

## Prevenzione oncologica e "interception": verso la medicina personalizzata

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### La rivoluzione epidemiologica del Millennio





Tasso di mortalità 1901 al 2000 e principali Malattie infettive (INF), tumori (TUM), cardiovascolari (CARD), cerebrovascolari (CER), respiratorie e influenzali (RESP), apparato digerente (DIG) e incidenti (ACC).

LA MORTALITÀ PER MOLTE CAUSE È DIMINUITA E L'ASPETTATIVA DI VITA AUMENTATA

De Flora S. et al. Faseb J, Vol 8:892-7

#### Prevenzione vs Terapia



L'aspettativa di vita aumenta e dunque cresce la fascia di popolazione anziana. In particolare, vivono mediamente più a lungo le **Donne** rispetto agli **Uomini.** 



Christensen K, et al Lancet. Oct 3;374(9696):1196-208.



La speranza di vita nel 2019 dai nostri calcoli (con qualche approssimazione rispetto ai calcoli Istat) risulta di 83,2 anni alla nascita e di 21,1 a 65 anni di età, aggiungendo i decessi Covid-19 si passa a 82,1 e 20,2 ed aggiungendo ancore il 10% di decessi Covid in più si arriva a 82,0 e 20,1.



#### Sopravvivenza media relativa a 5-anni per tipo di tumore (uomini e donne) in diversi Paesi Europei



## La Repubblica (Sull'aumentata speranza Di vita)

## Gli italiani i più longevi d'Europa

Classifica di Lancet. E gli esperti confermano: "Qui si vive meglio"

(segue dalla prima pagina) <b>EIENDISI</b> PARCIER Se la donne sono delle francesi (1854 anni contro inostri 85,3), nelcomples- osi conferma che il nostro è il paese dove i giorni sono più lun- tione di la divisi di la divisi si conferma sul ragiori di questo primato. E lo fa in un momento the sembra studiato apposta peri	correlazione fra ricchezza, edu- cazione e durat della vita i mol- to strutta, sottolinea la curatrice dello studio. Carol lagger dell'u- niversità inglese di Lelcester. E nell'Europa 251 inucleo centra- nell'Europa 251 inucleo centra- listruzione e levrato, buon sistema sanitataio e alutti agli anziani	Aspettattiva di vita in Europa FRANCIA Donne (d cui 63 in buona salute) ITALIA 85,3 (di cui 71 in buone salute) SPAGNA 85 (di cui 63 in buone salute) ITALIA 80,4	Lincel. Il primato italiano ha cau- senotecome dieta, un sistema sa- nitario che funziona bene nono- stante qualchescandalo eumage- merale condizione di salute che si diario di su bassa di salute che si di su di su su su su su su su su su su accentuare i lati negativi della ni di su di su su su su su su su su su di su di su su su su su su su su su di su di su s	ran dal Consiglio Europee por tare al 50 per cento il livello di oc- cupazione dei lavoratori con più di 55 ami e far sittare gradual- mente l'età pensionabile verso i 70 ami. el ovoto che la fase di at Con il nostro pil si pone il problema delle pensioni e dovremo lavorare fino a 70 anni	Fasticella dei 70 anni. Per ogni anno che passa, al giorno d'oggi, la nostra aspettati- va di vita aumenta di almeno tre mesi, -è come se ogni anno du- programa della della della della su- to glialtri trevengono in uncer- serso depositai in hanca: ne sufruiremo sotto formadi alion- namento della vecchiata. Ma ano solo i giovani e i lavoratori tivi in genere. Anche perchè ne- luttimi quindici anni l'Europa è meciata auno ritemo mediamente	
pel, infaitt, si vive più a lungo e si invecchia con meno acciacchi laddove il livello di sitruzione è più elevato, il sistema sanitario pubblico è meglio finanziato e le politiche a favore degli anziani sono più supportate da fondi. La	le dei quindici offre panorami nettamente migliori rispetto ai dicei paesi arrivati dopo con eco- nomie più traballanti. Per Antonio Golini, che inse- gna Demografia alla Sapienza ed è membro dell'Accademia dei	(d) cut 70 in buona salute) SVEZIA (d) cut 70 in buona salute) FRANCIA (d) cut 68 in buona salute)	dura però solo un capitolo. In un paese che invecchia (così come tutto il continente) e ha un pil pri- vo di grinta non esiste altra solu- zione — sostengono la Jagger e i suoi ricercatori — che mettere in atto una raccomandazione avan-	tività di un individuo debba an- dare di pari passo con l'allunga- mento della sua vita dice Golini. Anche perché l'indice della salu- te — che indica l'età media in cui si presentano i primiacciacchi in- validanti — oltrepassa in Italia	India e Cina ci hanno sopravan- zato di circa dieci volte. La strada persa si recupera soltanto lavo- rando di più, non solo nel corso della settimanamanche in quel- lo della vita. Sembra sia il modo migliore per arrivare a cent'anni.	

Aspettattiva di vita in Europa Donne FRANCIA 85,4 (di cui 69 in buona salute) ITALIA 85.3 (di cui 71 in buona salute) SPAGNA 85 (di cui 68 in buona salute) Uomini ITALIA 80.4 (di cui 71 in buona salute) SVEZIA 80.3 (di cui 70 in buona salute) FRANCIA 79,5 (di cui 68 in buona salute)

#### Quali sono i fattori di rischio dei tumori?

*Le cause note* delle alterazioni del DNA nella genesi del cancro sono di vari ordini: si ipotizzano cause di tipo ambientale, genetiche, infettive, legate agli stili di vita e *fattori casuali.* La quota di tumori attribuibili ai vari fattori di rischio è riportata nella Tabella 1: negli USA il fumo di tabacco da solo è responsabile del 33% delle neoplasie; un altro 33% è legato ai cosiddetti *stili di vita* (dieta, sovrappeso, abuso di alcool e inattività fisica).

Fattore di rischio		Quota di tumori attribuibi		
		USA, 2012*	Regno Unito, 2010**	
		%	%	-
	Tabacco	33	19	
	Dieta	5	19	
	Sovrappeso, obesità	20	5	
	Inattività fisica	5	1	
	Abuso di bevande alcoliche	3	4	
	Fattori occupazionali	5	4	
	Infezioni	8	3	
	Radiazioni ionizzanti e esposizione a raggi UV	2	5	
	Inquinamento ambientale	2	-	

#### TABELLA 1. Quota di tumori attribuibili a vari fattori di rischio

\*American Association for Cancer Research, 2013.

\*\* Parkin DM. The fraction of cancer attributable to lifestyle and environmental factors in UK in 2010. Br J Cancer, 2011.

