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PHYSICAL ACTIVITY AND CANCER PREVENTION

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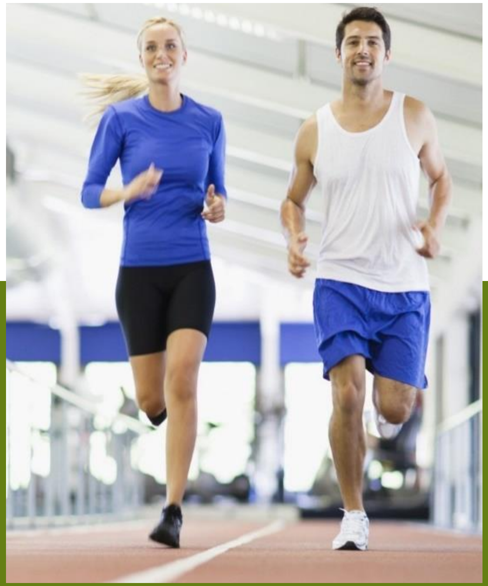


- Most cancers arise from a complex etiology involving genetic, environmental and lifestyle factors, and their interactions, and there is great need and opportunity for cancer prevention through lifestyle change. Increasingly, recognition of the role of host factors in cancer survival has supported the increased focus on lifestyle changes to improve these factors.
- Some of the major risk factors associated with cancer include **physical inactivity, sedentary behavior, and obesity.**

the International Agency for Research on Cancer (IARC) established that there is convincing evidence that excess body fatness (i.e., *highest BMI category evaluated versus normal BMI of 18.5–24.9 kg/m/2*) is associated with an increased risk of at least 13 different types of cancers.

. Summary of the observational epidemiologic evidence on the association between obesity and cancer risk by cancer site. Summary evidence was acquired from Lauby-Secretan *et al.* [19].

Cancer site	Overall classification of evidence	Magnitude of relative risk increase for BMI $\geq$ 25 versus BMI < 25	Evidence for dose–response effect	Biologic plausibility
Colorectal	Strong	10–30%	Yes	Yes
Gastric cardia	Strong	20–80%	Yes	Yes
Esophagus	Strong	15–480%	Yes	Yes
Liver	Strong	50–80%	Yes	Yes
Postmenopausal breast	Strong	10–12%	Yes	Yes
Gallbladder	Strong	20–60%	Yes	Yes
Endometrial	Strong	50–710%	Yes	Yes
Renal/kidney	Strong	30–80%	Yes	Yes
Meningioma	Strong/Moderate	40–213%	Limited	Limited
Pancreatic	Strong	20–50%	Yes	Yes
Multiple myeloma	Strong/Moderate	15–52%	Limited	Limited
Ovarian	Moderate	10–20%	Yes	Yes
Thyroid	Moderate	4–17%	Yes	Yes

- An estimated 30–40% of cancers can be prevented through changes in modifiable lifestyle and environmental risk factors known to be associated with cancer incidence.
- Decades of epidemiologic research have identified a physically active lifestyle as protective against the occurrence of some common cancers, but comprehensive reviews were lacking.

