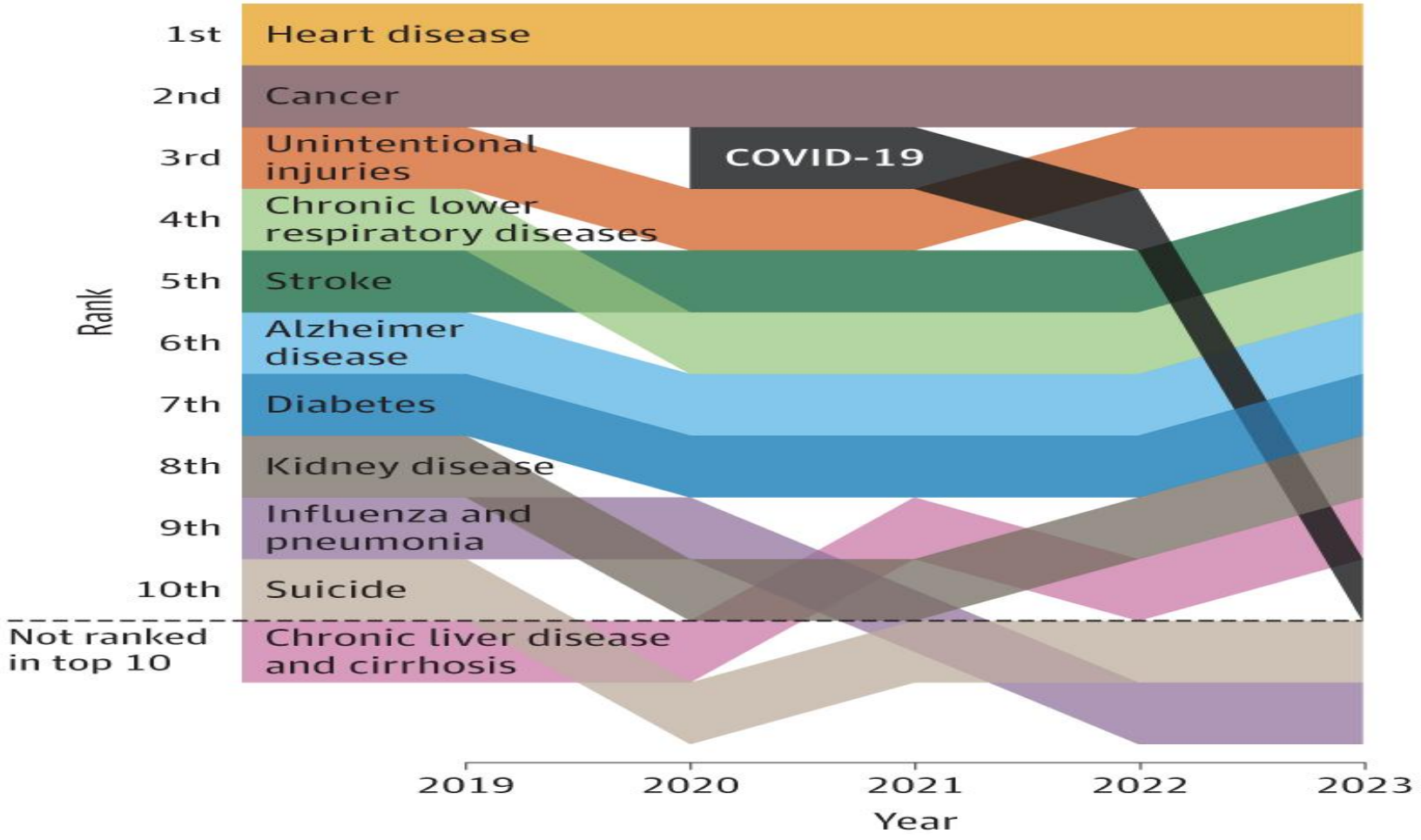
ACTEL 30 gennaio 2025

L’approccio moderno per prevenire i tumori e invecchiare in salute

Federico Bozzetti

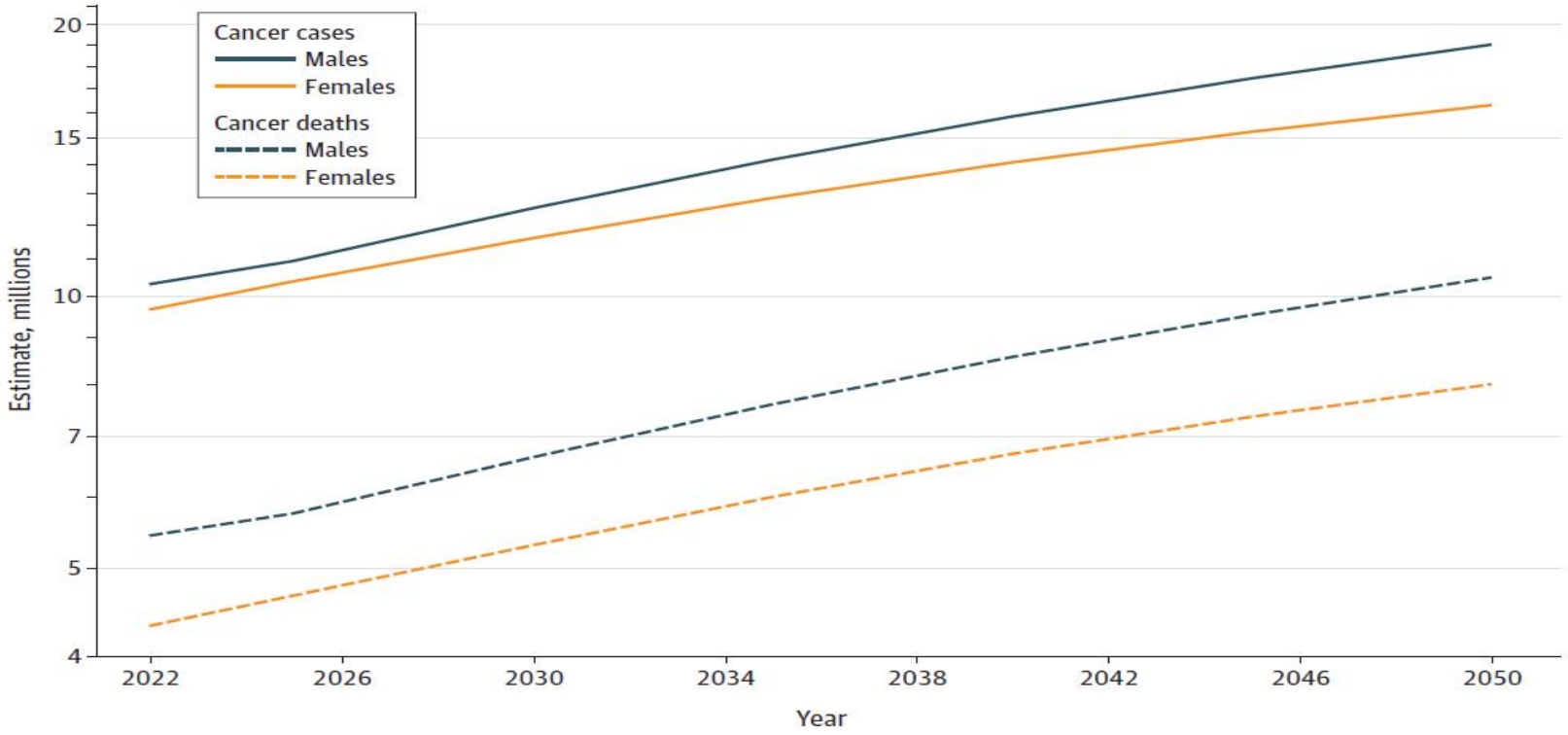
Ahmad et al. Leading Causes of Death in the US, 2019-2023. JAMA. 2024 Aug 8. doi: 10.1001/jama.2024.15563



Bizuayehu et al. Global Disparities of Cancer and Its Projected Burden in 2050. JAMA Netw Open. 2024 Nov 4;7(11):e2443198. doi: 10.1001/jamanetworkopen.2024.43198.

Nel 2024 in Italia 390.100 nuove diagnosi di tumore

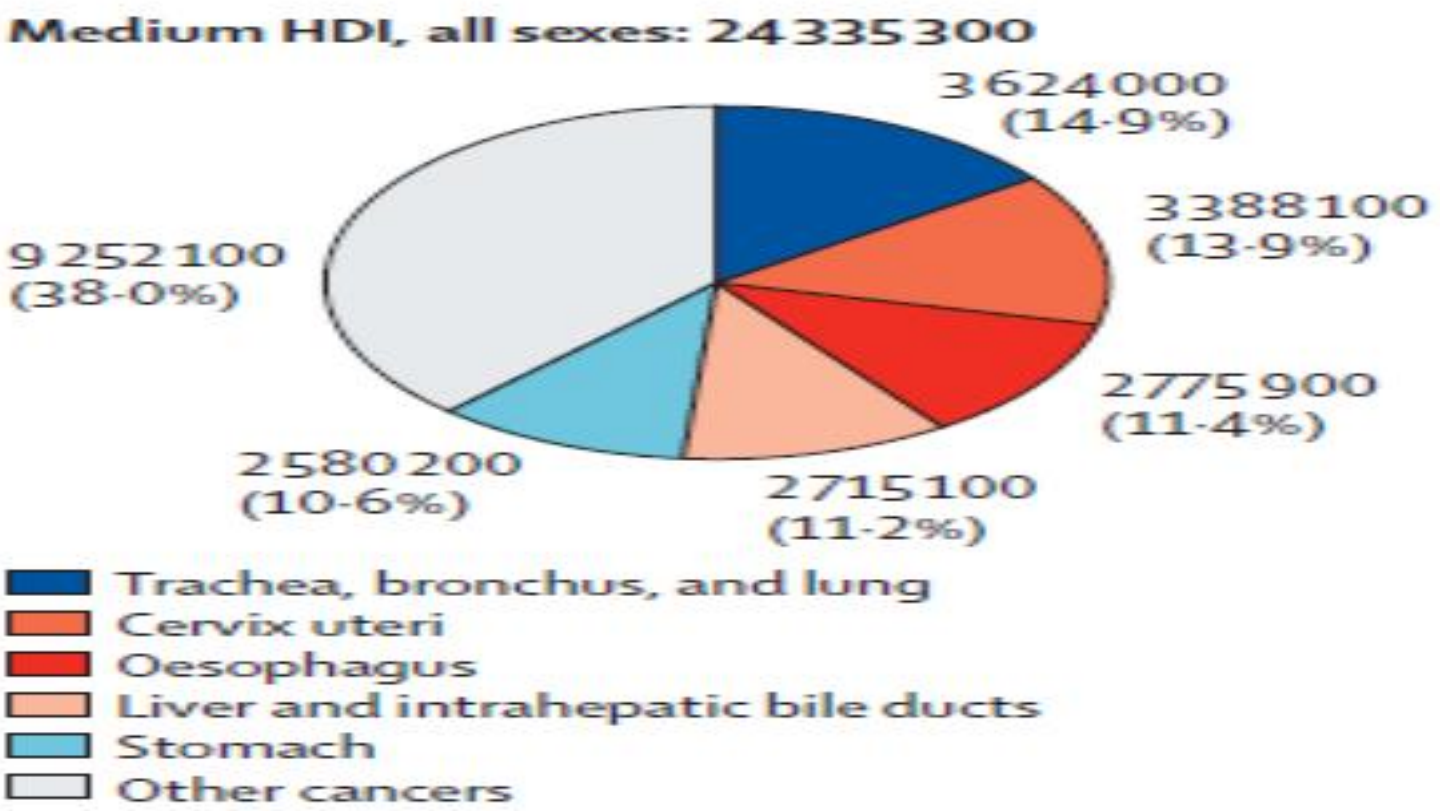
Figure 1. Worldwide Projected Number of Cancer Cases and Deaths by Sex, 2022-2050



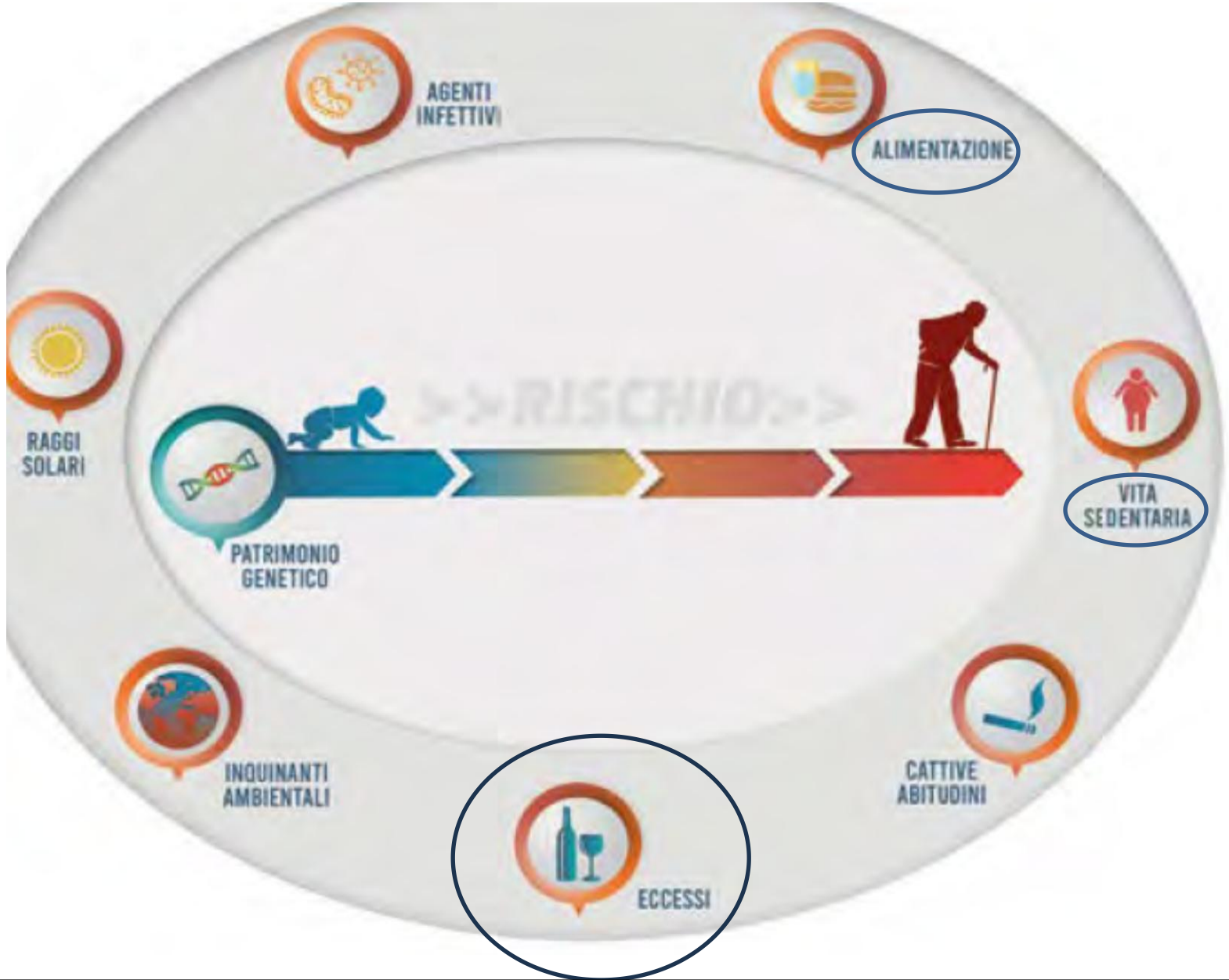
Lloyd-Jones et al. Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association. Circulation. 2022 Aug 2;146(5):e18-e43.

Frick et al. Quantitative estimates of preventable and treatable deaths from 36 cancers worldwide: a population-based study.
Lancet Glob Health 2023; 11: e1700–12

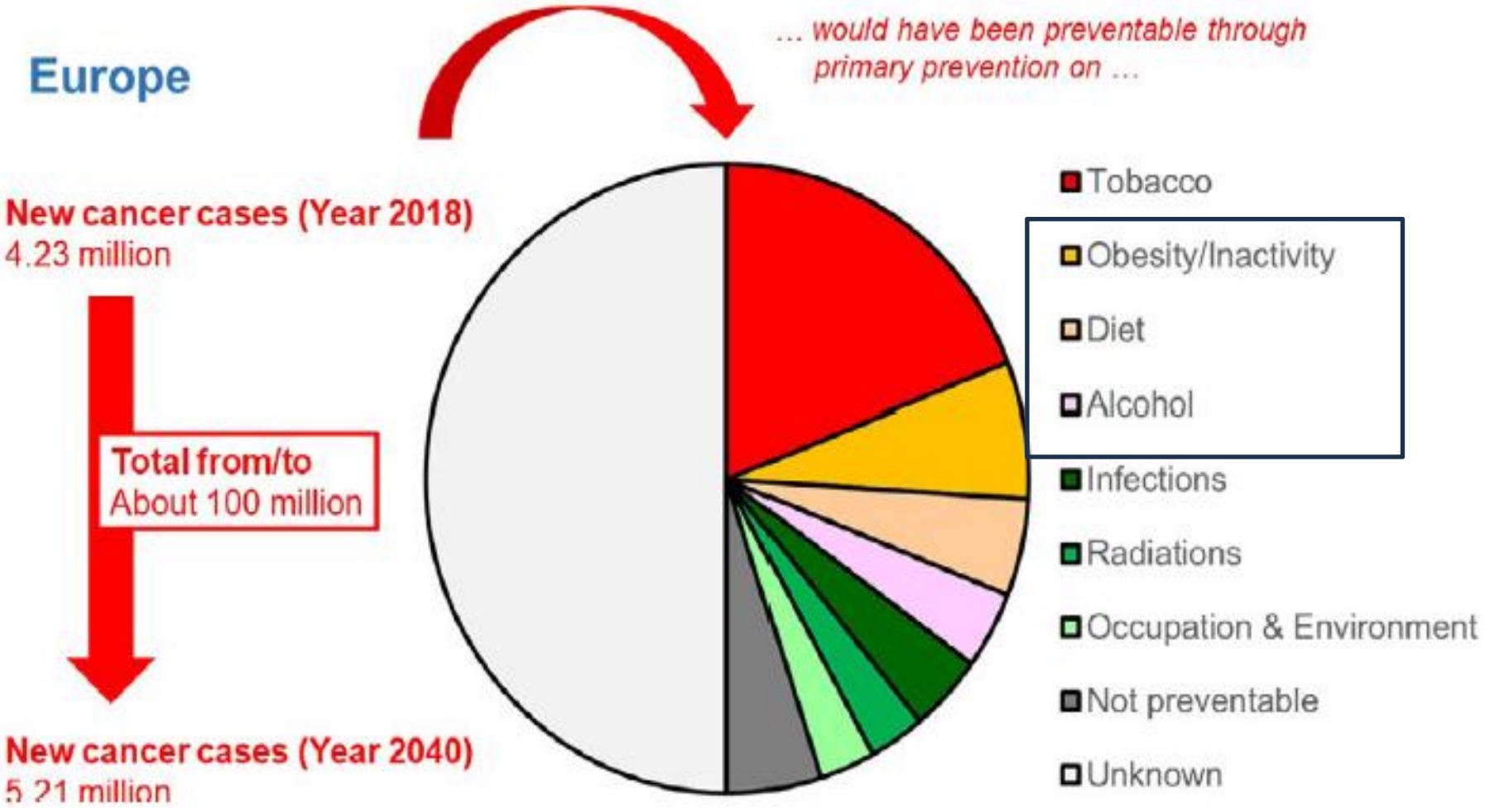
This study estimates premature deaths at ages 30–69 years and distinguishes these as deaths that are preventable (avertable through primary or secondary prevention)



¾ circa dei tumori nel nostro paese puo' esser prevenuto

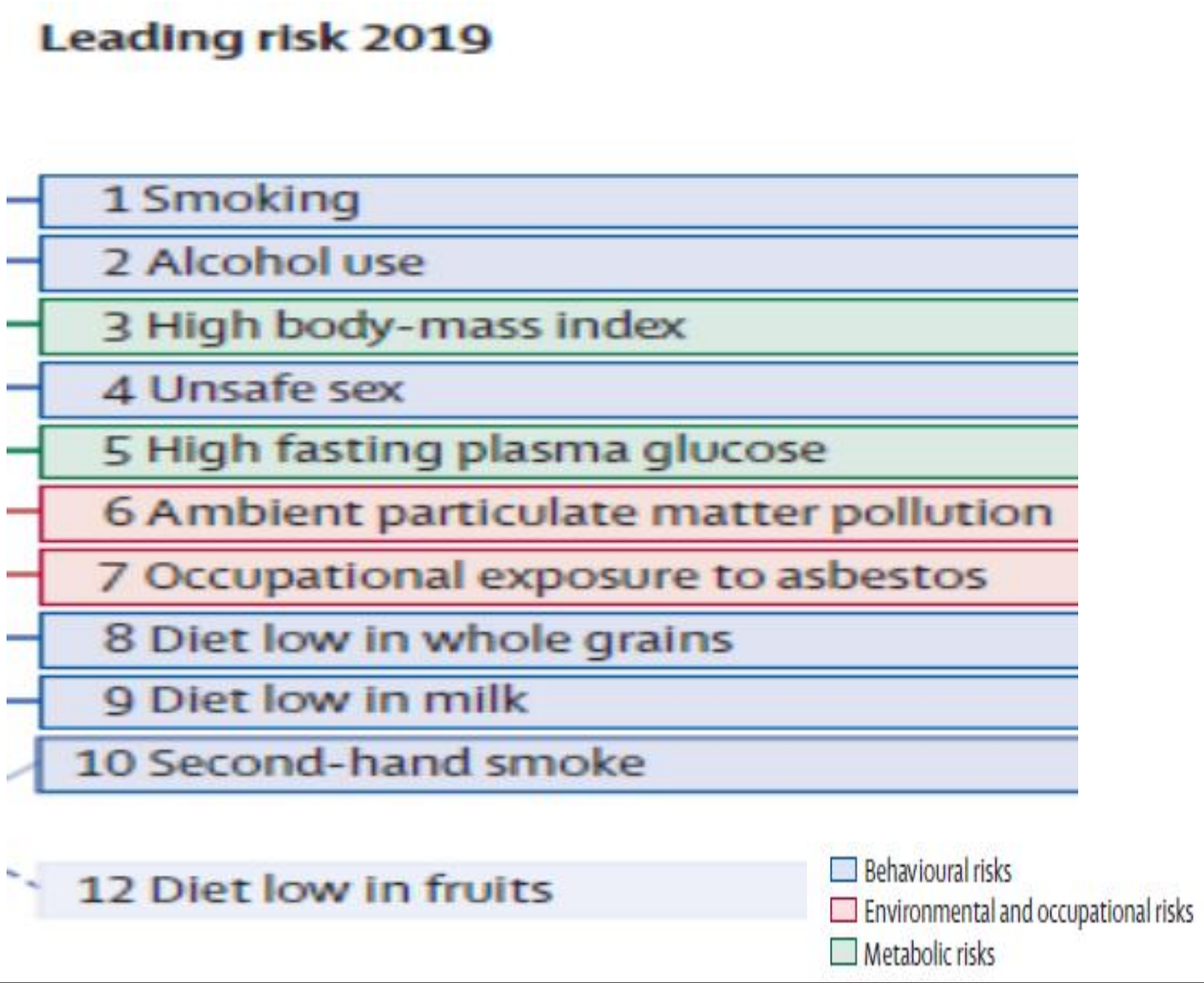

AGENTI INFETTIVI
ALIMENTAZIONE
RAGGI SOLARI
>>RISCHIO>>
VITA SEDENTARIA
PATRIMONIO GENETICO
INQUINANTI AMBIENTALI
CATTIVE ABITUDINI
ECCESSI

Berns et al. Towards a cancer mission in Horizon Europe: recommendations. Molecular Oncology 14 (2020) 1589–1615



The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019
GBD 2019 Cancer Risk Factors Collaborators*Lancet 2022; 400: 563–91

1 tumore su 3 e' causato dal fumo
Il fumo e' responsabile di 17 tipi di tumore
L' alcool e' reponsabile in Europa del 4% di tutte le morti
L'obesita' e' responsabile di 13 tipi di tumore



Su 281.300 morti per tumore in Italia nel 2021,
il 23% poteva esser evitato

Fattore di rischio	Uomini	Donne
Fumo	33.569	9.922
Consumo elevato di bevande alcoliche	8.031	4.811
Fattori nutrizionali	6.328	4.323
Eccesso ponderale	3.808	3.173
Inattività fisica	392	606
Combinato*	44.083	20.385

TABELLA 4. Numero di morti evitabili per tumori attribuibili a stili di vita individuali in Italia

(Fonte: Carreras G et al, Epi Prev 2019)

*La somma non corrisponde al totale combinato per la possibile concomitanza di stili di vita individuali.

ARGOMENTI

- Dieta scorretta
- Abuso di alcool
- Alterazione del metabolismo: sovrappeso/iperglicemia
- Inattivita’ fisica

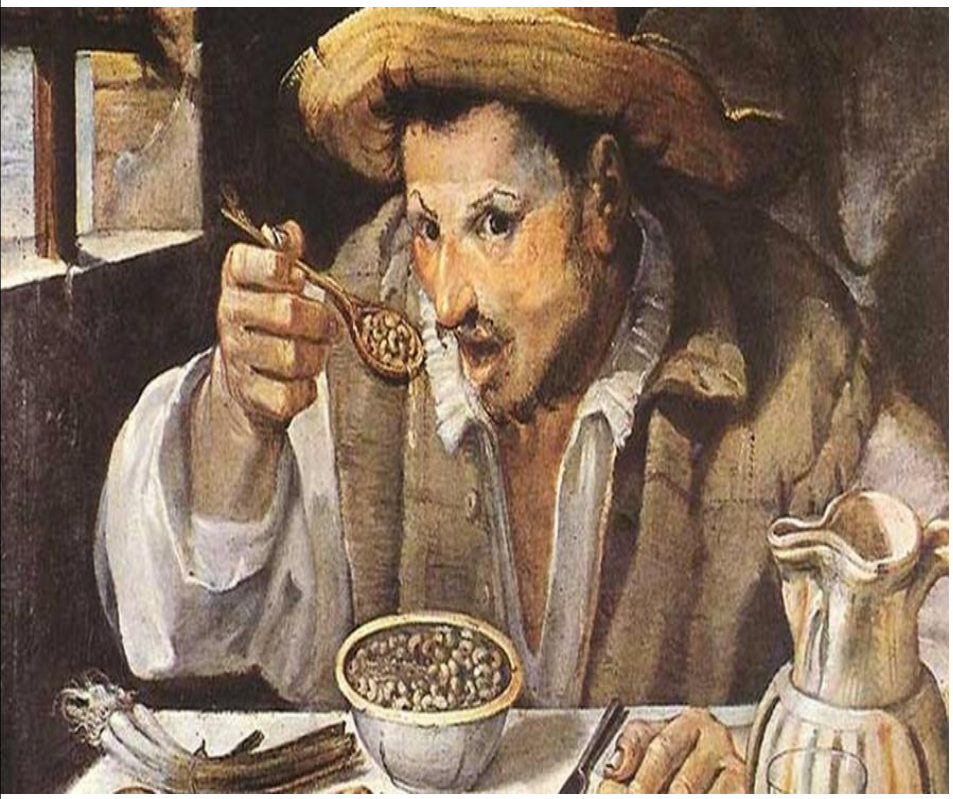
ARGOMENTI

- Dieta scorretta

  - abuso di carne rossa, cibi (ultra)processati, bevande zuccherate
  - carenza di frutta, verdura, carote e broccoli

- Abuso di alcool
- Alterazione del metabolismo: sovrappeso/iperglicemia
- Inattivita’ fisica

DIETA SCORRETTA E CANCRO



Fattori confondenti nel concetto di alimentazione come fattore di rischio oncologico

- Nutrienti nocivi (es. acidi grassi saturi)
- Alimenti nocivi (es. salumi)
- Processamento degli alimenti (es. cibi ultra-processati)

Esempi di cibi ultraprocessati

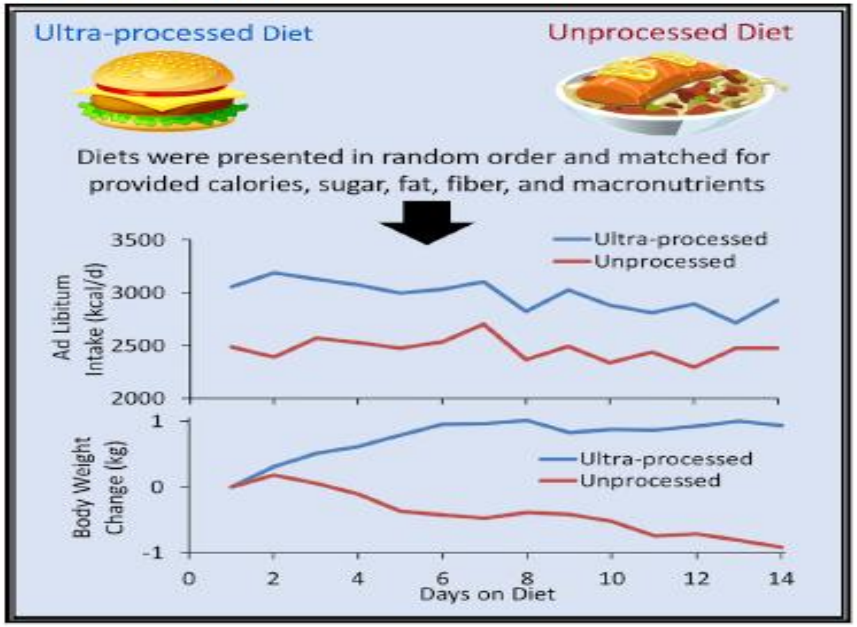
semel in anno licet insanire

Clinical and Translational Report

Cell Metabolism

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of *Ad Libitum* Food Intake

Graphical Abstract



Authors

Kevin D. Hall, Alexis Ayuketah, Robert Brychta, ..., Peter J. Walter, Shanna Yang, Megan Zhou

Correspondence

kevinh@nih.gov

In Brief

Hall et al. investigated 20 inpatient adults who were exposed to ultra-processed versus unprocessed diets for 14 days each, in random order. The ultra-processed diet caused increased *ad libitum* energy intake and weight gain despite being matched to the unprocessed diet for presented calories, sugar, fat, sodium, fiber, and macronutrients.

