

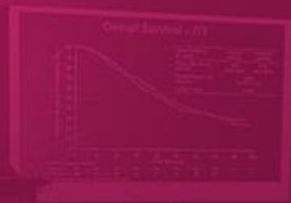
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SABCS



CONFERÊNCIA BRASILEIRA DE  
**CÂNCER DE MAMA**

LACOG - GBECAM 2023

LACOG - GBECAM



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LACOG - GBECAM 2024

REALIZAÇÃO



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APOIO

Instituto Projeto



GERENCIAMENTO  
E PRODUÇÃO



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*you*

# Novas evidências em “*surveillance*”

Dieta, exercício e controle de peso

# Declaração de conflito de interesses

De acordo com a Resolução 1595/2000 do Conselho Federal de Medicina e RDC 96, Art. 42 § 2º da ANVISA e do Código de Conduta da Interfarma, declaro que:

**Nenhum conflito de interesses a declarar**

Ricardo Caponero, LACOG-GBECAN 15 de Março de 2024

CONFERÊNCIA BRASILEIRA DE  
**CÂNCER DE MAMA** REALIZAÇÃO  
LACOG - GBECAM 2024



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APOIO



# Ressalva...



=

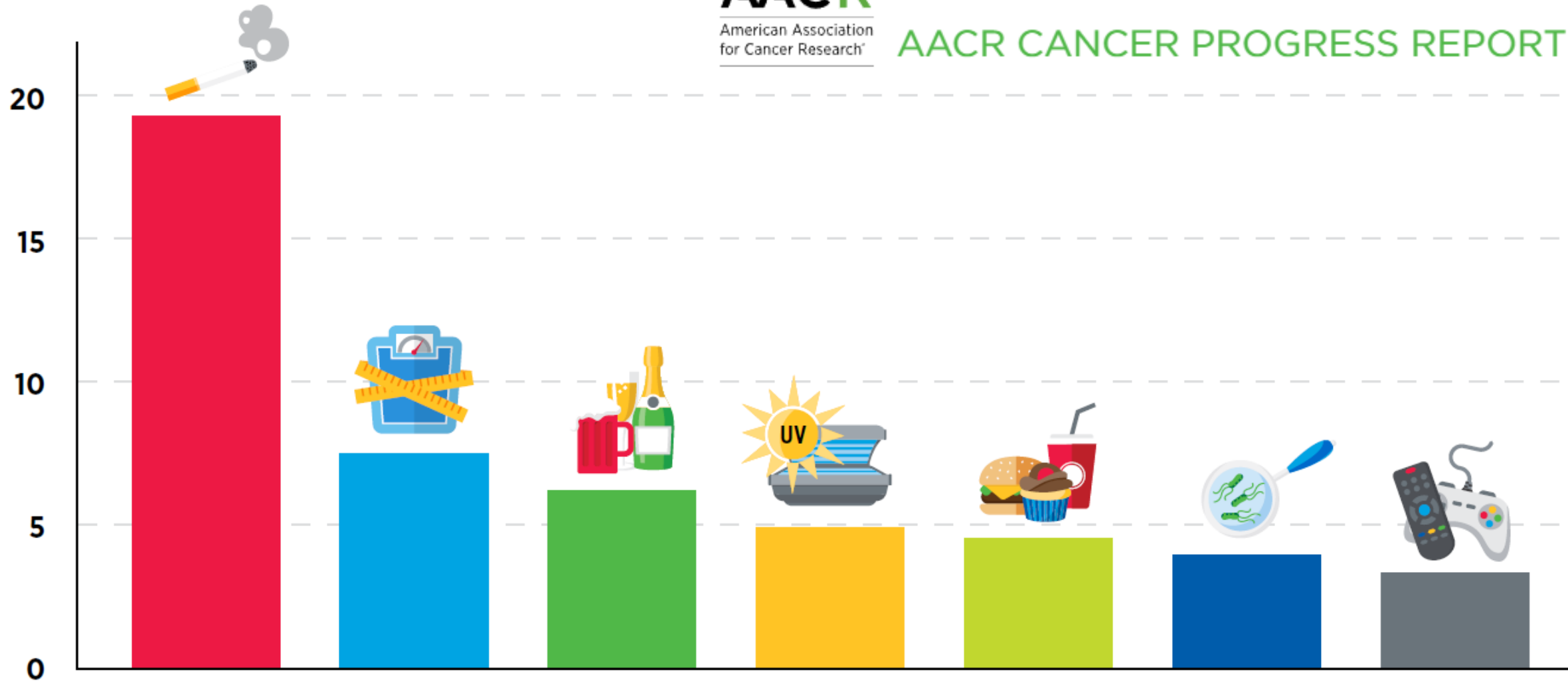


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# Riscos na carcinogênese

**Também valem para segunda neoplasias primárias**

% U.S. CANCER CASES ATTRIBUTABLE TO  
SELECTED FACTORS IN ADULTS AGE >30



**Tobacco  
Smoking**

**Excess  
Body Weight**

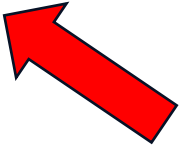
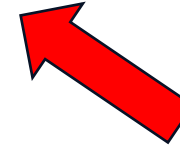
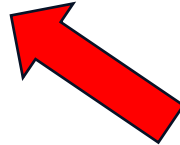
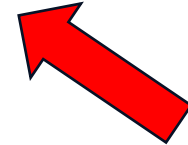
**Alcohol  
Consumption**

**Ultraviolet  
Radiation  
Exposure**

**Poor Diet**

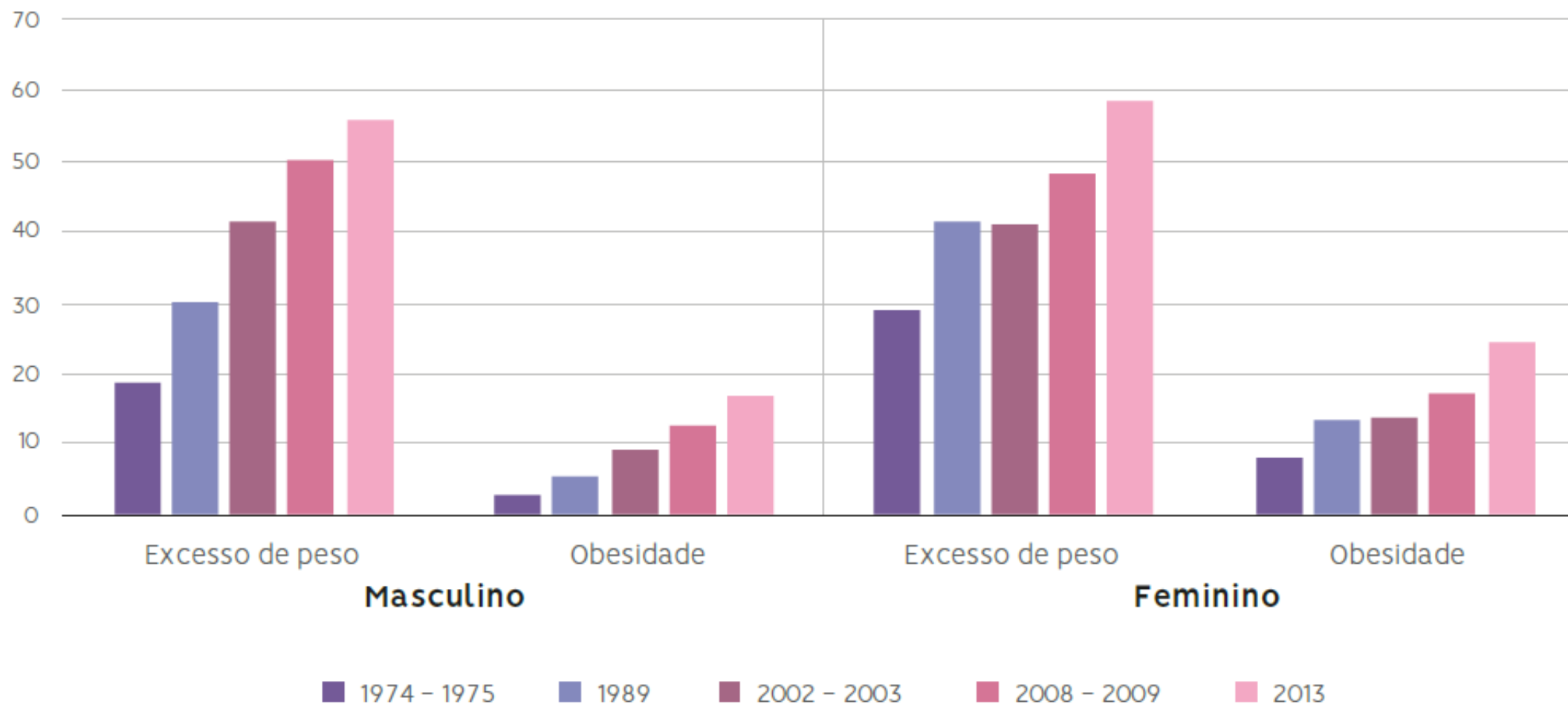
**Pathogenic  
Infections**

**Physical  
Inactivity**



# Prevalência de excesso de peso, Brasil

Prevalência (%)

