JORNADAS
DE MEDICINA
IPO PORTO

Estilos de vida e prevenção do cancro e das suas sequelas

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**Desde os anos 50-60 do século XX
o estilo de vida nos países mais desenvolvidos mudou**
(e mais recentemente, está a mudar nos países emergentes)

https://pt.dreamstime.com/ilustra%C3%A7%C3%A3o-stock
-evolu%C3%A7%C3%A3o-da-obesidade-image42846576

As Epidemias do Século XXI

Covid-19

Guerras

Doenças não Transmissíveis

Recomendações de Sociedades Científicas para prevenção da DCV e Doenças Endócrino-Metabólicas

American Heart Association (AHA)

European Society of Endocrinology (ESE)

Aumento da Incidência e Mortalidade por Cancro –
A catástrofe anunciada

Explore the future of cancer burden

2020

2040

19 300 000

30 200 000

= 500 000

Demographic changes
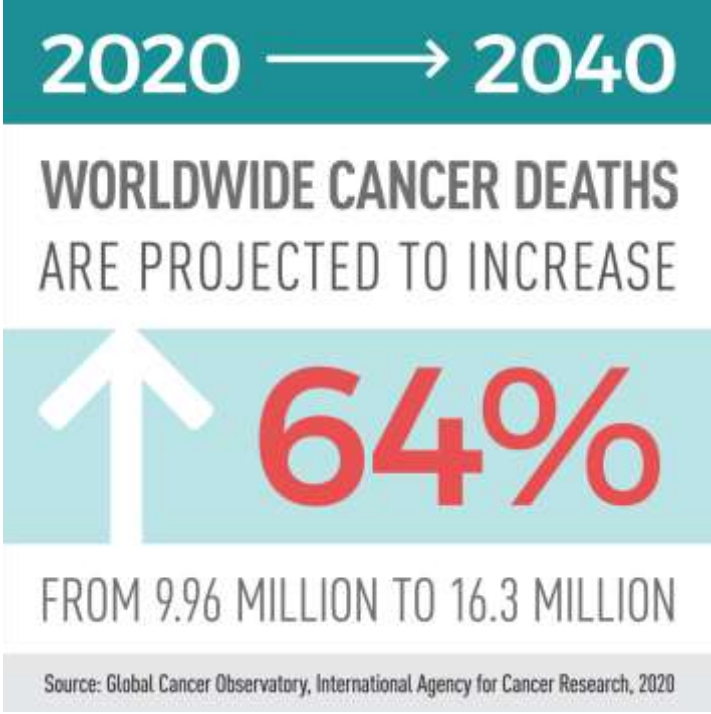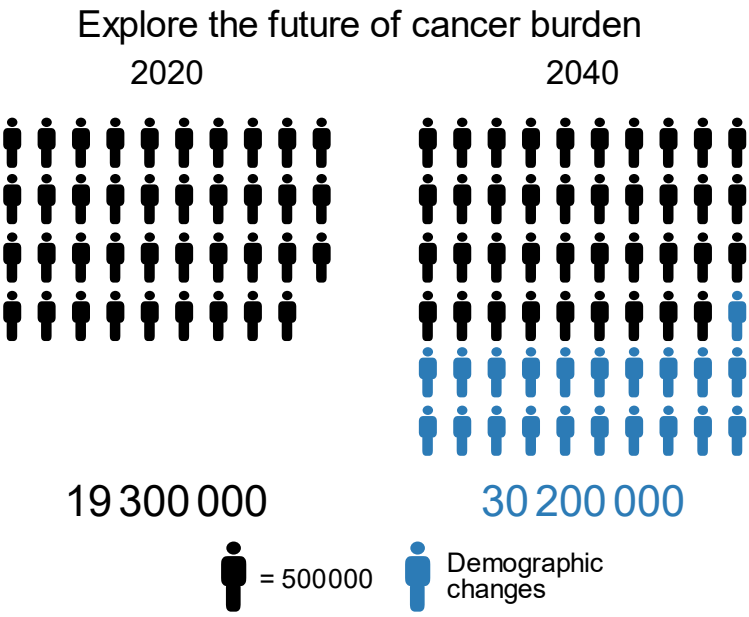
https://visualsonline.cancer.gov/details.cfm?cid=eb_govdel&imageid=12610

2020 ⟶ 2040

WORLDWIDE CANCER DEATHS ARE PROJECTED TO INCREASE

64%

FROM 9.96 MILLION TO 16.3 MILLION

Source: Global Cancer Observatory, International Agency for Cancer Research, 2020

Previsões para 2045 (WHO)

Novos casos

Mortes

Projected number of new cases for all cancers combined (both sexes combined) in 2050 according to the four-tier Human Development Index (HDI).

Source: GLOBOCAN 2022.
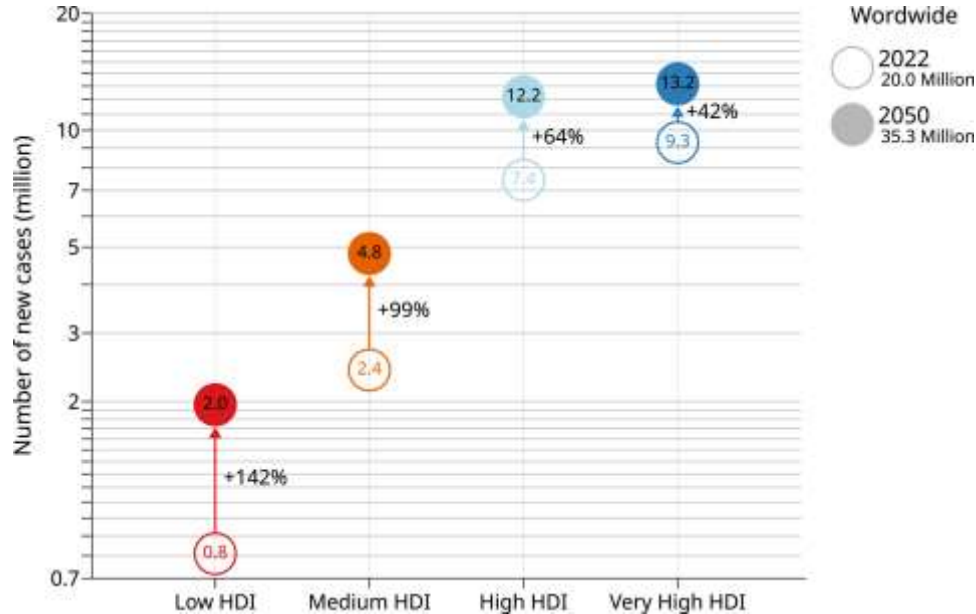
The shift in global disease burden, and share of non-communicable diseases by world regions (European Environment Agency)
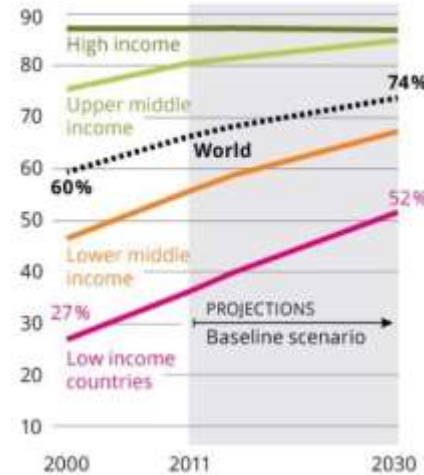
Cancro precoce em crescimento
Geração X e millennials sob alerta máximo

- POR J. PLACIDO JÚNIOR

TABLE 3 Probability (%) of developing invasive cancer within selected age intervals by sex, United States, 2017–2019.[a]

Cancer site	Sex	Probability, %				
		Birth to 49 years	50–64 years	65–84 years	85 years and older	Birth to death
All sites[b]	Male	3.5 (1 in 29)	11.8 (1 in 8)	31.9 (1 in 3)	19.1 (1 in 5)	41.6 (1 in 2)