I numeri del Cancro in Italia 2018

#### Numero di morti evitabili per tumori attribuibili a stili di vita individuali in Italia

Fattore di rischio	Maschi	Femmine
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

I NUMERI DEL CANCRO In Italia 2020

## Leading Sites of New Cancer Cases and Deaths – 2022 Estimates

	Male			Female		
	Prostate	268,490	27%	Breast	287,850	31%
S	Lung & bronchus	117,910	12%	Lung & bronchus	118,830	13%
	Colon & rectum	80,690	8%	Colon & rectum	70,340	8%
	Urinary bladder	61,700	6%	Uterine corpus	65,950	7%
	Melanoma of the skin	57,180	6%	Melanoma of the skin	42,600	5%
	Kidney & renal pelvis	50,290	5%	Non-Hodgkin lymphoma	36,350	4%
	Non-Hodgkin lymphoma	44,120	4%	Thyroid	31,940	3%
	Oral cavity & pharynx	38,700	4%	Pancreas	29,240	3%
	Leukemia	35,810	4%	Kidney & renal pelvis	28,710	3%
	Pancreas	32,970	3%	Leukemia	24,840	3%
	All sites	983,160		All sites	934,870	
				Female		
	Lung & bronchus	68,820	21%	Lung & bronchus	61,360	21%
	Prostate	34,500	11%	Breast	43,250	15%
	Colon & rectum	28,400	9%	Colon & rectum	24,180	8%
	Pancreas	25,970	8%	Pancreas	23,860	8%
2	Liver & intrahepatic bile duct	20,420	6%	Ovary	12,810	4%
	Leukemia	14,020	4%	Uterine corpus	12,550	4%
5	Esophagus	13,250	4%	Liver & intrahepatic bile duct	10,100	4%
	Urinary bladder	12,120	4%	Leukemia	9,980	3%
3	Non-Hodgkin lymphoma	11,700	4%	Non-Hodgkin lymphoma	8,550	3%
	Brain & other nervous system	10,710	3%	Brain & other nervous system	7,570	3%
	All sites	322.090		All sites	287.270	

MAMMELLA	
Incidenza Si stima che nel 2019 verranno diagnosticati in Italia circa 53.000 nuovi casi di carcinomi mammella femminile (dati AIRTUM).	
Mortalità Anche per il 2016 il carcinoma mammario ha rappresentato la prima causa di morte per tumo nelle donne, con oltre 12.000 decessi (dati ISTAT).	
Sopravvivenza Risulta in Italia essere pari a 87%.	
Sopravvivenza a 10 anni La sopravvivenza dopo 10 anni dalla diagnosi è pari a 80%.	
Fattori di rischio	Le donne sopra i 50 anni d'età hanno un maggior rischio di sviluppare un tumore mammario. Sono stati identificati altri fattori di rischio legati a <b>fattori riproduttivi</b> (menarca precoce e una menopausa tardiva; nulliparità,una prima gravidanza a termine dopo i 30 anni, il mancato allattamento al seno], <b>fattori ormonali</b> (terapia ormonale sostitutiva assunta durante la menopausa), <b>fattori dietetici e metabolici</b> (elevato consumo di alcol e di grassi animali e
	basso consumo di fibre vegetali), <b>pregressa radioterapia</b> (a livello toracico e specialmente se prima dei 30 anni d'età) e <b>precedenti displasie o neoplasie mammarie</b> . Inoltre, il 5-7% dei tumori mammari risulta essere legato a <b>fattori ereditari</b> ,1/4 dei quali determinati dalla mutazione di due geni, BRCA1e/o BRCA2.
Diagnosi	Leggere i paragrafi sottostanti. Per ulteriori approfondimenti consultare Linee Guida AIOM nel
Trattamento	

I NUMERI DEL CANCRO In Italia 2019

PROSTATA			
Incidenza	Il tumore della prostata è la neoplasia più frequente tra i soggetti di sesso maschile (19%). Per il 2019 sono attesi 37.000 nuovi casi.		
Mortalità	Nel 2016 si sono osservati 7.540 decessi per cancro prostatico (ISTAT).		
Sopravvivenza a 5 anni	La sopravvivenza a 5 anni degli uomini con tumore della prostata in Italia è pari a 92%. Per i pazienti in vita dopo 1 e 5 anni l'aspettativa di vita si mantiene stabile.		
Sopravvivenza a 10 anni	za La sopravvivenza a 10 anni degli uomini con tumore della prostata in Italia è pari a 90%.		
Fattori di rischio L'emergere di forme clinicamente silenti e biologicamente non aggressive ha in difficile l'interpretazione degli studi eziologici e la valutazione della diversa dist fattori di rischio in passato correlati all'insorgenza di questa malattia, tra i qual elevato di carne e latticini, dieta ricca di calcio (con conseguente elevata concer			
	di IGF-lematico) e alti livelli di androgeni nel sangue. La malattia appare per altro legata a fattori ereditari in una minoranza di casi (<15%).		
Diagnosi	Leggere i paragrafi sottostanti. Per ulteriori approfondimenti consultare		
Trattamento	Linee Guida AIOM nel sito www.aiom.it		

I NUMERI DEL CANCRO In Italia 2019

#### Proposal For a common Risk Scorecard

#### Two "Scorecards" for Risk Assessment for either Cardiovascular Disease or Cancer

	Established Scorecard for Cardiovascular Risk (European Society of Cardiology)	Proposed New Scorecard for Cancer Risk
Personal and Lifestyle	Age and sex	Age and sex
Components	Smoking	Smoking Exercise Dietary habits Obesity Reproductive history
Genetic Analysis	Family history	Family history Oncogene/tumor suppressor mutations Metabolic activity polymorphisms
Laboratory Measurements	Mean LDL cholesterol Mean HDL cholesterol / LDL:HDL ratio Mean systolic blood pressure Indications of diabetes	DNA adducts DNA oxidative damage score Proteomics score: Tissue proteomics Serum proteomics Microbiopsy dysplasia score hormone status Chronic infection ( <i>e.g. H. pvlori</i> ) Any new biochemical markers that will be devaloped

Albini A and Sporn M Nature Reviews Cancer



## Fattori di rischio per tumore

Fattori di rischio non modificabili	Fattori di rischio modificabili	Fattori di rischio trattabili
Età	Tabacco	Infiammazione cronica
Genetica	Sovrappeso ed obesità	Infezioni virali
Mutazioni ereditarie e somatiche	Nutrizione	Infezioni batteriche
Sesso	Attività fisica	Diabete
Etnia	Esposizione ad agenti cancerogeni	Irradiazione
Anamnesi familiare	Alcool	Stato ormonale
Anamnesi personale	Allattamento*	
Storia riproduttiva*,†		
Regione del mondo†		

- Per donne.
- +In alcuni casi, le persone possono scegliere la propria storia riproduttiva e la propria regione mondiale; per altri, questa non è una scelta specifica.
- Strategies to Prevent "Bad Luck" in Cancer. Albini A, Cavuto S, Apolone G, Noonan DM. J Natl Cancer Inst. 2015 Aug 4;107(10). pii: djv213. doi: 10.1093/jnci/djv213. Print 2015 Oct.

# Non fumare: molti tumori (non solo polmonari aumentano col fumo di sigaretta)





Age-standardised smoking prevalence in 2017 and estimated hypothetical prevalence with the highest-level of tobacco control policies (TCP) implementation (measured by the Tobacco Control Scale), by sex and country.



## Estimated number of new cancer cases in 2020 attributable to alcohol drinking worldwide and in Europe in both sexes



#### Aumento della Percentuale di persone in sovrappeso USA negli ultimi venti anni



# Ci sono più persone sovrappeso che persone con un peso "sano" o normale



### L' obesità è in crescita nel mondo occidentale



Ministry of Health. 2015. Understanding excess body weight. NZ Health Survey.

## Estimated number of new cancer cases in 2012 attributable to obesity worldwide and in Europe in both sexes



#### Obesity reduction is also beneficial to cancer prevention



Adapted from "An Equity-Oriented Prevention Framework", National Academy of Medicine, 2017 The scheme might it be beneficial for cancer prevention & screening to more closely align with prevention & screening for other diseases (e.g., obesity cardiovascular, metabolic, diabetes)

#### Some points in prevention and screening

- •Learning from reducing HPV-associated cancer
- •Alignment between prevention & screening for cancer
- •Screening for additional types of cancer and new approaches for cancer screening
- •Working on life style
- Health disparities and technology

Interventions against cervical cancer: Opportunities at each step of the process

HPV vaccination	Primary prevention	
Cervical cancer screening	Secondary prevention	
Treatment of invasive cervical cancer	Tertiary prevention	

### Prevention, screening, and early detection: HPVassociated cancer

**Good news:** We can do a tremendous amount for primary & secondary prevention

Bad news: The tools are underutilized

We need to figure out how to better utilize vaccinations and screening We can't stop at the "what" (interventions).