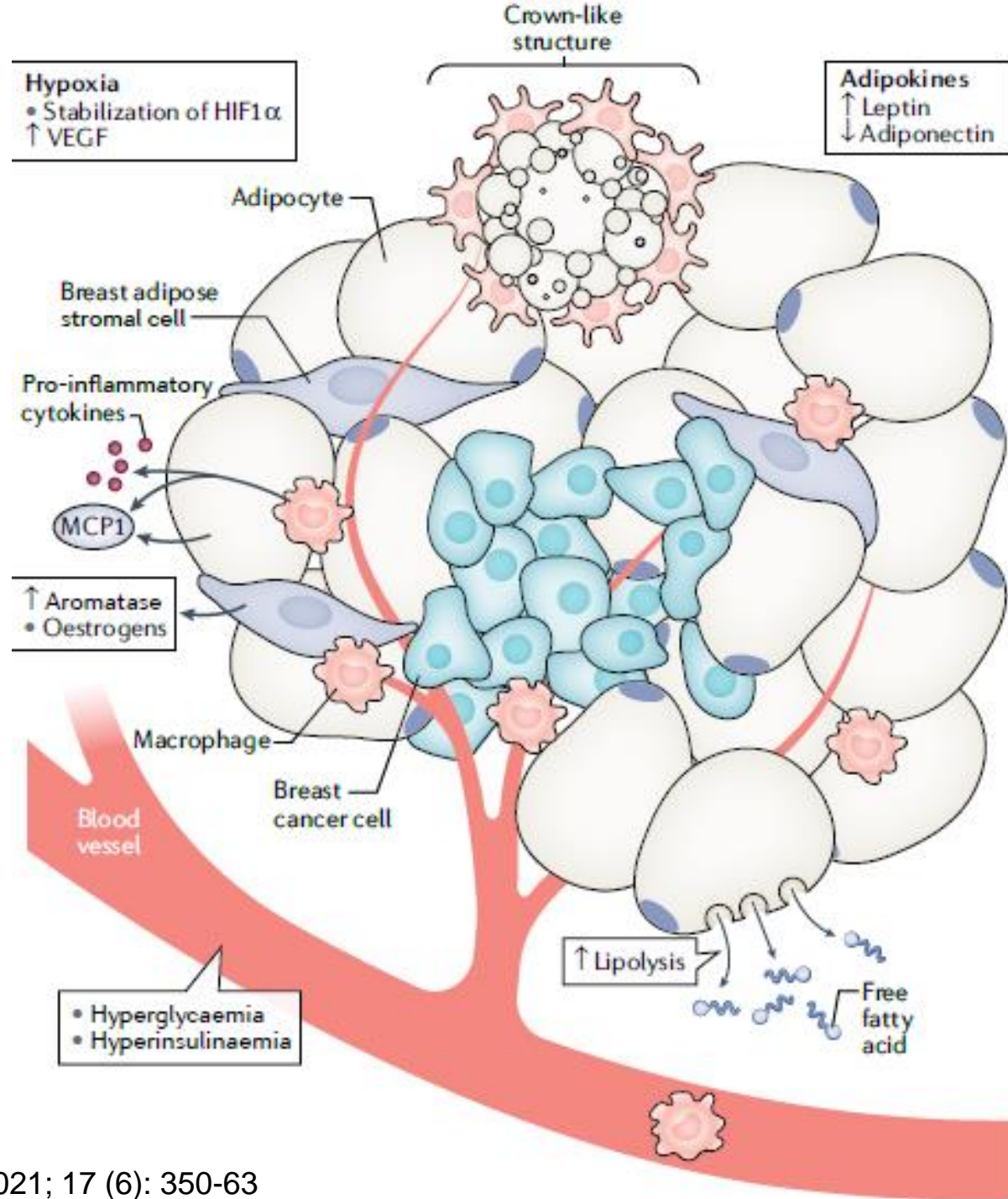


**Instituto Nacional de Câncer José Alencar Gomes da Silva.**

A situação do câncer de mama no Brasil: síntese de dados dos sistemas de informação  
Instituto Nacional de Câncer José Alencar Gomes da Silva. – Rio de Janeiro: INCA, 2019.  
ISBN 978-85-7318-377-1 (versão eletrônica)