Revista Visão 2024

TABLE 3 Probability (%) of developing invasive cancer within selected age intervals by sex, United States, 2017–2019.[a]

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	Female	5.9 (1 in 17)	10.8 (1 in 9)	24.3 (1 in 4)	14.4 (1 in 7)	39.6 (1 in 3)
	Female		0.1 (1 in 738)	1.1 (1 in 90)	4.3 (1 in 23)	1.9 (1 in 52)	5.9 (1 in 17)
Melanoma of the skin[c]	Male	0.4 (1 in 243)	0.9 (1 in 116)	2.4 (1 in 42)	1.4 (1 in 73)	3.6 (1 in 28)
	Female	0.6 (1 in 160)	0.7 (1 in 153)	1.1 (1 in 92)	0.5 (1 in 188)	2.5 (1 in 41)
Non-Hodgkin lymphoma	Male	0.3 (1 in 395)	0.5 (1 in 196)	1.6 (1 in 63)	0.9 (1 in 105)	2.4 (1 in 42)
	Female	0.2 (1 in 528)	0.4 (1 in 264)	1.2 (1 in 86)	0.7 (1 in 153)	1.9 (1 in 52)
Prostate	Male	0.2 (1 in 449)	3.9 (1 in 26)	10.4 (1 in 10)	3.1 (1 in 32)	12.9 (1 in 8)
Thyroid	Male	0.2 (1 in 483)	0.2 (1 in 480)	0.3 (1 in 354)	0.1 (1 in 1429)	0.7 (1 in 153)
	Female	0.8 (1 in 124)	0.5 (1 in 200)	0.5 (1 in 217)	0.1 (1 in 1194)	1.7 (1 in 58)
Uterine cervix	Female	0.3 (1 in 337)	0.2 (1 in 554)	0.2 (1 in 564)	0.1 (1 in 1535)	0.7 (1 in 152)
Uterine corpus	Female	0.3 (1 in 303)	1.1 (1 in 91)	1.7 (1 in 58)	0.4 (1 in 239)	3.1 (1 in 32)

[a]For people free of cancer at the beginning of the age interval.
[b]All sites exclude basal cell and squamous cell skin cancers and in situ cancers except urinary bladder.
[c]Probabilities for non-Hispanic White individuals.

Cancro - Genética ou Ambiente?

Dados Migratórios

Cancer inheritance

Hereditary cancer 10-15%

Familial cancer 5-15%

Sporadic cancer 70-80%

Up to 30% of all cancers run in families

genosalut

https://www.genosalut.com/en/
genetic-testing-and-counselling/cancer/
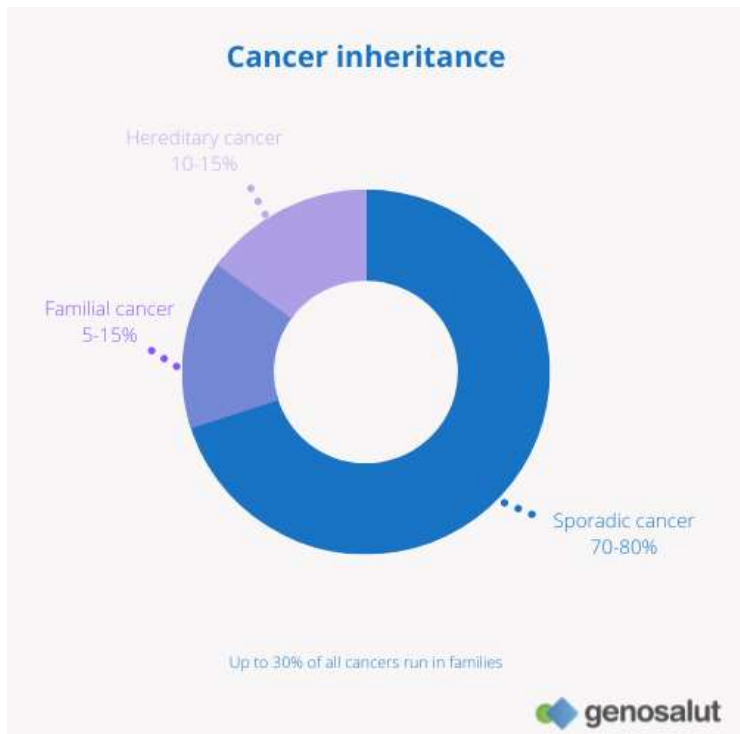
Figure 1.2.20 Cancer incidence for selected cancers in Japanese women by generation in Hawaii and Japan, 1968–1977

Stomach
Colon, rectum
Breast

Rate per 100,000

Japan (Miyagi)   Hawaii (1st generation)   Hawaii (2nd generation)
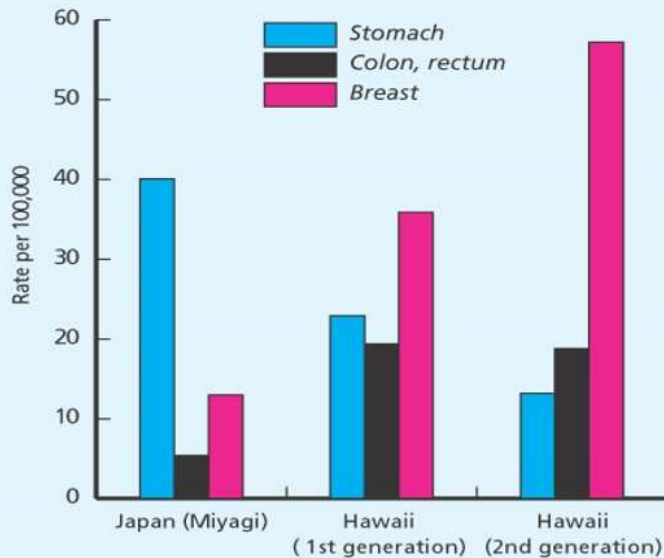
Age-adjusted to the World Standard Population
(From Kolonel et al, 1980)

dietandcancereport.org

Evaluating intrinsic and non-intrinsic cancer risk factors
Song Wu, et. Al. Nature Communications, 2018

INTRINSIC RFs	NON INTRINSIC RFs	
Random errors in DNA replication (non modifiable)	Endogenous RFs (partially modifiable)	Exogenous RFs (modifiable)
	Aging	Radiação
	Genetic Susceptibility	Carcinogénicos Quimicos
	DNA repair machinery	Virus-associated neoplasia
	Hormones	Smoking, sedentarism, nutrient imbalance….
	Growth Factors	
	Inflammation…	

✓ **50% das neoplasias seriam evitáveis se fossem reduzidos os FRs modificáveis para cancro**

✓ **30% das neoplasias seriam evitáveis com adoção de um estilo de vida saudável**

Fatores Modificáveis para Cancro e Diagnóstico Precoce

Tabaco e Cancro

Radiação e Cancro

Exposição solar e Cancro

Agentes Infeciosos e Cancro

Ambiente e Cancro

Cumulative risk of death from lung cancer in men in the United Kingdom for continuing smokers and for former smokers, according to the age when quitting (death rates in 1990 are shown). From Peto et al. BMJ 321 (2000) 323–329.
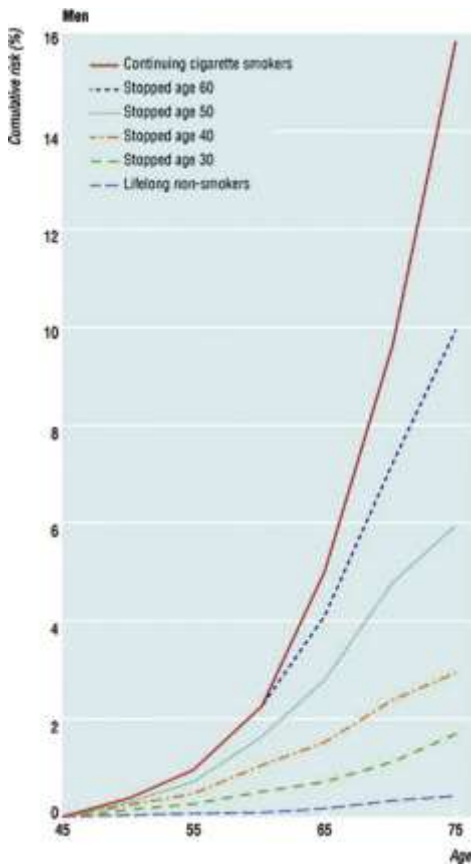
Tabaco e Cancro