We need to work on the "how" (implementation, delivery)

### Global Disparities in Cervical Cancer Cases & Deaths: Manyfold higher in Africa than in U.S.



#### Low- and middle-income countries:

~90% of cervical cancer *cases* and *deaths* (projected to increase by 2% each year)

#### Africa vs. North America:

- >4-fold difference in incidence rate
- >8-fold difference in mortality rates

Cervical cancer represents 90% of HPVassociated cancer

*Great opportunity for prevention, screening, and early detection – through technology.* 

Bray et al, Global cancer statistics 2018, Cancer 2018.

## Health care provider recommendation associated with increased HPV vaccine uptake



Source: Lu et al, Human papillomavirus vaccination trends among adolescents: 2015 to 2020. Pediatrics, 2022.

### Herd protection in 14-24 year-old women 12 years after HPV vaccine introduction in the U.S.



Rosenblum et al, Annals Int. Med. 2022

Some important clinical results against HPV types targeted by the HPV vaccine

Vaccine has very high	Vaccine confers sterilizing
efficacy (>95%) & long	immunity
duration of protection	Prevents infection in most
(>10 years)	vaccinees
Vaccine induces herd immunity even with sub- optimal vaccine uptake	Learning from reducing HPV-associated cancer

Schiller & Lowy, *Vaccine*, 2018; Hildesheim et al, *American Journal of Obstetrics and Gynecology*, 2016; Rosenblum et al, *CDC Morbidity and Mortality Weekly Report (MMWR)*, 2021

## Cost-effective, high quality "See and Treat" approach for cervical cancer screening

Undergoing international large-scale clinical trials for lowand middle-income AND high-income countries



Rapid, inexpensive, on-site HPV DNA test



**On-site automated visual evaluation** of cervix with smartphone and AI algorithm (HPV-positive women)



On-site thermal ablation

For more: Desai et al, Int J Cancer, 2022: "Redesign of a rapid, low-cost HPV typing assay to support riskbased cervical screening and management" and "The development of "automated visual evaluation" for cervical cancer screening"

### Efforts to expand screening

Additional forms of cancer	Risk-based treatment
Simplifying screening methods	Starting screening closer to home

#### PREVENZIONE E "INTERCETTAZIONE": UNA NUOVA ERA NELLA CHEMOPREVENZIONE

#### Perspective

## Cancer Prevention and Interception: A New Era for Chemopreventive Approaches 🛚

Adriana Albini<sup>1</sup>, Andrea DeCensi<sup>2</sup>, Franco Cavalli<sup>3</sup>, and Alberto Costa<sup>4</sup>

#### Table 1. A potential "to do" list in cancer prevention and preventive interception

	Prevention	Interception
1	Do not smoke.	-Quit smoking (often requires a multitask, structured intervention). Take low- dose aspirin or other chemoprevention measures.
2	Avoid chemical carcinogens in the environment and at work place. Make your environment smoke free.	<ul> <li>Fight for your rights: receive attention if you have been exposed to asbestos, PAH, and other carcinogens in the work place or environment.</li> </ul>
3	Avoid physical carcinogens, example: overexposure to sunlight and other sources of UV.	-Do periodic screening for premalignant skin lesions.
4	Avoid biologic carcinogens. Vaccines for virally induced cancer (example: HPV).	-Antibiotics for bacterial-associated cancer (example: <i>Helicobacter pylori</i> ). Do periodic screening for premalignant lesions in the uterine cervix
5	Avoid overweight and obesity, eat properly	Lose weight, change dietary habits
6	Avoid foods that might be potentially carcinogenic	-Limit salt, red and processed meat; avoid soft drinks
7	Limit alcohol. Do not overcome 1 glass per day in women and 2 glasses in men	-Cut back or quit drinking
8	Keep your gut flora and your microbiota "healthy"	<ul> <li>Restore your intestinal flora with a healthy life style and diet. Near future: dietary supplements containing "healthy" microbiome components</li> </ul>
9	Avoid a sedentary lifestyle, be physically active	-Get on an exercise program
10	Control risk factors: inflammation, metabolic syndrome	<ul> <li>With low level risk conditions, take some chemopreventive strategies with few side effects: aspirin, metformin, flavonoids, curcumin</li> </ul>
11	Prefer breast feeding your children rather than using formula	<ul> <li>Monitor changes in your body (e.g., breast lumps).</li> </ul>
12	If there are familial cases of cancer, get genetic counseling and do relevant chemoprevention for the cancers at risk.	<ul> <li>Do periodic screening for premalignant lesions for breast, colon and prostate.</li> <li>With high risk consider a chemoprevention trial. Near future: precision prevention.</li> </ul>

Abbreviations: PAH, polycyclic aromatic hydrocarbons; UV, ultraviolet light.

Clin Cancer Res; 22(17) September 1, 2016

Clinical

Cancer Research

### **Precision Medicine and Prevention**

Interventions to prevent, screen, diagnose, or treat a disease (e.g., cancer), based on a molecular and mechanistic understanding of the causes, pathogenesis, and/or pathology of the disease

*Precision medicine can be better than traditional approaches in cancer prevention* 

 Evidence is required to determine that a precision approach is superior to a more traditional approach



A theoretical advantage of precision medicine over traditional approaches:

Potential for conceptually-based improvements, while traditional approaches depend mainly on empiricism

### MC(E)Ds: Multicancer "early" detection tests

## Current goal: Detect asymptomatic cancer stages I-III



## Some critical differences from traditional cancer screening:

- 1) Not specific for cancer at particular site
- 2) Not geared mainly to identify pre-cancer or stage I cancer
- Is geared to identify several stages of cancer

prevention.cancer.gov

### Some current MC(E)D issues

Will MCDs reduce mortality rates?

Will MCDs be **useful for all cancer stages** (I-III) for which they screen?

Will advances in cancer **treatment** increase, decrease, or have no **impact** on the utility of MCD tests?

Will benefits clearly outweigh harms?

• Will it be possible for people with limited insurance to get tested and, if their result is positive, to have appropriate diagnostic evaluation and treatment?




### **Imaging Advances**

### **Cancer Detection and Staging**

- Diagnosis at earlier stage
- Clearer picture of disease spread
- Helps patients get optimal treatment
- Permits more limited, minimally invasive surgical techniques



- Informs treatment continuation
  - or discontinuation

- Digital mammograms
- PET scanning
- Low-dose CT
- Enhanced MRI technologies

## Cancer Genomics in screening and prevention

### Advent of the "precision medicine" era

• But cancer's biology is far more complex than we had imagined



## Alimentazione e salute

Alcuni alimenti (verdure, frutta, spezie, bevande, condimenti)

Contribuiscono alla nostra salute prevenendo:

- Malattie Cardiovascolari
- Diabete
- Tumori
- Malattie neurodegenerative



Un importante concetto emergente utile per aiutarci a stare in salute con i cibi è che gli schemi dietetici e le associazioni fra cibi possono essere <u>nel loro insieme</u> protettivi



# Molti componenti della dieta hanno proprietà protettive per la salute



Fonte: Araldi et al. Albini A. Current Cancer Drug Target, 8:146-155

# Molti componenti della dieta hanno proprietà chemiopreventive



Fonte: Araldi et al. Albini A. Current Cancer Drug Target, 8:146-155



**Figure 2: Polyphenols from Mediterranean Diet.** Polyphenols protect and reduce inflammation by different pathways (through mechanisms of down-regulation, balance and up-regulation) preventing obesity, cancer and age-related diseases, in which inflammation has an important pathological role [240].