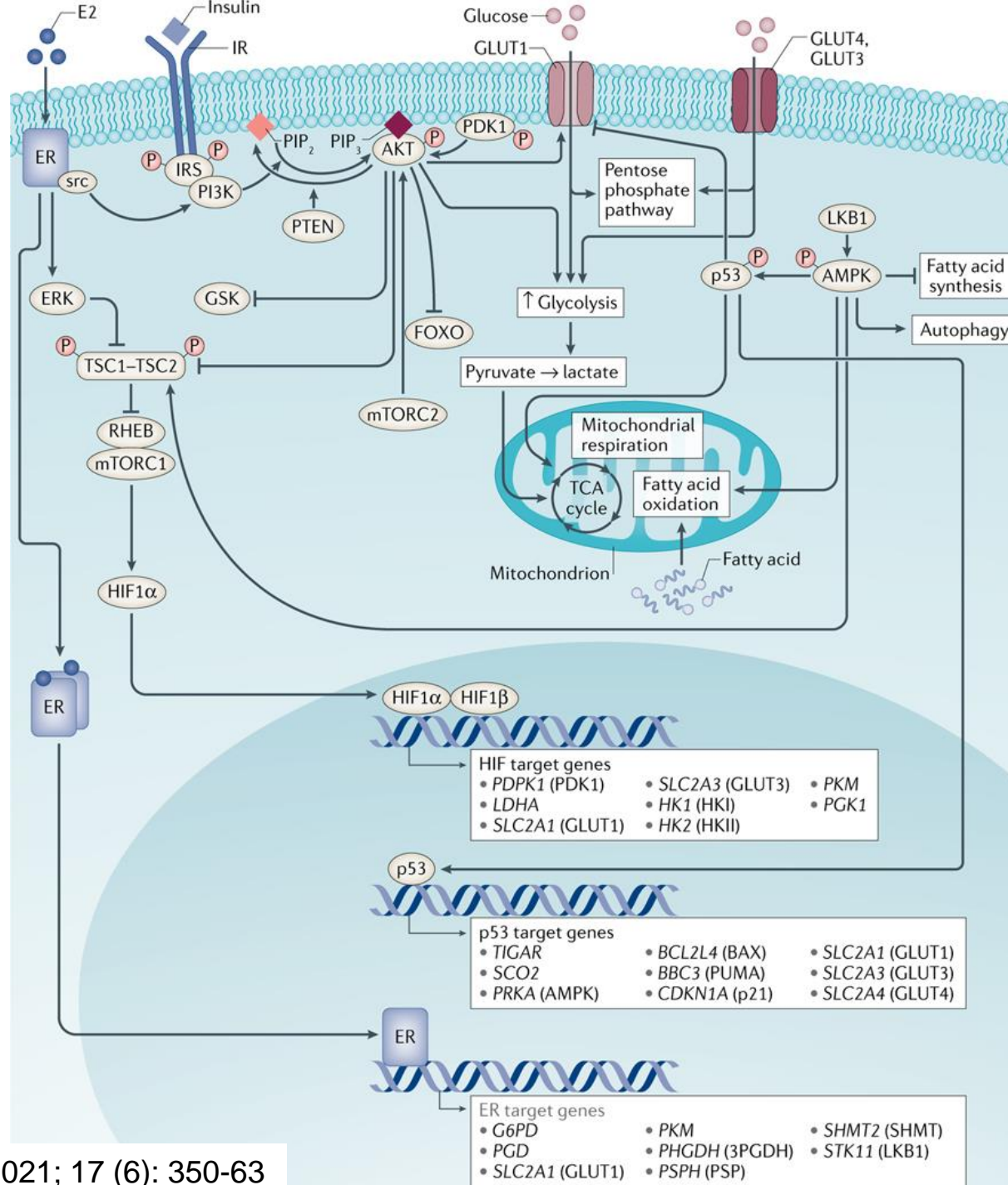
# Fisiopatologia da obesidade e câncer



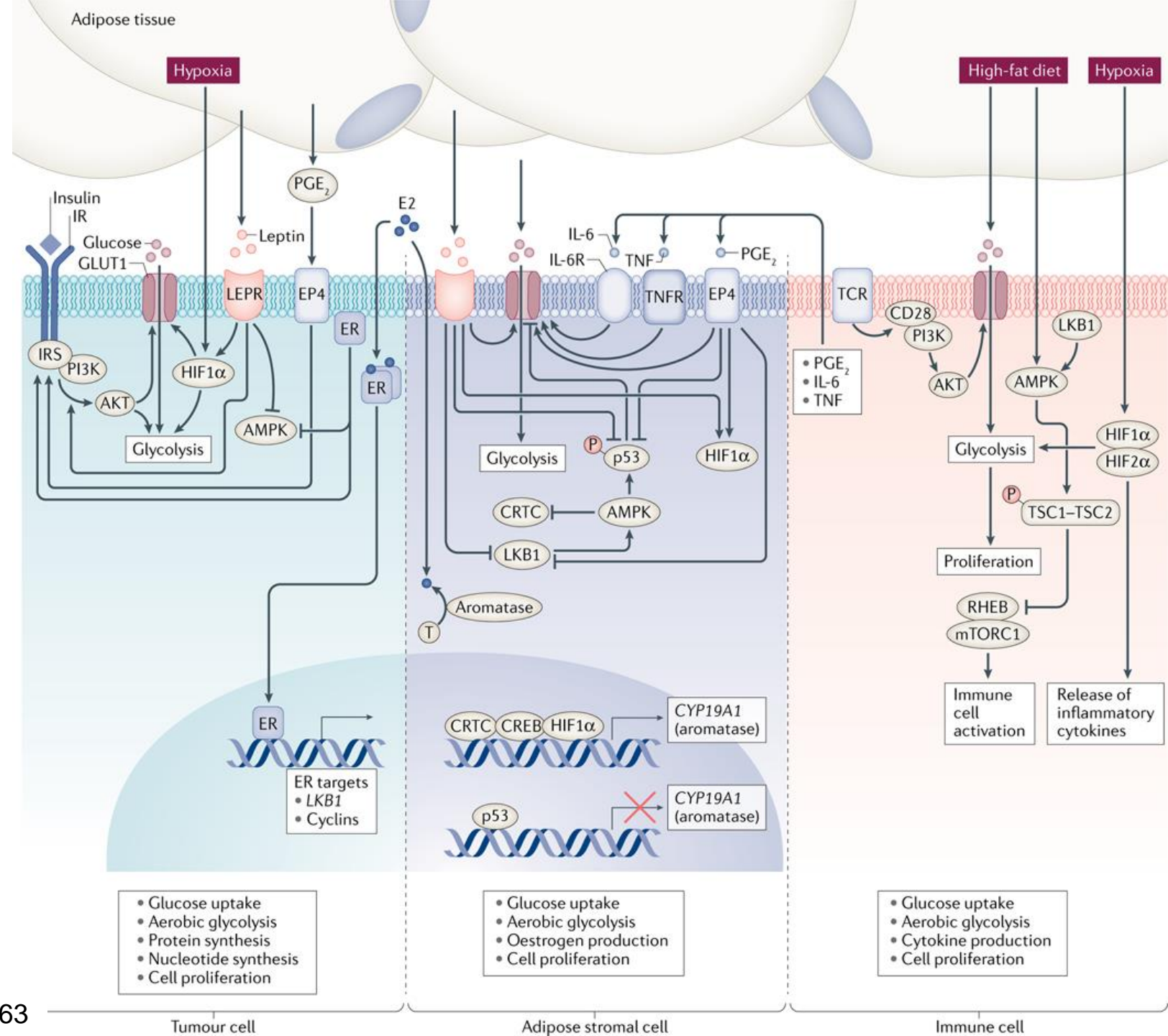


# Vias metabólicas principais no câncer de mama

Célula do câncer de mama



# Vias metabólicas desreguladas no câncer de mama e células do estroma adiposo no contexto da obesidade





## OBSESITY

### CHROMATIN MODIFICATIONS

- Hypomethylation leads to structural changes in chromatin.