Highlights

- 20 inpatient adults received ultra-processed and unprocessed diets for 14 days each
- Diets were matched for presented calories, sugar, fat, fiber, and macronutrients
- *Ad libitum* intake was ~500 kcal/day more on the ultra-processed versus unprocessed diet
- Body weight changes were highly correlated with diet differences in energy intake

Definizione di cibi ultraprocessati

- I cibi ultraprocessati sono soprattutto preparati industriali confezionati alla scopo di massimizzarne la palatabilita' ed il consumo, mediante una combinazione di ingredienti ad alta densita' calorica e additivi chimici con finalita' cosmetiche.

- I cibi ultraprocessati hanno per lo piu' una scarsa qualita' nutrizionale, contengono molti zuccheri, sali, grassi saturi, mentre sono poveri di fibre, minerali e vitamine.

- L'impatto negativo sul nostro stato di salute, pero', e' parzialmente indipendente dal loro contenuto in nutrienti.

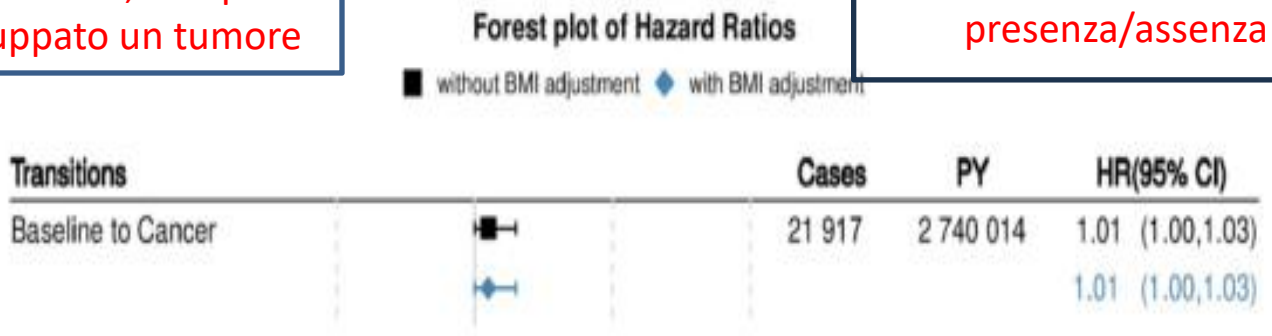
Scala NOVA

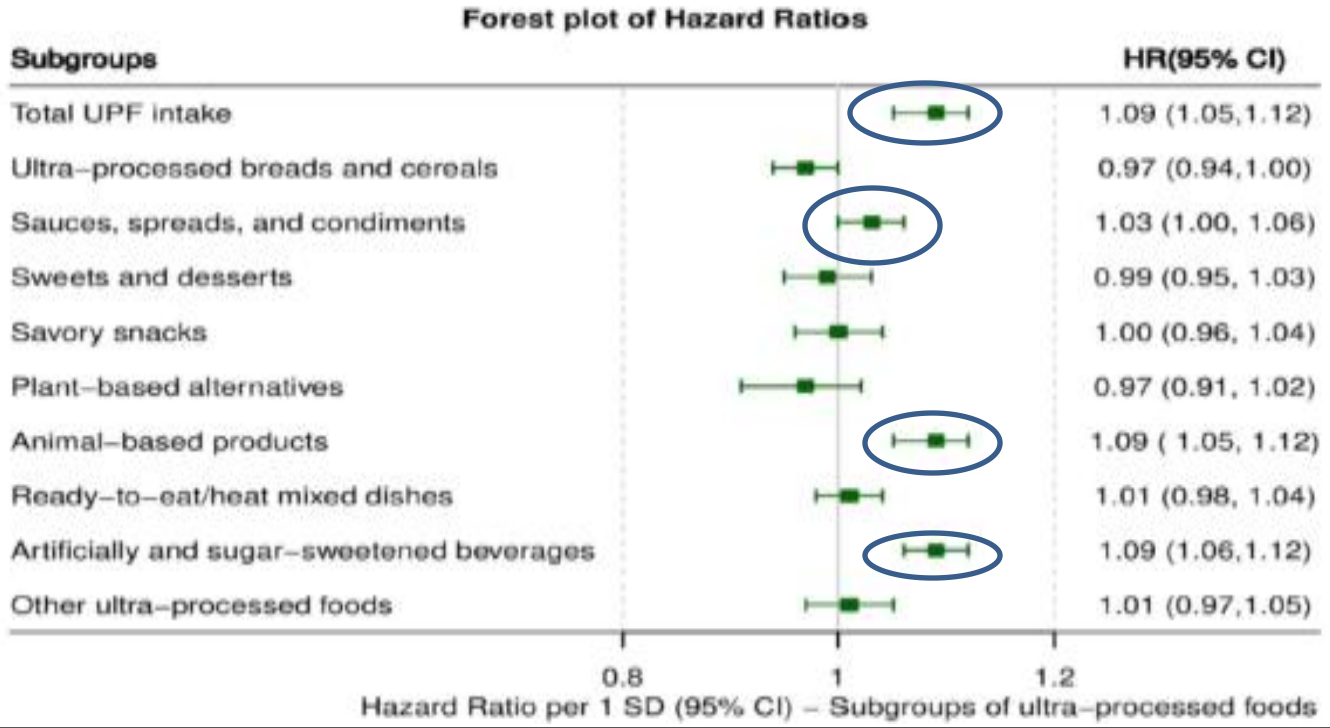
- La categoria **Nova 1** è costituita da **alimenti naturali o minimamente lavorati** come verdure, legumi, latte pastorizzato, farina integrale.
- I **Nova 2** sono **ingredienti parzialmente trasformati** attraverso metodi come pressatura e macinatura dei cereali: le farine raffinate, il sale, lo zucchero, il burro o l'olio d'oliva.
- Il **gruppo 3** comprende **verdure in scatola**, legumi in barattolo, carne o pesce essiccati o affumicati, formaggio tradizionale, certi tipi di frutta secca in busta: sono prodotti preparati **con conservanti o antiossidanti naturali** (quali sale o acido citrico) ma con ingredienti riconoscibili.
- **È nella classe Nova 4 che rientrano gli alimenti ultra-processati**. Secondo l'OMS si definiscono tali quei prodotti che, oltre alle aggiunte di zuccheri, sale, oli e grassi, **contengono sostanze che non si usano nelle preparazioni casalinghe.** A essere ultra-processati spesso sono crocchette di pollo surgelate, barrette proteiche, molti salumi e insaccati e le bibite "zero", per l'aggiunta di edulcoranti chimici artificiali.

Cordova et al. Consumption of ultra-processed foods and risk of multimorbidity of cancer and cardiometabolic diseases: a multinational cohort study. The Lancet Regional Health - Europe 2023;•: 100771

Studio su 266 666 partecipanti, seguiti per 11 anni, dei quali l'8% ha sviluppato un tumore

HR = rapporto di rischio:
Il tasso di rischio di un evento in presenza/assenza di un fattore

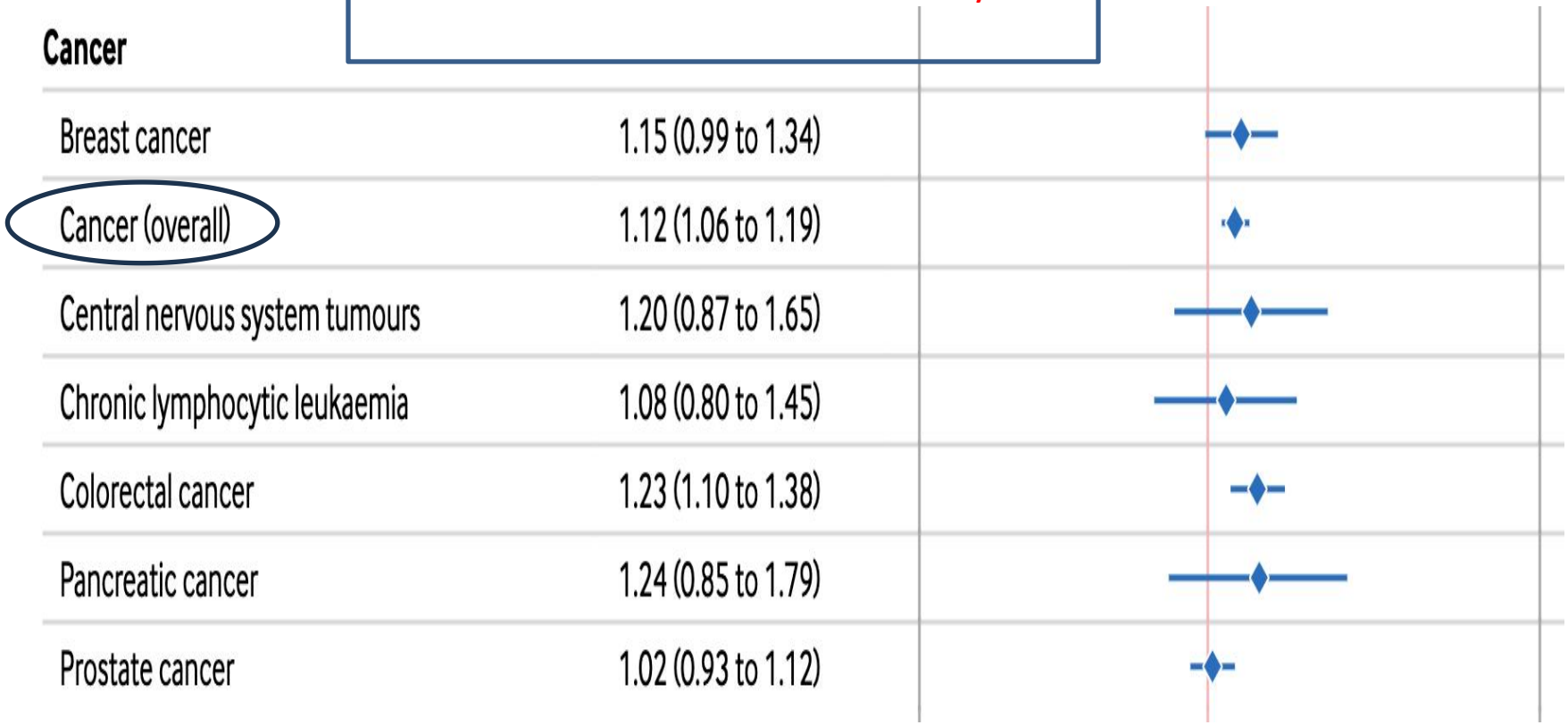




Lane et al. Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. BMJ. 2024 Feb 28;384:e077310.

A study of 9 888 373 partecipants

Odds ratio for cancer mortality



Cancer	
Breast cancer	1.15 (0.99 to 1.34)
Cancer (overall)	1.12 (1.06 to 1.19)
Central nervous system tumours	1.20 (0.87 to 1.65)
Chronic lymphocytic leukaemia	1.08 (0.80 to 1.45)
Colorectal cancer	1.23 (1.10 to 1.38)
Pancreatic cancer	1.24 (0.85 to 1.79)
Prostate cancer	1.02 (0.93 to 1.12)

Bevel et al. Association of Food Deserts° and Food Swamps°° With Obesity-Related Cancer Mortality in the US. JAMA Oncol. 2023 Jul 1;9(7):909-916

° aree abitative lontane da rifornimenti di cibi sani, °°ambienti urbani con pochi negozi di alimentari ma diverse opzioni alimentari non nutrienti come negozi all'angolo o ristoranti fast-food

Table 2. Association of Food Environment Measures With Obesity-Related Cancer Mortality Among 3038 US Counties or County Equivalents

Variable	Odds of high obesity-related cancer mortality		
	Counties with low obesity-related cancer mortality, No. (%) (n = 2283)[a,b]	Counties with high obesity-related cancer mortality, No. (%) (n = 758)[a,b]	AOR (95% CI)
Food desert			
Low	800 (35.0)	215 (28.4)	1 [Reference]
Moderate	781 (34.2)	235 (31.0)	1.12 (0.91-1.38)
High	708 (31.0)	307 (40.5)	1.59 (1.29-1.94)
Food swamp (comprehensive RFEI)			
Low	794 (34.8)	219 (28.9)	1 [Reference]
Moderate	785 (34.4)	229 (30.2)	1.15 (0.93-1.43)
High	708 (31.0)	306 (40.4)	1.77 (1.43-2.19)

RFEI: indice ambientale alimentare al dettaglio

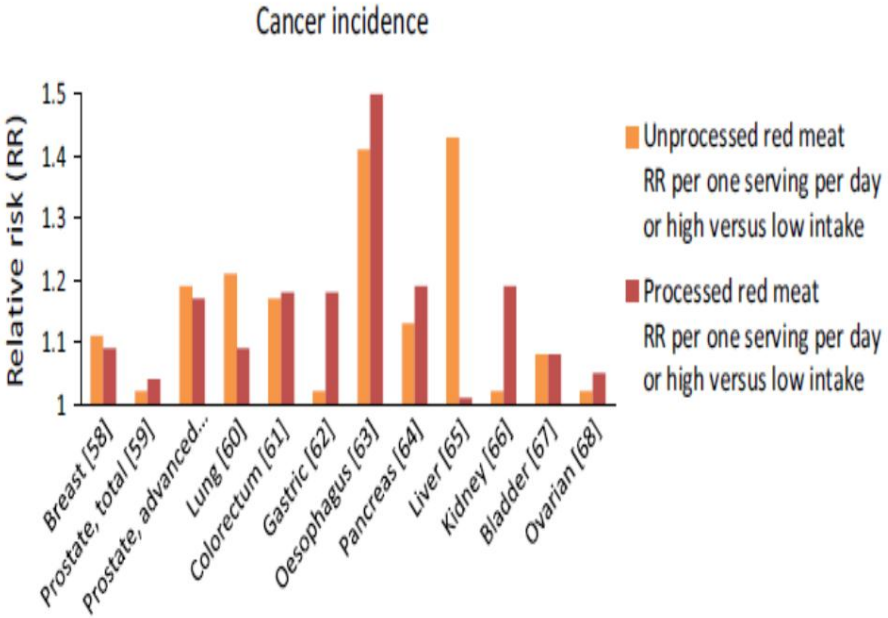
Klieman N et al. Food processing and cancer risk in Europe: results from the prospective EPIC cohort study. Lancet Planet Health. 2023 Mar;7(3):e219-e232.

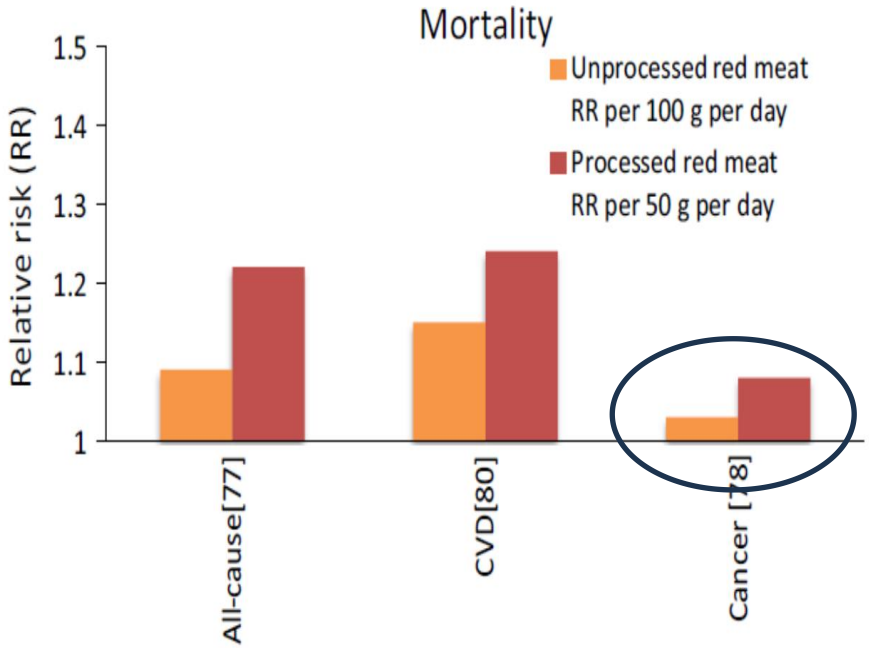
Dati su 450 111 partecipanti raccolti tra il 1991 e il 2011

La sostituzione del 10% dei cibi processati con una ugual quantità di cibi minimamente processati si associa ad una riduzione del rischio globale di cancro rispettivamente del 4% e precisamente:

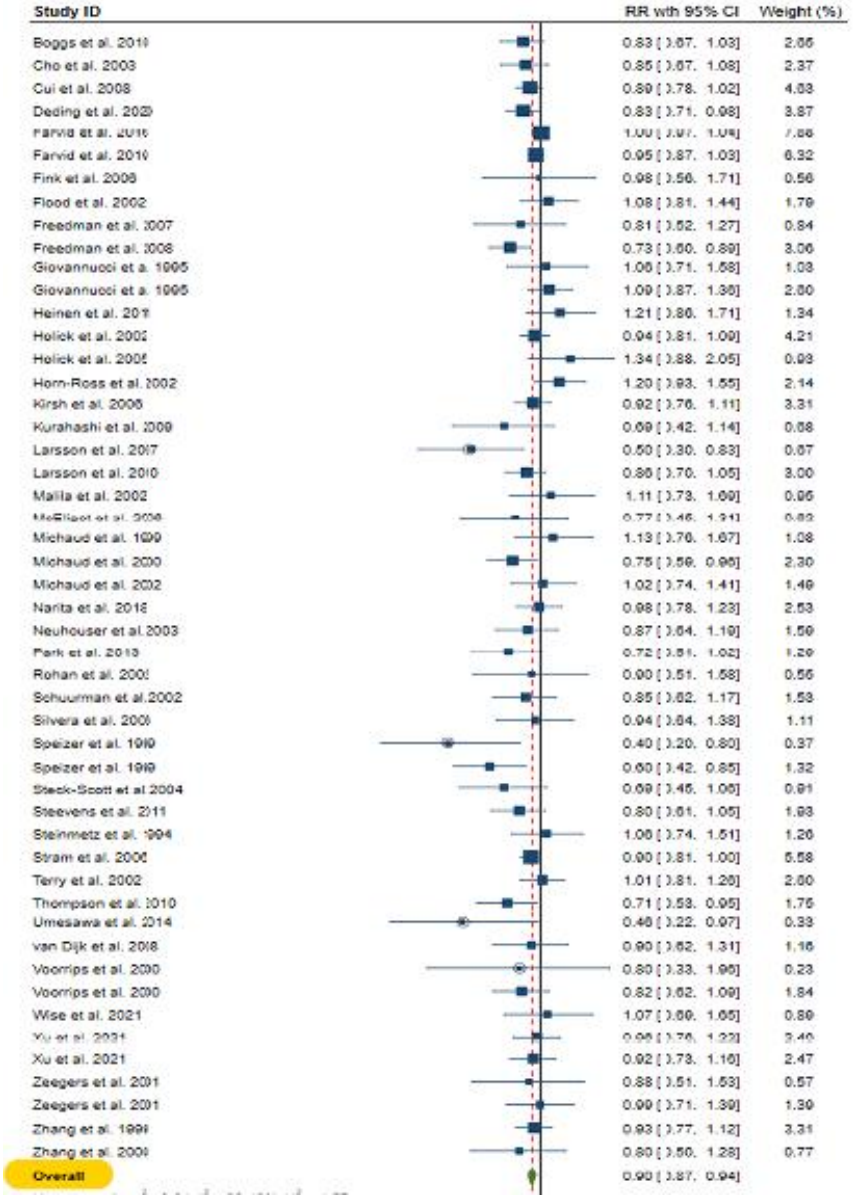
- Tumori della testa e del collo: **20%**
- Tumore spinocellulare dell'esofago: **43%**
- Tumore del colon cancer: **12%**
- Tumore del retto **: 10%**
- Tumore del fegato: **23%**
- Tumore della mammella postmenopausa: **7%**

Wolk et al. Potential health hazards of eating red meat
J Intern Med 2017; 281: 106–122.



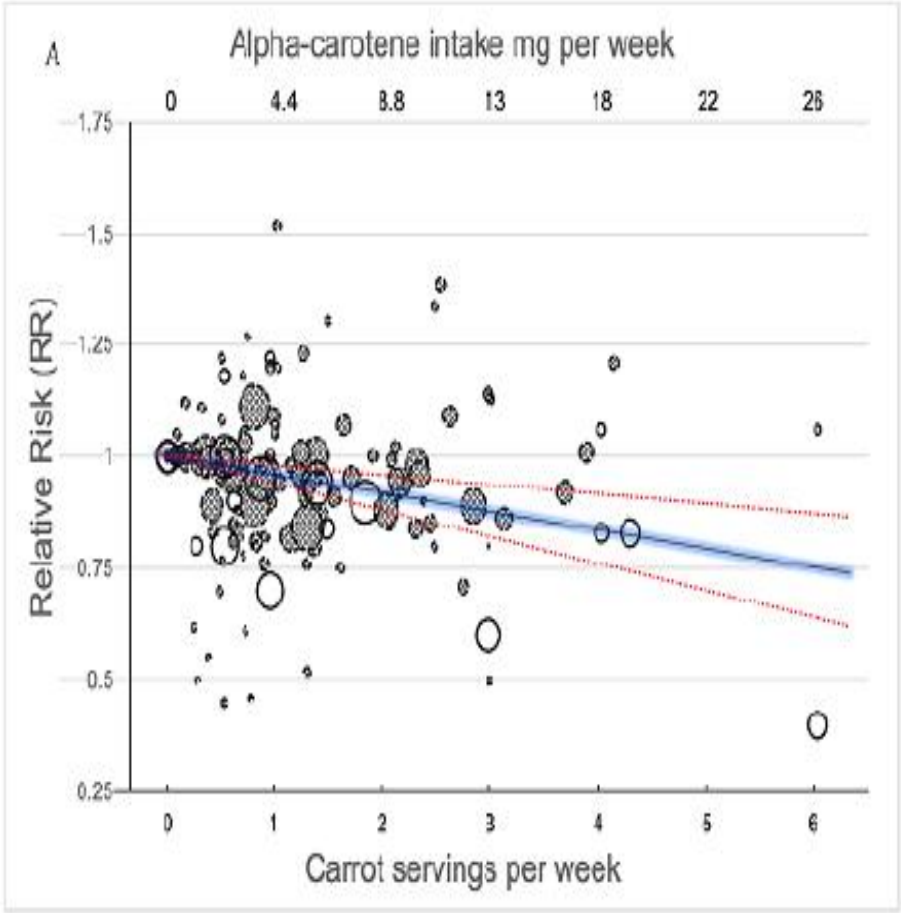


Ojobor CC et al. Carrot intake is consistently negatively associated with cancer incidence: A systematic review and meta-analysis of prospective observational studies. Crit Rev Food Sci Nutr. 2023 Dec 17:1-13



50 prospective studies with 52 000 cases recording carrot intake, the cancer-risk was substantially reduced (R= 0.90)

1 serving = 80 g di carote



Baladia et al. Broccoli Consumption and Risk of Cancer: An Updated Systematic Review and Meta-Analysis of Observational Studies. Nutrients. 2024 May 23;16(11):1583.

- E’ uno studio di 770 734 soggetti
- Una grande assunzione di broccoli e’ quella di un consumo giornaliero o settimanale, mentre una bassa assunzione e’ quella nulla o non settimanale o comunque meno di 3 volte al mese.
- Una grande assuzione di broccoli si associa auna ridotta incidenza di tumore del pancreas, della prostata e della vescica.

L'organizzazione Mondiale della Sanità consiglia di non superare i 350 g di carne rossa e lavorata alla settimana, di cui 50 g di salumi e insaccati.

Nel mese di ottobre 2015 l'**International Agency for Research on Cancer (IARC)** di Lione, un'agenzia dell'Organizzazione mondiale della sanità che valuta e classifica le prove di cancerogenicità delle sostanze, ha definito la **carne rossa** come probabilmente cancerogena (classe 2A della classificazione dello IARC) e la **carne rossa lavorata** (**insaccati** e **salumi**) come sicuramente cancerogena (classe 1 della classificazione dello IARC).