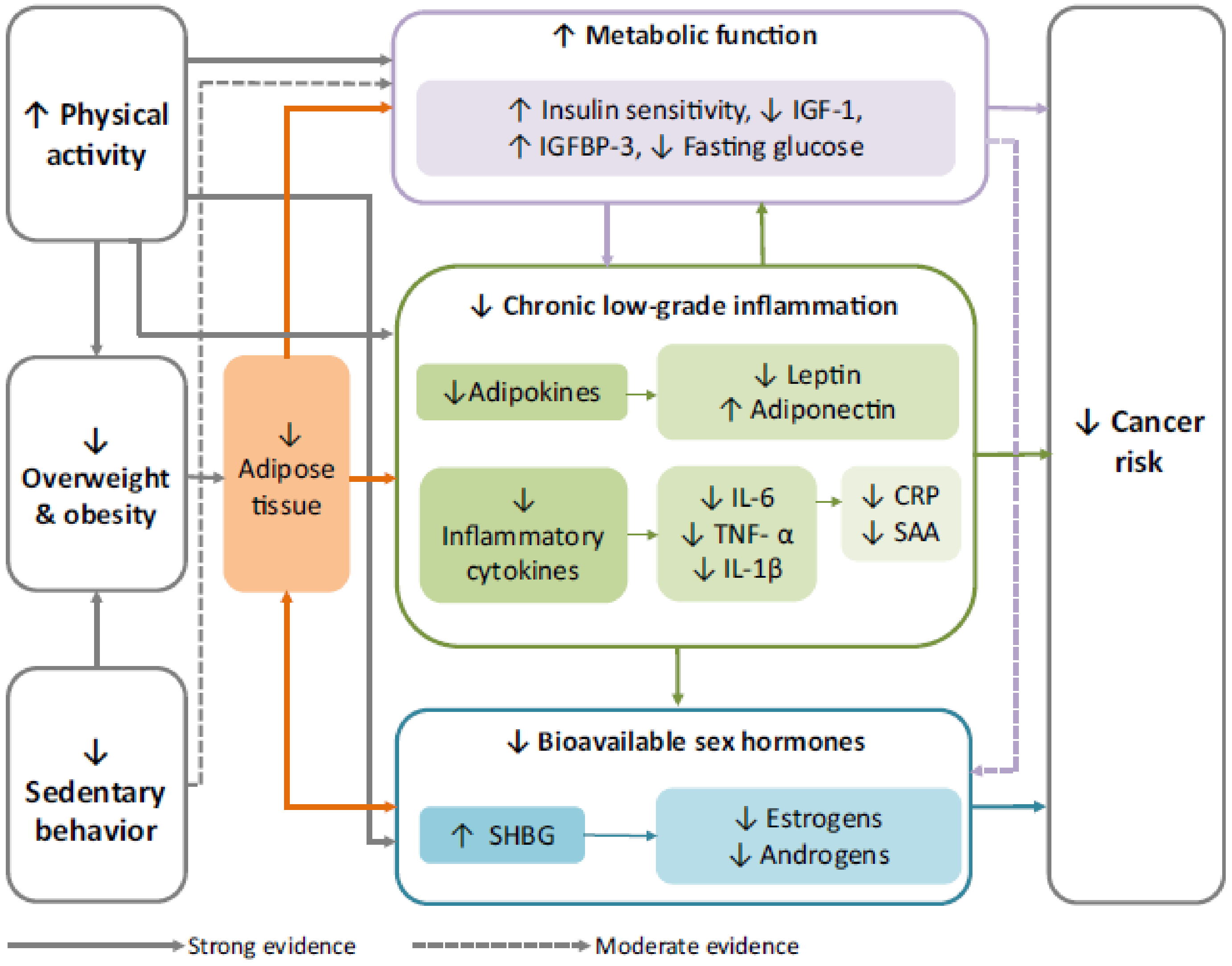
2018 Physical Activity Guidelines Advisory Committee Evidence on Relationship between Physical Activity and Risk of Developing Invasive Cancer

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

2018 Physical Activity Guidelines Advisory Committee Evidence on Relationship Between Physical Activity and Mortality in Cancer Survivors

All-cause Mortality		
Cancer	Evidence Grade	Approximate % Relative Risk Reduction
Breast	Moderate	48%
Colorectal	Moderate	42%
Prostate	Limited	37-49%
Cancer-specific Mortality		
Breast	Moderate	38%
Colorectal	Moderate	38%
Prostate	Moderate	38%

Hypothesized biologic mechanisms linking physical activity, excess body fat, and sedentary behavior to cancer risk.



EMERGING HYPOTHESES

- Physical activity is hypothesized to affect the **balance between reactive oxygen species (ROS) and antioxidant defenses** that can result in oxidative stress. ROS may cause chromosomal abnormalities, DNA damage, and mutations in tumor-suppressing genes. **Acute exercise appears** to promote oxidative stress and a pro-oxidant environment but as physical activity is **repeated,** adaptations to this stress occur and eventually antioxidant defenses are built up.

EMERGING HYPOTHESES

- A similar pattern emerges from the relationship between physical activity and immune function, whereby the body responds differently to acute and prolonged bouts of exertion. Bouts of unusually heavy and/or long exertions (e.g., running a marathon) can lead to transient immune dysfunction, while shorter duration aerobic physical activity stimulates short-term increases in immunoglobulins, neutrophils, natural killer cells, cytotoxic T cells, and immature B cells, which over time, enhance immunosurveillance .

EMERGING HYPOTHESES

- Physical activity may affect the development of cancer through epigenetic alterations to chromosomes, DNA methylation, expression of microRNA, and chromatic structure. Telomere length, a prognostic marker of aging and disease, has been shown to be longer in men with healthy eating and exercise habits.