- Structural changes curb body weight regulation.

### HISTONE MODIFICATIONS

#### METHYLATED REGIONS

- ↓ On H4K27 in p16<sup>INK4a</sup> gene region
- ↑ Regions involved in metabolism
- ↓ Regions involved in inflammation

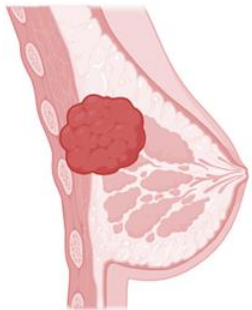
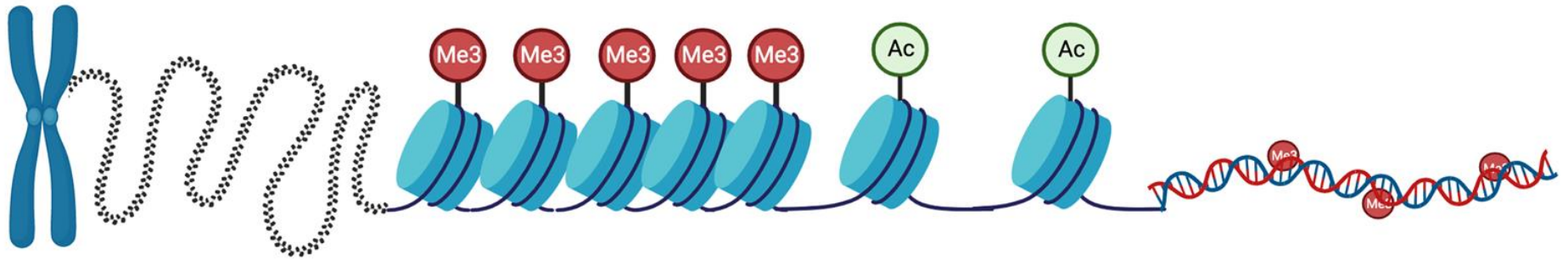
#### ACETYLATED REGIONS