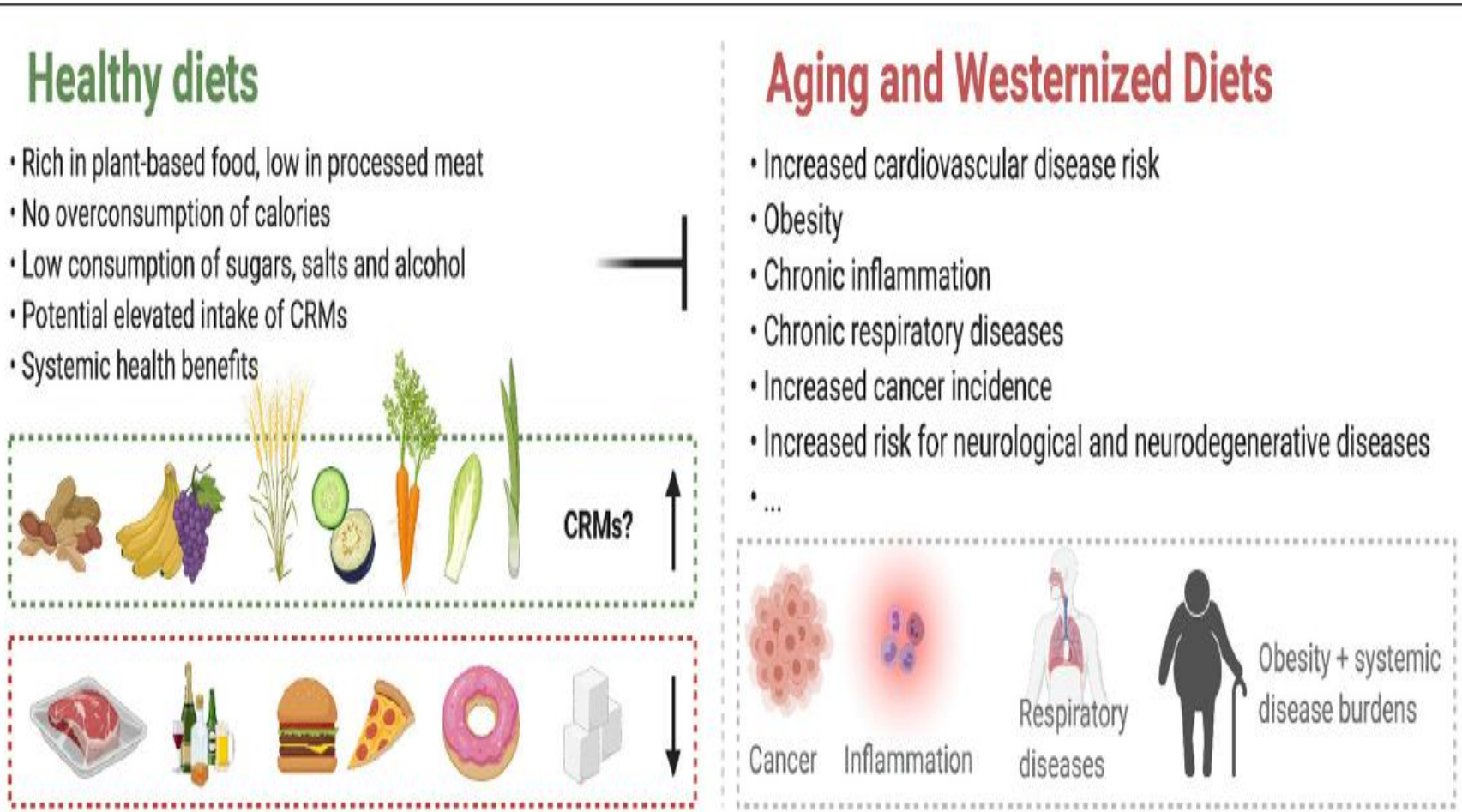


FIGURE 1 | Healthy diet plans stand opposite to Westernized Diets and counteract age-associated deteriorations. The contribution of Caloric Restriction Mimetics (CRMs) to the effects of healthy diets is currently largely undetermined.

in sintesi

Una dieta corretta comprende:

- Frutta e verdura (in particolare carote e broccoli)
- Carne bianca e pesce
- Cibi con zuccheri complessi

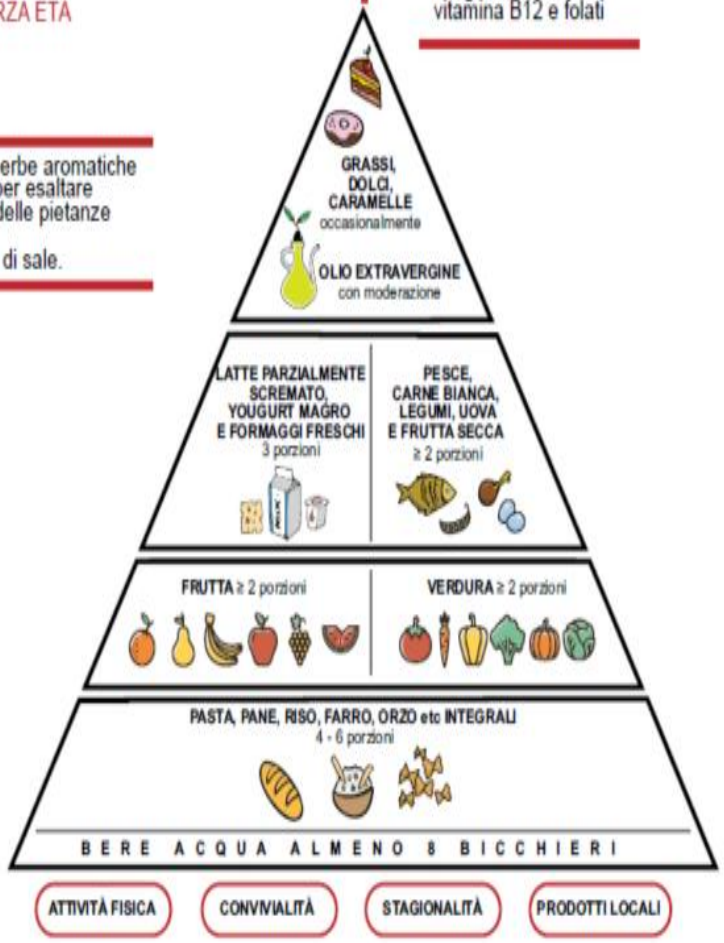
Una dieta corretta non comprende:

- Carne rossa (manzo) e lavorata in quantita' ≥350 g di carne rossa e lavorata alla settimana, di cui 50 g di salumi e insaccati
- Prodotti ultraprocessati (prodotti animali, bevande zuccherate/dolcificate)
- Cibi ricchi di zuccheri semplici e grassi saturi

PIRAMIDE ALIMENTARE
GIORNALIERA
DELLA TERZA ETÀ

Supplementazione
con vitamina D
Da valutare l'eventuale
integrazione con
vitamina B12 e folati

Utilizzare erbe aromatiche
e spezie per esaltare
il sapore delle pietanze
e ridurre
l'aggiunta di sale.



DIETA OCCIDENTALE

DIETA MEDITERRANEA

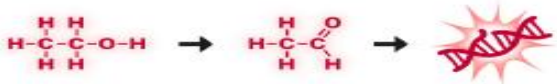
ARGOMENTI

- Dieta scorretta
- Abuso di alcool
- Alterazione del metabolismo: sovrappeso/iperglicemia
- Inattivita’ fisica

Four ways alcohol can cause cancer

MECHANISM A

Alcohol breaks down into **acetaldehyde** which damages DNA in multiple ways, causing an increased risk of cancer.



Ethanol (Pure alcohol) → Acetaldehyde → DNA damage

MECHANISM B

Alcohol induces **oxidative stress**, increasing the risk of cancer by damaging DNA, proteins, and cells and increasing inflammation.

Reactive oxygen species → Oxydative stress → DNA, proteins, and lipids damage

MECHANISM C

Alcohol alters **levels of multiple hormones**, including estrogen, which can increase breast cancer risk.

Increases estrogen → Alters breast tissue → DNA damage

MECHANISM D

Alcohol leads to greater absorption of **carcinogens.**

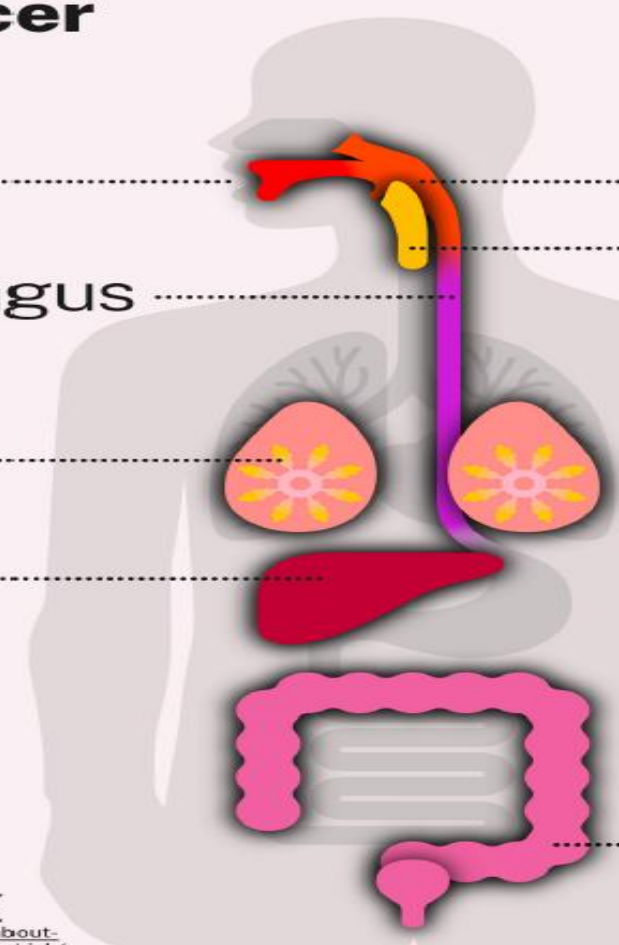
Carcinogens dissolve in alcohol + Alcohol alters cells in mouth and throat → Carcinogens more easily absorbed

*Rumgay et al. (2021) reviewed these four mechanisms through which alcohol can cause cancer along with several other possible pathways that appear to influence cancer risk. These include disruption of one-carbon metabolism, alteration of retinoid metabolism, and impaired immune function among others.

Source: Rumgay H, Murphy N, Ferrari P, Soerjomataram I. Alcohol and Cancer: Epidemiology and Biological Mechanisms. *Nutrients*. Sep 11 2021;13(9) doi:10.3390/nu13093173

Office *of the* U.S. Surgeon General

Consuming alcohol increases the risk of developing at least 7 types of cancer



Mouth
(Oral Cavity)

Throat
(Pharynx)

Voice Box
(Larynx)

Esophagus

Breast
(in Women)

Liver

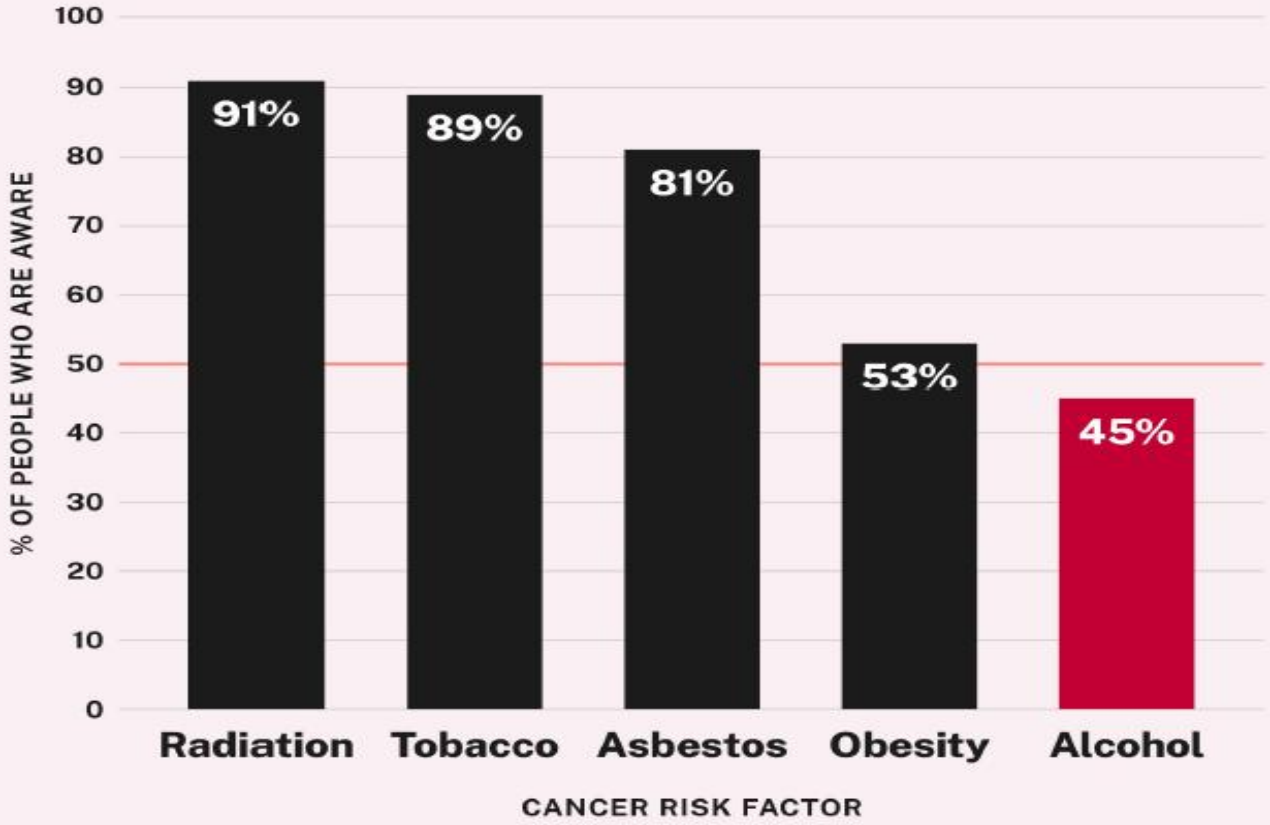
Colon &
Rectum

Source:
"Alcohol and Cancer Risk."
National Cancer Institute.
https://www.cancer.gov/about-cancer/causes-prevention/risk/alcohol/alcohol-fact-sheet

Office *of the*
U.S. Surgeon General

Less than half of Americans are aware that alcohol consumption increases cancer risk

Survey of a nationally representative sample of U.S. adults ages 18 and older*



L’alcool è la II causa di tumori….

- Il 70% degli intervistati pensa effettivamente che l’alcool sia una frequente causa di tumori dopo il fumo e la dieta scorretta, ma…..

- ¼ degli intervistati ritiene che bere un po’ di vino diminuisca il rischio di tumore piuttosto che non berne assolutamente.

741,300 cancer cases worldwide were attributable to alcohol consumption in 2020

The risk of cancer is lower at lower levels of consumption. However, many more people consume ≤2 drinks per day, thus leading to a **similar number of overall cancer cases at lower levels as higher levels of consumption.**

185,100 cancer cases (25.0%)

209,800 cancer cases (28.3%)

192,900 cancer cases (26.0%)

153,400 cancer cases (20.7%)

DAILY ALCOHOL CONSUMPTION

One standard drink in the U.S. contains 14 grams (0.6 fl oz) of pure alcohol:

5 fl oz **wine** or 12 fl oz **beer** or 1.5 fl oz **liquor**

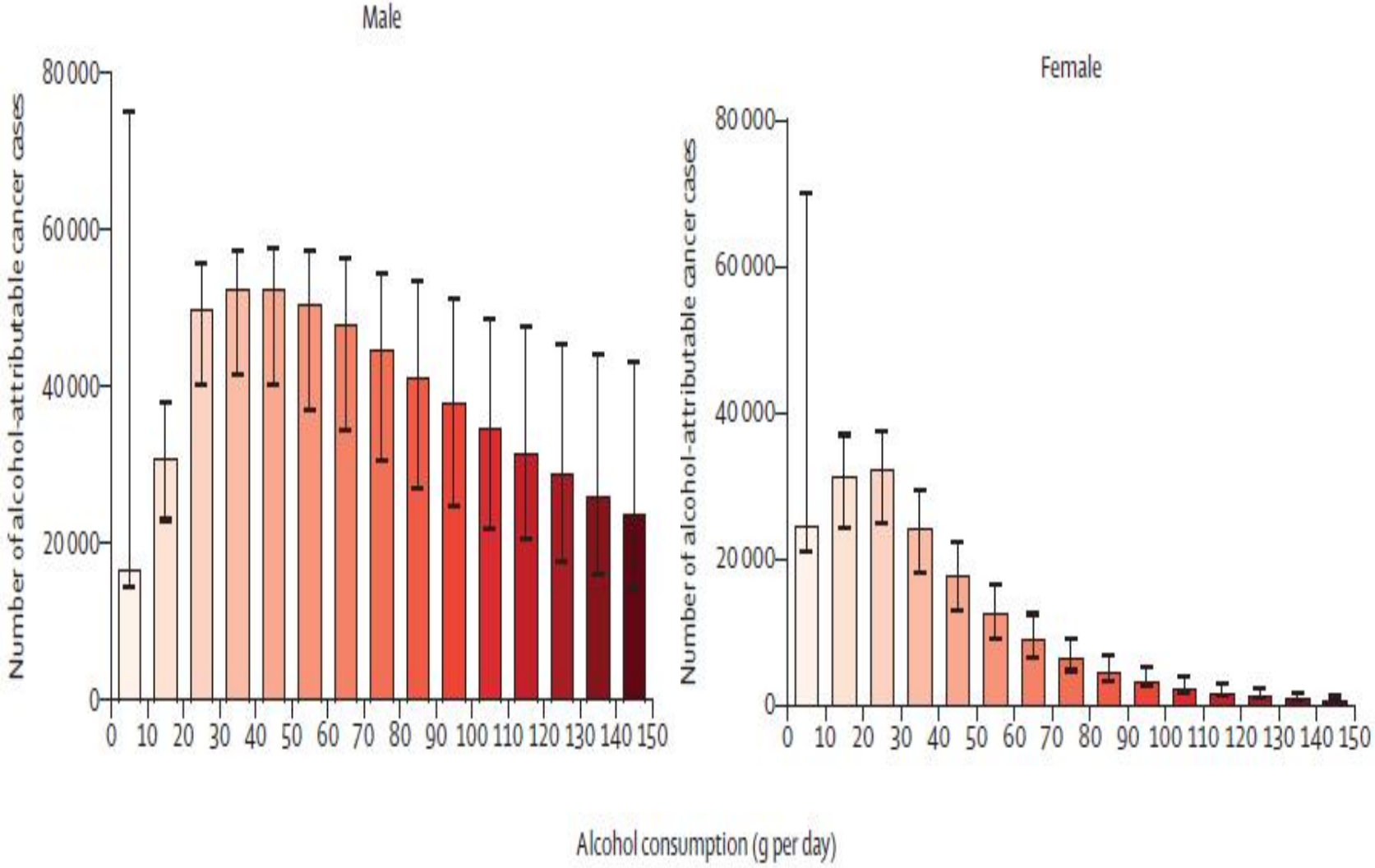
Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study

Harriet Rumgay, Kevin Shield, Hadrien Charvat, Pietro Ferrari, Bundit Sornpaisarn, Isidore Obot, Farhad Islami, Valery E P P Lemmens, Jürgen Rehm, Isabelle Soerjomataram

Summary

Background Alcohol use is causally linked to multiple cancers. We present global, regional, and national estimates of alcohol-attributable cancer burden in 2020 to inform alcohol policy and cancer control across different settings globally.

Lancet Oncol 2021; 22: 1071–80
Published Online



Hydes et al. A comparison of gender-linked population cancer risks between alcohol and tobacco: how many cigarettes are there in a bottle of wine? BMC Public Health. 2019 Mar 28;19(1):316

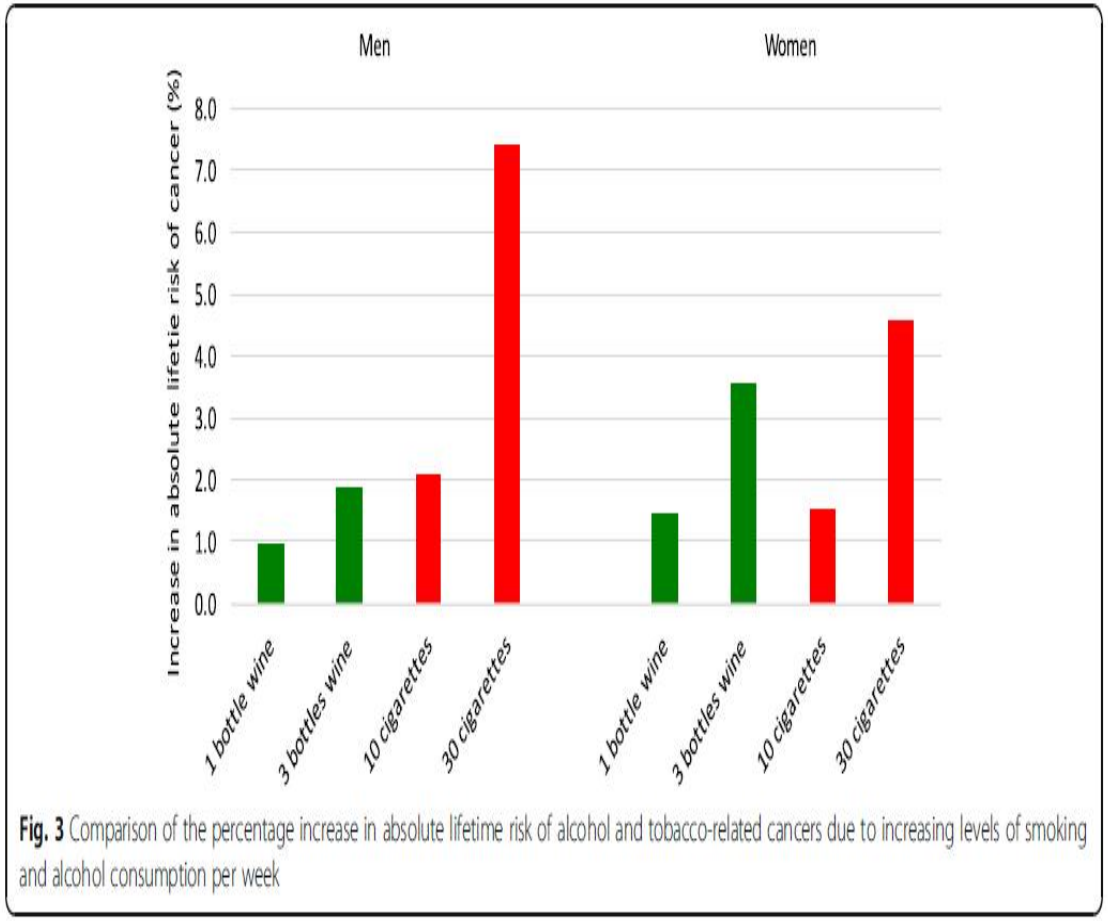
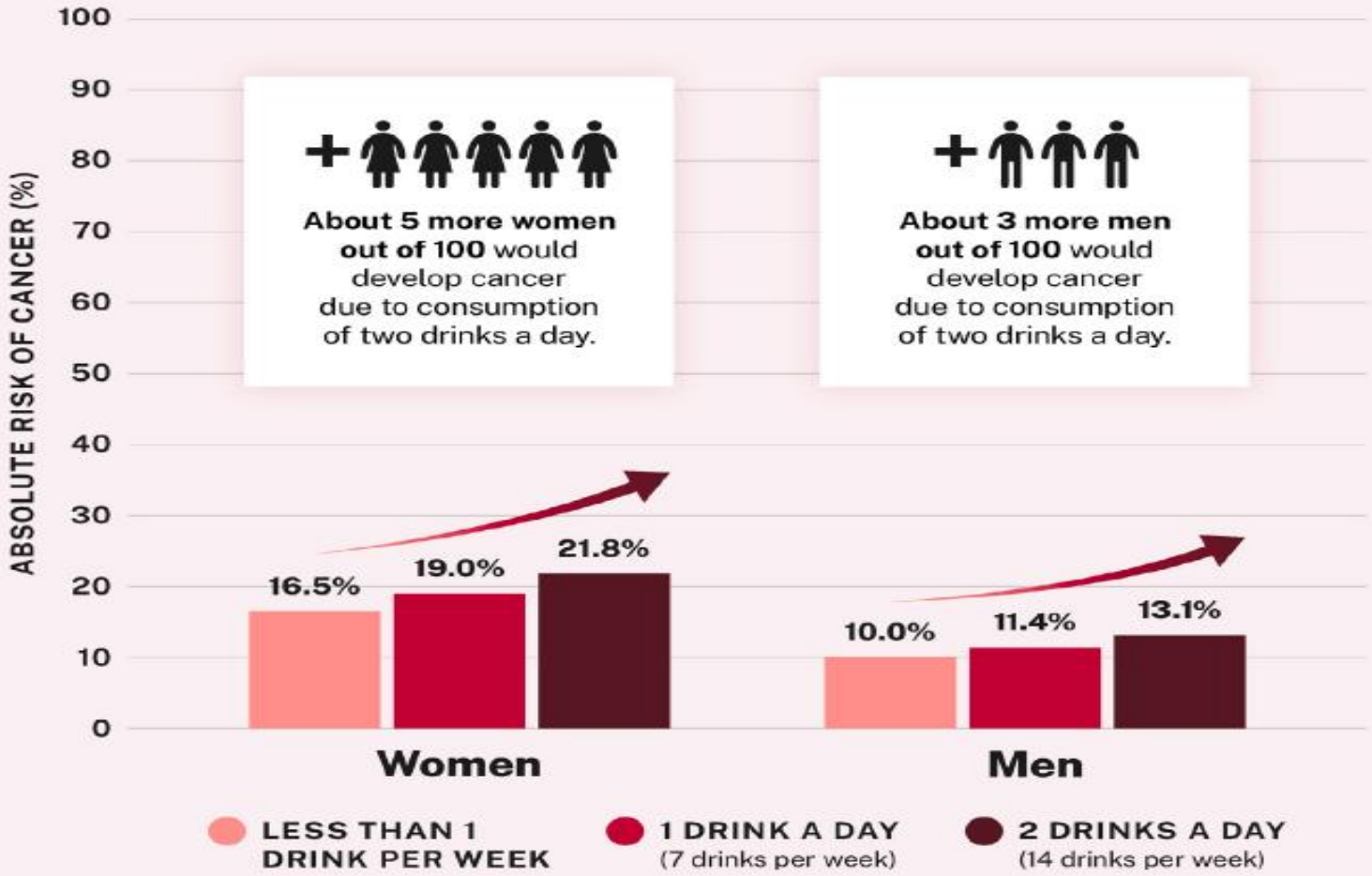


Fig. 3 Comparison of the percentage increase in absolute lifetime risk of alcohol and tobacco-related cancers due to increasing levels of smoking and alcohol consumption per week

In Italia, il 36,9% delle donne è sedentario, il 26,8% è in sovrappeso e l'11,1% obeso, il 15,3% fuma e l'8,7% consuma alcol in quantità a rischio. La soglia limite del consumo alcolico, è pari a 20 g al giorno per gli uomini (due bicchieri di vino da 125 ml) e 10 g al giorno per le donne (circa un bicchiere di vino).

Higher alcohol consumption increases alcohol-related cancer risk in women and men



JAMA Network Open 2022;5(8):e2228544.