MAIOR RISCO DE CANCRO:

- ✓ Pulmão
- ✓ Cabeça e Pescoço
- ✓ Esófago
- ✓ Pâncreas
- ✓ ...
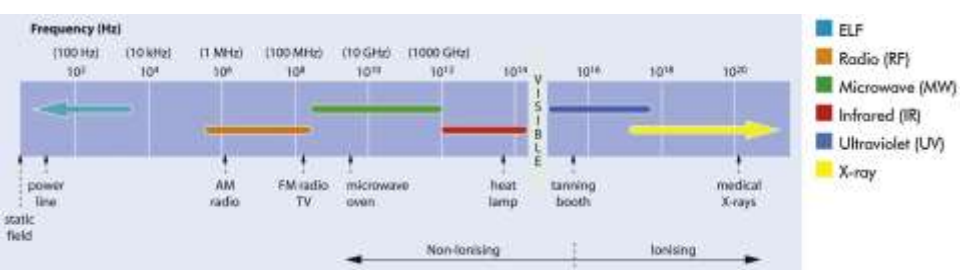
The electromagnetic spectrum extends from below the low frequencies used for modern radio communication to gamma radiation at the shortest wavelength and highest frequency. Reproduced from the European Commission, Research Directorate-General, European Communities (2005).

☢ **Radiação e Cancro**

Excess relative risk per unite dose (Sv⁻¹)ᵃ

Map of radon in Europe (<=2014). Radiat. Prot. Dosimetry 2014;162: 129–34.
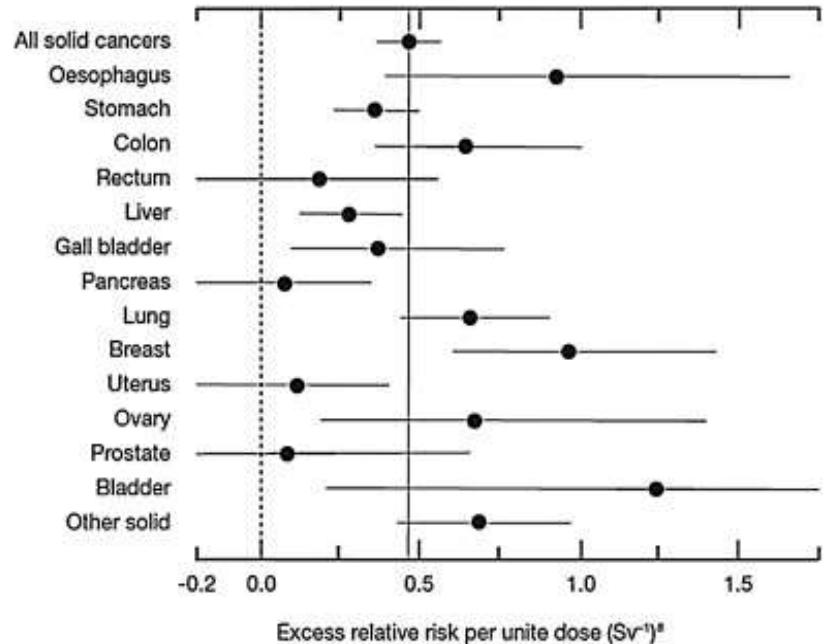
Estimates of solid cancer mortality risk for different organs from studies of the survivors of the atomic bombings in Japan. The figure shows the excess relative risk per unit dose (Sv1) of various cancer types from radiation exposure among the survivors of the atomic bombings in Japan. (ONU)
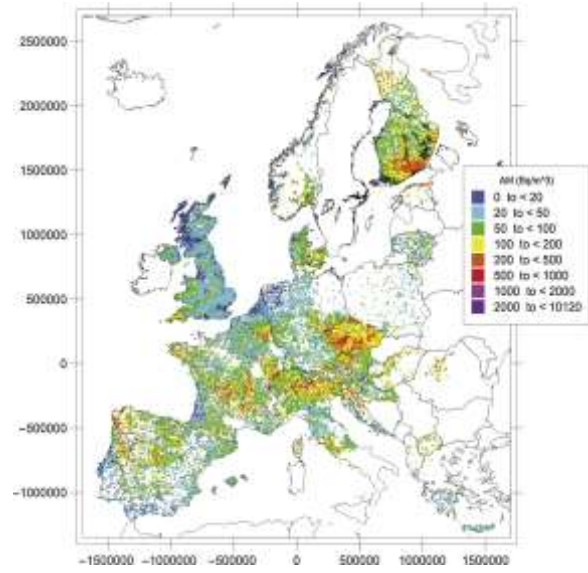
☀ Radiação UV (UVA e UVB) e Cancro

	Phenotype	UV sensitivity		Skin cancer risk
Type I	Very fair, pale white, light coloured or red hair, often freckled	++++	Skin burns very easily, and never, or hardly ever, develops a tan	Greatest risk of skin cancer
Type II	Fair, white skin, light hair, and blue or brown eyes. Some may have dark hair	+++	Skin burns easily, and tans slowly	High risk of skin cancer
Type III	Light brown, light olive skin with dark hair and brown or green eyes	++	Skin does not burn easily, and develops a tan	High risk of skin cancer
Type IV	Moderate brown, brown eyes and dark hair	+	Skin hardly ever burns, and develops a tan easily (Mediterranean skin type)	At risk of skin cancer
Type V	Dark brown, brown eyes and dark hair	+/_	Skin never burns, naturally darker skin (Asian skin types)	Skin cancers are relatively rare, but those that occur are often detected at later, more dangerous stage.
Type VI	Deeply pigmented dark brown to black, dark brown eyes and black hair	_	Skin never burns, naturally dark-coloured skin (Negroid skin types)	Skin cancers are relatively rare, but those that occur are often detected at later, more dangerous stage.

Melanoma

Carcinoma Espinocelular

Carcinoma Basocelular

Mecanismos:
- ✓ Danos DNA
- ✓ Imunosupressão
- ✓ Melanogénese
- ✓ Vit. D

Risco acrescido se exposição na infância

Solários - carcinogénicos

Infecção e Cancro

✓ **Vírus Hepatite B (HBV)**
✓ **Vírus Hepatite C (HCV)**
✓ **Vírus Imunodeficiência Humana (HIV)**
✓ **Vírus Papiloma Humano (HPV)**
✓ **Helicobacter Pilori (HP)**

Carcinoma Hepatocelular (HBV, HCV)

Sarcoma de Kaposi, LNH, Cancro Cabeça e Pescoço (HIV)

Cancro Genital e Cabeça e Pescoço (HPV)