Oncotarget, 2017, Vol. 8, (No. 5), pp: 8947-8979



## Lo studio EPIC



### **European Prospective Investigation into Cancer and nutrition**



~ 520,000 volontari reclutati in 10 Paesi Europei **OBIETTIVO**: studiare il ruolo dei fattori alimentari e legati allo stile di vita nell' eziologia dei tumori e di altre malattie cronico-degenerative.

### Raccolta dei dati

Questionario anamnestico



- ≻FFQ → dieta
- >Misure antropometriche

➢ Prelievo

**EPIC Italia:** ~ 47,000 volontari in 5 centri

Da dove vengono I dati scientifici che provano che con la corretta alimentazione si prevengono I tumori? Lo studio EPIC

Epidemiological and Large Population Studies, like for instance the EPIC Study

### Italian Mediterranean Index and risk of colorectal cancer in the Italian section of the EPIC cohort

Claudia Agnoli<sup>1</sup>, Sara Grioni<sup>1</sup>, Sabina Sieri<sup>1</sup>, Domenico Palli<sup>2</sup>, Giovanna Masala<sup>2</sup>, Carlotta Sacerdote<sup>3,4</sup>, Paolo Vineis<sup>4,5</sup>, Rosario Tumino<sup>6</sup>, Maria Concetta Giurdanella<sup>6</sup>, Valeria Pala<sup>1</sup>, Franco Berrino<sup>7</sup>, Amalia Mattiello<sup>8</sup>, Salvatore Panico<sup>8</sup> and Vittorio Krogh<sup>1</sup>

Int. J. Cancer: 132, 1404-1411 (2013) © 2012 UICC



La dieta mediterranea riduce l'incidenza di tumori:EPIC

Mediterranean dietary pattern and cancer risk in the EPIC cohort

E Couto<sup>1,2</sup>, P Boffetta<sup>\*,1,3,4</sup>, P Lagiou<sup>5</sup>, P Ferrari<sup>6</sup>, G Buckland<sup>7</sup>, K Overvad<sup>8</sup>, CC Dahm<sup>9</sup>, A Tjønneland<sup>10</sup>, A Olsen<sup>10</sup>, F Clavel-Chapelon<sup>11,12</sup>, M-C Boutron-Ruault<sup>11,12</sup>, V Cottet<sup>11,12</sup>, D Trichopoulos<sup>4,13,14</sup>, A Naska<sup>5</sup>, V Benetou<sup>5</sup>, R Kaaks<sup>15</sup>, S Rohrmann<sup>15</sup>, H Boeing<sup>16</sup>, A von Ruesten<sup>16</sup>, S Panico<sup>17</sup>, V Pala<sup>18</sup>, P Vineis<sup>19,20</sup>, D Palli<sup>21</sup>, R Tumino<sup>22</sup>, A May<sup>23</sup>, PH Peeters<sup>23</sup>, HB Bueno-de-Mesquita<sup>24,25</sup>, FL Büchner<sup>24,26</sup>, E Lund<sup>27</sup>, G Skeie<sup>27</sup>, D Engeset<sup>27</sup>, CA Gonzalez<sup>7</sup>, C Navarro<sup>28,29</sup>, L Rodríguez<sup>30</sup>, M-J Sánchez<sup>28,31</sup>, P Amiano<sup>28,32</sup>, A Barricarte<sup>28,33</sup>, G Hallmans<sup>34</sup>, I Johansson<sup>35</sup>, J Manjer<sup>36</sup>, E Wirfärt<sup>37</sup>, NE Allen<sup>38</sup>, F Crowe<sup>38</sup>, K-T Khaw<sup>39</sup>, N Wareham<sup>39</sup>, A Moskal<sup>1</sup>, N Slimani<sup>1</sup>, M Jenab<sup>1</sup>, D Romaguera<sup>19</sup>, T Mouw<sup>19</sup>, T Norat<sup>19</sup>, E Riboli<sup>19</sup> and A Trichopoulou<sup>4,5</sup>

Br J Cancer (2011) 104, 1493 – 1499 Table 3 Hazard ratios for all cancers associated with categories of the Mediterranean diet score

Meno tumori con L'adesione alla dieta Mediterraneanea

Score	Cohort members	Cases	HR <sup>a</sup> (95% CI)	
Both sexes				
0-3	154052	10 349	1.00	
4	105 936	6849	0.96 (0.93–0.99	
5	99 672	6225	0.92 (0.89-0.95	
6-9	118818	7308	0.93 (0.90-0.96	
		P  for trend = 0.00001		
Men				
0-3	43 [6]	3044	1.00	
4	30.770	2121	0.99 (0.93-1.04	
5	29766	2049	0.97(0.92 - 1.03)	
6-9	38908	2455	0.93 (0.88-0.99	
0 /	50,000	2 IJJ P fo	0.95(0.0000.000)	
		7 10		
Women				
0-3	110891	7305	1.00	
4	75   66	4728	0.95 (0.91-0.98	
5	69 906	4176	0.90 (0.87–0.94	
6-9	79910	4853	0.93 (0.89-0.96	
		P for trend = 0.000 l		



### 6

Legumi Fibre di cereali Multivitamine Vitamina A Vitamina B<sub>6</sub> Acido Folico Vitamina D Vitamina E

Magnesio

#### Original Investigation | Oncology Role of Diet in Colorectal Cancer Incidence Umbrella Review of Meta-analyses of Prospective Observational Studies

Sajesh K. Veettil, PhD; Tse Yee Wong, B Pharm; Yee Shen Loo, B Pharm; Mary C. Playdon, PhD; Nai Ming Lai, MRCPCH; Edward L. Giovannucci, MD, ScD; Nathorn Chaiyakunapruk, PharmD, PhD

Associazione tra il ruolo della dieta e la riduzione dell'incidenza del cancro del colon-retto					
Alimento o regime dietetico	Evidenza Statistica*				
Fibra alimentare totale	+++				
Latticini	+++				
Cereali integrali	+++				
Verdura	+++				
Frutta	+++				
Calcio alimentare	++				
Yogurt	++				
Alimentazione sana	++				
Latte non fermentato	++				
Zinco	++				
Dieta Pesco-vegetariana	+				
Dieta semi-vegetariana	+				
Integrazione di Calcio	+				

### Associazione tra il ruolo della dieta e l'aumento dell'incidenza del cancro del colon-retto

Alimento o regime dietetico	Evidenza Statistica*
Carne Rossa	+++
Carne lavorata	+++
Uova	+++
Dieta occidentale	++
Consumo di alcool	++
Birra	++
Alimentazione non sana	+
Carne di maiale	+
Ferro eme	+/-

\*AMSTAR-2: Strumento di misurazione per valutare le revisioni sistematiche

da: Sajesh K. Veettil et al. JAMA Network Open. 2021;4(2):e2037341. doi:10.1001/jamanetworkopen.2020.37341

#### \*AMSTAR-2: Strumento di misurazione per valutare le revisioni sistematiche da: Sajesh K. Veettil et al. JAMA Network Open. 2021;4(2):e2037341.

+ +/-

doi:10.1001/jamanetworkopen.2020.37341



# Cosa mangiare? La piramide alimentare anti-cancro e le linee guida

- Consuma la giusta quantità di calorie.
- Bevi abbondante acqua (e non bibite carbonate)
- Mangia molti cibi di origine vegetale: verdure, legumi
- frutta, noci, fibre
- Usa olio di oliva, spezie, erbe per condire
- Limita il sale, le carni lavorate, gli insaccati, I dolciumi
- Limita alcool ed evita superalcolici

"30% dei tumori potrebbero essere prevenuti con una corretta alimentazione -American Institute for Cancer Research





Long-term disease control against recalcitrant cancers

• Game-changing discoveries – more coming



### The tumor microenvironment



Johanna A. Joyce & Jeffrey W. Pollard Nature Reviews Cancer 9, 239-252 (April 2009) doi:10.1038/nrc2618

# In inflammation and in tumor progression similar cellular activations occur in the microenvironment



Albini A, Sporn MB. The tumour microenvironment as a target for chemoprevention. Nat Rev Cancer. 7:139-47; 2007

## MICROAMBIENTE: ruolo nei tumori



Phenotype Switching in Leukocytes Polarization of native immunity cells

Huang Y, Snuderl M, Jain RK. Polarization of tumor-associated macrophages: a novel strategy for vascular normalization and antitumor immunity. Cancer Cell. 2011 Jan 18;19(1):1-2.