Original Investigation | Oncology

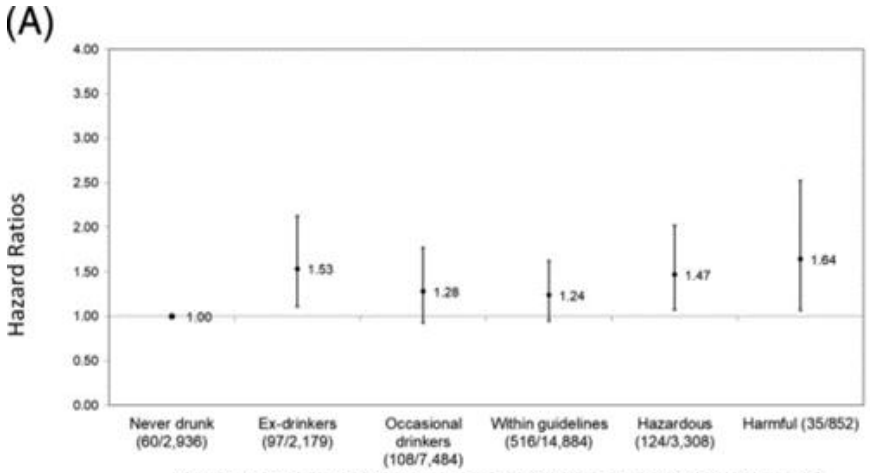
Association Between Changes in Alcohol Consumption and Cancer Risk

Jung Eun Yoo, MD, PhD; Kyungdo Han, PhD; Dong Wook Shin, MD, MBA, DrPH; Dahye Kim, BS; Bong-seong Kim, MS; Sohyun Chun, MD; Keun Hye Jeon, MD; Wonyoung Jung, MD; Jinsung Park, MD, PhD; Jin Ho Park, MD, PhD; Kui Son Choi, PhD; Joo Sung Kim, MD, PhD

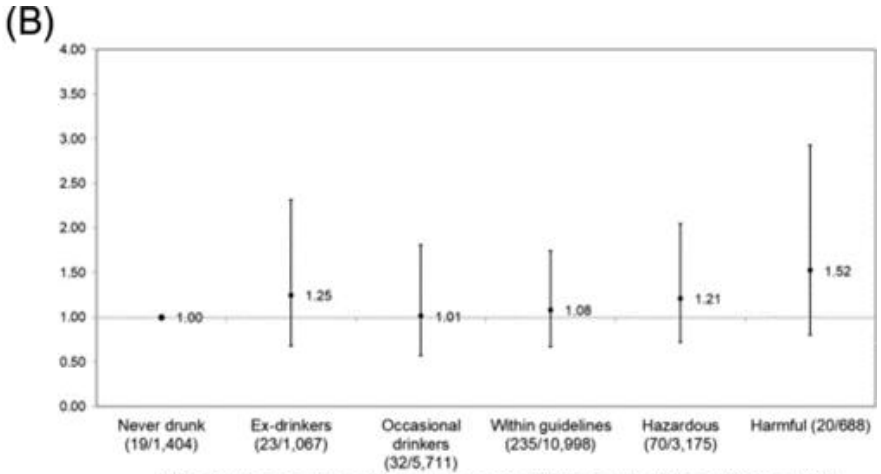
- Among the 4 513 746 participants (mean age, 53.6 years), the incidence rate of cancer was 7.7 per 1000 person-years during a median follow-up of 6.4 years

- Results of this study showed that increased alcohol consumption from 0 g/d, *mild* (<15 g/d), *moderate* (15-29.9 g/d) or *heavy* (30 g/d) was **associated with higher risks for** alcohol-related diseases and **all cancers,** whereas sustained quitting and reduced drinking were associated with lower risks of alcohol-related and all cancers

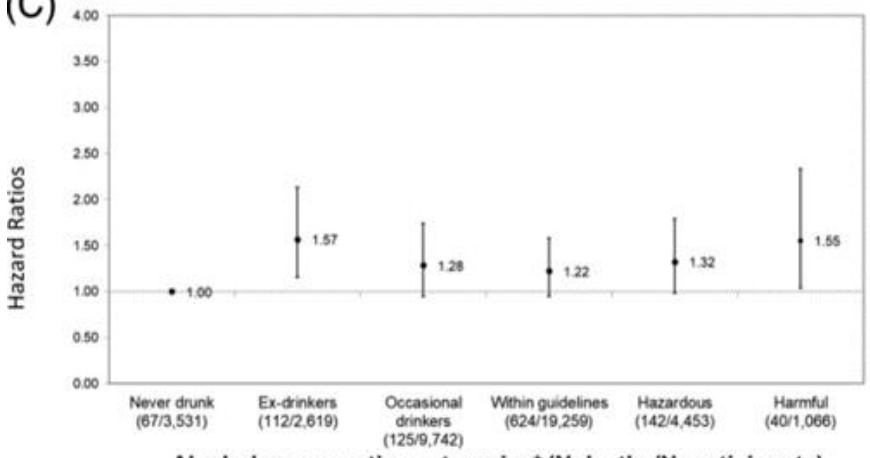
Feng et al. Does adequate physical activity attenuate the associations of alcohol and alcohol-related cancer mortality? A pooled study of 54 686 British adults. Int J Cancer. 2020 Nov 15;147(10):2754-2763.



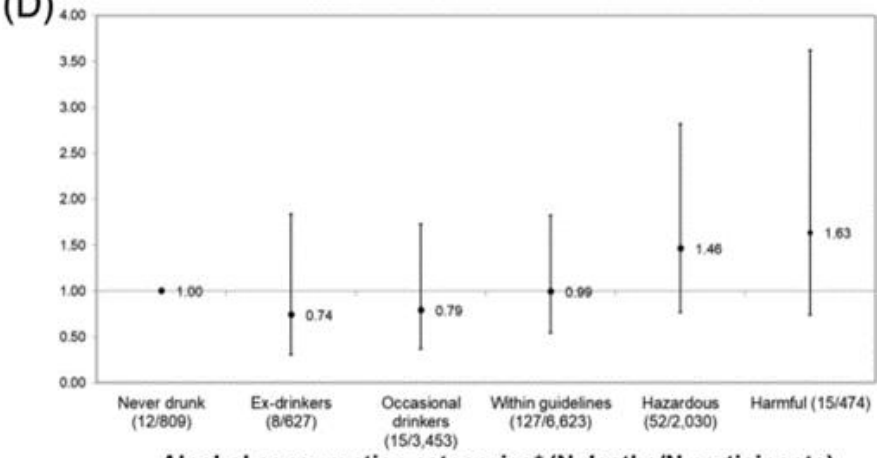
< 7.5MET-hour/week



=7.5 MET-hour/week



<15 MET-hour/week



≥ 15 MET-hour/week

ARGOMENTI

- Dieta scorretta
- Abuso di alcool
- Alterazione del metabolismo: sovrappeso/iperglicemia
- Inattivita’ fisica

CONTRASTARE L'OBESITA'

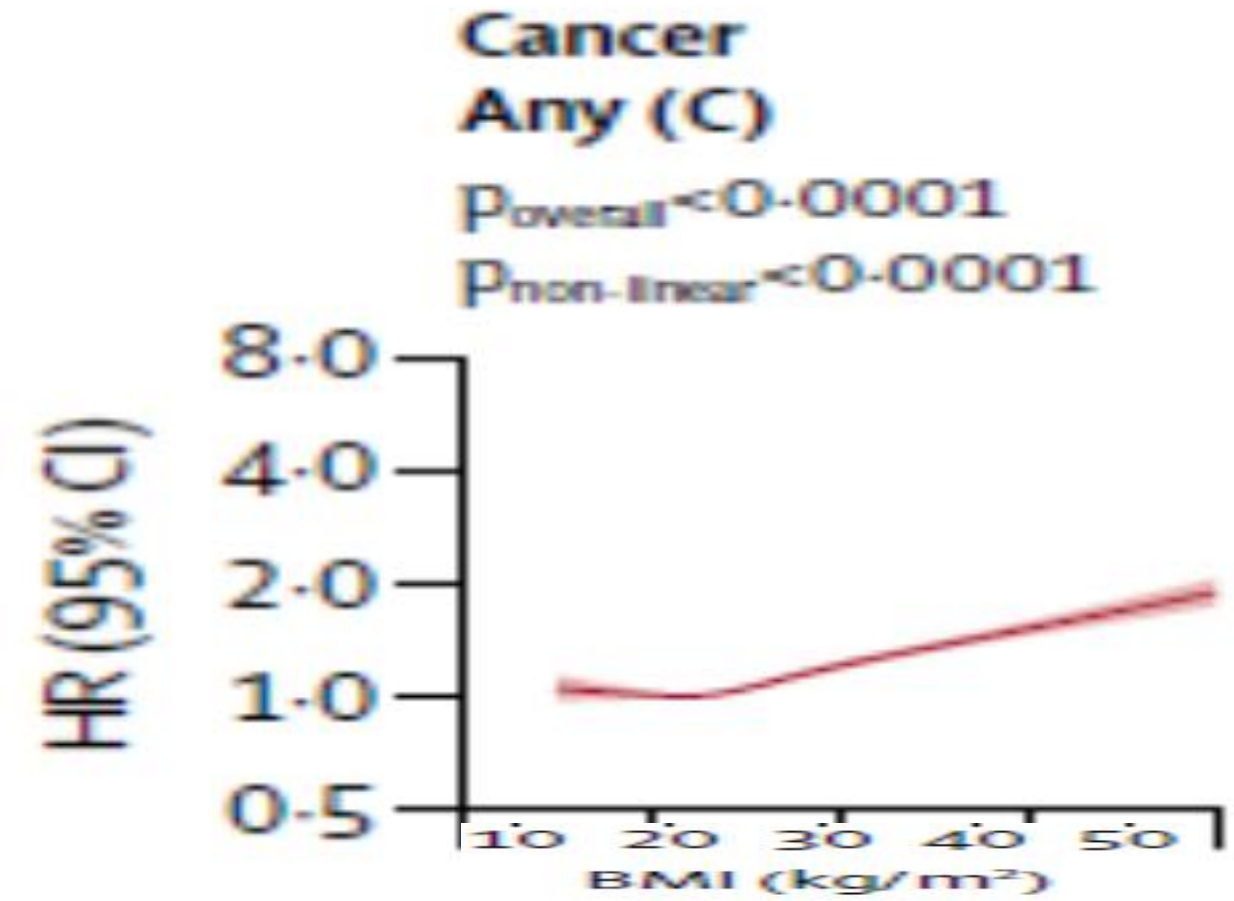
PARAMETRI ANTROPOMETRICI

- L’Indice di massa corporea (BMI) si ottiene dividendo il peso espresso in chilogrammi per l'altezza al quadrato espressa in metri. Si distinguono 4 classi:

- sottopeso se il valore è inferiore a 18,5
- normopeso se il valore è compreso tra 18,5 – 24,9
- sovrappeso se va dai 25 – 29,9
- obesità se è tra i 30 e 40
- obesità estrema se supera i 40

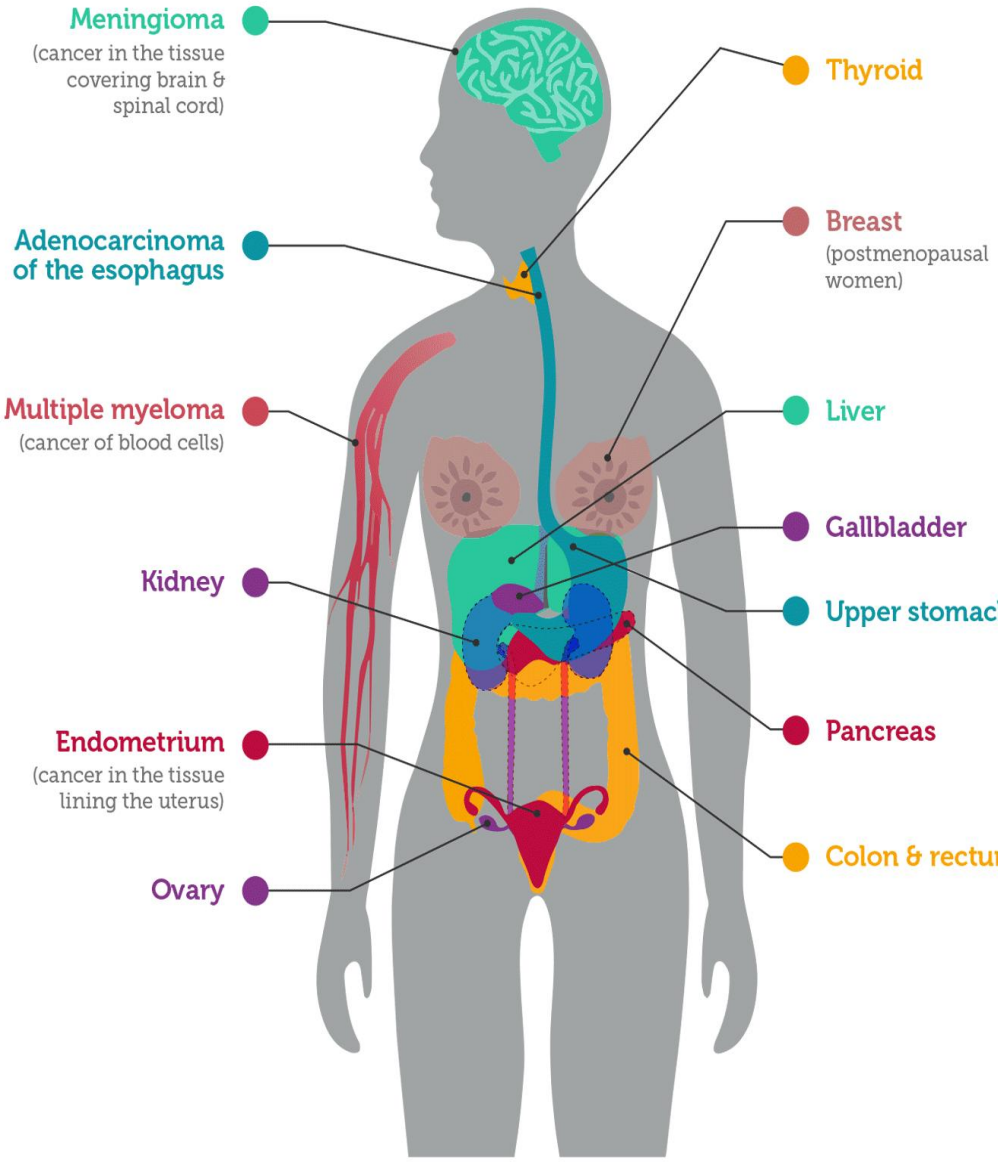
- Il rapporto vita/fianchi dovrebbe essere inferiore a 0,8 nelle donne e a 0,9 negli uomini. Se il rapporto WHR (waist-to-hip ratio) è maggiore di 0,85, si parla di obesità androide, se è inferiore a 0,79 si parla di obesità ginoide.

Bhaskaran et al. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol. 2018 Dec;6(12):944-953.



NATIONAL CANCER INSTITUTE

Cancers Associated with Overweight & Obesity



cancer.gov/obesity-fact-she

Adapted from Centers for Disease Control & Preventi

AUMENTO DEL RISCHIO DI TUMORE NELLA OBESITA'

TIPO DI TUMORE	AUMENTO DEL RISCHIO
Endometrio, esofago,	2-4 volte
Stomaco (cardias), fegato, rene	2 volte
Pancreas	50%
Colecisti	20-60%
Meningioma	20-50%
Mammella	20-40%
Mieloma	10-20%
Ovario, tiroide	10% ogni 5 unita' di BMI

Pati et al. Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management. Cancers (Basel). 2023 Jan 12;15(2):485.

Table 2. Gender-specific summary of cancer risk for each 5 kg per m^2 increase in BMI for major cancers with strong evidence of relationship with obesity.

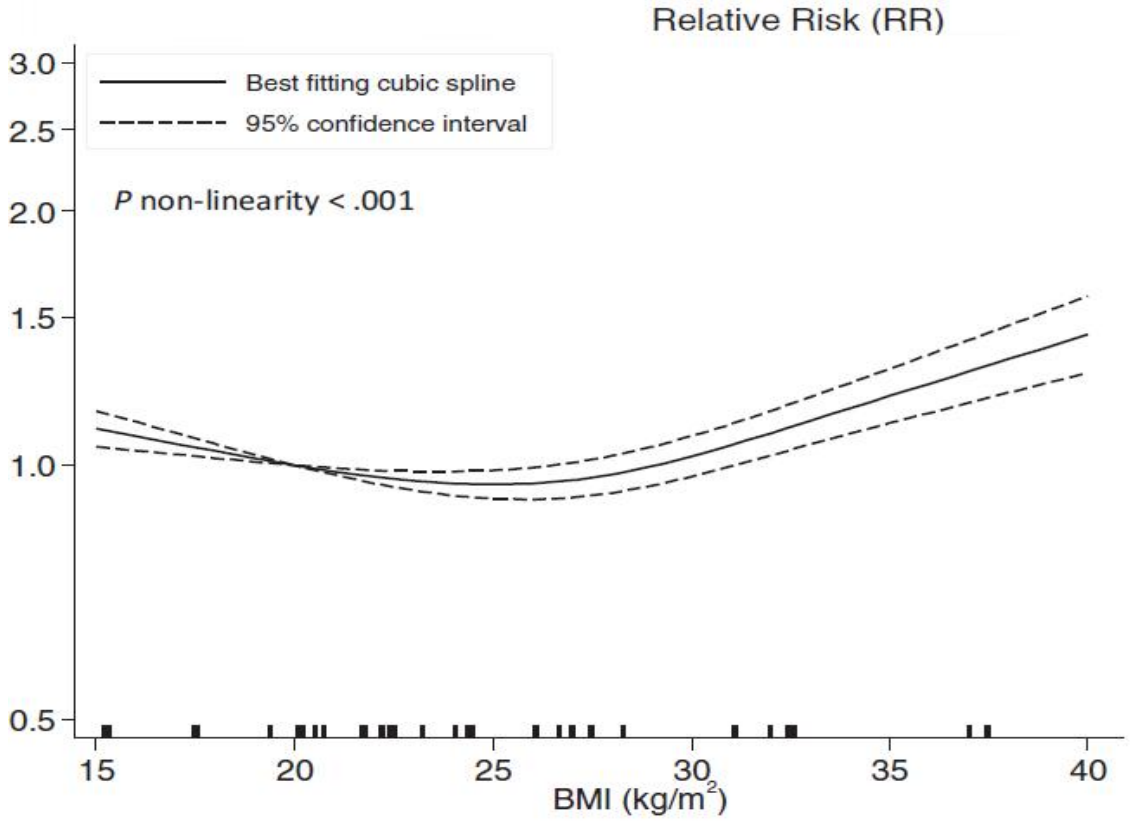
BMI = Peso (Kg)/altezza (m2)

Type of Cancer	Number of Cohorts	Relative Risk (95% Confidence Interval)	
		Women	Men
Endometrial cancer [4]	19	1.59 (1.50–1.68)	NA
Gallbladder cancer [4]	4	1.59 (1.02–2.47)	1.09 (0.99–1.21)
Esophageal adenocarcinoma [4]	5	1.51 (1.31–1.74)	1.52 (1.33–1.74)
Kidney cancer [4]	12	1.34 (1.25–1.43)	1.24 (1.15–1.34)
Postmenopausal breast cancer [4]	34	1.12 (1.08–1.16)	NA
Hpatocellular cancer [19]	9	1.12 (1.03–1.22)	1.19 (1.09–1.29)
Pancreatic adenocarcinoma [23]	23	1.10 (1.04–1.16)	1.13 (1.04–1.22)
Colon cancer [4]	29	1.09 (1.05–1.13)	1.24 (1.20–1.28)
Ovarian cancer [77]	34	1.06 (1.00–1.12)	NA
Stomach cancer [4]	8	1.04 (0.90–1.20)	0.97 (0.88–1.06)
Rectal cancer [4]	29	1.02 (1.00–1.05)	1.09 (1.06–1.12)
Later stage prostate cancer [73]	23	NA	1.08 (1.04–1.12)

NA = not available.

Chan et al. Postdiagnosis body fatness, weight change and breast cancer prognosis: Global Cancer Update Program (CUP global) systematic literature review and meta-analysis. Int J Cancer. 2023 Feb 15;152(4):572-599.

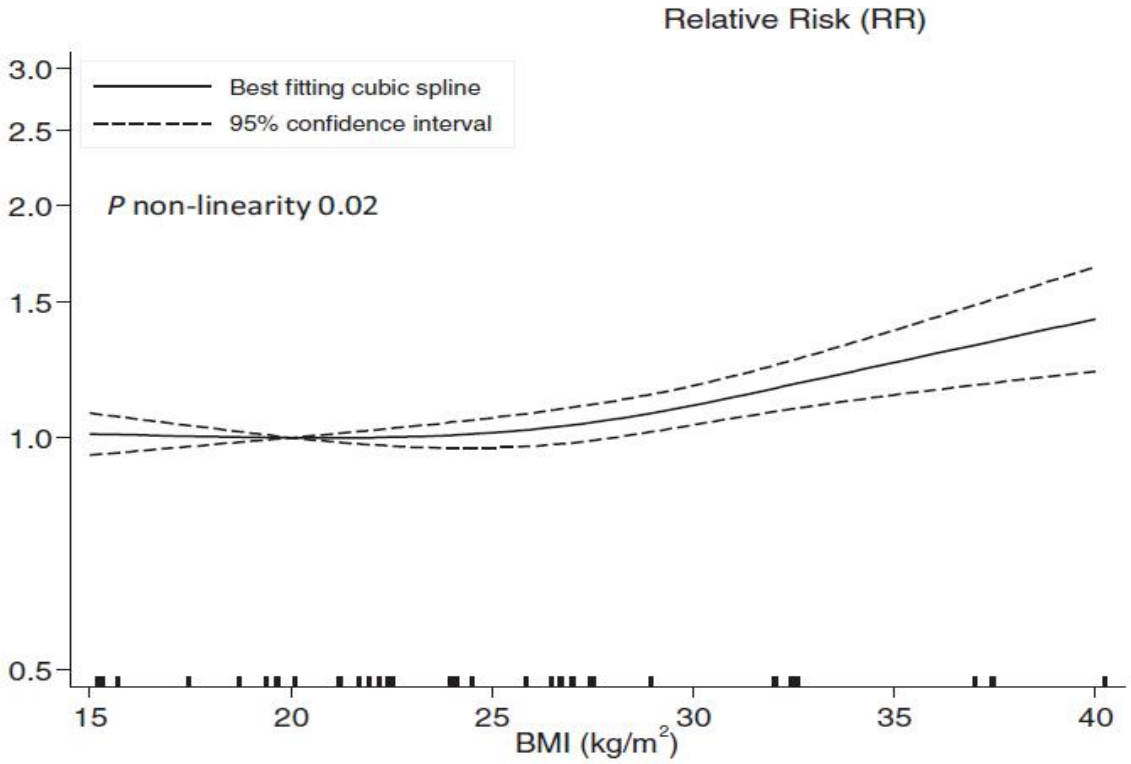
An analysis of 226 studies including over 456 000 women diagnosed with BC



BMI (kg/m²)	RR estimates (95% CI)
16	1.08 (1.04-1.13)
18	1.04 (1.02-1.06)
20	1.00
22	0.97 (0.95-0.99)
25	0.95 (0.91-0.99)
27	0.96 (0.92-1.01)
30	1.02 (0.97-1.08)
32	1.09 (1.03-1.16)
35	1.21 (1.12-1.30)
37	1.29 (1.19-1.41)

BMI and overall mortality

Chan et al. Postdiagnosis body fatness, weight change and breast cancer prognosis: Global Cancer Update Program (CUP global) systematic literature review and meta-analysis. Int J Cancer. 2023 Feb 15;152(4):572-599.

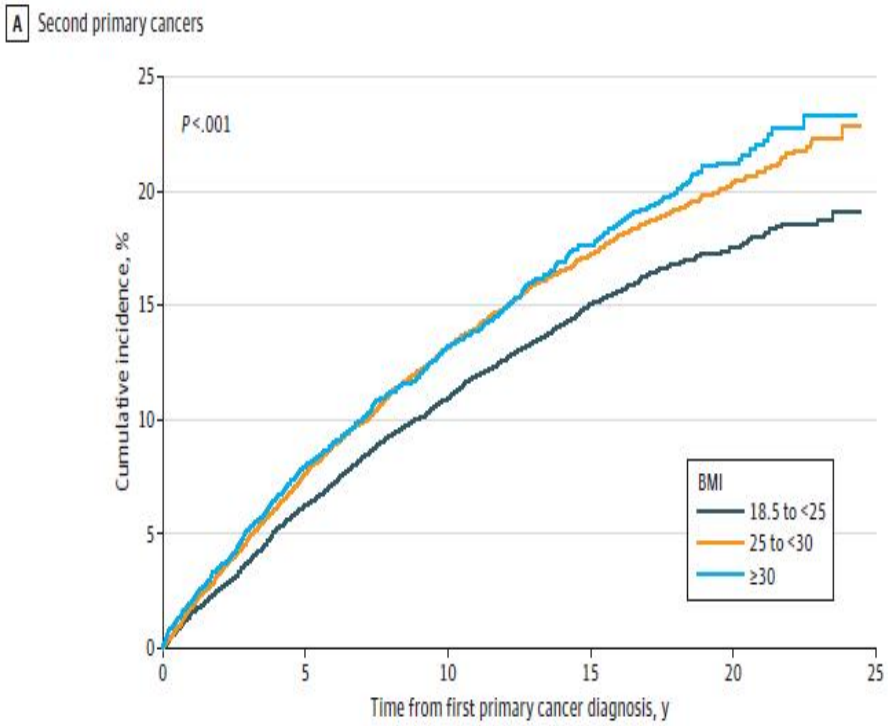


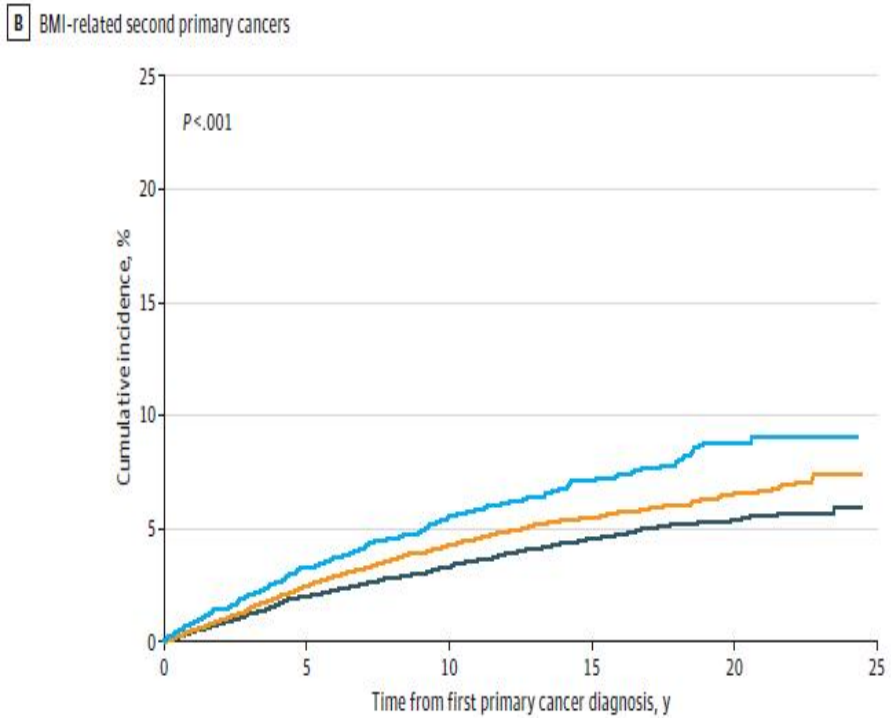
BMI (kg/m²)	RR estimates (95% CI)
16	1.01 (0.96-1.06)
18	1.00 (0.98-1.03)
20	1.00
22	1.00 (0.98-1.02)
25	1.01 (0.97-1.06)
27	1.04 (0.98-1.09)
29	1.08 (1.02-1.14)
32	1.16 (1.08-1.24)
35	1.25 (1.13-1.39)
37	1.32 (1.16-1.50)

BMI and breast cancer specific mortality

Bodelon et al. Excess Body Weight and the Risk of Second Primary Cancers Among Cancer Survivors. JAMA Netw Open. 2024 Sep 3;7(9):e2433132.