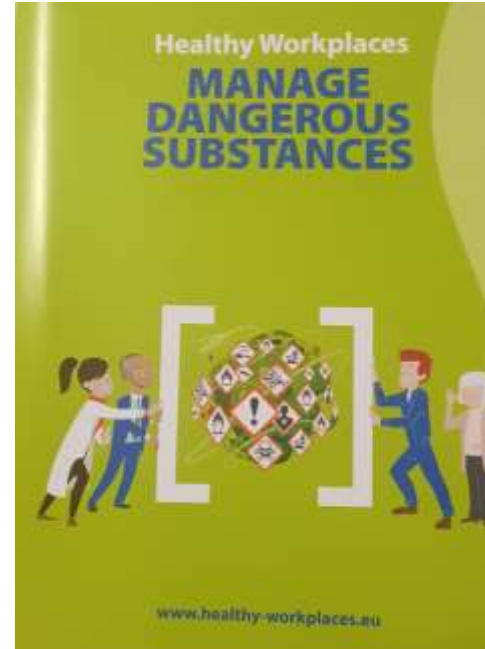**Cancro Gástrico (HP)**

Ambiente e Cancro
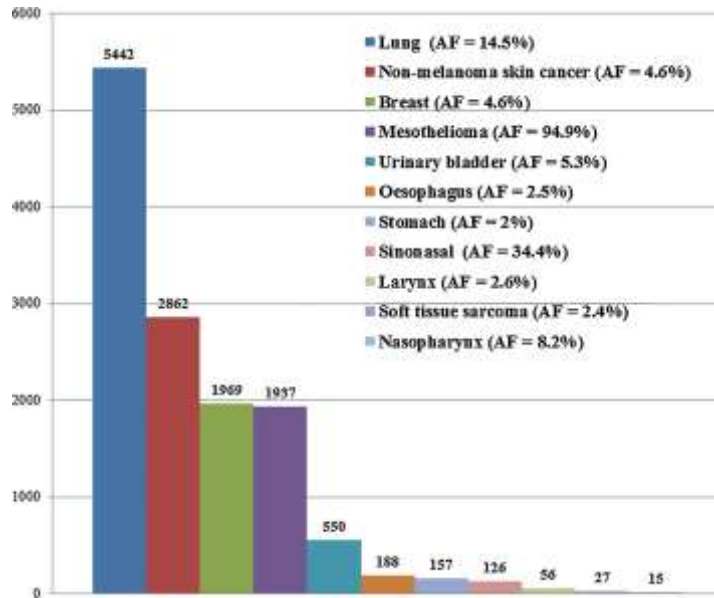
Estimated numbers (cases in men and women together) attributable
to occupational exposures by cancer site (and attributable fraction
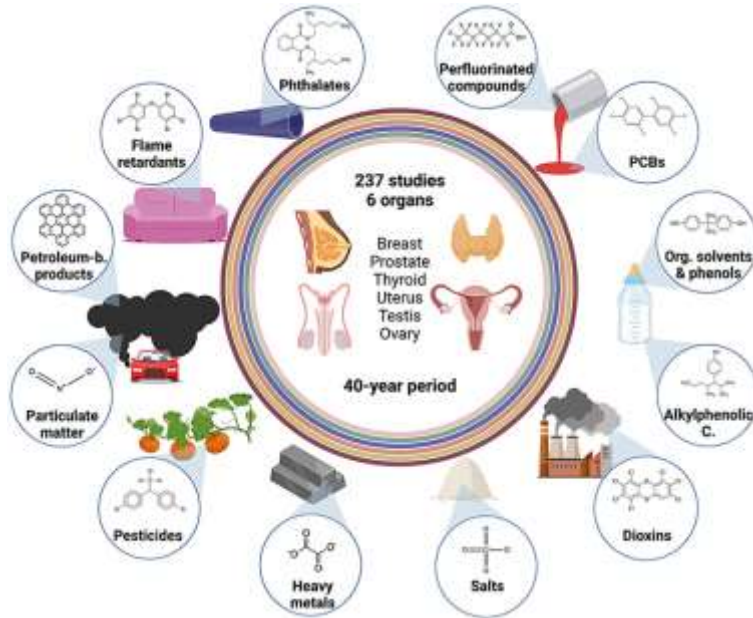(AF) for men and women together indicated in parenthesis).
Br. J. Cancer, 107 (Suppl 1) (2012 Jun), pp. S3-S7

✓ **POLUIÇÃO AMBIENTAL**

✓ **EXPOSIÇÃO OCUPACIONAL**

Disruptores Endócrinos e Cancro

Sofia Macedo, …Paula Soares et. Al. Environmental Research Volume 218, 1 February 2023, 114869

✓ **Pesticides** were the most studied EDCs. **Phthalates, Heavy Metals, and Particulate Matter (silica dust)were the EDCs most frequently associated with neoplasia**.

✓ **EDCs were associated with increased neoplasia risk in 43-67%** of the studies, with a lowest value for the ovary (43%) and a highest value for thyroid (67%).

✓ **Thyroid was the endocrine organ** with more studies showing a positive effect size for cancer risk.

✓ **The additive effect of EDCs mixtures** could exacerbate adverse effects on human health and should be addressed.

Fatores Modificáveis para Cancro e Diagnóstico Precoce

Álcool e Cancro

Alimentação e Cancro
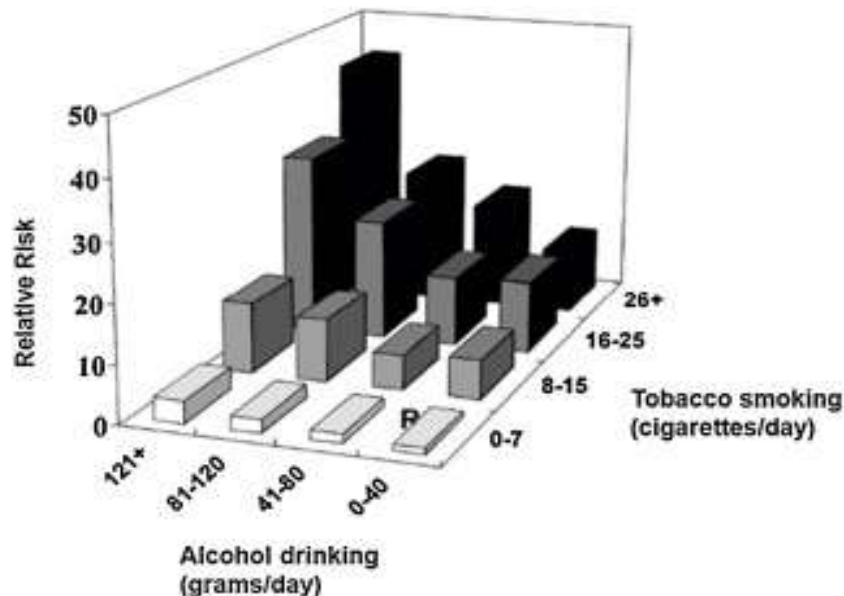
Sedentarismo e Cancro

Obesidade e Cancro

Amamentação, Menopausa e Cancro

Estimated relative risk (RR) for the interaction between tobacco smoking and alcohol drinking on cancers of the upper respiratory tract (reference category, risk = 1). Combined exposure to alcohol drinking and tobacco smoking increases the risk of upper digestive and respiratory tract neoplasms in a supra-multiplicative manner. From P. Boyle, Annals of Oncology 2003, 14: 973– 1005.