Noonan, Albini et al, Cancer Metastasis Reviews

# Immune cell plasticity



frontiers n Immunology

🕈 frontiers

in Immunology

published: 0: doi: 10.3389./\*--

Contribution to Tumor Angiogenesis

From Innate Immune Cells Within the Tumor Microenvironment:

0

Phenotype switch of innate immune cells in cancer

### Nurturing NK cells and cytotoxic ones:





Albini A, Noonan DM, Cancer Discovery, jan 2021

Figure 1. Nurturing NK cells and cytotoxic ones: a double-edged sword in pregnancy and antitumor action. NK cells in various states: A, CD56<sup>bright</sup>CD16<sup>-</sup>, CD9<sup>-</sup>, CD43<sup>-</sup> dNK cells nurturing in the reproductive system, helping embryo implant and fetal development. dNK cells produce proangiogenic factors (including VEFCF CXCIB anotonenin and agate-trin-1) MMP9 and elycohelin B, CD56<sup>bright</sup>CD16<sup>-</sup>, CD9<sup>-</sup>, and CD49<sup>-</sup> dNK-like cells. disclaving cortumor

> Ing in cancer. dNK-like cells produce proangiogenic Tactors (including VEDF, CXLLB, and angiogenin), MMP9, and LIMP II activation responsible for miscarriage and pregnancy los. Cytotoxic dNK had increased perforin, granzyme B and destroy the cytotoxic activities active in antitumor behavior. Cytotoxic NK cells release perforin and granzyme B and destroy the produced by the NK cells. The figure Published OnlineFirst December 4, 2020; DOI: 10.1158/2159-8250.CD-20-0795

## Il microbiota

Possiamo definire il microbiota intestinale umano come l'insieme dei microorganismi che si trovano nel tubo digerente dell'uomo. Qui vivono dalle 500 alle 1000 specie differenti di microorganismi, i più numerosi dei quali sono batteri seguiti da miceti e virus.



Il microbiota intestinale partecipa al metabolismo dei carboidrati, delle proteine e dei lipidi, regola la secrezione degli ormoni, del pH e degli ioni H, nonché la produzione di composti anti-batterici

Di recente, i ricercatori hanno stabilito un legame tra il microbiota intestinale e il peso corporeo. Le persone obese tendono ad avere una composizione diversa dei batteri intestinali paragonati ad individui magri.

Gli studi mostrano che la composizione del microbiota intestinale si modifica con la perdita di peso e/o con l'aumento di peso; tuttavia, il significato di tali cambiamenti per la salute umana è ancora dibattuto



Buoni germi per buona salute e longevità: il microbiota (alias: flora intestinale)



Nature Reviews | Microbiology

# Profili metabolici in seguito al consumo di alimenti



## Chemoprevention

### The concept of Chemoprevention:

In 1976, Michael Sporn defined chemoprevention:

"The use of specific agents to reverse, suppress or prevent the carcinogenic process to invasive cancer."

Michael Sporn



## Aspirin in Chemoprevention

Targeting inflammation: Several types of cancers are prevented

Warfarin had no effect over the same time period

Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials Rothwell PM et al Lancet. 2011;377(9759):31-41



# From diabetes cure to cancer prevention ... via angioprevention?

### METFORMIN



A decreased risk of breast cancer was observed in female patients with type 2 diabetes using metformin on a long-term basis.

Bodmer M et al, Diabetes Care 2010

Evans JM et al. BMJ 2005

Epidemiological studies have confirmed that metformin, but not other anti-diabetic drugs, significantly reduces cancer incidence and improves cancer patients' survival in tipe 2 diabetics. **Combination Chemoprevention (to the** micreonvironment): Metformin + Aspirin?

# SCIENTIFIC REPORTS

**OPEN** Aspirin and atenolol enhance

### metformin activity against breast cancer by targeting both neoplastic and microenvironment cells Received: 01 June 2015

Accepted: 23 November 2015 Published: 05 January 2016

Giovanna Talarico<sup>1,\*</sup>, Stefania Orecchioni<sup>1,\*</sup>, Katiuscia Dallaglio<sup>2</sup>, Francesca Reggiani<sup>1</sup>, Patrizia Mancuso<sup>1</sup>, Angelica Calleri<sup>1</sup>, Giuliana Gregato<sup>1</sup>, Valentina Labanca<sup>1</sup>, Teresa Rossi<sup>2</sup>, Douglas M. Noonan<sup>3,4</sup>, Adriana Albini<sup>3,\*</sup> & Francesco Bertolini<sup>1,\*</sup>

Metformin can induce breast cancer (BC) cell apoptosis and reduce BC local and metastatic growth in preclinical models. Since Metformin is frequently used along with Aspirin or beta-blockers, we investigated the effect of Metformin, Aspirin and the beta-blocker Atenolol in several BC models. In vitro, Aspirin synergized with Metformin in inducing apoptosis of triple negative and endocrinesensitive BC cells, and in activating AMPK in BC and in white adipose tissue (WAT) progenitors known to cooperate to BC progression. Both Aspirin and Atenolol added to the inhibitory effect of Metformin against complex I of the respiratory chain. In both immune-deficient and immune-competent preclinical models, Atenolol increased Metformin activity against angiogenesis, local and metastatic growth of HER2+ and triple negative BC. Aspirin increased the activity of Metformin only in immune-competent HER2+ BC models. Both Aspirin and Atenolol, when added to Metformin, significantly reduced the endothelial cell component of tumor vessels, whereas pericytes were reduced by the addition of Atenolol but not by the addition of Aspirin. Our data indicate that the addition of Aspirin or of Atenolol to Metformin might be beneficial for BC control, and that this activity is likely due to effects on both BC and microenvironment cells.

## MOLECULES CHEMOPREVENTIVE **NUTRACEUTICHE-Nostro gruppo studio:**

to compre

ucoxantina

#### No nutrients

christophe brunet@szn it (C.B.)

Microalgal Derivatives as Potential Nutraceutical and

Christian Galasso <sup>1</sup>, Antonio Gentile <sup>1</sup>, Ida Orefice <sup>1</sup>, Adrianna Ianora <sup>1</sup>, Antonino Bruno <sup>2</sup>

Douglas M. Noonan 2,3, Clementina Sansone 1,\*, Adriana Albini 2,4,\* and Christophe Brunet 1 <sup>1</sup> Stazione Zoologica Anton Dohrn, Villa Comunale, 80121 Naples, Italy; christian.galasso@szn.it (C.G.);

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<sup>2</sup> Laboratory of Vascular Biology and Angiogenesis, IRCCS MultiMedica, 20138 Milan, Italy;

Department of Biotechnology and Life Sciences, University of Insubria, 211000 Varese, Italy

Food Supplements for Human Health: A Focus on

**Cancer Prevention and Interception** 

#### MDPI

#### 🖉 marine drugs

MDPI

MMP-9 and IL-1ß as Targets for Diatoxanthin and Related Microalgal Pigments: Potential Chemopreventive and **Photoprotective Agents** 