- ↑ On H4K27 in p16<sup>INK4a</sup> gene region
- ↑ On H3K27 after high fat diet

### DNA MODIFICATIONS

#### METHYLATED GENES

- ↑ Metabolism and mitochondrial function genes
- ↓ Genes related to inflammation and immunity



## BREAST CANCER

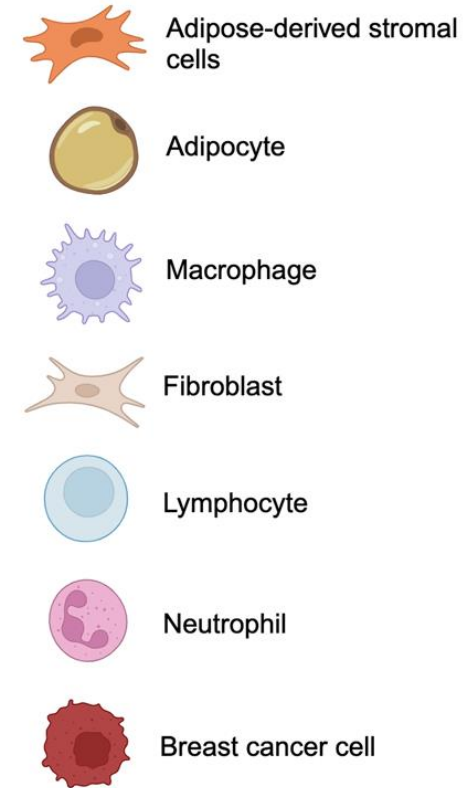
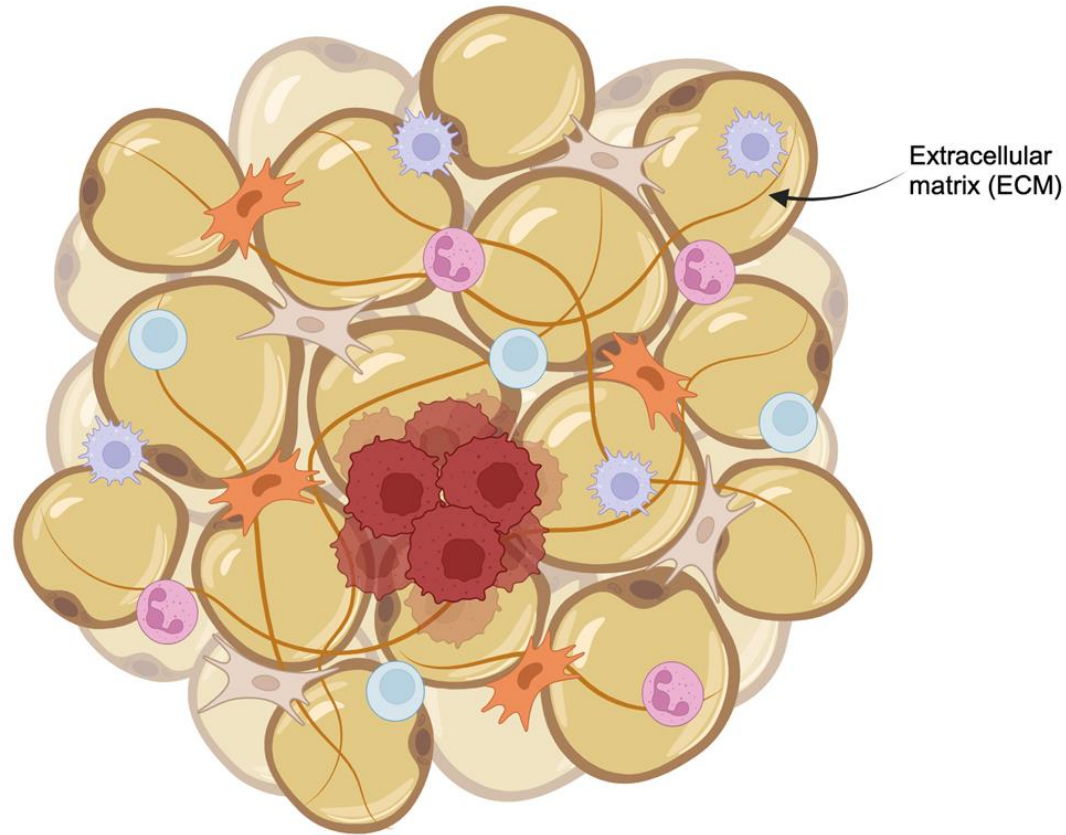
- Increase in global methylation alters chromatin structure.
- Structural changes curb transcriptional access to tumor suppressors.