Álcool e Cancro

MAIOR RISCO DE CANCRO:

- ✓ Cancro da Cavidade Oral, Faringe, esófago
- ✓ Cancro Colo-retal
- ✓ Carcinoma Hepatocelular
- ✓ Carcinoma da Mama Feminina

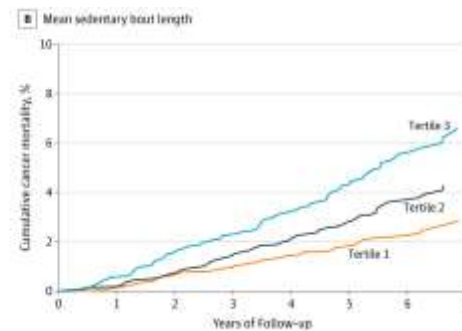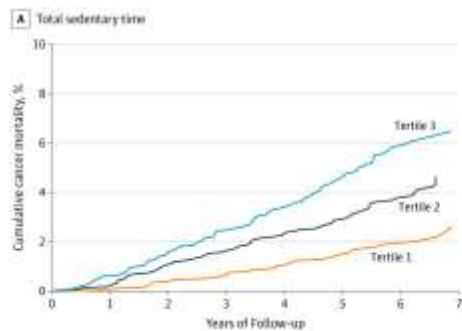# Alimentação e Cancro
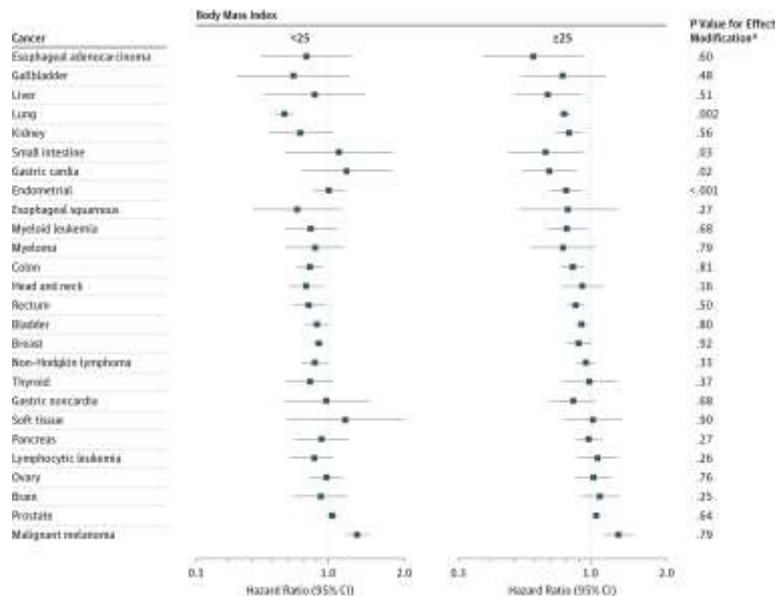

Dietary Habits and Cancer

- ✓ There is no good evidence that any one food prevents cancer.

- ✓ There aren't many foods that cause cancer, **but eating processed red meat can increase the risk of bowel cancer.**

- ✓ Foods such as burnt toast or crispy potatoes contain a chemical called acrylamide.

- ✓ Some tins and cans are lined with something called Bisphenol-A (BPA).

Sedentarismo e Cancro

Exercício Físico associado a menor incidência de cancro, sobretudo se Excesso de Peso /Obesidade

Sedentarismo associado a excesso de Mortalidade por Cancro.

Obesidade e Cancro

| Evidence level	Strength of Relative Risk Increase for Obesity and Cancer Risk		
	High (RR increase ≥3)	**Modest (RR increase: 1.50-2.99)**	**Little (RR increase: ≥1.0<1.49)**
Convincing / Sufficient	Endometrial Adenocarcinoma Esophageal Adenocarcinoma	Renal Adenocarcinoma Hepatocellular Cancer Pancreatic Adenocarcinoma Gastric Cardia Cancer Multiple Myeloma Meningioma	Colorectal Cancer Postmenopausal Breast Cancer Gallbladder cancer Ovarian cancer Thyroid cancer
Limited		Advanced Prostate Cancer Male Breast Cancer Diffuse Large T-Lymphoma	
Adapted from Avgerinos, 2019			

**Epidemiological Evidence Associating Overweight/Obesity and Cancer
by Level of Evidence and Strength of Relative Risk Increase for Overwheight/Obesity
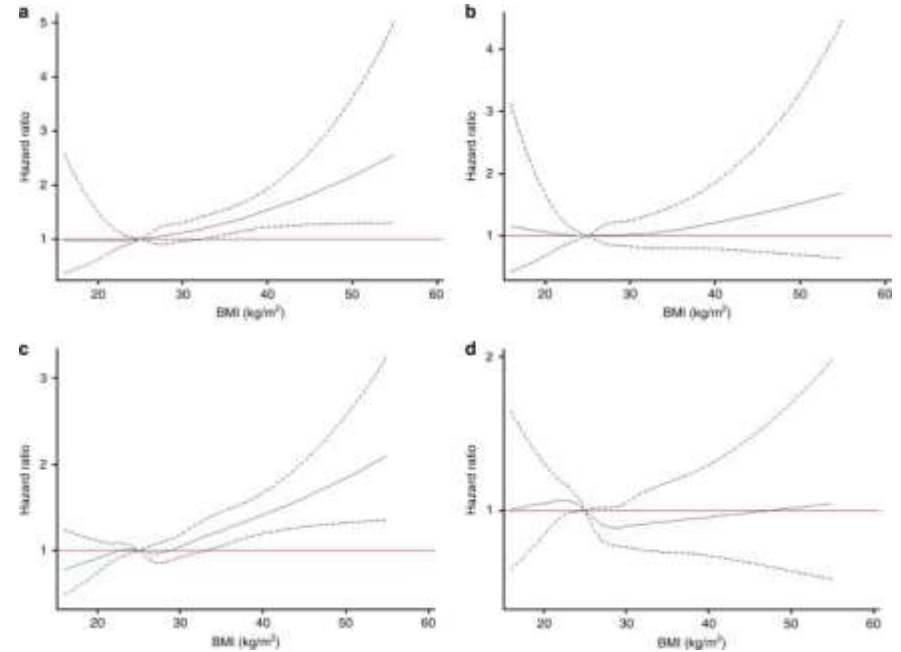In Comparison to Normal-Range Body Mass Index Defined by WHO as Synopsized by the IARC Working Group In 2017**

Central body fatness is a stronger predictor of cancer risk than overall body size

Amanda M. Barberio et. al., Nature Communications, 2019

IMC
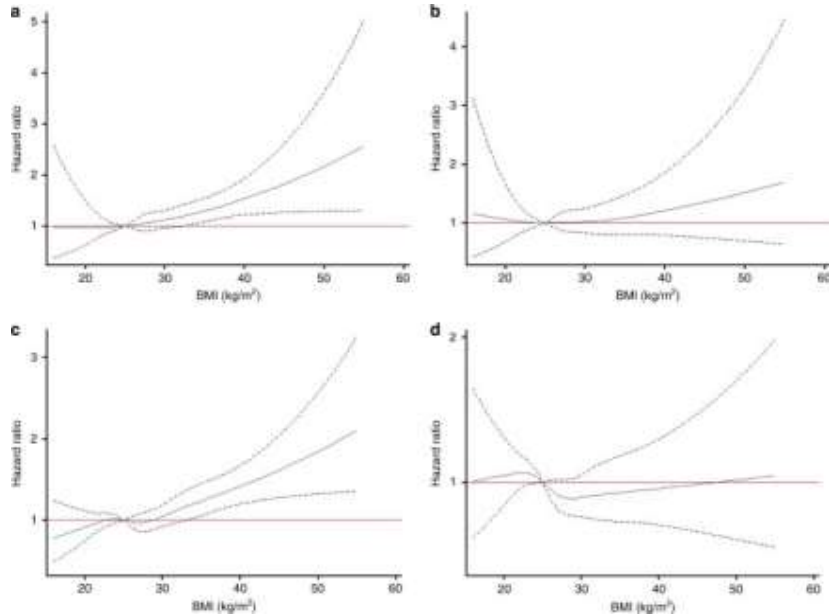
PC

These findings suggest that central adiposity measured by waist circumference is a stronger than BMI risk factor for all cancers

Síndrome Metabólica e Cancro

Metabolic syndrome is defined as having at least three of five components:

→ Elevated waist circumference (≥ 88 cm for women; ≥ 102 cm for men)

→ Elevated triglycerides (≥ 150 mg/dL) or drug treatment for elevated triglycerides