Luigi Pistelli<sup>1</sup>, Clementina Sansone<sup>1,\*</sup>, Arianna Smerilli<sup>1</sup>, Marco Festa<sup>2</sup>, Douglas M. Noonan<sup>3,4</sup>, Adriana Albini<sup>2</sup> and Christophe Brunet<sup>1</sup>

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Gnagnarella et al. BMC Cancer	(2022) 22:794
https://doi.org/10.1186/s12885	-022-09521-4

BMC Cancer

**Open Access** 

#### STUDY PROTOCOL

EDITORIAL

Life style and interaction with microbiota in prostate cancer patients undergoing radiotherapy: study protocol for a randomized controlled trial

Patrizla Gnagnarella<sup>1+1</sup><sup>o</sup>, Giulia Marvaso<sup>2,3†</sup>, Barbara Alicja Jereczek-Fossa<sup>2,3</sup>, Ottavio de Cobelli<sup>3,4</sup>, Maria Claudia Simoncini<sup>6</sup>, Luiz Felipe Nevola Teixeira<sup>5</sup>, Annarita Sabbatin<sup>6</sup>, Gabriella Pravettoni<sup>37</sup>, Harriet Johansson<sup>8</sup>, Luigi Nezl<sup>9</sup>, Paolo Muto<sup>10</sup>, Valentina Borzillo<sup>10</sup>, Egidio Celentano<sup>11</sup>, Anna Crispo<sup>11</sup>, Monica Pinto<sup>12</sup>, Ernesta Cavalcanti<sup>13</sup>, Sara Gandini<sup>9</sup> and for the MicroStyle Collaborative Group Editorial: Exploiting the effect of dietary fibre on the gut microbiota in patients with pelvic radiotherapy

www.nature.com/bi

(f) Check for updates

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British Journal of Cancer (2022) 127:1575-1576;

# Effetti benefici dell'attività fisica per la salute e la prevenzione

### Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study

Chi Pang Wen\*, Jackson Pui Man Wai\*, Min Kuang Tsai, Yi Chen Yang, Ting Yuan David Cheng, Meng-Chih Lee, Hui Ting Chan, Chwen Keng Tsao, Shan Pou Tsai, Xifeng Wu

#### Summary

Lancet 2011; 378: 1244-53 Published Online August 16, 2011 DOI:10.1016/50140-6736(11)60749-6 See Comment page 1202 \*These authors shared first authorship Institute of Population Science, National Health Research Institutes, Zhunan, Taiwan (C P Wen MD, M K Tsai MS, Y C Yang MS, HT Chan MS); China Medical University Hospital, Taichung, Taiwan (C P Wen, M K Tsai, Y C Yang); Laboratory for Exercise Physiology Research, Institute of Sport Science, National Taiwan Sport University, Taoyuan, Taiwan (IPM Wai PhD): Department of Epidemiology, University of Washington, Seattle, WA, USA (TYD Cheng MS): Institute of Medicine and Department of Family and Community Medicine, Chung Shan Medical

Background The health benefits of leisure-time physical activity are well known, but whether less exercise than the recommended 150 min a week can have life expectancy benefits is unclear. We assessed the health benefits of a range of volumes of physical activity in a Taiwanese population.

Methods In this prospective cohort study, 416175 individuals (199265 men and 216910 women) participated in a standard medical screening programme in Tawan between 1996 and 2008, with an average rollow-up of 8.05 years (SD 4.21). On the basis of the amount of weekly exercise indicated in a self-administered questionnaire, participants were placed into one of five categories of exercise volumes: inactive, or low, medium, high, or very high activity. We calculated hazard ratios (HR) for mortality risks for every group compared with the inactive group, and calculated life expectancy for every group.

Findings Compared with individuals in the inactive group, those in the low-volume activity group, who exercised for an average of 92 min per week (95% CI 71–112) or 15 min a day (SD 1·8), had a 14% reduced risk of all-cause mortality (0·86, 0·81–0·91), and had a 3 year longer life expectancy. Every additional 15 min of daily exercise beyond the minimum amount of 15 min a day further reduced all-cause mortality by 4% (95% CI 2·5–7·0) and all-cancer mortality by 1% (0·3–4·5). These benefits were applicable to all age groups and both sexes, and to those with cardiovascular disease risks. Individuals who were inactive had a 17% (HR 1·17, 95% CI 1·10–1·24) increased risk of mortality compared with individuals in the low-volume group.

A Interpretation 15 min a day or 90 min a week of moderate-intensity exercise might be of benefit, even for individuals of at risk of cardiovascular disease.

Family and Community cine, Chung Shan Medical University and Hospital.

### Quanto?

#### SPECIAL COMMUNICATIONS



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#### AMERICAN COLLEGE of SPORTS MEDICINE

POSITION STAND

Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise

This pronouncement was written for the American College of Sports Medicine by Carol Ewing Garber, Ph.D., FACSM, (Chair); Bryan Blissmer, Ph.D.; Michael R. Deschenes, Ph.D., FACSM; Barry A. Franklin, Ph.D., FACSM; Michael J. Lamonte, Ph.D., FACSM; I-Min Lee, M.D., Sc.D., FACSM; David C. Nieman, Ph.D., FACSM; and David P. Swain, Ph.D., FACSM.

Recommendations for physical activity					
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref		
It is recommended for healthy					
150 minutes a week of moderate intensity or 75 minutes a week of vigorous intensity aerobic PA or an	1	A	258–261		
equivalent combination eller con					
For additional benefits in healthy adults, a gradual increase in aerobic PA to 300 minutes a week of moderate intensity, or 150 minutes a week of vigorous intensity aerobic PA, or an equivalent combination thereof is recommended.	I	A	259, 260		
Regular assessment and counselling on PA is recommended to promote the engagement and, if necessary, to support an increase in PA volume over time. <sup>d</sup>	I	в	262–264		
PA is recommended in low-risk individuals without further assessment.	T	с	265, 266		
Multiple sessions of PA should be considered, each lasting ≥10 minutes and evenly spread throughout the week, i.e. on 4–5 days a week and preferably every day of the week.	lla	в	267, 268		
Clinical evaluation, including exercise testing, should be considered for sedentary people with CV risk factors who intend to engage in vigorous PAs or sports.	lla	с	265		

### Piepoli MF et al. Eur J Prev Cardiol 2016; 23: NP1-96

## 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease



Courtesy of Gaia Cattadori

### **Epidemiology and Prevention**

#### Dose–Response Relationship Between Physical Activity and Risk of Heart Failure A Meta-Analysis

Ambarish Pandey, MD; Sushil Garg, MD; Monica Khunger, MD; Douglas Darden, MD; Colby Ayers, MS; Dharam J. Kumbhani, MD, SM; Helen G. Mayo, MLS; James A. de Lemos, MD; Jarett D. Berry, MD, MS

- Background—Prior studies have reported an inverse association between physical activity (PA) and risk of heart failure (HF). However, a comprehensive assessment of the quantitative dose–response association between PA and HF risk has not been reported previously.
- Methods and Results—Prospective cohort studies with participants >18 years of age that reported association of baseline PA levels and incident HF were included. Categorical dose–response relationships between PA and HF risk were assessed with random-effects models. Generalized least-squares regression models were used to assess the quantitative relationship between PA (metabolic equivalent [MET]–min/wk) and HF risk across studies rangeting quantitative PA estimates. Twelve prospective cohort studies with 20203 HF events amor (370460 participants (53.5% women); hedian follow-up, 13 years) were included. The highest levels of PA were associated with a specific across studies and used with participants reporting no leisure-time PA, those who engaged in guideline-recommended minimum levels of PA (500 MET-min/wk; 2008 US federal guidelines) had modest reductions in HF risk (pooled hazard ratio, 0.90; 95% confidence interval, 0.87–0.92). In contrast, a substantial risk reduction was observed among individuals who engaged in PA at twice (hazard ratio for 1000 MET-min/wk, 0.81; 95% confidence interval, 0.77–0.86) and 4 times (hazard ratio for 2000 MET-min/wk, 0.65; 95% confidence interval, 0.58–0.73) the minimum guideline-recommended levels.
- Conclusions—There is an inverse dose–response relationship between PA and HF risk. Doses of PA in excess of the guideline-recommended minimum PA levels may be required for more substantial reductions in HF risk. (Circulation. 2015;132:1786-1794. DOI: 10.1161/CIRCULATIONAHA.115.015853.)