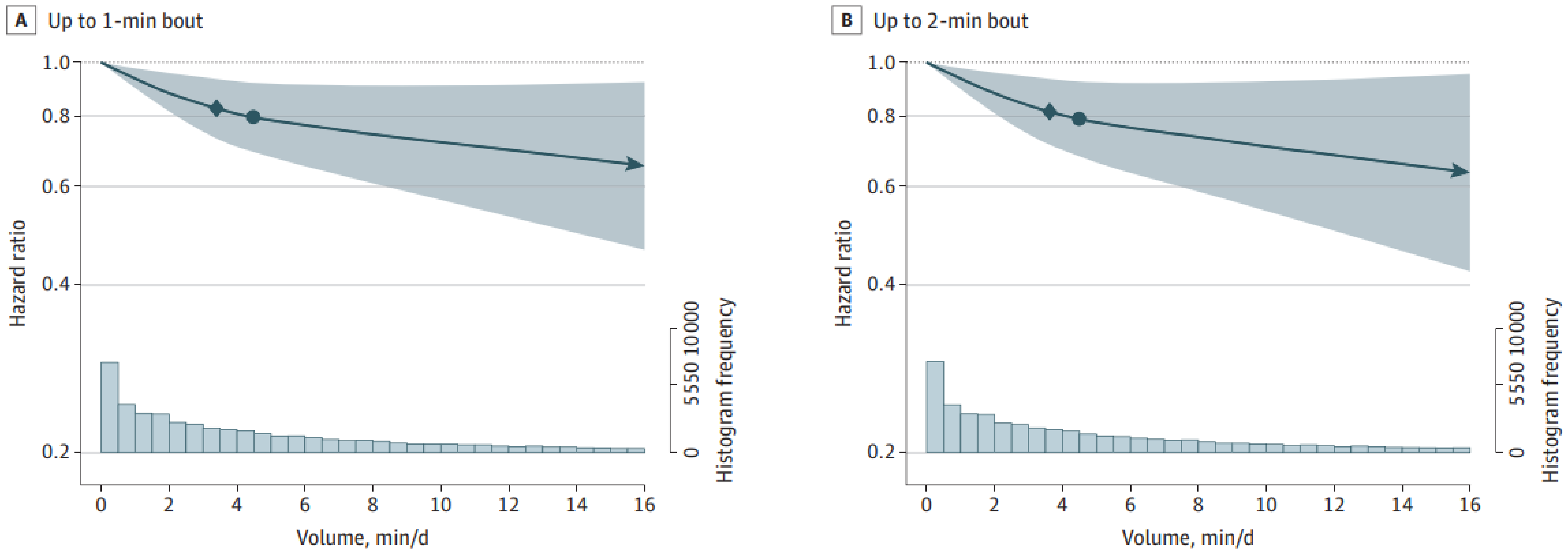
Vigorous Intermittent Lifestyle Physical Activity and Cancer Incidence Among Nonexercising Adults
The UK Biobank Accelerometry Study. Emmanuel Stamatakis, *et al.(2023)*

The association between physical activity (PA) intensity and certain cancer sites, such as breast and colon cancers, is dose dependent and has a greater risk reduction associated with vigorous physical activity (VPA) compared with lower intensities.

Although VPA is time efficient, structured exercise bouts may not be feasible or appealing to most middle-aged adults. Vigorous intermittent lifestyle physical activity (VILPA) refers to brief and sporadic (eg, up to 1-2 minutes [min]) bouts of VPA during daily living, eg, bursts of very fast walking or stair climbing.

A recent study found a beneficial association of daily VILPA with total cancer mortality, although the low number of cancer deaths precluded a detailed dose-response examination.

Figure 2. Dose-Response Association of Vigorous Intermittent Lifestyle Physical Activity (VILPA) Daily Duration, From Bouts of Up to 1 and 2 Minutes, With Total Cancer Incidence (n = 22 398; 2356 Events)



The diamond shape indicates the ED_{50} value, the minimal dose defined as the daily duration of VILPA associated with 50% of the optimal risk reduction; and the circle, the effect associated with the median VILPA value (the list of values is available in eTable 7 in Supplement 1) . Analyses were adjusted for age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), duration of light-intensity physical activity, duration of moderate-intensity physical activity, smoking status, alcohol consumption, accelerometer- estimated sleep duration, fruit and vegetable consumption, education level, medication use, self-reported parental history of cancer, and prevalent cardiovascular disease. All analyses were additionally adjusted for vigorous physical activity duration of more than 1 (bouts up to 1 minute exposure) minute or more than 2 (bouts up to 2 minutes exposure) minutes. Hazard ratios were calculated using Fine-Gray models.

This cohort study found that daily VILPA duration was inversely associated with incident cancer risk in a near-linear manner, with steeper dose-response for PA-related cancers. As few as 4 to 5 min of VILPA daily was associated with a substantially lower cancer risk.

With little variation between bouts of up to 1 or 2 min, a minimum of 3.4 to 3.6 min of VILPA/d was associated with a 17% to 18% reduction in total incident cancer risk (compared with no VILPA). The study sample median of 4.5 VILPA min/d was associated with a 31% to 32% reduction in PA-related cancer incidence.