→ Low HDL cholesterol (< 40 mg/dL for men; < 50 mg/dL for women) or drug treatment for low HDL

→ Elevated blood pressure (systolic ≥ 130 mm Hg or diastolic ≥ 85 mm Hg) or hypertensive drug treatment

→ Elevated fasting glucose (≥ 100 mg/dL) or drug treatment for elevated glucose

✓ **Metabolic dysfunction associations with breast and colorectal cancer risk have been observed independently of BMI,**

✓ with **increased risk in individuals with metabolically unhealthy normal weight or overweight/obese** compared with metabolically healthy normal weight
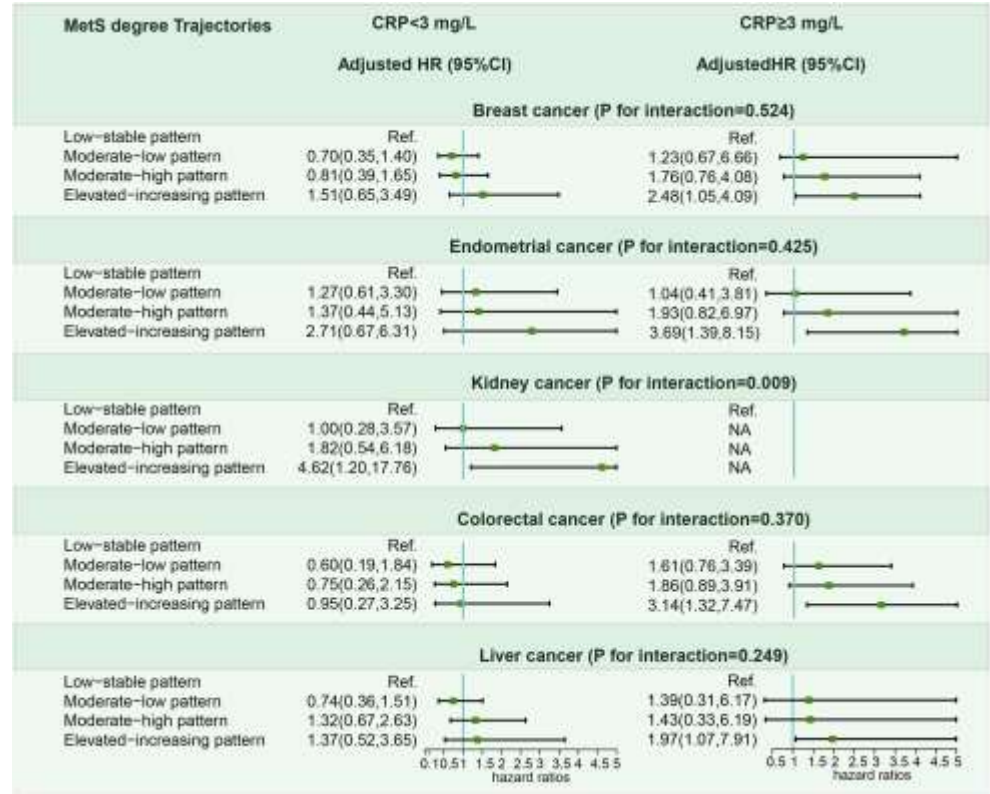
Deng et. al. Cancer. 2024;130:2150–2159.

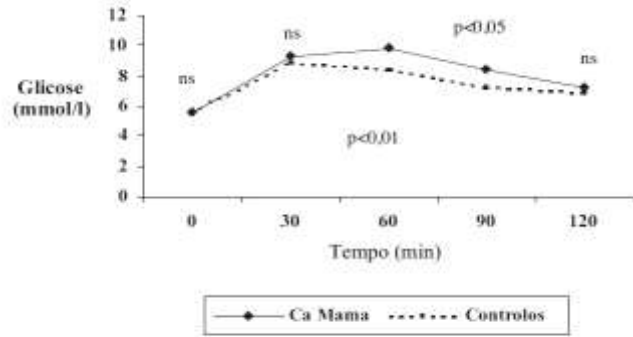# Case- control study (43 controls vs 43 naive treatment breast cancer pts)
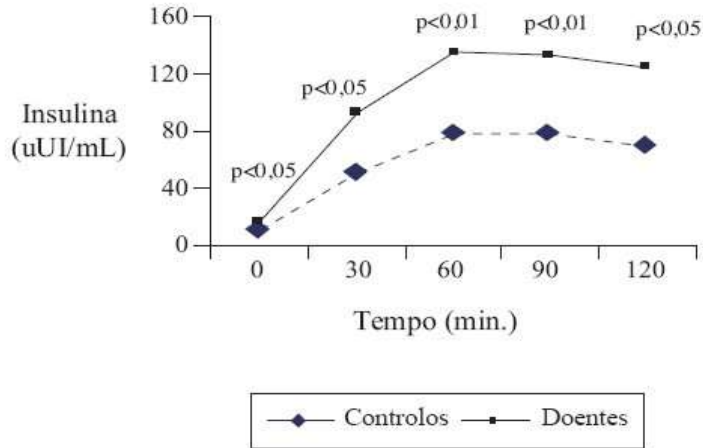

Fig. 8 – Curva de Glicemia (PTGO).


Fig. 9 – Curva de insulina (PTGO)

Breast Cancer associated with:

- Fetal Macrossomia
- High WC
- High Blood Pressure
- Metabolic Syndrome
- Insulin resistance (HOMA-RI>2.2)

**The risk was proportional to the number of MetS components**

Ana Paula Santos. Falência dos Mecanismos de Regulação Endócrina na Obesidade e sua relação com a Carcinogénese Mamária. 2004. http://hdl.handle.net/10216/14341.

RISCO DE CANCRO e RESISTÊNCIA À INSULINA
Um modelo multi-dimensional

- ✓ Efeito mitogénico da insulina
- ✓ F. Crescimento (Insulina, IgF1)
- ✓ Hormonas (Estrogénios, Androgénios, Leptina…)
- ✓ Citoquinas pro-inflamatórias
- ✓ PAI-1
- ✓ Microbiota

Adaptado de Jee et al. Yonsei Med J 2005; 46(4):449

PI3K/Akt/mTOR pathway is a major key in establishing the connection between metabolism (Insulin Resistance and Hyperinsulinism) and Cancer
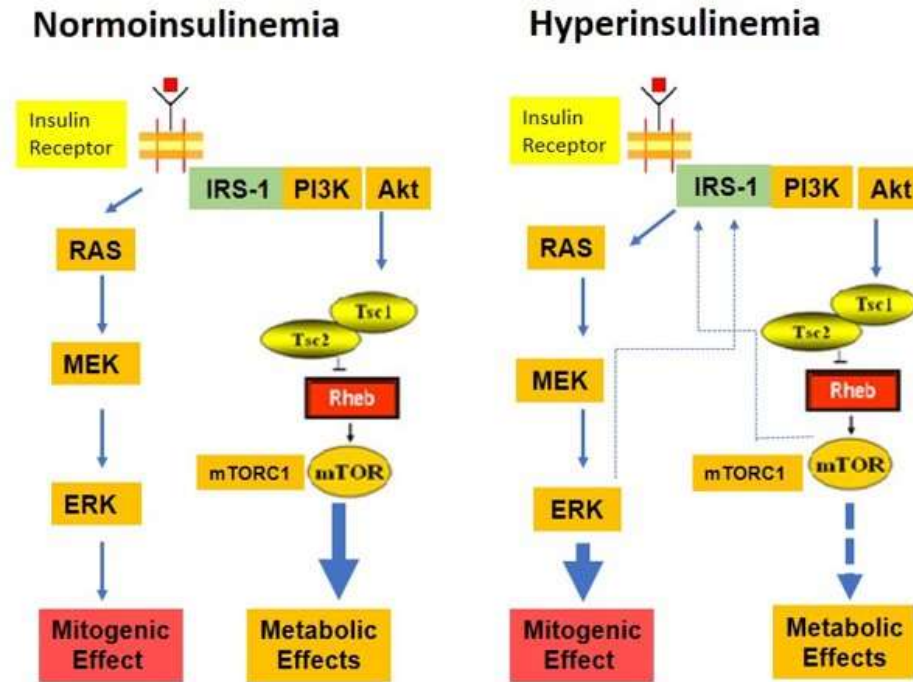
(Adapted from "Diabetes and cancer. Paolo Vigneri, et. al. ERC, 2009)