### Prevenzione Primaria
#### **Advances in Heart Failure**

#### Exercise Training as Therapy for Heart Failure Current Status and Future Directions

Secondaria

Jerome L. Fleg, MD; Lawton S. Cooper, MD, MPH; Barry A. Borlaug, MD; Mark J. Haykowsky, PhD; William E. Kraus, MD; Benjamin D. Levine, MD; Marc A. Pfeffer, MD, PhD; Ileana L. Piña, MD, MPH; David C. Poole, PhD, DSc; Gordon R. Reeves, MD, MPT; David J. Whellan, MD, MHS; Dalane W. Kitzman, MD; Results from a National Heart, Lung, and Blood Institute Working Group

#### Background

Despite a variety of pharmacological and device therapies for persons with chronic heart failure (HF), prognosis and quality of life (QOL) remain poor. The need for new effective strategies to improve outcomes for patients with HF is underscored by persistently high mortality, morbidity, healthcare use, and costs associated with HF, with >1 million US HF hospitalizations at an estimated direct and indirect cost in the US of \$40 billion in 2012.<sup>1</sup>

Exercise intolerance is a primary symptom in patients with chronic HF, both those with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF), and is a strong determinant of prognosis and of reduced OOL<sup>2</sup> Exercise training improves exercise intolerance and QOL in patients with chronic stable HFrEF, and has become an accepted adjunct therapy for these patients (Class B level of evidence) based on a fairly extensive evidence base of ran-

domized trials, mostly small.

of aerobic exercise, including high-intensity interval training (HIIT), and resistance, training relative to aerobic training; combination of exercise training with other therapies; optimization of adherence; benefit for older patients with HF, those with HFpEF or multiple comorbidities, and those with acute decompensated HF.

The National Heart, Lung, and Blood Institute convened a working group of experts on June 11, 2012 in Bethesda, MD to identify knowledge gaps and to suggest general approaches to filling those gaps for exercise training as a treatment for HF. The National Heart, Lung, and Blood Institute invited experts in a variety of areas, including basic and clinical exercise physiologists, HF and cardiac rehabilitation (CR) specialists, and clinical trial specialists to address these issues. Workshop participants were asked to identify knowledge gaps and to suggest general approaches in basic and clinical investigation to evaluate, to optimize, and to translate the potential role of exercise training in the treatment of HF.

(Circ Heart Fail. 2015;8:209-220. DOI: 10.1161/CIRCHEARTFAILURE.113.001420.)





POSITION STATEMENT

## Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation

Massimo F. Piepoli<sup>1\*</sup>, Viviane Conraads<sup>2</sup>, Ugo Corrà<sup>3</sup>, Kenneth Dickstein<sup>4,5</sup>, Darrel P. Francis<sup>6</sup>, Tiny Jaarsma<sup>7</sup>, John McMurray<sup>8</sup>, Burkert Pieske<sup>9</sup>, Ewa Piotrowicz<sup>10</sup>, Jean-Paul Schmid<sup>11,12</sup>, Stefan D. Anker<sup>13</sup>, Alain Cohen Solal<sup>14</sup>, Gerasimos S. Filippatos<sup>15</sup>, Arno W. Hoes<sup>16</sup>, Stefan Gielen<sup>17</sup>, Pantaleo Giannuzzi<sup>3</sup>, and Piotr P. Ponikowski<sup>18</sup>





# Physical Activity Guidelines for Americans

# 2<sup>nd</sup> edition











# **Exercise Training in Post-COVID-19 Patients: The Need for a Multifactorial Protocol for a Multifactorial Pathophysiology**

Gaia Cattadori<sup>1,\*</sup>, Silvia Di Marco<sup>1</sup>, Massimo Baravelli<sup>1</sup>, Anna Picozzi<sup>1</sup> and Giuseppe Ambrosio<sup>2</sup>

J. Clin. Med. 2022, 11, 2228. https://doi.org/10.3390/jcm11082228

#### 3. Inflammation and Exercise Training

Exercise training is known to positively affect immune system and inflammation [3]. The acute inflammatory response may be reduced by a regular physical activity through at least five mechanisms: (1) reducing the inflammatory signalling pathway mediated by Toll-like receptors; (2) increasing anti-inflammatory cytokines such as Interleukin-10 and 37, which could inhibit the inflammatory cascade; (3) reducing lung inflammation promoting the conversion from Angiotensin II to Angiotensin 1–7; (4) activating the Angiotensinconverting enzyme 2 receptor vasodilator pathway to reduce lung inflammation; and (5) restoring nitric oxide levels in order to counteract endothelial dysfunction [8]. However, different physical activities in terms of intensity and type have different effects on the immune system and inflammation: intense exercise can actually lead to a higher level of inflammatory mediators and to increase the risk of injury and chronic inflammation, effert with appropriate resting periods can achieve maximum while mode benefit [9] The "J curve" concept hypothesizes hat excessive bouts of prolonged training can impair immune function, and high intensity exercise may thus be dangerous, helping to exacerbate virus infection, such as COVID-19. On the contrary, moderate intensity exercise improves the immune system and it should be recommended as a non-pharmacological inexpensive and viable way to cope with COVID-19 virus The "Forrest Gump" theory states, based on study on ACE axis unbalance, that "regular one's risk of getting infected with SARS-CoV-2 but it would reduce one's risk of getting severe disease [10,11]". Moreover, several studies have demonstrated that both acute and chronic exercise training at moderate intensity, improve endothelial dysfunction, muscular blood supply, peripheral O2 extraction, muscular strength, ventilator efficacy, resulting in clinically significant benefits in terms of improved exercise capacity, quality of life and cardio-pulmonary function. Exercise programs in adults hospitalized with an acute or an exacerbation of a chronic respiratory condition, even if disparate, were well tolerated, and adverse events were infrequent with movement out of bed within 24 h of hospitalization with progressive daily movement and progression titrated based on symptoms [12].

Courtesy of Gaia Cattadori

# Inattività fisica associata a un rischio più elevato di COVID grave

#### Studio di Kaiser Permenente nel sud della California USA

- •48 440 adulti con diagnosi di COVID 19
- Livelli di attività fisica riportati due anni prima
- Confronto inattivo con attivo (= esercizio 150 min)
- Ricovero in terapia intensiva e morte

L'inattività fisica aumenta il rischio:

- 126% di ricovero
- •73% di cura in terapia intensiva
- •149% di morte

# Fattori di rischio nell'infanzia-(ruolo della famiglia)

- •Dislipidemia
- Obesità
- •Alta pressione sanguigna
- •Fumo passivo
- Inattività fisica
- •Dieta malsana
- •Stato socioeconomico basso
- •Mancanza di istruzione
- •Disuguaglianze sanitarie
- •Scarsa alfabetizzazione sanitaria

## Effetti benefici dell'attività fisica:

Miglioramento della salute delle ossa e del peso per i bambini dai 3 ai 5 anni.

Miglioramento della funzione cognitiva per i giovani dai 6 ai 13 anni.