For comparison, **1 metabolic equivalent unit increase in cardiorespiratory fitness (3.5 mL of oxygen uptake/kg/min) is associated with a 7% reduction in total cancer risk.**

Physical Activity and Mortality in Cancer Survivors: A Systematic Review and Meta-Analysis(136 studies). Christine M, *at al.*(2019)

Physical Activity before or after cancer diagnosis was associated with statistically significant decreased hazards of cancer-specific and all-cause mortality in at least 11 different cancer sites. In addition, we found that hazard of CVD mortality among cancer survivors was also reduced with PA.

PHYSICAL ACTIVITY AND EXERCISE RECOMMENDATION

- Specific recommendations for physical activity include aerobic exercise, resistance training, or a combination of both for expected patient benefits.
- Greater amounts of physical activity, particularly moderate-to-vigorous–intensity physical activity, conferred a greater risk reduction for breast cancer-specific and all-cause mortality.

Methods of Estimating Intensity of Cardiorespiratory and Resistance Exercise

	Cardiorespiratory Endurance Exercise											Resistance Exercise
	Relative Intensity				Intensity ($\%\dot{V}O_{2max}$) Relative to Maximal Exercise Capacity in MET			Absolute Intensity	Absolute Intensity (MET) by Age			Relative Intensity
Intensity	%HRR or $\%\dot{V}O_2R$	$\%HR_{max}$	$\%\dot{V}O_{2max}$	Perceived Exertion (Rating on 6–20 RPE Scale)	20 METs $\%\dot{V}O_{2max}$	10 METs $\%\dot{V}O_{2max}$	5 METs $\%\dot{V}O_{2max}$	METs	Young (20–39 yr)	Middle Age (40–64 yr)	Older (≥65 yr)	% One Repetition Maximum
Very light	<30	<57	<37	Very light (RPE <9)	<34	<37	<44	<2.0	<2.4	<2.0	<1.6	<30
Light	30–39	57–63	37–45	Very light to fairly light (RPE 9–11)	34–42	37–45	44–51	2.0–2.9	2.4–4.7	2.0–3.9	1.6–3.1	30–49
Moderate	40–59	64–76	46–63	Fairly light to somewhat hard (RPE 12–13)	43–61	46–63	52–67	3.0–5.9	4.8–7.1	4.0–5.9	3.2–4.7	50–69
Vigorous	60–89	77–95	64–90	Somewhat hard to very hard (RPE 14–17)	62–90	64–90	68–91	6.0–8.7	7.2–10.1	6.0–8.4	4.8–6.7	70–84
Near maximal to maximal	≥90	≥96	≥91	≥ Very hard (RPE ≥18)	≥91	≥91	≥92	≥8.8	≥10.2	≥8.5	≥6.8	≥85

Commonly Used Equations for Estimating Maximal Heart Rate

Author	Equation	Population
Fox et al. (35)	$HR_{max} = 220 - age$	Small group of men and women
Astrand (8)	$HR_{max} = 216.6 - (0.84 \times age)$	Men and women age 4–34 yr
Tanaka et al. (101)	$HR_{max} = 208 - (0.7 \times age)$	Healthy men and women
Gellish et al. (38)	$HR_{max} = 207 - (0.7 \times age)$	Men and women participants in an adult fitness program with broad range of age and fitness levels
Gulati et al. (47)	$HR_{max} = 206 - (0.88 \times age)$	Asymptomatic middle-aged women referred for stress testing

Methods for Prescribing Exercise Intensity

- HR method: Target HR = $HR_{max/peak}$[a] $\times$ % intensity desired
- HRR method: Target HR (THR) = [($HR_{max/peak}$[a] − HR_{rest}) $\times$ % intensity desired] + HR_{rest}

FITT RECOMMENDATIONS FOR INDIVIDUALS WITH OVERWEIGHT AND OBESITY

	Aerobic	Resistance	Flexibility
Frequency	≥5 d · wk^{-1}	2–3 d · wk^{-1}	≥2–3 d · wk^{-1}
Intensity	Initial intensity should be moderate (40%–59% $\dot{V}O_2R$ or HRR); progress to vigorous (≥60% $\dot{V}O_2R$ or HRR) for greater health benefits.	60%–70% of 1-RM; gradually increase to enhance strength and muscle mass.	Stretch to the point of feeling tightness or slight discomfort.
Time	30 min · d^{-1} (150 min · wk^{-1}); increase to 60 min · d^{-1} or more (250–300 min · wk^{-1}).	2–4 sets of 8–12 repetitions for each of the major muscle groups	Hold static stretch for 10–30 s; 2–4 repetitions of each exercise
Type	Prolonged, rhythmic activities using large muscle groups (*e.g.*, walking, cycling, swimming)	Resistance machines and/or free weights	Static, dynamic, and/or PNF

1-RM, one repetition maximum; HRR, heart rate reserve; PNF, proprioceptive neuromuscular facilitation; $\dot{V}O_2R$, oxygen uptake reserve.

THANK YOU FOR YOUR ATTENTION