26 894 pazienti con tumore primitivo non metastatico varia sede seguiti per una mediana di 8 anni





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journal homepage: www.elsevier.com/locate/pmedr

Relationship between obesity indexes and triglyceride glucose index with gastrointestinal cancer among the US population

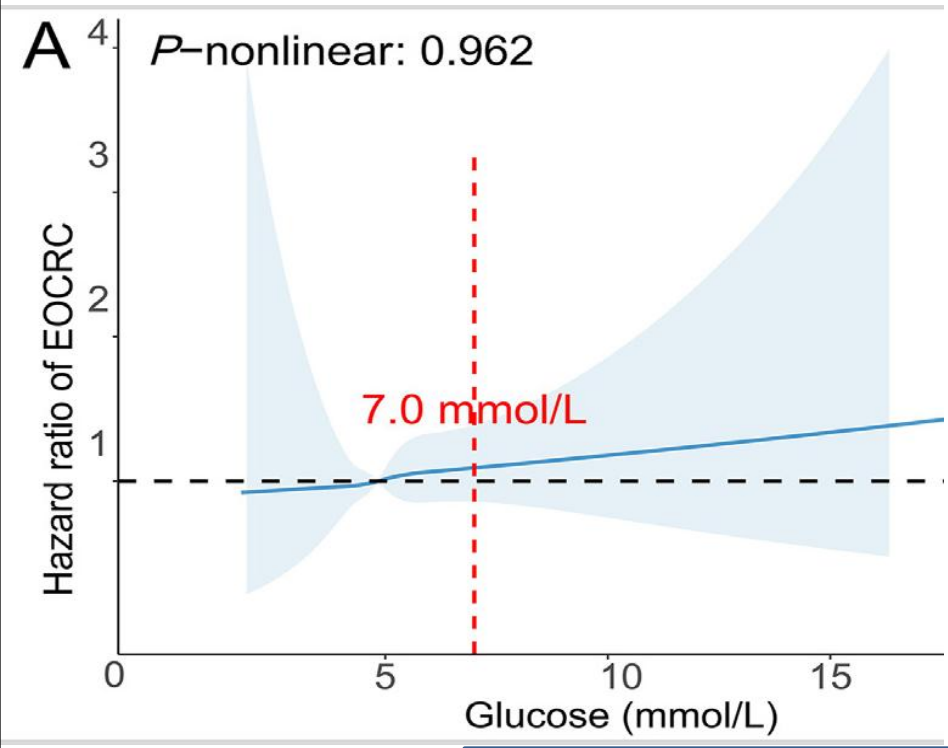
Bowen Zha [1], Angshu Cai [1], Guiqi Wang [*]

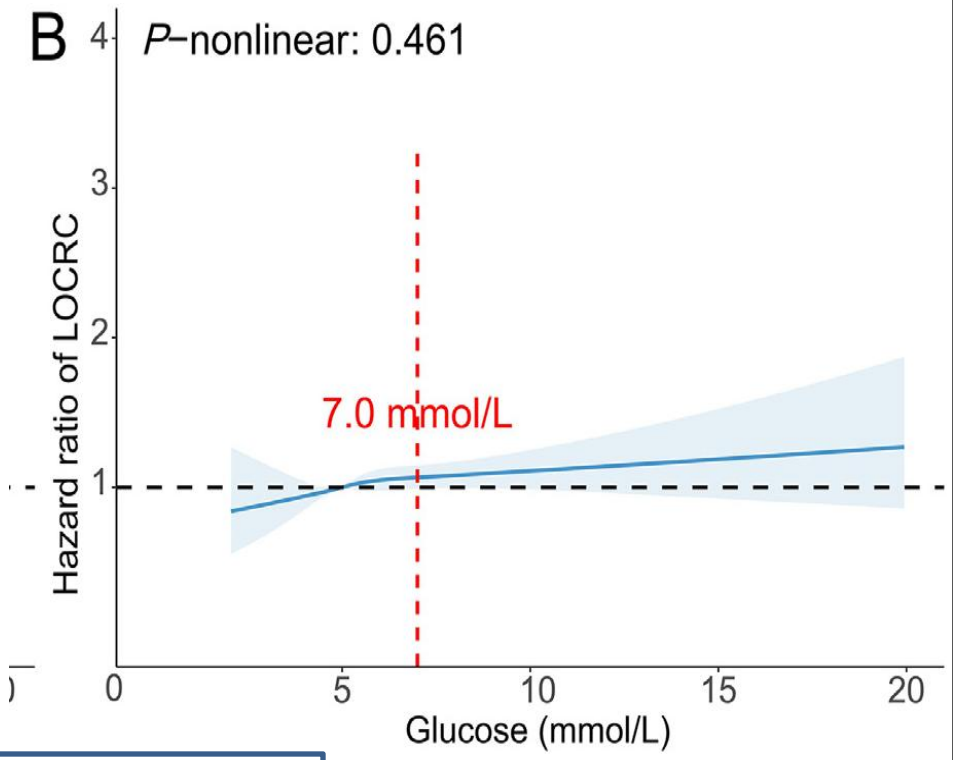
Department of Endoscopy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, People's Republic of China

- 21 411 partecipanti inclusi 187 pazienti with GIC.
- L'indice TyG (trigliceridemia a diguno [mg/dL] x glicemia a digiuno [mg/dL])/2 e' fortemente associato con la comparsa di di GIC
- Il BMI e' correlato con la sopravvivenza dei pazienti che hanno sviluppato un tumore gastrointestinale (maggiore il BMI, peggiore la sopravvivenza)

Luo C et al. Associations between blood glucose and early- and late-onset colorectal cancer: evidence from two prospective cohorts and Mendelian randomization analyses. J Natl Cancer Cent. 2024 Jun 22;4(3):241-248.

the UK Biobank recruited > 500,000 individuals (40 to 69 yrs.) between 2006 and 2010 and analyzed data between April 2023 and 2024





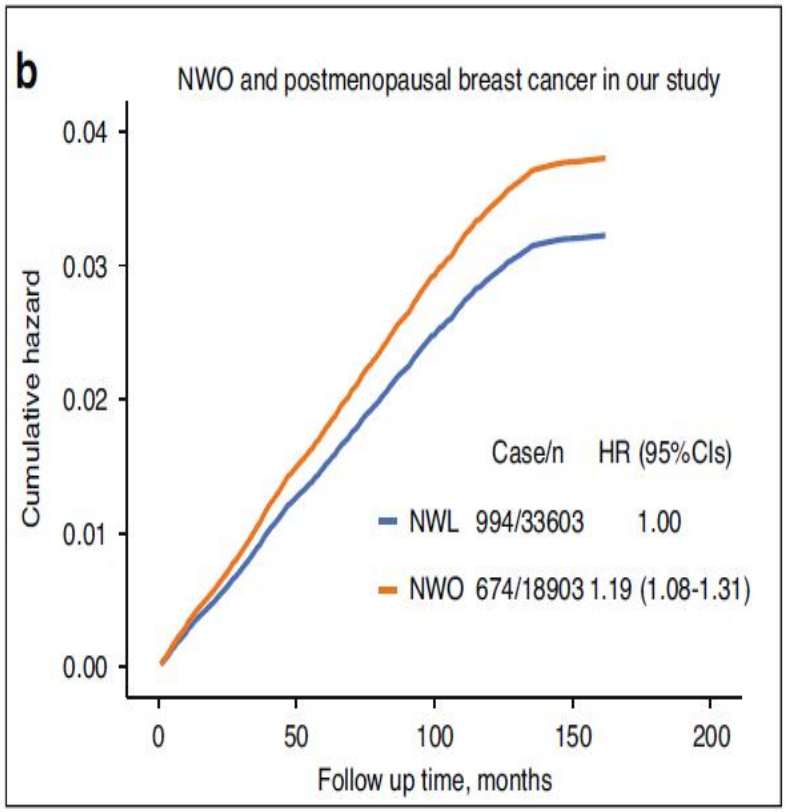
EOCRC vs LOCRC:≤55 yrs vs>55 yrs

7mmol/L=126mg/dL
1 mmol/L = 18 mg/dL

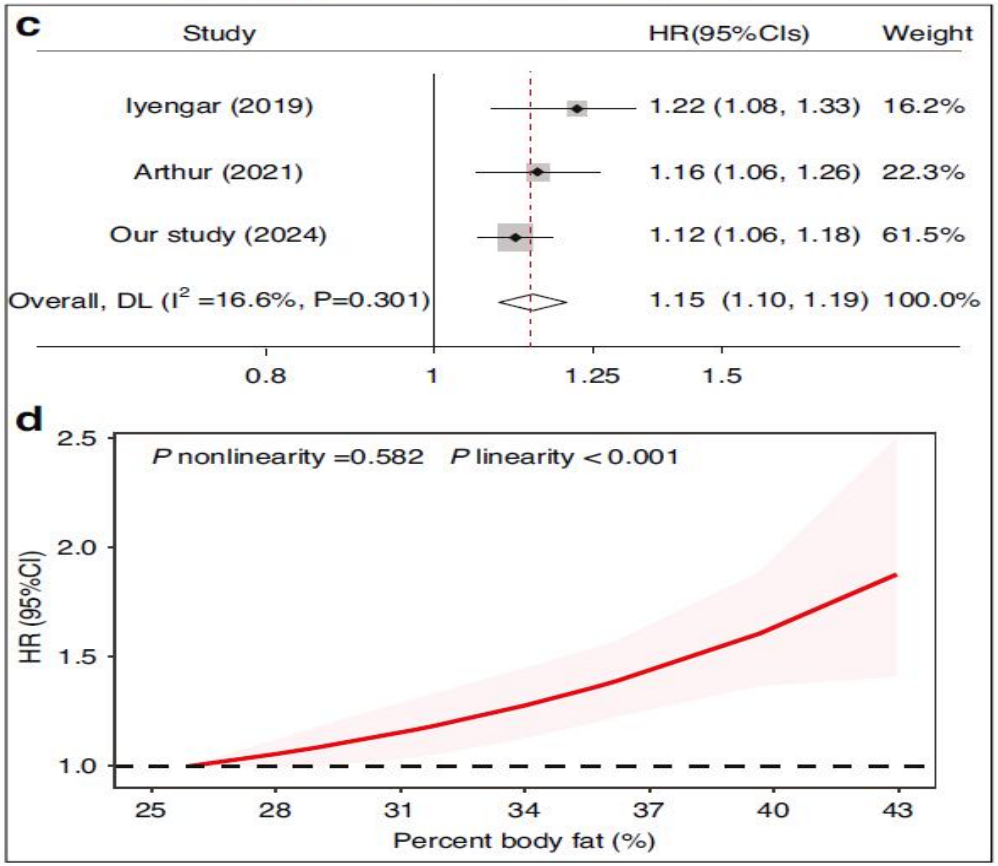
WANG et al. Normal weight obesity, circulating biomarkers and risk of breast cancer: a prospective cohort study and meta-analysis. Br J Cancer. 2024 Nov 28

This study included 52,506 postmenopausal females with normal BMI followed for 15 years. NWO was defined as a normal BMI (18.5–24.9 kg/m2) and an excess percent body fat (PBF › 33.3%).

Postmenopausal breast cancer

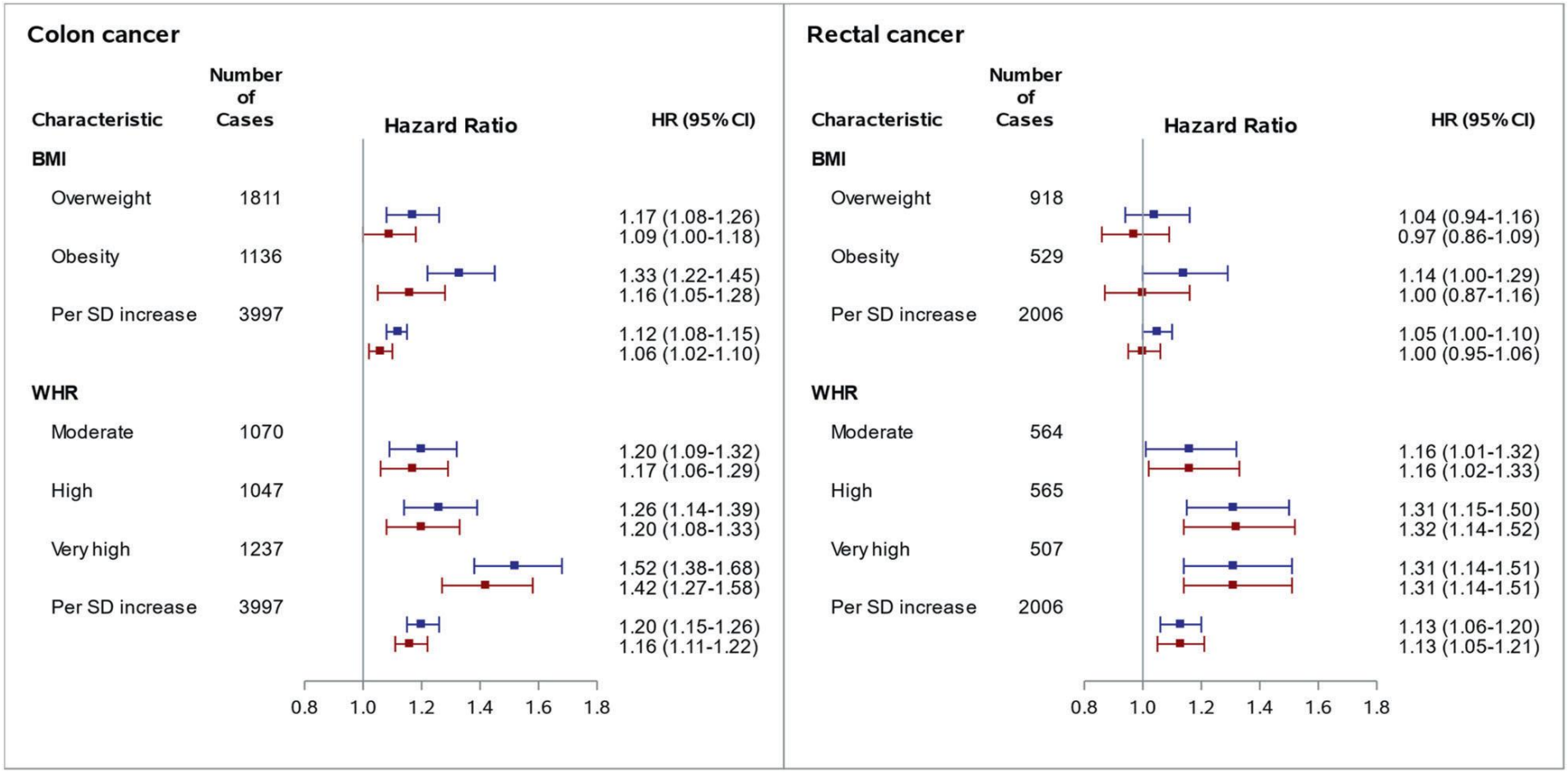


Meta-analysis of our study and two other studies



Safizadeh et al. Central obesity may account for most of the colorectal cancer risk linked to obesity: evidence from the UK Biobank prospective cohort. Int J Obes (Lond). 2024 Nov 19.

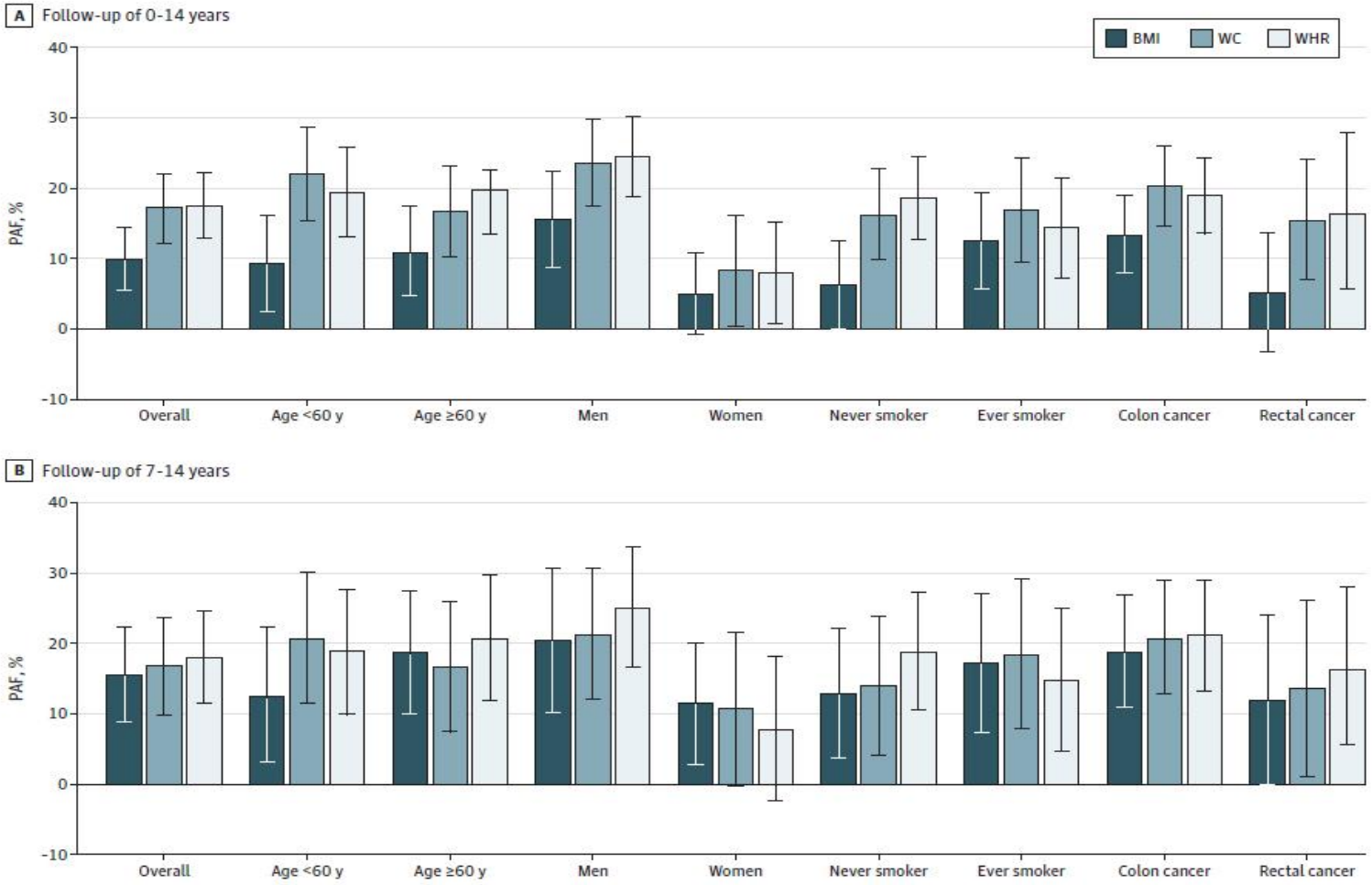
During a median follow-up of 12.5 years, of 460 784 participants, 5 977 developed CRC.



Hazard ratios (HR) and their 95% confidence intervals (CI) for incident colorectal cancer risk associated with increased BMI and WHR

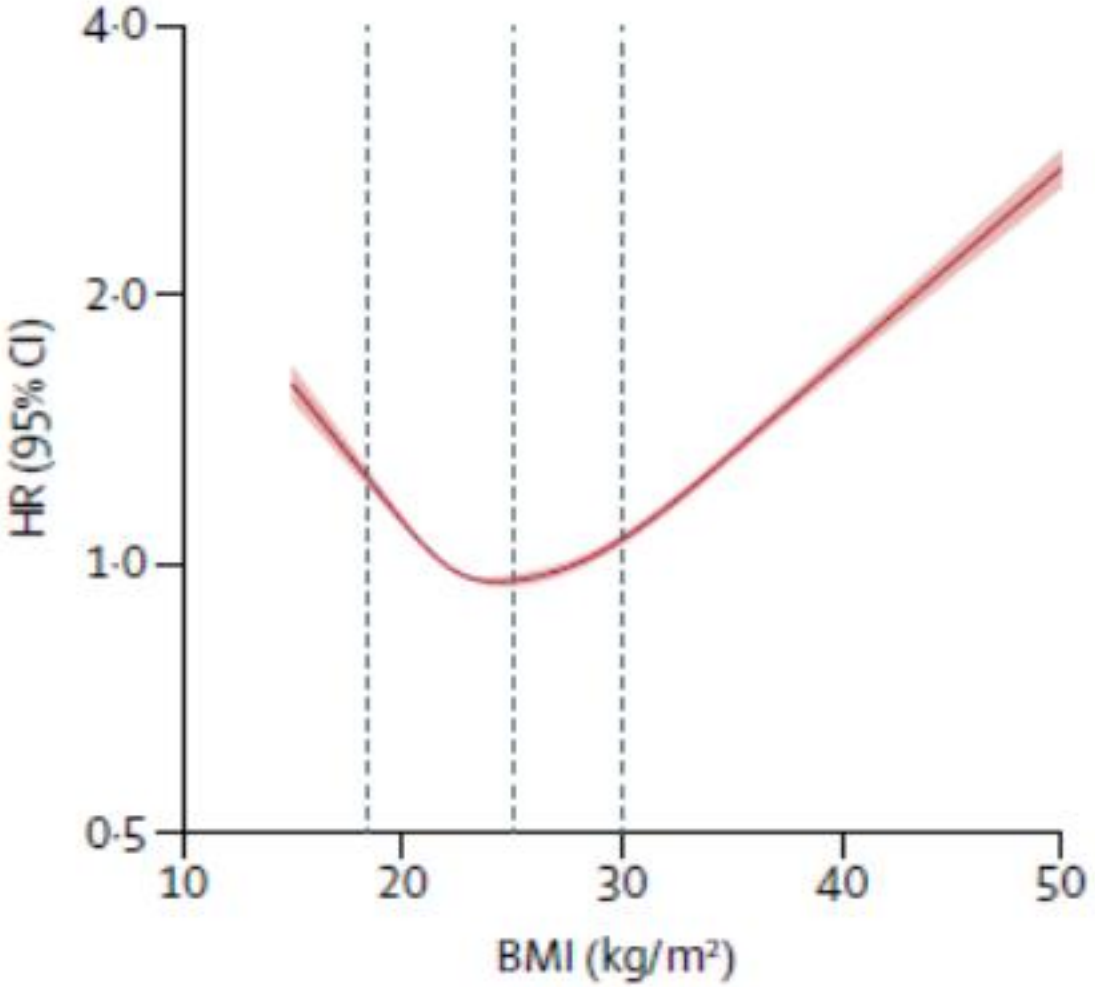
Safizadeh et al. Colorectal Cancer and Central Obesity. JAMA Netw Open. 2025 Jan 2;8(1):e2454753.

Figure 2. Population Attributable Fractions (PAFs) of Colorectal Cancer Cases Attributable to High Body Mass Index (BMI), Waist Circumference (WC), and Waist to Hip Ratio (WHR)



ne’ troppo grassi……ne’ troppo magri

Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol. 2018 Dec;6(12):944-953



***Hussain SM et al.**

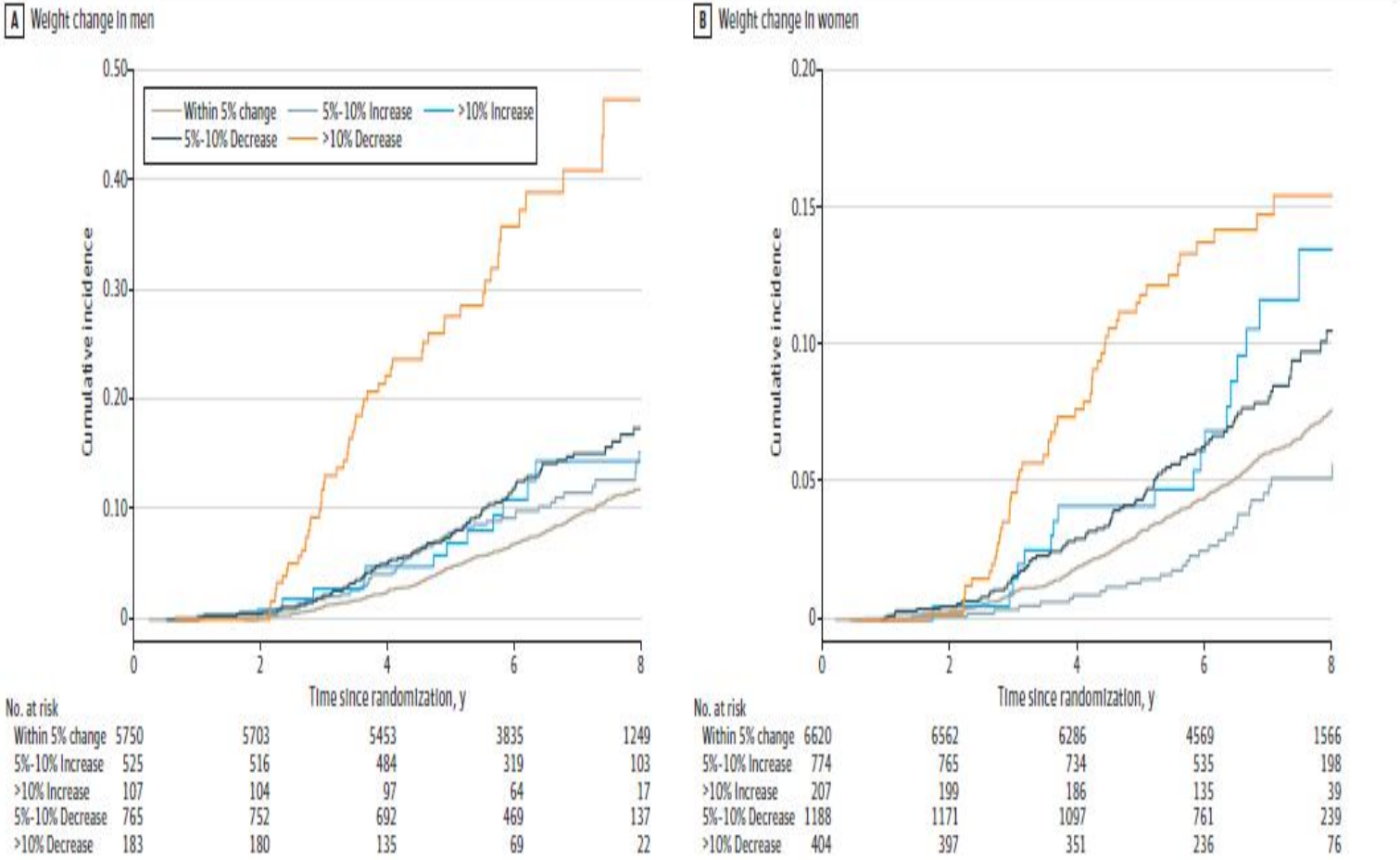
Associations of Change in Body Size With All-Cause and Cause-Specific Mortality Among Healthy Older Adults. JAMA Netw Open. 2023 Apr 3;6(4):e237482.

Weight loss in the first 2 years was associated with a higher cancer-specific mortality

Men: >10% decrease : HR 3.49

Women: 5%-10% decrease: HR, 1.44; >10% decrease: HR, 2.78

Figure 2. Associations of Changes in Body Size and All-Cause Mortality in the Aspirin in Reducing Events in the Elderly Trial



ARGOMENTI

- Dieta scorretta
- Abuso di alcool
- Alterazione del metabolismo: sovrappeso/iperglicemia
- Inattivita’ fisica

Definizioni collegate all'Attività Fisica

Physical activity:	comprende tutti i movimenti del corpo che comportano un dispendio energetico. Sono comprese le attività domestiche, la spesa, il lavoro.
Physical exercise:	comprende i movimenti ripetitivi programmati e strutturati specificatamente destinati al miglioramento della forma fisica e della salute.
Sport:	Attività fisica che comporta situazioni competitive strutturate e sottoposte a regole.
Fitness:	Una serie di attributi quali resistenza, mobilità e forza correlati alla capacità di praticare attività fisica.