Benefici per la salute del cervello, tra cui possibile miglioramento della funzione cognitiva, riduzione del rischio di ansia e depressione e miglioramento del sonno e della qualità della vita.

Per le donne in gravidanza, rischio ridotto di aumento di peso eccessivo, diabete gestazionale e depressione postpartum.

Per gli anziani, rischio ridotto di lesioni da caduta.

Per le persone con varie condizioni mediche croniche, ridotto rischio di mortalità per tutte le cause e specifiche per malattia, miglioramento della funzione fisica e migliore qualità della vita.

Ridotto rischio di cancro in gran numero di siti.

Rapporto tra esercizio fisico da moderato a vigoroso, tempo di sedentarieta e rischio di mortalità per tutte le cause negli adulti



Risk of all-cause mortality decreases as one moves from red to green.

Source: This heat map is adapted from data found in Ekelund U, Steene-Johannessen J, Brown WJ. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonized meta-analysis of data from more than 1 million men and women. Lancet. 2016;388:1302-1310. doi:10.1016/S0140-6736(16)30370-1.

# Relationship of Moderate-to-Vigorous Physical Activity to All-Cause Mortality



Source: Adapted from data found in Moore SC, Patel AV, Matthews CE. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. PLoS Med. 2012;9(11):e1001335. doi:10.1371/journal.pmed.1001335.

# Many types of physical activity may lower risk of death for older adults (age 59-82)

In older adults getting regular physical activity\*, **risk of death decreased** – *regardless of type of activity*.





\*7.5 to 15 MET per week



Watts EL, et al. Association of Leisure Time Physical Activity Types and Risks of All-Cause, Cardiovascular, and Cancer Mortality Among Older Adults. JAMA Network Open. August 24, 2022.

### American Cancer Society Guideline for Diet and Physical Activity for Cancer Prevention

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Abstract: The American Cancer Society (ACS) publishes the Diet and Physical Activity Guideline to serve as a foundation for its communication, policy, and community strategies and, ultimately, to affect dietary and physical activity patterns among Americans. This guideline is developed by a national panel of experts in cancer research, prevention, epidemiology, public health, and policy, and reflects the most current scientific evidence related to dietary and activity patterns and cancer risk. The ACS guideline focuses on recommendations for individual choices regarding diet and physical activity patterns, but those choices occur within a community context that either facilitates or creates barriers to healthy behaviors. Therefore, this committee presents recommendations for community action to accompany the 4 recommendations for individual choices to reduce cancer risk. These recommendations for community action recognize that a supportive social and physical environment is indispensable if individuals at all levels of society are to have genuine opportunities to choose healthy behaviors. This 2020 ACS guideline is consistent with guidelines from the American Heart Association and the American Diabetes Association for the prevention of coronary heart disease and diabetes as well as for general health promotion, as defined by the 2015 to 2020 Dietary Guidelines for Americans and the 2018 Physical Activity Guidelines for Americans. CA Cancer J Clin 2020;70:245-271. © 2020 American Cancer Society.

Keywords: cancer prevention, dietary patterns, nutrition, physical activity

How do we incentivize a healthy lifestyle and/or disincentivize an unhealthy lifestyle?



## Barriere sistemiche allo stile di vita sano

#### Sfide per aderire a modelli dietetici sani

Fattori socioeconomici e insicurezza alimentare e nutrizionale

Discriminazione strutturale e segregazione di quartiere

Marketing mirato di cibi e bevande malsane

#### Barriere ambientali da esercitare

Mancanza di accesso alla palestra e alle strutture per l'allenamento

Pochi parchi o spazi verdi

Mancanza di posti sicuri e convenienti per camminare o andare in bicicletta



Source: NCI Surveillance, Epidemiology, and End Results Program (SEER), seer.cancer.gov

For more, see Lawrence, et al: Trends in Cancer Mortality Among Black Individuals in the U.S. From 1999 to 2019 – *JAMA Oncology*, May 19, 2022



More education

is associated with:

 ✓ healthier lifestyle factors
 ✓ greater use of cancer screening tests

Sauer et al, Cancer Epidemiol Biomarkers Prevent 28: 629-42, 2019

### To do:

Closer integration with prevention and screening for neoplastic disease

Addressing health disparities in addition to other disparities

Making it easier for people to adopt healthy lifestyles, prevention, and screening

Implications for health disparities from the beginning when developing new technology

Simplified screening approaches to detect a wider range of cancers hold great potential, provided they are evidence-based and can be equitably deployed

#### CANCER PREVENTION RESEARCH | COMMENTARY

#### Cancer Prevention Prioritized at AACR Annual Meeting and a New Working Group



Adriana Albini

#### ABSTRACT

Scientific advances in the late 19th century set the stage for progress in understanding and treating cancer, a disease that was previously considered almost hopeless. One hundred years later, cancer prevention is becoming an increasingly important focus for oncology research. New tools and ideas bring to the field some extremely promising molecular, organizational, social, and political approaches, which were a focus of the *American Association for Cancer Research* 2022 Annual Meeting and of the newly launched AACR Cancer Prevention Working Group (CPWG). We are moving toward precision prevention, better tools for early detection and for risk assessment, the use of a Precancer Atlas, unveiling of new biomarkers. Besides improving lifestyle, by avoiding risk factors such as tobacco use, excessive UV exposure, infectious agents, as well as poor dietary habits, lack of exercise, overweight, and obesity, many other factors can impact cancer risk, which is a warning to consider a multifaceted molecular but also social approach. Gender, ethnicity, geographic, and economic lines are associated with disparities in prevention, which we want to overcome. Here we summarize some challenges and priorities in cancer prevention emerging from the work of AACR and CPWG.

Cancer Prev Res 2022;15:475-80 dot 10.1158/1940-6207.CAPR-22-0310 ©2022 American Association for Cancer Research

# CPWG actions to accomplish its mission

The AACR Cancer Prevention Working Group will accomplish its mission by working to:

Foster transdisciplinary approaches to the study of cancer prevention

Promote the incorporation of molecular and biochemical concepts and techniques as well as novel data science tools into well-designed cancer prevention studies

Provide an ongoing forum(s) for the scholarly discussion and development of effective approaches to the conduct and interpretation of cancer prevention studies

Foster collaborations with individuals engaged in other scientific disciplines, as needed

Recommend scientific and educational programs that will serve to advance the field

Assist with the professional advancement of early- and mid-career investigators engaged in cancer prevention research

Establish a community of individuals expert in or interested in advancing progress in cancer prevention

Figure 1.

CPWG actions to accomplish its mission. Adapted from CPWG Charter (https://www.aacr.org/professionals/membership/scientific-working-groups/cancerprevention- working-group/cpwg-charter/).

Albini A. Cancer Prevention Prioritized at AACR Annual Meeting and a New Working Group. Cancer Prev Res 2022;15:475–80

# Cancer: Progress by Many Measures



- Precision medicine
- Immunotherapy

#### Prevention

- Interventions for infection-related cancers
- Cancer susceptibility genes
- Drug and surgical risk reduction strategies
- Disparities

## Quality of Life

- Better toxicity
  management
- Less intensive therapies
- Palliative care integration

## Survivorship

- Growing research area
- Late effects identified
- Surveillance strategies established

# Fare sport o attività fisica

LO SPORT ASSIEME ALLA DIETA MANTIENE IN SALUTE: UNA SCHERMITRICE ARMATA CONTRO IL CANCRO



# Stile di vita NON salutare



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# La dieta Hi- tech



# Il Carrello della spesa intelligente



Dotato di uno strumento per la nutrizione virtuale che, tramite la lettura dei codici a barre, **riconoscerà l'ammontare totale di calorie, grassi e zuccheri** dei prodotti che si intende acquistare segnalando in caso di sgarri eccessivi e sconsigliando gli alimenti poco sani.