Body mass index and cancer risk among adults with and without cardiometabolic diseases: evidence from the EPIC and UK Biobank prospective cohort studies. Emma Fontvieille, et. Al.*BMC Medicine* **volume 21**, 418 (2023)
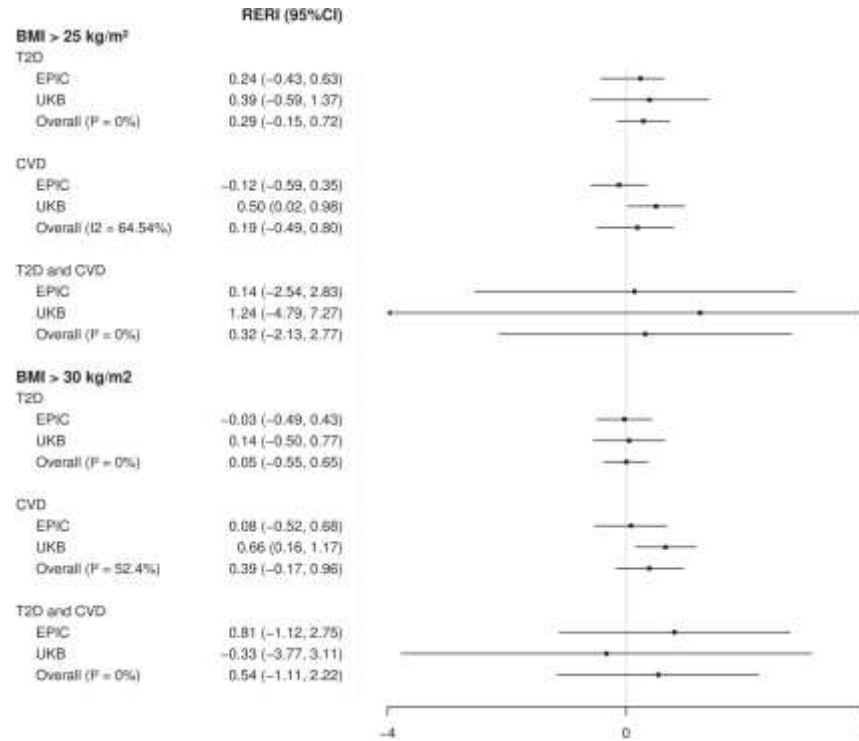
- ➤ Irrespective of CMD status, **higher BMI increased the risk of obesity-related cancer** among European adults.

- ➤ The additive interaction between obesity and CVD suggests **that obesity prevention would translate into a greater cancer risk reduction among population groups with CVD** than among the general population.

Health & Medicine

Obesity could overtake smoking as biggest preventable cause of cancer in women

by Cancer Research UK | News
24 September 2018

💬 0 comments
🕐 3 mins read

"Right now, obesity is projected to replace tobacco as the leading modifiable risk factor for many cancers," said ASCO Immediate Past President Clifford A. Hudis, MD, FACP m(2014).

When addressing ASCO membership at the 2014 ASCO Annual Meeting, Dr. Hudis stressed that **obesity has the potential to reverse the gains oncologists have made in fighting cancer during the past 50 years.**

Factores Modificáveis para Cancro e Diagnóstico Precoce

Álcool e Cancro

Sedentarismo e Cancro

Alimentação e Cancro

Obesidade e Cancro

Amamentação, Menopausa e Cancro da Mama

Amamentação e Cancro da Mama
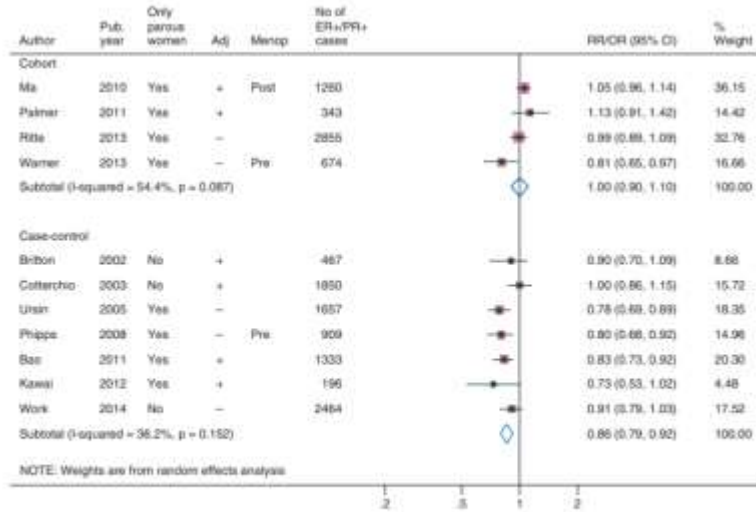
Figure 4. Association between ever breastfeeding and the breast cancers that were positive for both estrogen and progesterone receptors. Adj, adjusted for at least age, body mass index, parity, and family history of breast cancer; Menop, menopausal status of study participants ('Pre' and 'Post' indicate that participants were premenopausal or postmenopausal women, respectively); Pub. year, publication year.
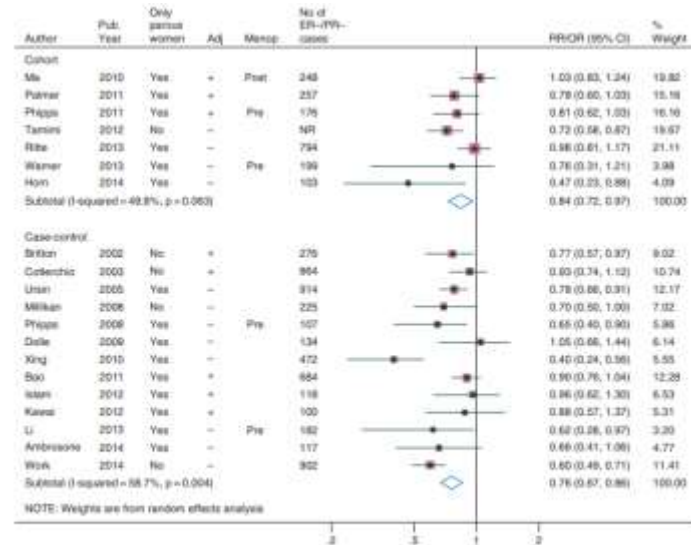
Figure 2. Association between ever breastfeeding and the breast cancers that are negative for both estrogen and progesterone receptors. Adj, adjusted for at least age, body mass index, parity, and family history of breast cancer; Menop, menopausal status of study participants ('Pre' and 'Post' indicate that participants were premenopausal or postmenopausal women, respectively); NR, not reported; Pub. year, publication year.

✓ The relative **risk of breast cancer is decreased by 4.3% (CI 2.9–5.8) for every 12 months of breastfeeding**, which was in addition to the 7.0% (CI 5.0–9.0) decrease in risk observed for each birth.

✓ In the context of a high-income country such as the UK**, a woman who has two children and breastfed for 12 months with each child will have reduced her risk of breast cancer by 8.6%.**

✓ **No reduction in the risk for hormone-receptor positive (HR+) BC** associated with breastfeeding but found **a 20% reduction in the risk of triple-negative BC (TNBC)**. Association of Breastfeeding and HER+ and BC is controversial.