EUFIC – European food information council
«fondamenti 06/2006 l'attività fisica»

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 = 3,5 mL O2/Kg/min
circa 1 Kcal/Kg/ora
circa 24 Kcal/Kg/die

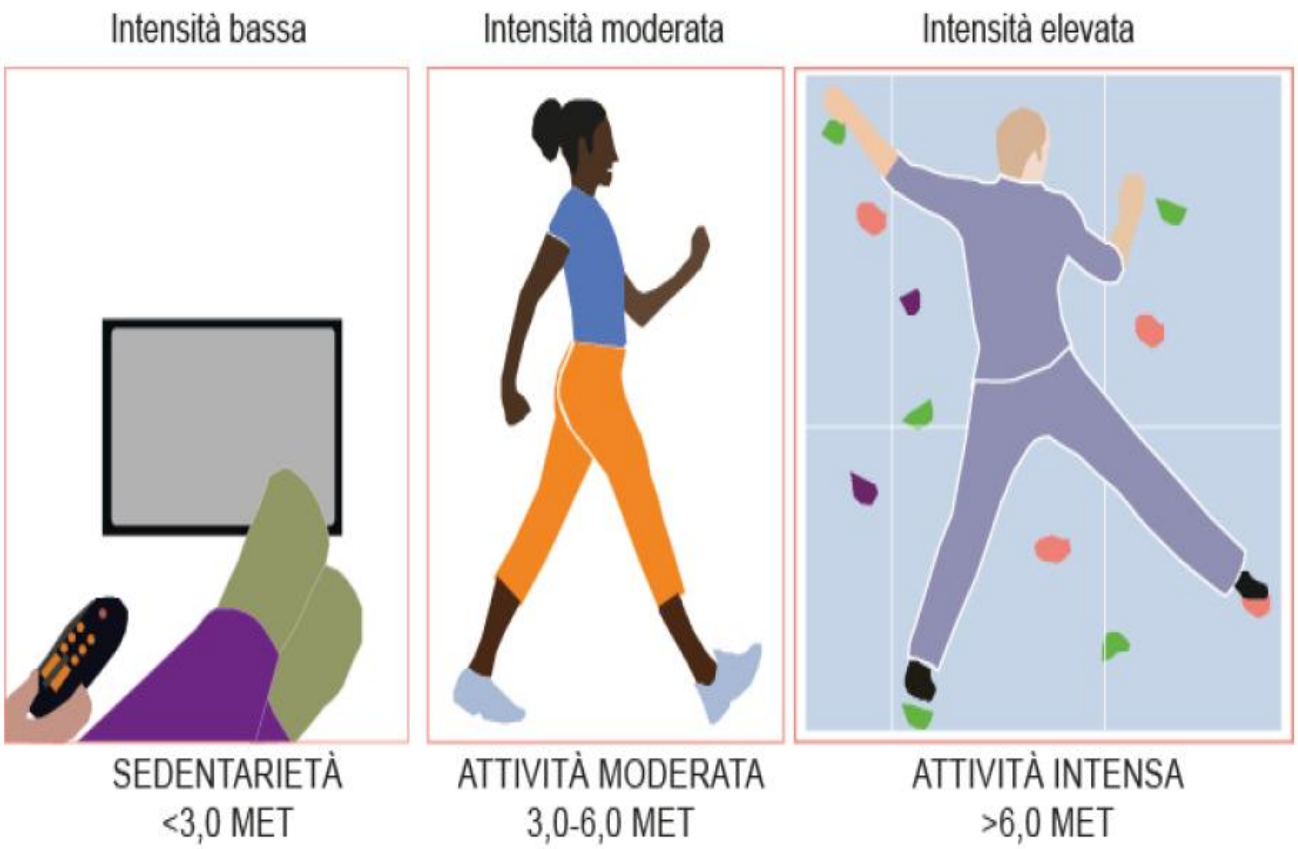
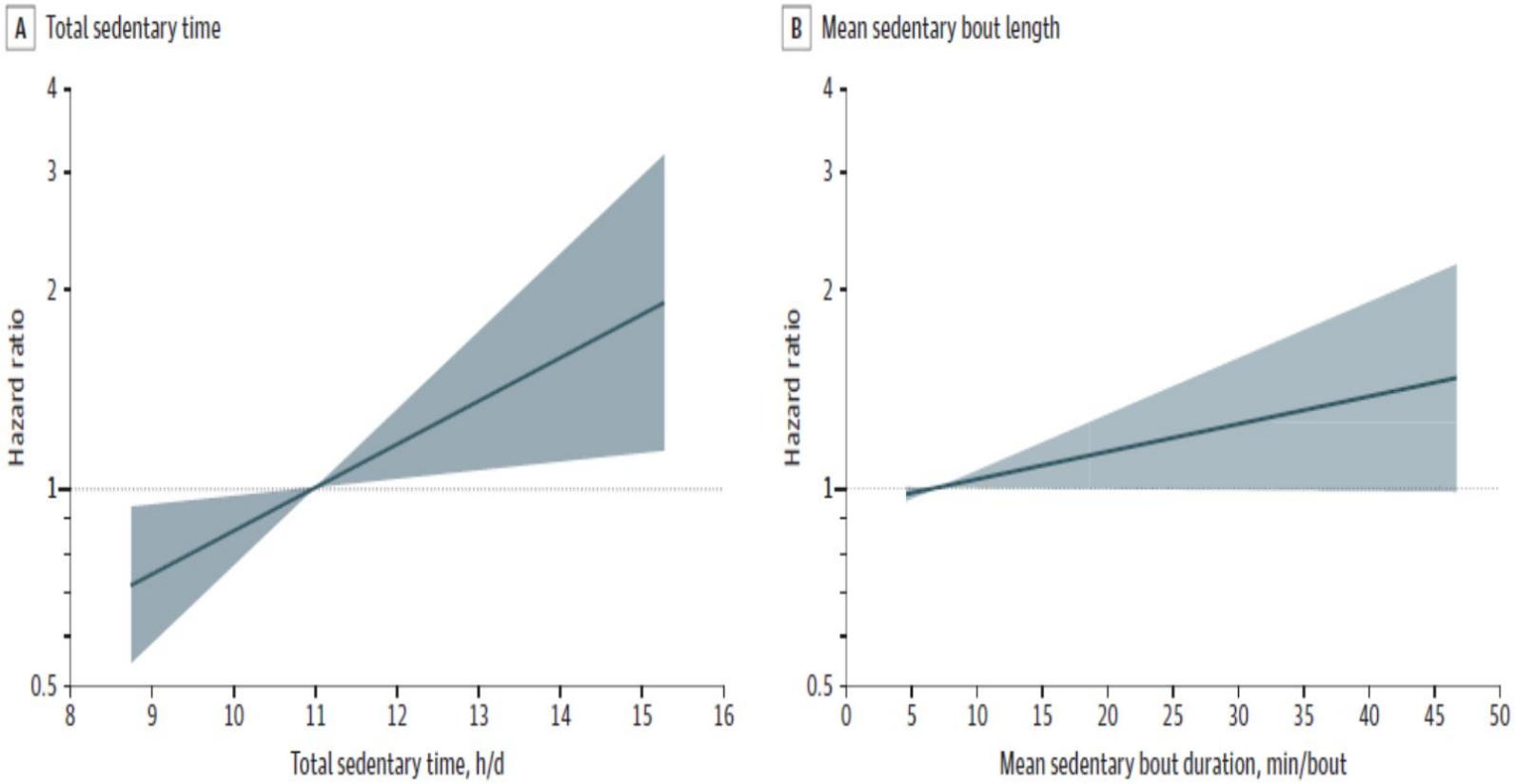


Figura 2.1. Livelli di intensità dell'esercizio fisico in MET

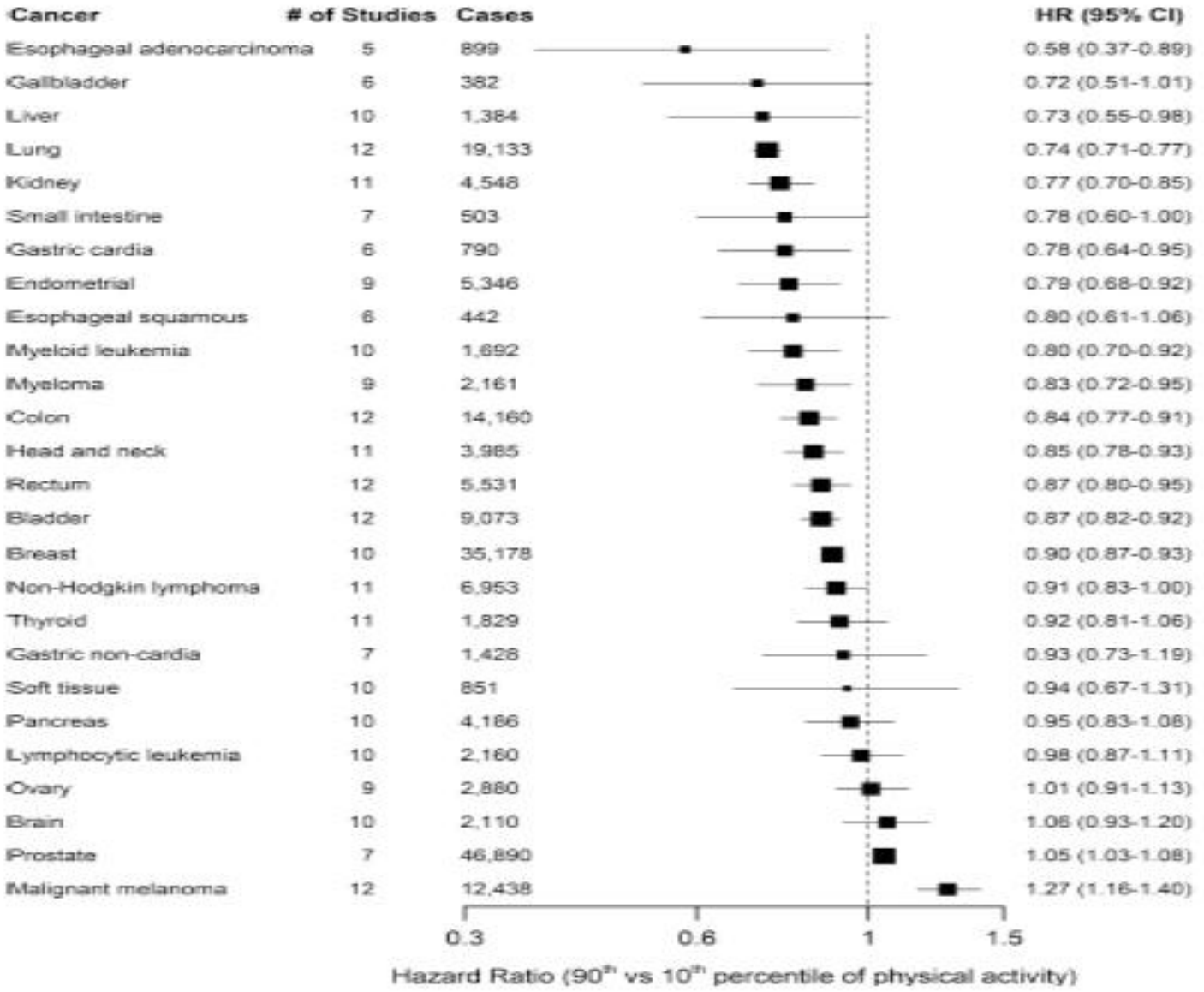
Gilchrist SC et al. Association of Sedentary Behavior With Cancer Mortality in Middle-aged and Older US Adults. JAMA Oncol. 2020 Aug 1;6(8):1210-1217.

8002 adults aged 45 yrs or older measured with a hip-mounted accelerometer for 7 consecutive days, with a follow uo of 5.5 yrs

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



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.



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

- 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 (HR=0.87)
- Mammella (HR=0.90).
- Melanoma (HR=1.27)
- Prostate (HR=1.05).

ATTIVITA' FISICA

- Definizione e classificazione di attività fisica
- Attività fisica: quale e quanta per ridurre il rischio di tumore
- Attività fisica «vigorosa e intermittente»

ATTIVITA' FISICA

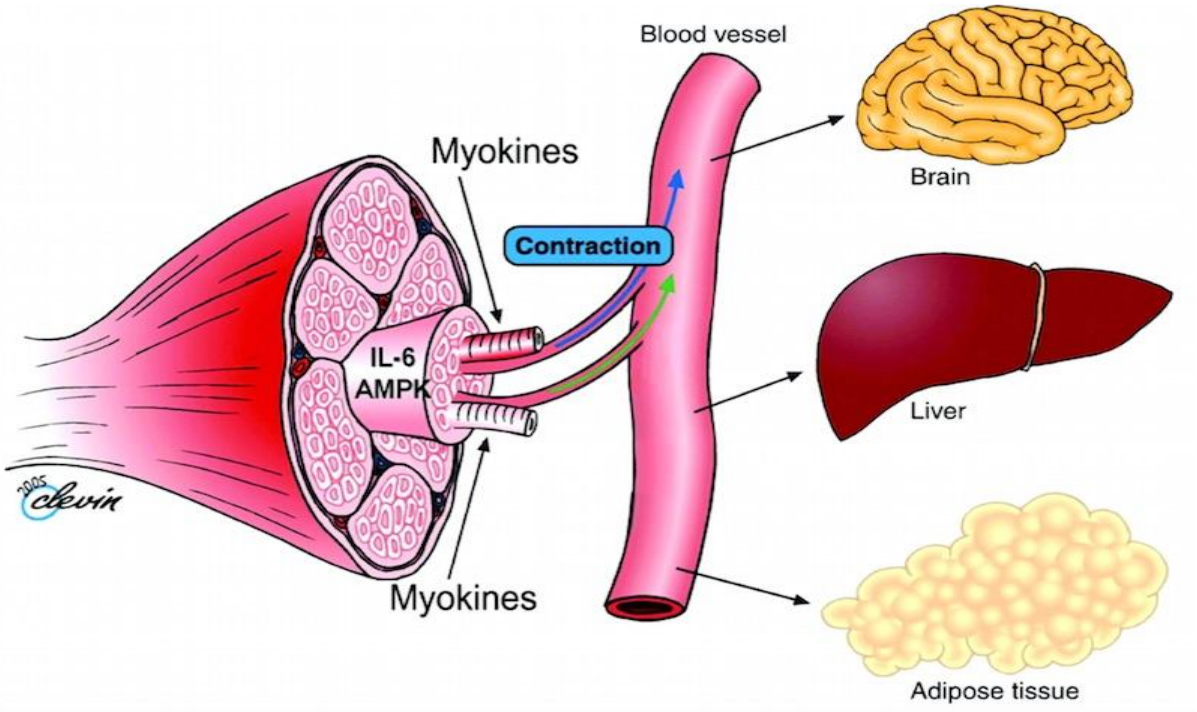
- Definizione e classificazione di attività fisica
- Attività fisica: quale e quanta per ridurre il rischio di tumore
- Attività fisica «vigorosa e intermittente»

L'entità di fatica consigliata e’12-14 Borg

Scala di Borg	Entità della dispnea
0	Nullo
0,5	Estremamente lieve
1	Molto Lieve
2	Lieve
3	Discreto
4	Piuttosto intenso
5/6	Intenso
7	Molto Intenso
8	
9	Quasi insopportabile
10	Insopportabile

Scala di Borg	Entità della fatica
6	Nessuna sensazione di esaurimento
7/8	Estremamente lieve
9	Lieve
10/12	Moderata
13/14	Un po' forte
15	Forte
16	
17	Molto forte
18	
19	Estremamente forte
20	Massimo sforzo

MYOKINES


Blood vessel
Myokines
Contraction
IL-6
AMPK
Myokines
Brain
Liver
Adipose tissue

ATTIVITA' FISICA

- Definizione e classificazione di attività fisica
- Attività fisica: **quanta** e quale per ridurre il rischio di tumore
- Attività fisica «vigorosa e intermittente»

La attività fisica protegge da molte malattie gravi

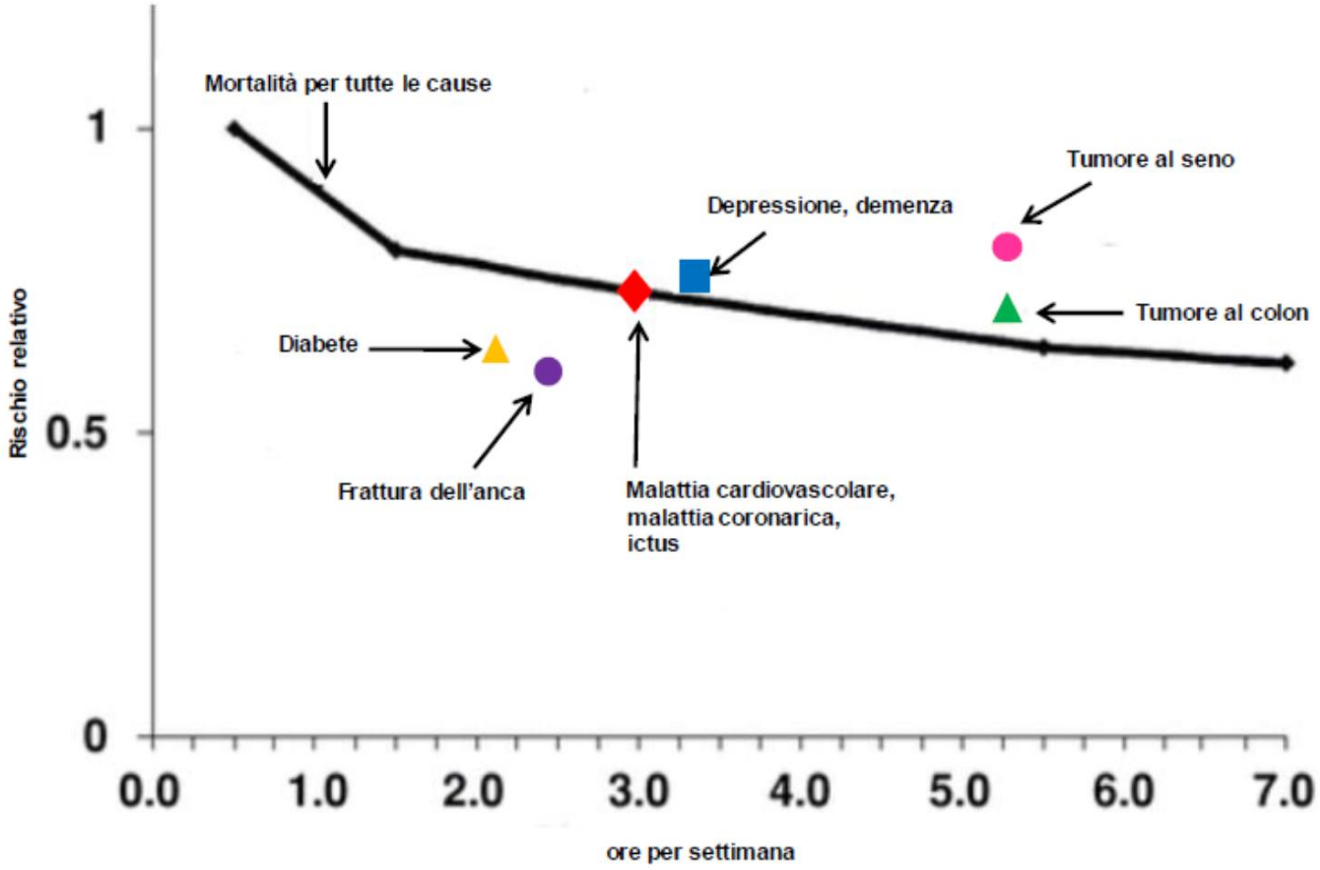
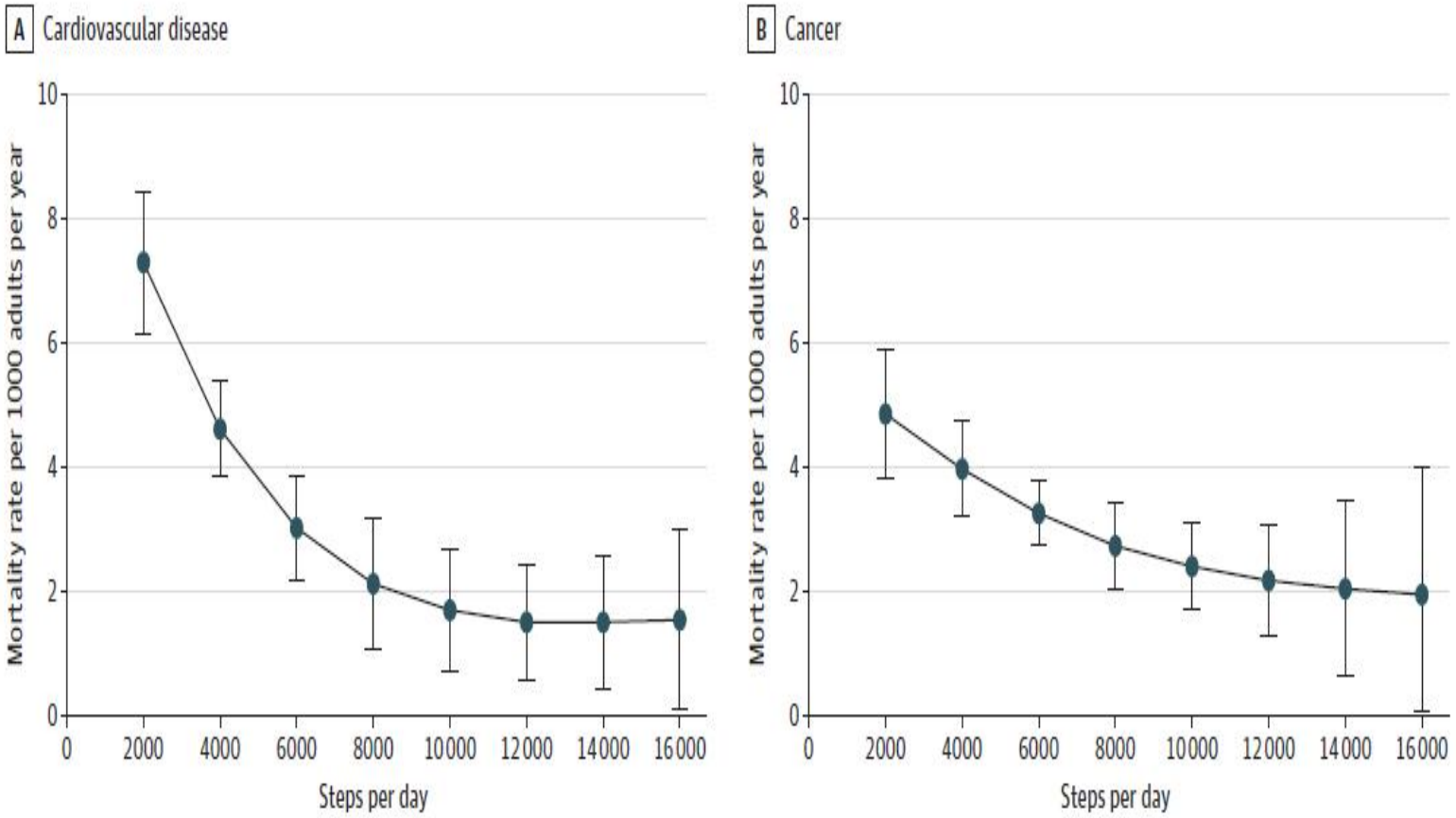


Figura 4.1. Associazione tra attività fisica moderata-intensa con eventi chiave di salute, inclusa la mortalità per tutte le cause

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 pazienti consecutivi seguiti per 7,7 anni (mediana)

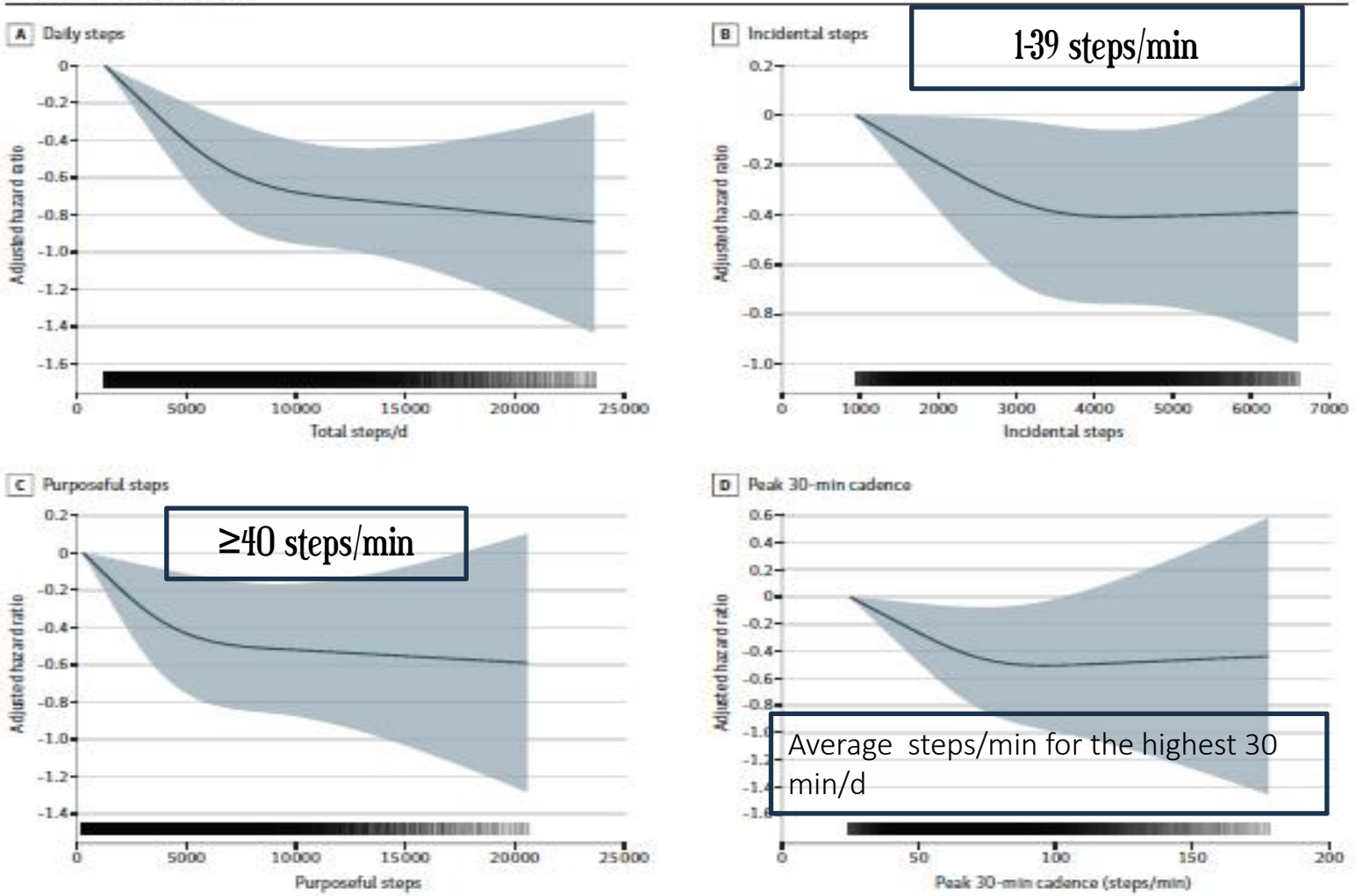
Figure 4. Steps per Day and Mortality From Cardiovascular Disease (CVD) and Cancer in a Study of the Association of Daily Step Count and Step Intensity With Mortality Among US Adults Aged at Least 40 Years