- ↑ Global methylation
- ↑ Regions encoding tumor suppressors
- ↓ Regions encoding oncogenes

- ↓ Global acetylation
- ↓ Acetylation due to activity from HDAC2

- ↑ Tumor suppressor genes (i.e. BRCA, HOXA5, RASSF1A)
- ↓ Cancer promoting oncogenes (i.e. TSTD1, YAP1)

# Tumor Microenvironment (TME)



## Obese ME

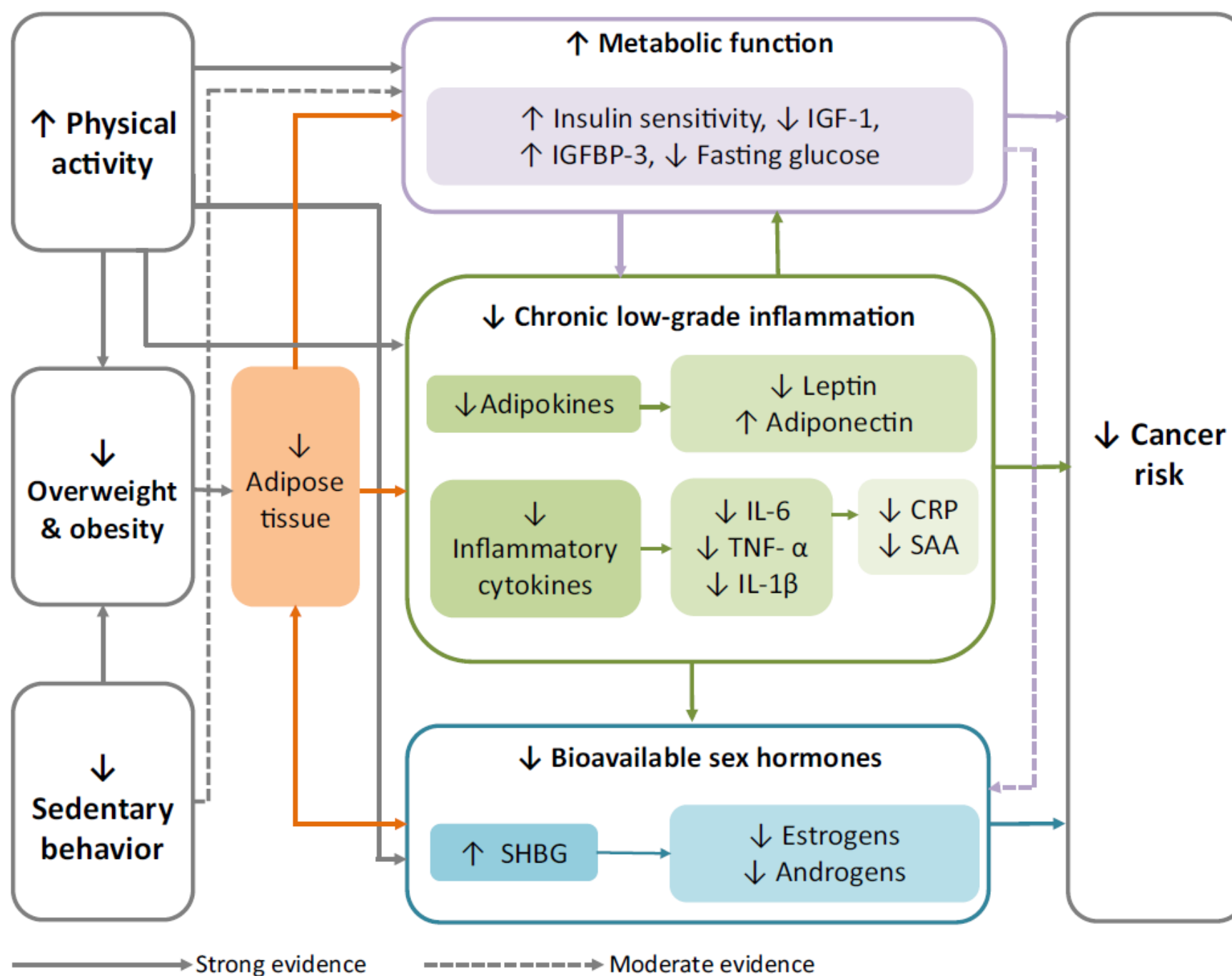
- ↑ Inflammation: TNF- $\alpha$  by macrophages
- ↑ Adipocyte hypermethylation and hypertrophy
- ↑ Immune hypomethylation
- ↑ Immune circulation
- ↑ DNMT
- ↓ Browning
- Accelerated epigenetic aging