Islami F, Liu Y, Jemal A, et al. Ann Oncol. 2015;26(12):2398-2407

Terapêutica Hormonal Substituição (THS) na Menopausa e Cancro da Mama

	Cases	HR (95% CI)
Oral ET		
<1 year	28	1.56 (1.04–2.33)
1–4.9 years	24	1.26 (0.82–1.92)
≥ 5 years	162	1.27 (1.08–1.50)
Unknown duration	289	1.47 (1.29–1.66)
Vaginal ET		
<1 year	291	0.98 (0.86–1.11)
1–2.9 years	225	1.12 (0.98–1.29)
3–4.9 years	85	1.06 (0.84–1.33)
≥ 5 years	252	0.90 (0.79–1.02)
Unknown duration	603	1.00 (0.92–1.10)
Oral oestrogen-NETA		
<1 year	92	1.23 (0.99–1.54)
1–2.9 years	92	2.01 (1.60–2.53)
3–4.9 years	34	1.85 (1.28–2.67)
≥ 5 years	613	3.47 (3.16–3.82)
Unknown duration	1141	2.18 (2.04–2.34)
Oral tibolone		
<4.9 years	21	1.19 (0.76–1.88)
≥ 5 years	91	2.43 (1.93–3.07)
Unknown duration	165	1.72 (1.46–2.04)

0.71 1.0 1.41 4.0

The use of oral and transdermal HT was associated with an increased risk of BC. The associations varied according to HT type, individual drugs, molecular subtype, detection mode and BMI. British Journal of Cancer (2024) 131:126–137

- ✓ **Combination therapy with E/P demonstrated a significantly increased risk**, with a hazard ratio of 1.2.

- ✓ This **risk remained elevated for several years** after discontinuation HRT but then declined rapidly.

- ✓ After the **results of the WHI study were made public, a decline in BC incidence** was noted in the US.

- ✓ In the WHI study, **postmenopausal women on combination E/P HRT had an average increase of 6% in mammographic density** vs aprox 1% decrease in placebo group over the same period.

🔍 Rastreio do Cancro – Diagnóstico Precoce (Prevenção Secundária)
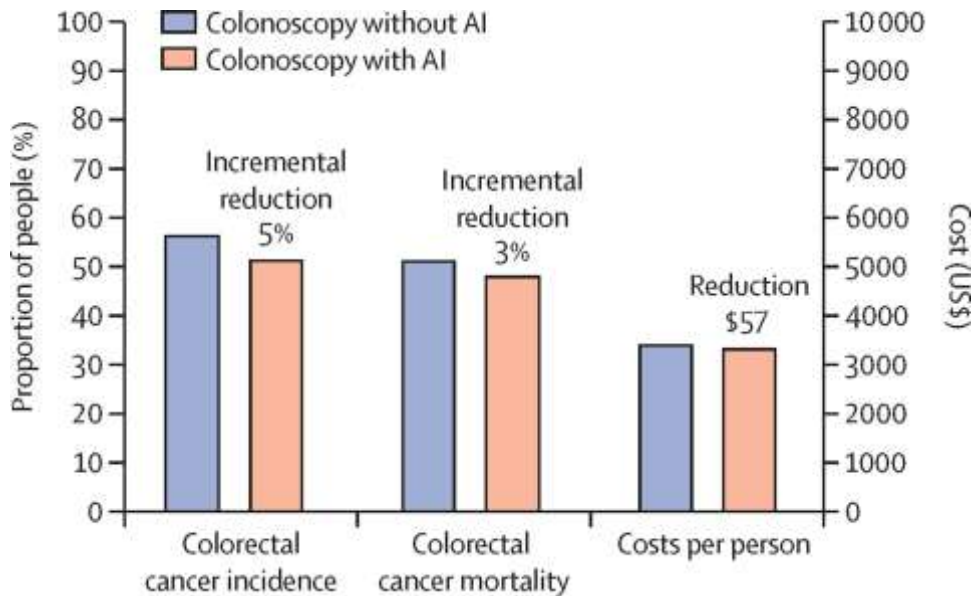
Expected risk of colorectal cancer incidence and mortality of colonoscopy screening with and without AI compared with non-screening. Estimated costs per person are also presented. Lancet Digit Health 2022 Published Online April 13, 2022 https://doi.org/10.1016/ S2589-7500(22)00042-5-

✓ **Colo Útero**
✓ **Cancro da Mama**
✓ **Cancro Coloretal**

✓ **Pele**
✓ **Cavidade Oral**
✓ **Estômago**
✓ **Ovário**
✓ **Pulmão......**

Estilo de Vida nos doentes com Cancro (Prevenção terciária)

Postdiagnosis body fatness, recreational physical activity, dietary factors and breast cancer prognosis: Global Cancer Update Programme (CUP Global) summary of evidence grading

✓ **Após o Diagnóstico**

✓ **Evitar recidivas**

✓ **Reduzir Mortalidade**

✓ **Manter a QoL**

Em Resumo….
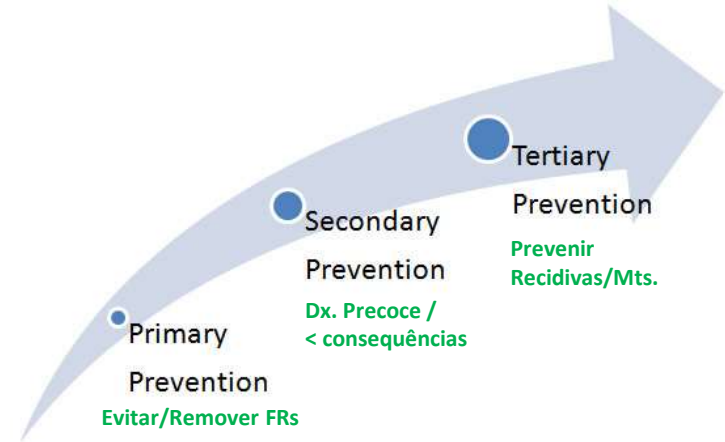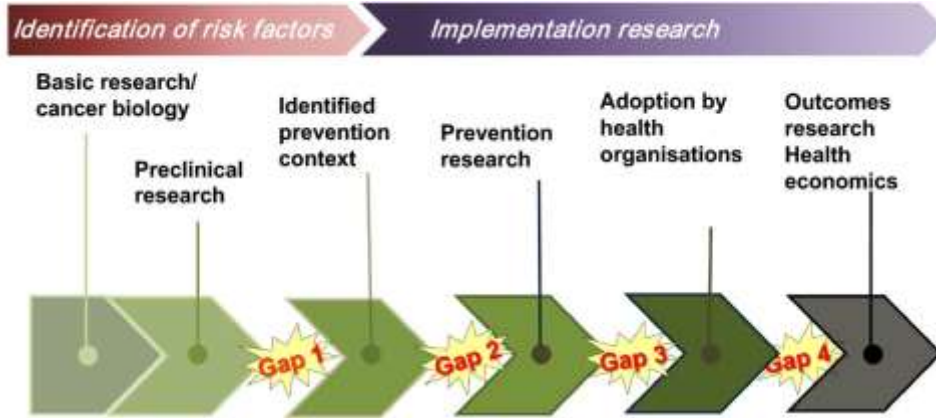
- ✓ The growing cancer problem **can only be significantly modified by concerted action involving prevention to decrease incidence, early detection and treatment** to increase the cure rate,

- ✓ and **personalised/precision cancer medicine to adapt early detection and treatment to the biology of a tumour**

- ✓ with **the aim of increasing the cure rate, prolonging survival and improving health-related quality of life**.

**'This Food Will Kill You,
That Food Will Save You'**

(Freedhoff, Y . Medscape Diabetes & Endocrinology, 2021)

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WAYS TO REDUCE YOUR CANCER RISK

Muito Obrigada!