Del Pozo G et al. Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. JAMA Intern Med. doi:10.1001/jamainternmed.2022.4

78 500 individui seguiti per 7 anni: **i passi effettuati ad una cadenza maggiore si associano ad un'ulteriore riduzione del rischio**

Figure 3. Dose-Response Association Between Primary Exposures and Cancer Composite of 13 Sites With a Known Relationship With Low Physical Activity[28]



Marshall et al. Cardiorespiratory fitness and incident lung and colorectal cancer in men and women: Results from the Henry Ford Exercise Testing (FIT) cohort. Cancer. 2019 May 6. doi: 10.1002/cncr.32085

Studio di 49.143 adulti (con un follow up mediano of 7.7 anni): quelli con la piu' alta categoria di fitness (METs ≥12) avevano una riduzione del rischio pari al 77% di tumore polmonare e del 61% di tumore colorettale

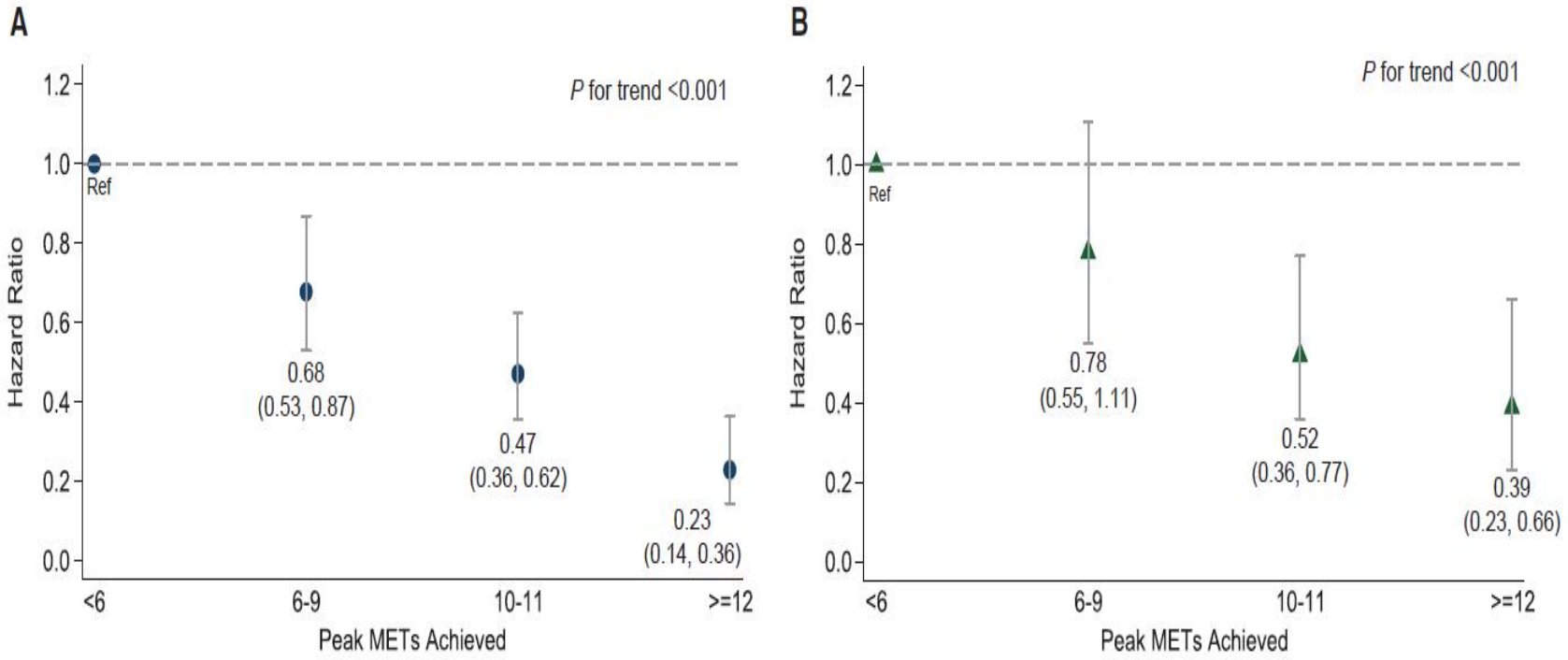
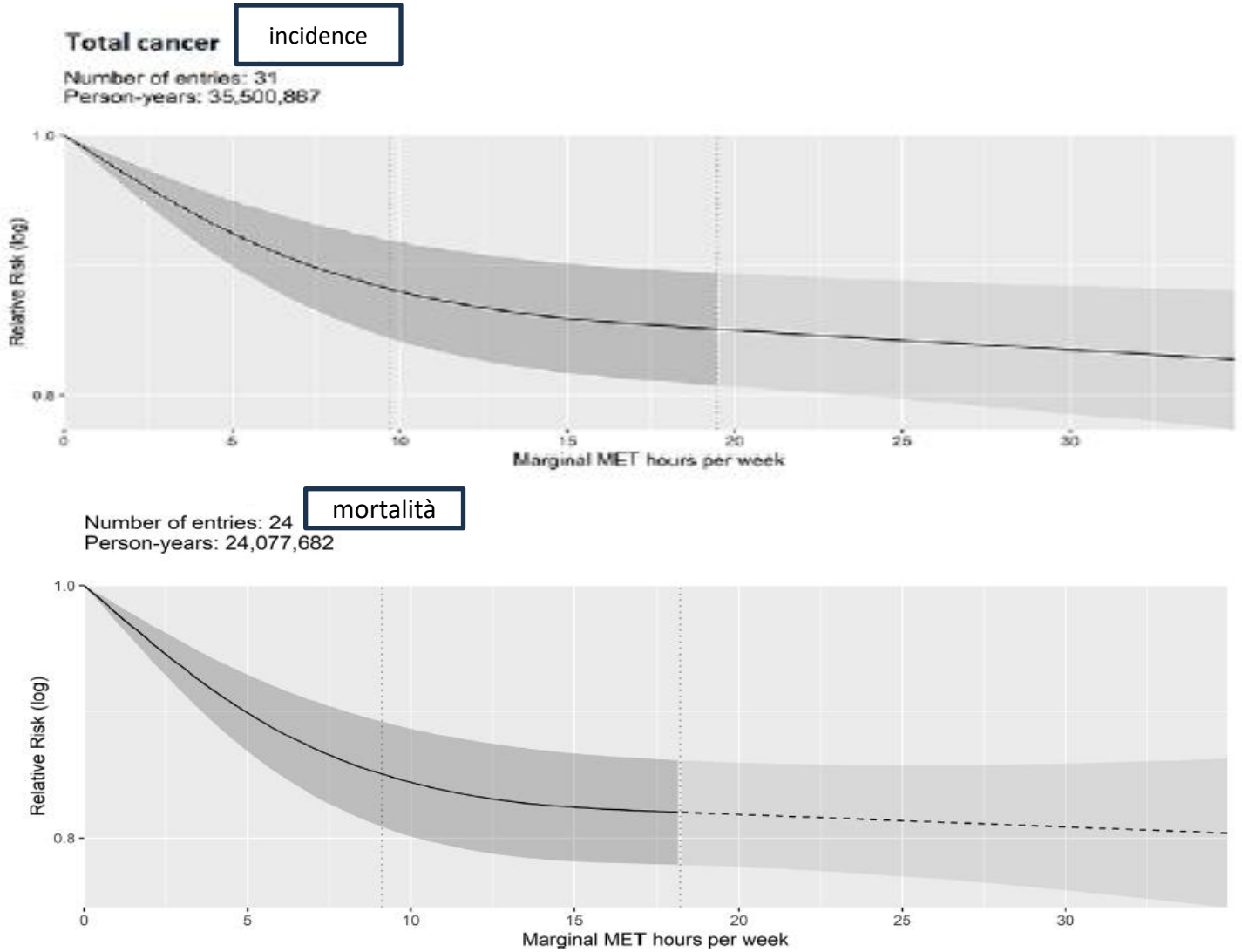


Figure 1. Hazard ratios and 95% CIs for risk of incident (A) lung and (B) colorectal cancer after adjusting for age, race, sex, smoking history, body mass index, diabetes for lung cancer incidence, and aspirin and statin use for colorectal cancer incidence. METs indicates metabolic equivalents of task; Ref, reference.

Garcia et al. Non-occupational physical activity and risk of cardiovascular disease, cancer and mortality outcomes: a dose–response meta-analysis of large prospective studies. Br J Sports Med 2023;57:979–989

35 500 867 person-years, 185 870 events



Garcia et al. Non-occupational physical activity and risk of cardiovascular disease, cancer and mortality outcomes: a dose–response meta-analysis of large prospective studies. Br J Sports Med 2023;57:979–989

> 30 million participants with a follow up of 163 415 543 person-years

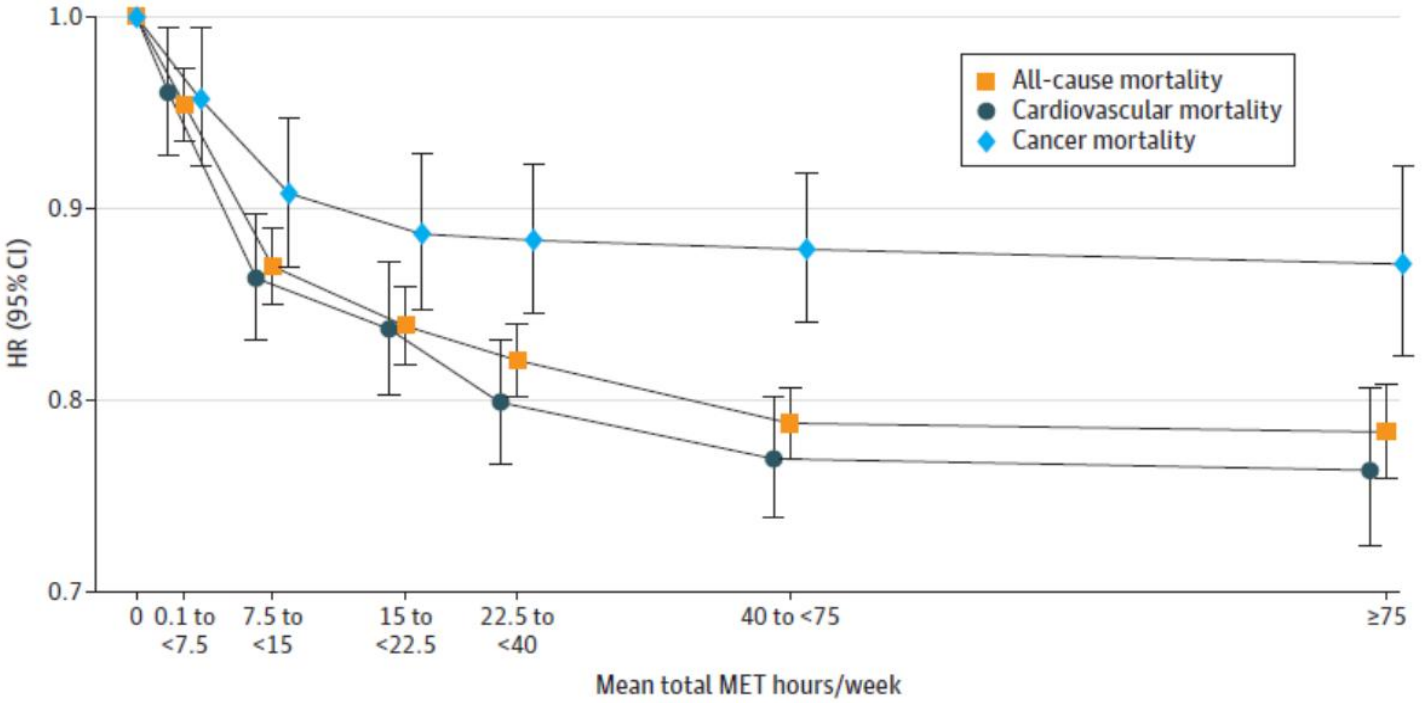
- These findings suggest an appreciably lower risk of cancers from the equivalent **of 75 min/week or less** of moderate-intensity aerobic physical activity (ie, half the recommended minimum levels).

- These results include the first dose–response meta-analysis of 9 site-specific cancers: bladder, esophageal, gastric cardia, head and neck, kidney, liver, lung, myeloid leukaemia and myeloma.

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.

272 550 participants, mean age 70.5 yrs, mean follow-up of 12.4 yrs

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

ATTIVITA' FISICA

- Definizione e classificazione di attività fisica
- Attività fisica: quanta e **quale** per ridurre il rischio di tumore
- Attività fisica «vigorosa e intermittente»

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 adults aged 18 years or older with a follow up of 5.9 years

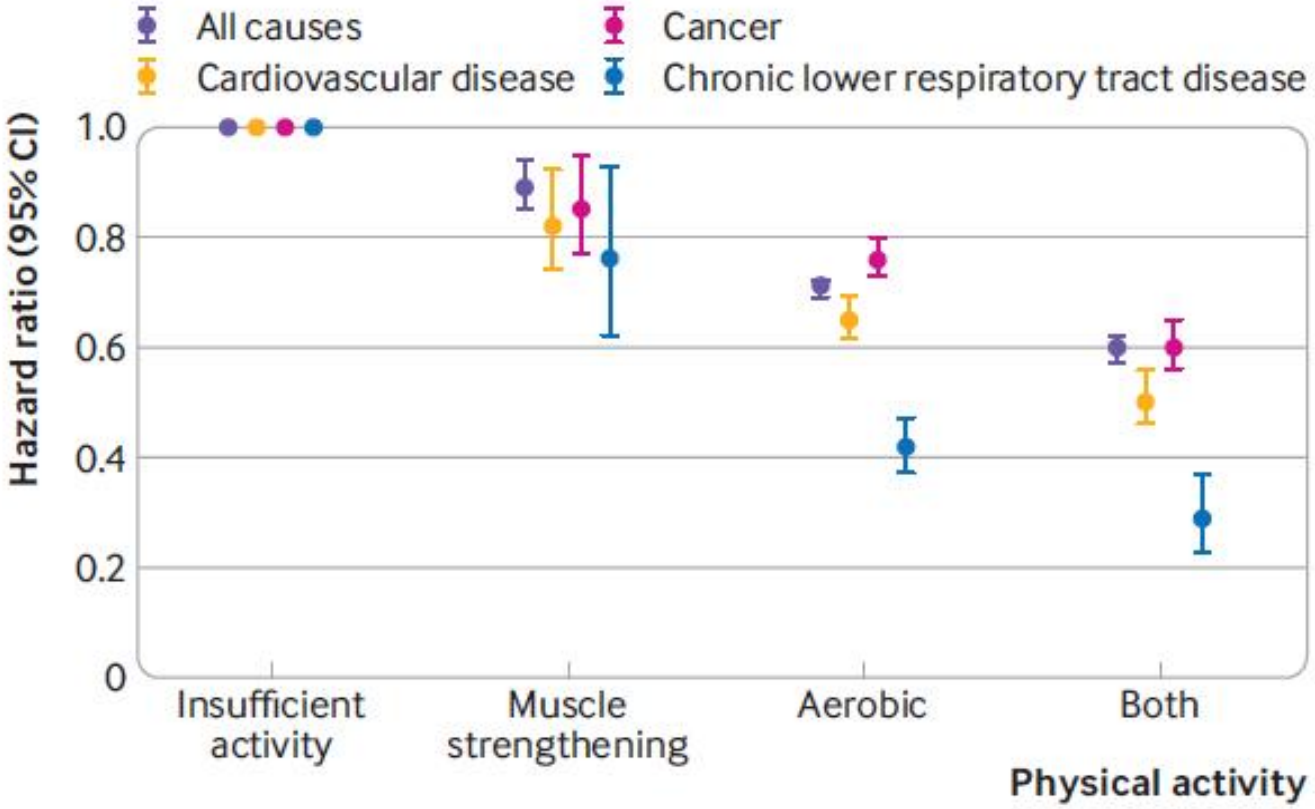
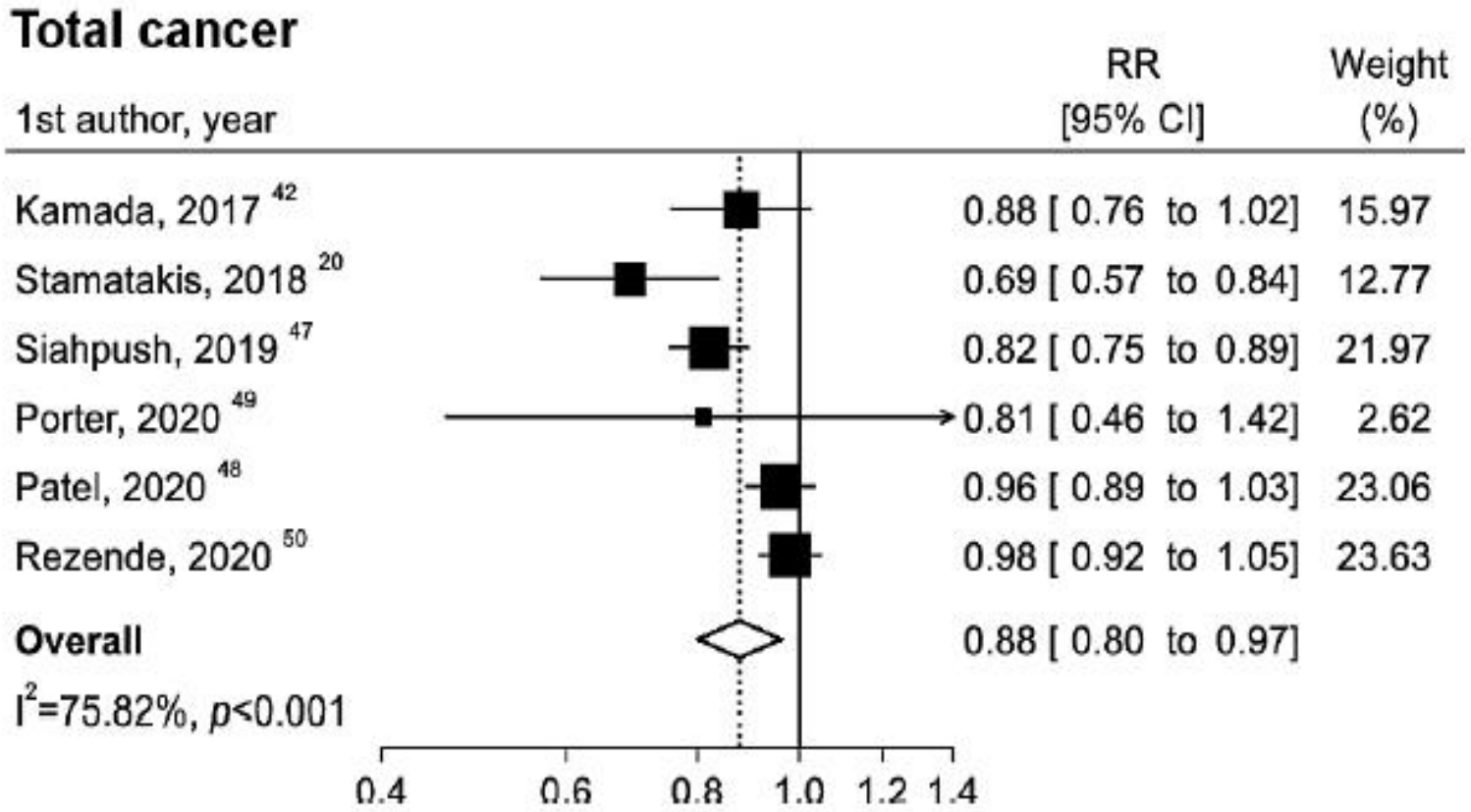


Fig 1 | Association between meeting the 2018 physical activity guidelines for Americans and all cause and cause specific mortality from three diseases. Estimates are from the fully adjusted model that includes the covariates of sex, age, race/ethnicity, education, marital status, body mass index, smoking,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

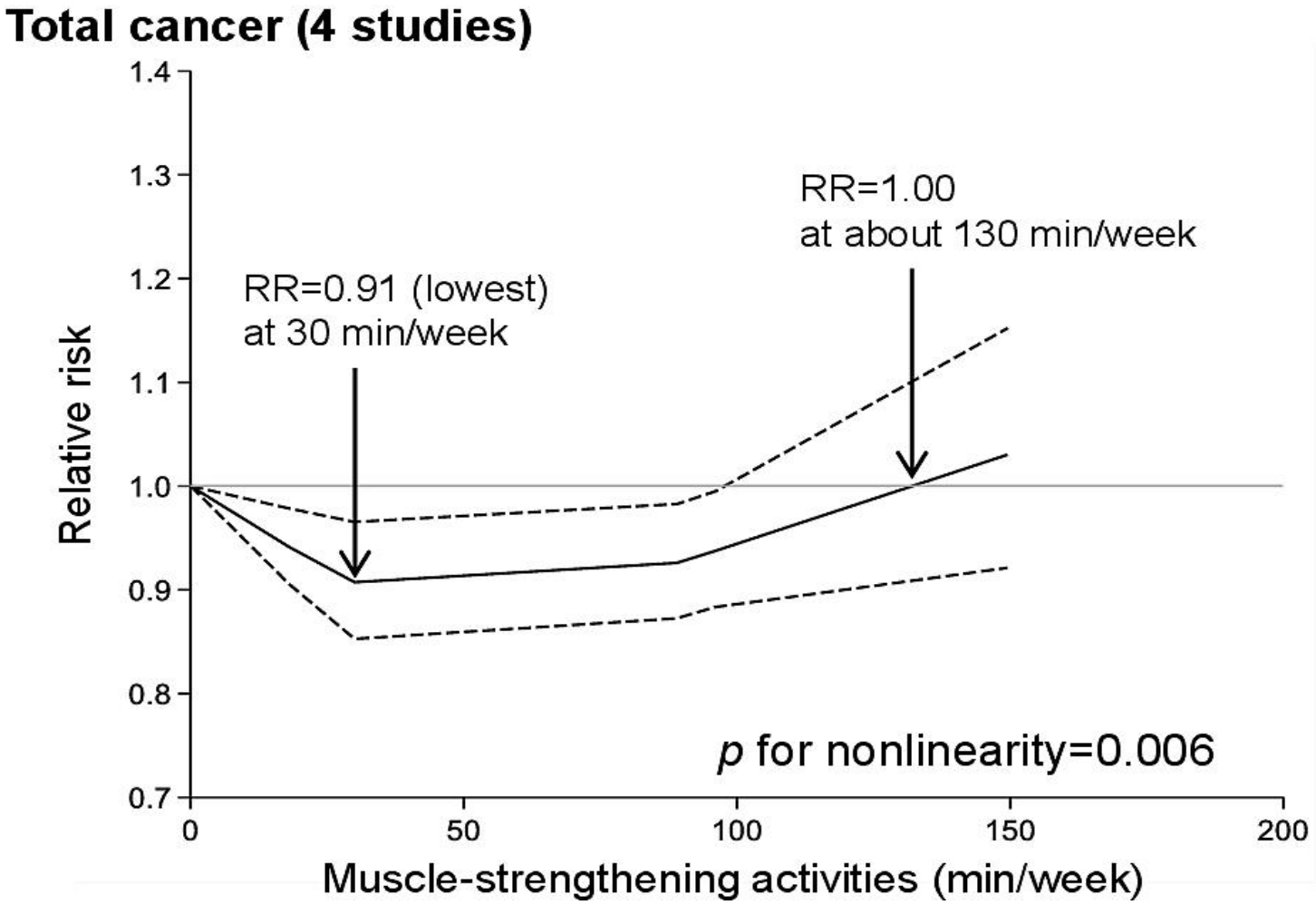
Momma et al. Muscle-strengthening activities are associated with lower risk and mortality in major non-communicable diseases: a systematic review and meta-analysis of cohort studies. Br J Sports Med. 2022 Jul;56(13):755-763

Associations between no versus any muscle-strengthening activities and cancer mortality in 540 343 partecipants (mean age <60 yrs) and 21253 cases of cancer (median follow-up 25.2 yrs)



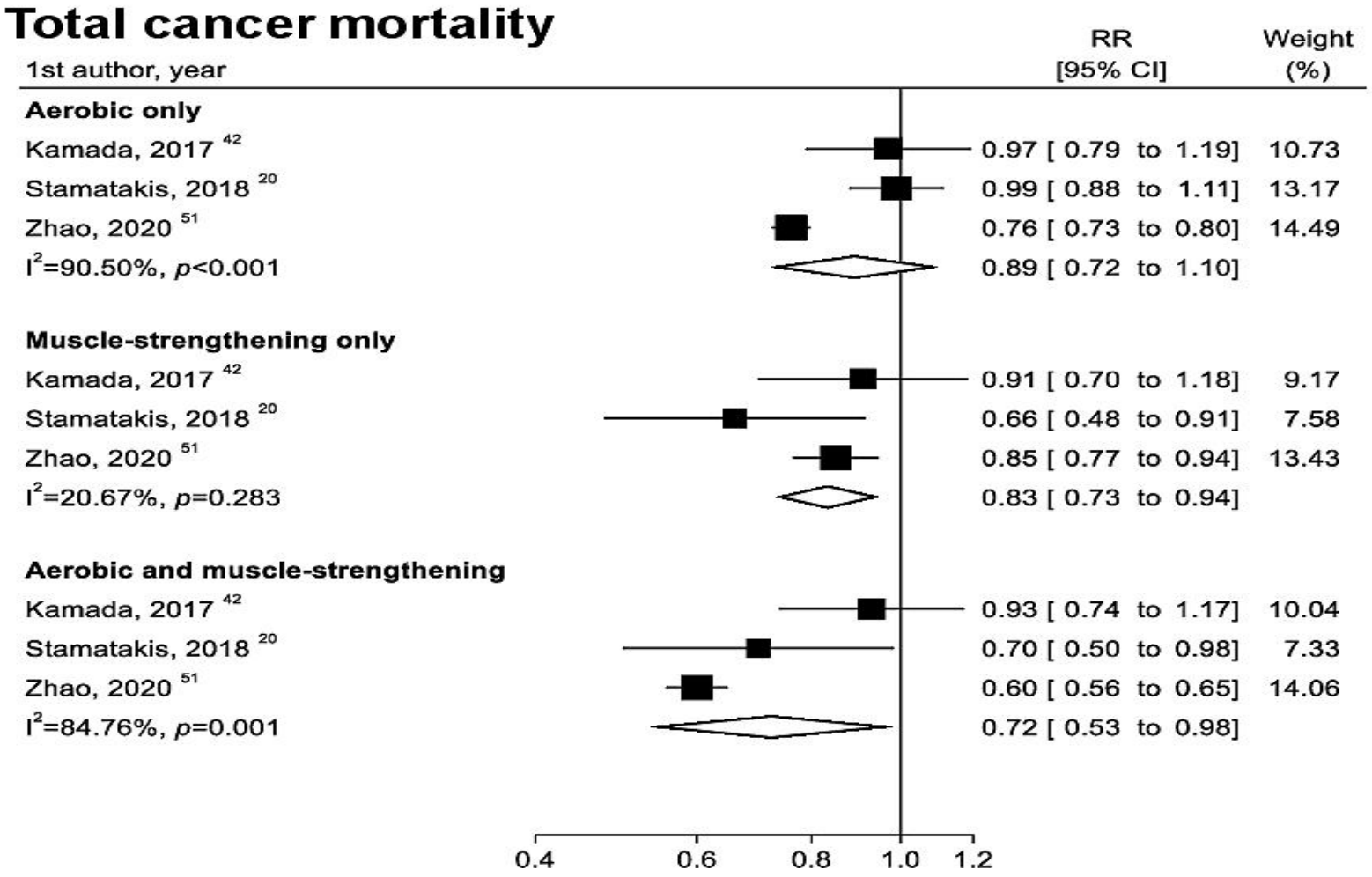
Momma et al. Muscle-strengthening activities are associated with lower risk and mortality in major non-communicable diseases: a systematic review and meta-analysis of cohort studies. Br J Sports Med. 2022 Jul;56(13):755-763.

maximum mortality risk reduction (≈10–20%) at ≈ 30–60 min/week of muscle-strengthening activities (non-linear association, mean age <60 yrs)

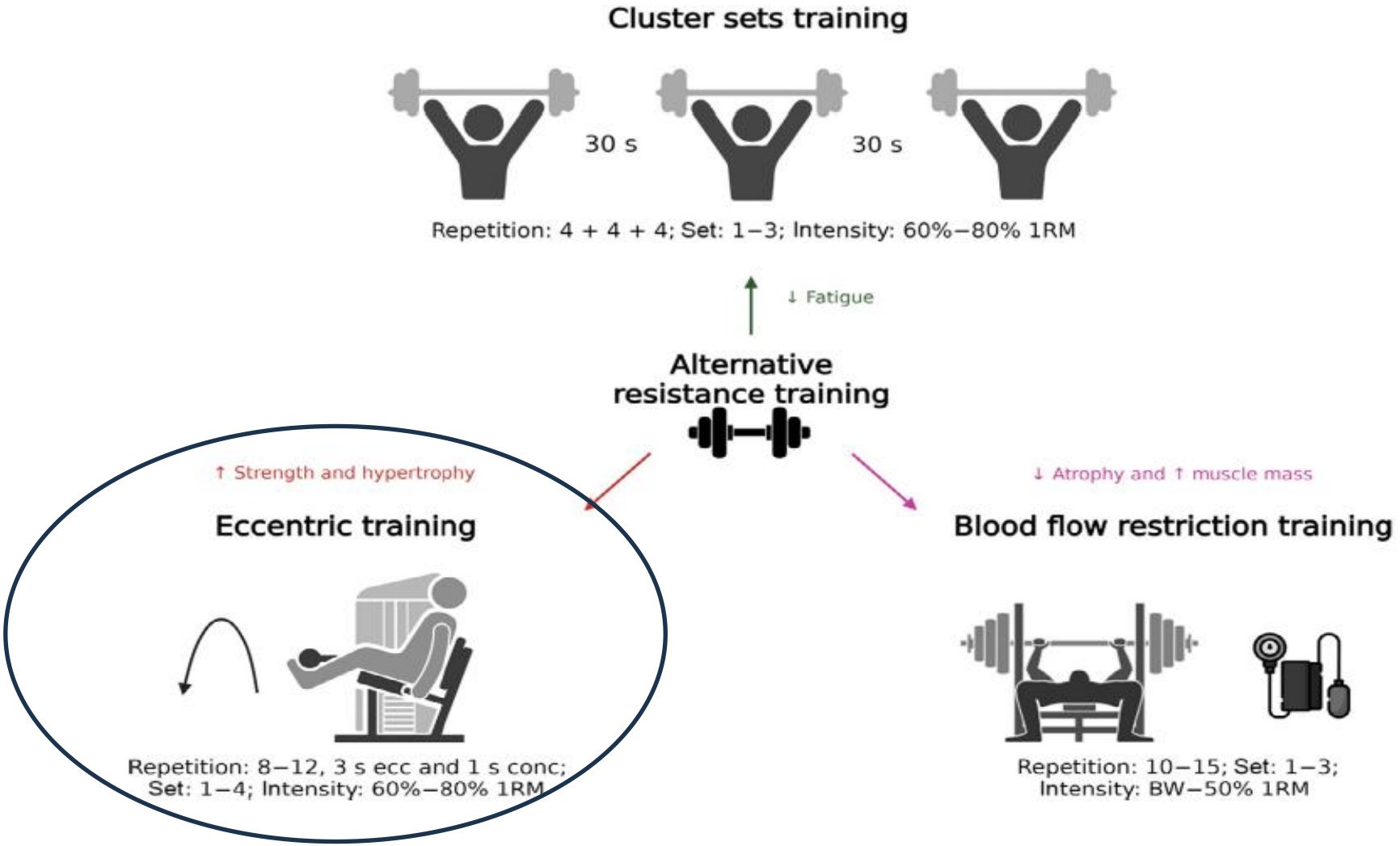


Momma et al. Muscle-strengthening activities are associated with lower risk and mortality in major non-communicable diseases: a systematic review and meta-analysis of cohort studies. Br J Sports Med. 2022 Jul;56(13):755-763.

The combination of muscle-strengthening and aerobic activities provides a greater benefit for reducing total cancer mortality (mean age < 60 yrs)



ESERCIZI ALTERNATIVI



McTiernan et al. 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE*. Physical Activity in Cancer Prevention and Survival: A Systematic Review. Med Sci Sports Exerc. 2019 Jun;51(6):1252-126

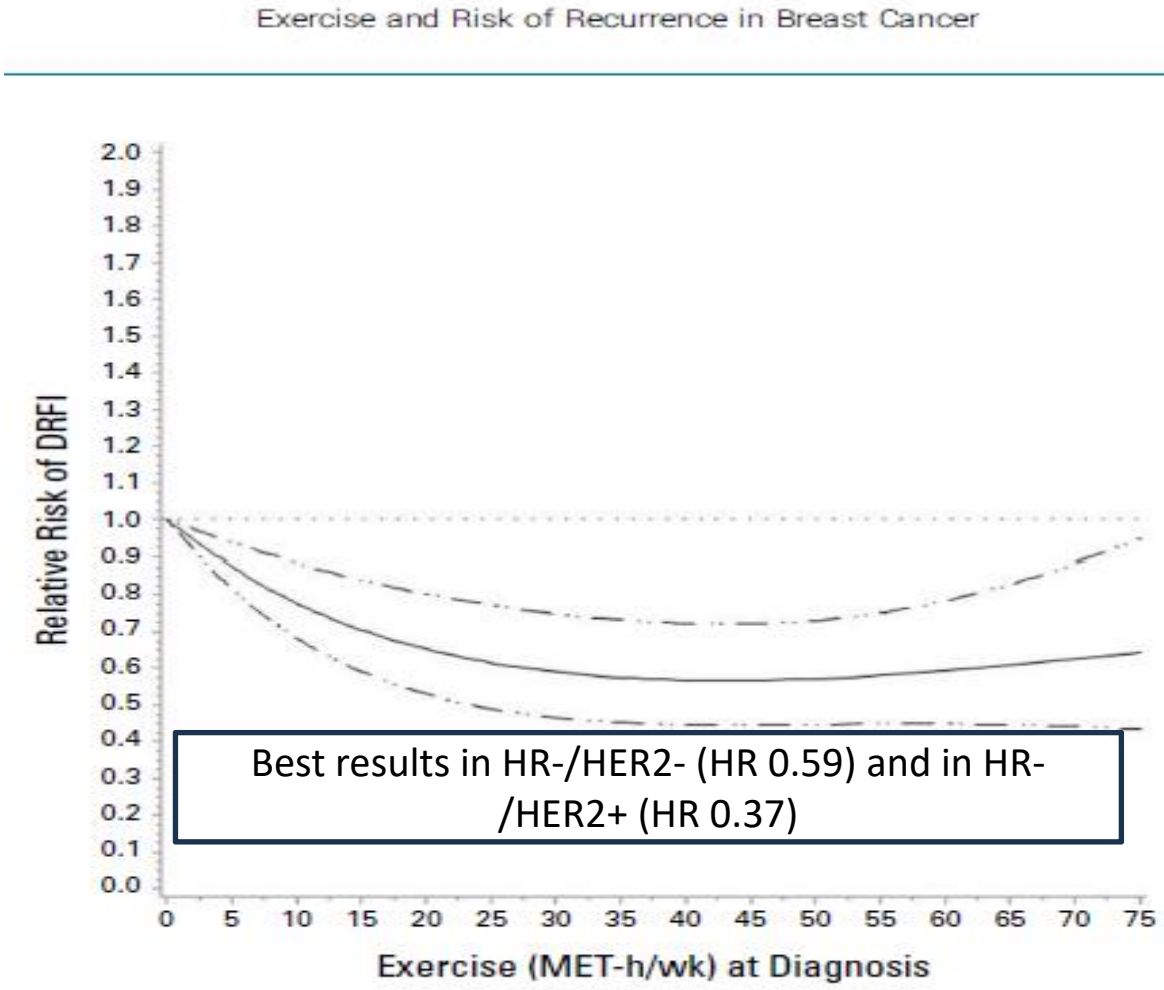
PRIMARY PREVENTION

2018 Physical Activity Guidelines Advisory Committee Evidence on Relationship between Physical Activity and Risk of Developing Invasive Cancer

Cancer	Overall Evidence Grade	Approximate % Relative Risk Reduction	Dose-response? Grade
Bladder	Strong	15%	Yes, moderate
Breast	Strong	12 – 21%	Yes, strong
Colon	Strong	19%	Yes, strong
Endometrium	Strong	20%	Yes, moderate
Esophagus (adenocarcinoma)	Strong	21%	No, limited
Gastric	Strong	19%	Yes, moderate
Renal	Strong	12%	Yes, limited
Lung	Moderate	21 – 25%	Yes, limited
Hematologic	Limited	Variable effect sizes	Not assignable
Head & Neck	Limited	Variable effect sizes	Not assignable
Ovary	Limited	8%	Yes, limited
Pancreas	Limited	11%	No, limited
Prostate	Limited	Variable effect sizes	Not assignable
Brain	Grade not assignable	Variable effect sizes	Not assignable
Thyroid	Limited	0	Not assignable
Rectal	Limited	0	Not assignable

Soldato et al. Dose/Exposure Relationship of Exercise and Distant Recurrence in Primary Breast Cancer. J Clin Oncol. 2024 Jun 5:JCO2301959.

Data on 10359 BC patients



Best results in HR-/HER2- (HR 0.59) and in HR-/HER2+ (HR 0.37)

Morishita et al. Effect of Exercise on Mortality and Recurrence in Patients With Cancer: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2020 Jan-Dec;19:153473542091746 2.

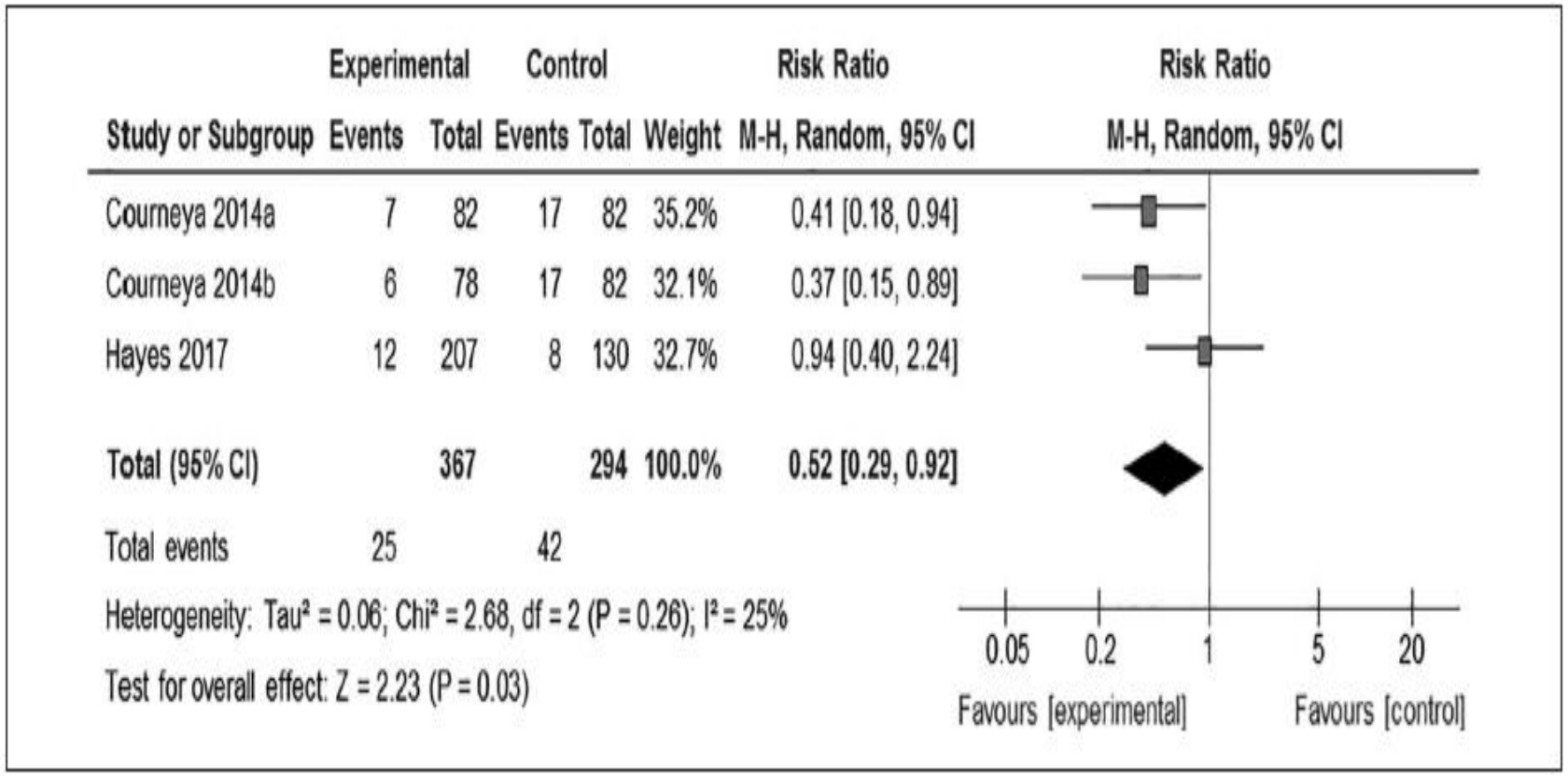


Figure 5. Risk ratio for the effect of exercise on recurrence in cancer survivors.

Morishita et al. Effect of Exercise on Mortality and Recurrence in Patients With Cancer: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2020 Jan-Dec;19:1534735420917462.

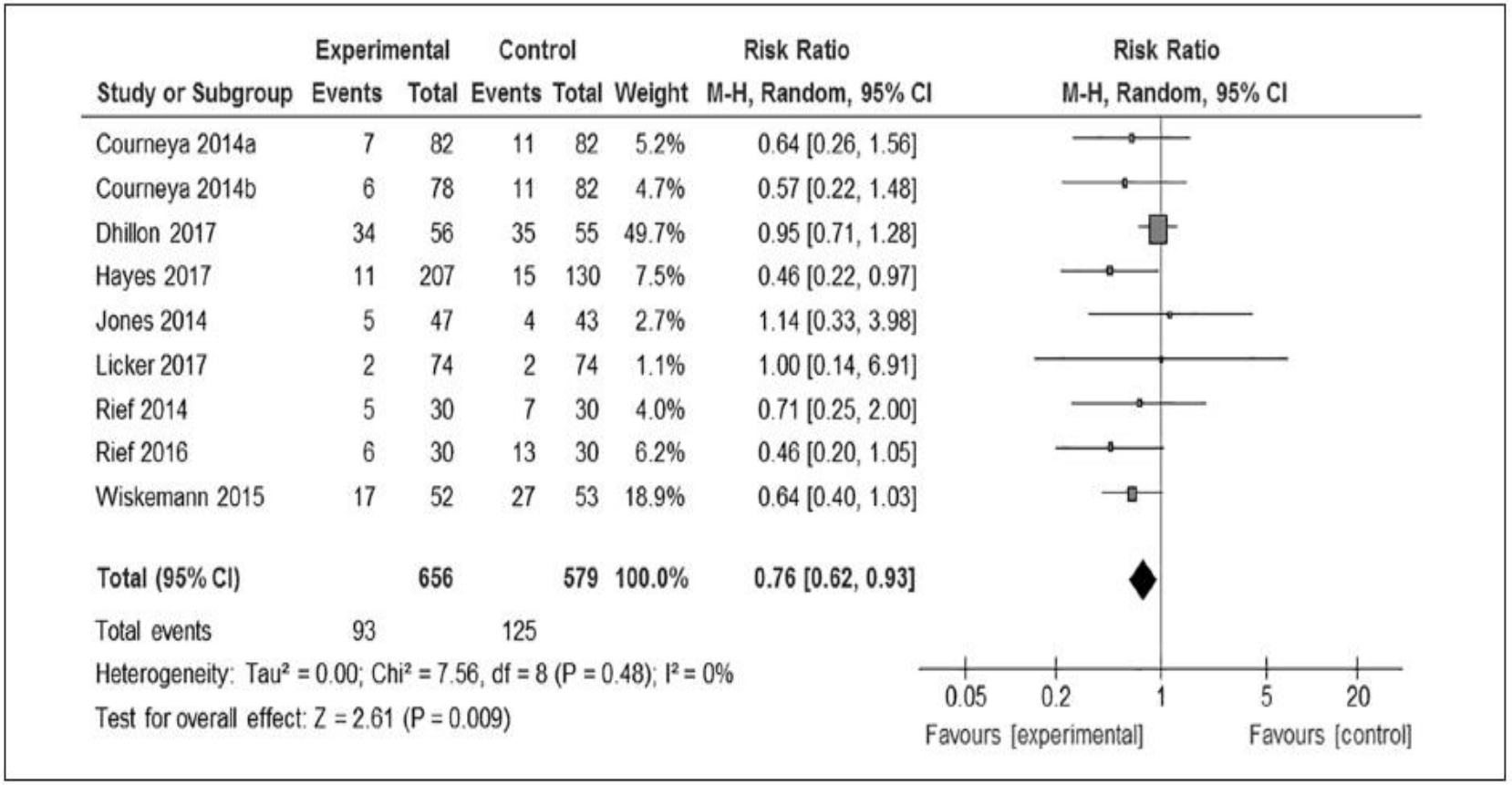


Figure 4. Risk ratio for the effect of exercise on mortality in cancer patients and survivors.

QUANTA ATTIVITA' FISICA
Indicazione classica (OMS)

ADULTI (18-64)

- **150 ai 300 min di attività fisica aerobica di intensità moderata a settimana**, oppure **almeno 75-150 minuti di attività fisica aerobica intensa**. Questi obiettivi possono essere raggiunti, per esempio, con 5 sessioni di esercizio moderato a settimana di almeno 30-60 minuti oppure svolgendo almeno 25-50 minuti 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**

QUANTA ATTIVITA FISICA
Indicazione classica (OMS)

OVER-65

- **attività fisica aerobica di intensità moderata per almeno 150-300 minuti o attività fisica aerobica intensa per 75-150 minuti**. 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.

QUANTA ATTIVITA' FISICA

Indicazioni recenti

Garcia et al: Br J Sports Med 2023;57:979–989

(studio su 35milioni persona/anno)

I dati indicano che una notevole riduzione del rischio di mortalita' per tumore si puo' ottenere con **75 min/settimana o meno di attivita' aerobica moderata** (cioe' meta' dei livelli minimi raccomandati)

Thus, our findings support the recent change in public health messaging to

'doing some PA is better than doing none',

and suggest that he emphasis on threshold-based recommendations could be further reduced.

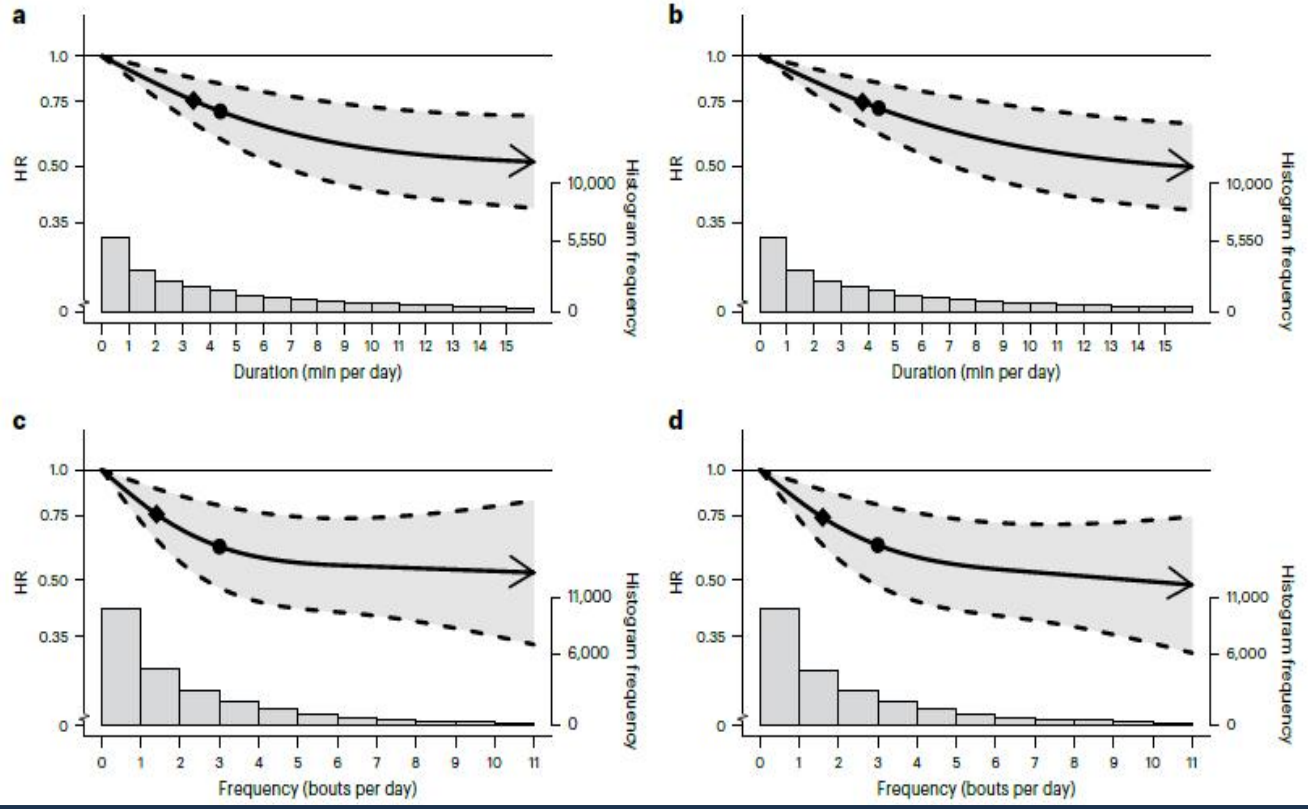
ATTIVITA' FISICA

- Definizione e classificazione di attività fisica
- Attività fisica: quanta e quale per ridurre il rischio di tumore
- Attività fisica «vigorosa e intermittente»

Stamatakis et al. Association of wearable device-measured vigorous intermittent lifestyle physical activity with mortality. Nat Med. 2022 Dec;28(12):2521-2529.

25 241 persone che non fanno esercizi seguite per una media di 6.9 anni

a) durata degli episodi (1 min); b) durata degli episodi (2 min); c) frequenza degli episodi (1 min); d) frequenza degli episodi (2 min)

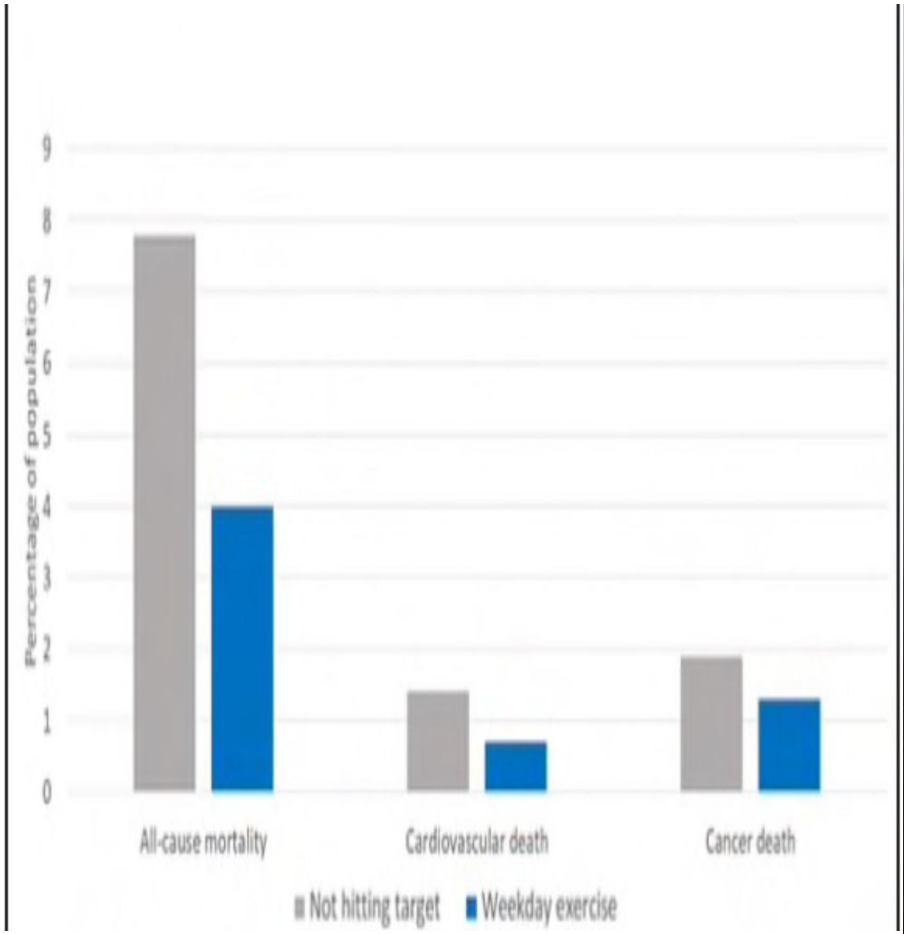


Diamond: minimal dose which estimates the daily duration/frequency of VILPA associated with 50% of optimal risk reduction. Circle: HR associated with the median VILPA value

In chi non pratica esercizi fisici, una attività vigorosa intermittente di 4,4 min al giorno si associa ad una riduzione del 26-30% della mortalità per tumore

Dos Santos et al. Association of the "Weekend Warrior" and Other Leisure-time Physical Activity Patterns With All-Cause and Cause-Specific Mortality: A Nationwide Cohort Study. JAMA Intern Med. 2022 Aug 1;182(8):840-848.

A study on 350 978 adults: 150 min or more of moderate-vigorous physical activity (or 75 min of vigorous activity) per week may experience similar health benefits whether the sessions are spread throughout the week or concentrated in a weekend.



M E S S A G G I C H I A V E

- **Dieta scorretta (poca frutta e verdura, abuso di cibi ultraprocessati e alcool), sovrappeso, iperglicemia e inattività fisica si associano ad un maggior rischio di tumore**

- **Per ridurre il rischio occorre una attività fisica settimanale aerobica**

  - **moderata ≥ 150-300 min o intensa 75-150 min., più 2 volte di rafforzamento muscolare (ma recenti dati suggeriscono la metà può esser sufficiente) o**
  - **10-12000 passi al giorno, meglio se ad alta frequenza, o**
  - **attività compresa tra 7.5 e > 15 MET/ ore per settimana**

- **Il semplice potenziamento muscolare riduce il rischio, ma e' meglio se si associa ad attivita' aerobica**

- **Anche la attivita' moderata (150 min) o vigorosa (75 min) concentrata nel week-end riduce il rischio**

- **L'attività fisica riduce anche il rischo di recidiva e mortalità nei pazienti curati per tumore (esperienza più consolidata nel carcinoma mammario)**

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