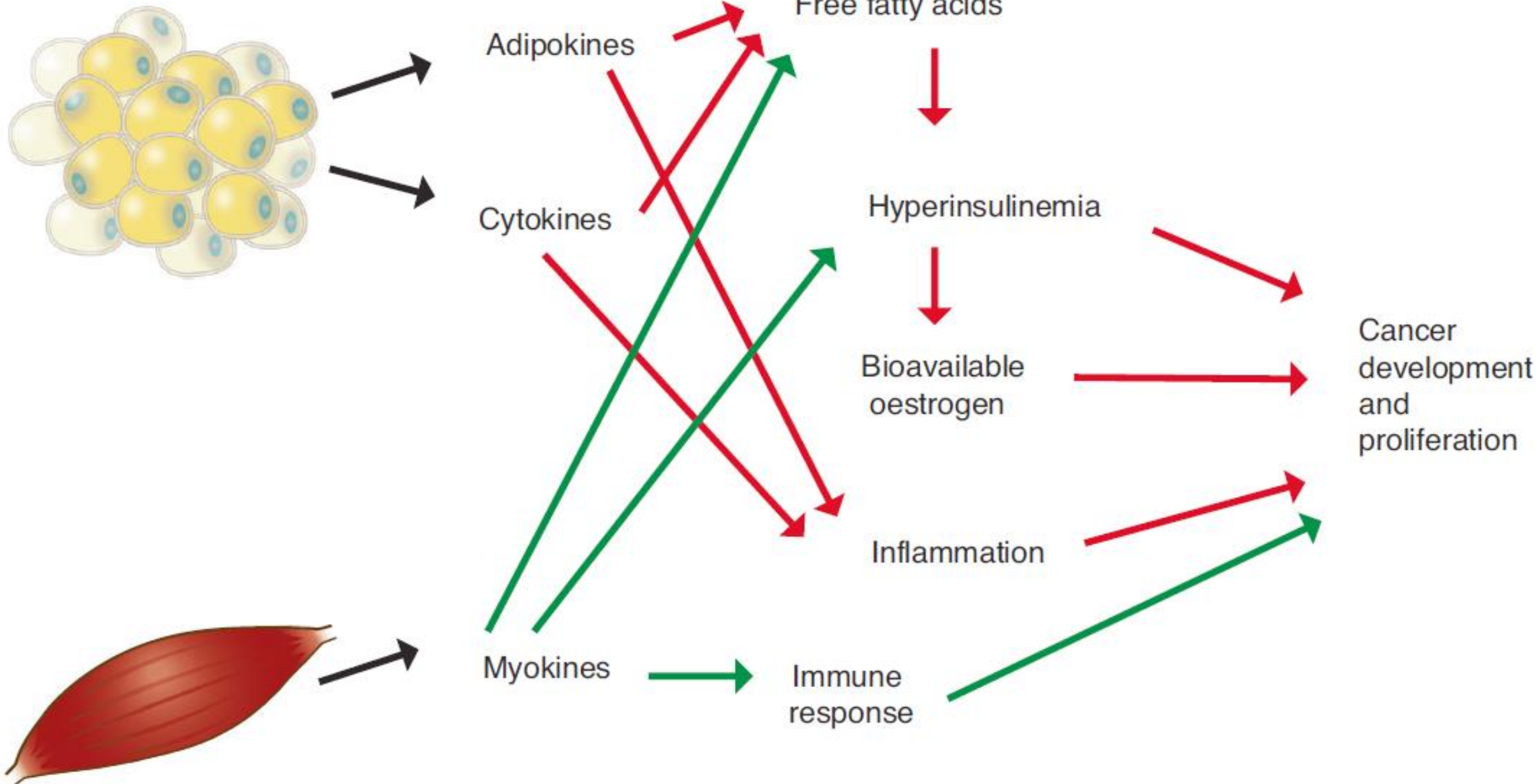
## Obese BC TME

- Hypermethylation of genes involved in immune response
- Accelerated epigenetic aging
- Worse prognosis

## BC TME

- ↑ HDAC  $\rightarrow$  ↑ IFN- $\gamma$
- ↑ HAT
- ↑ Tumor associated macrophages
- ↓ T-cell infiltration (LSD1)
- ↑ LSD1  $\rightarrow$  ↓ CD8 + T-cells
- Immune cell alterations





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# Recomendações na prevenção primária



# Grupos alimentares e risco (Mama)

15 estudos de coorte e 34 estudos caso-controle

Tipo de alimento	RR (IC95%)	Risco
Frutas	0,71 (0,55-0,93)	↓ 29%
Vegetais	0,71 (0,53-0,95)	↓ 29%
Carne, alimentos com soja, chá verde	p > 0,05	
Proteína de soja	0,65 (0,51-0,83)	↓ 35%
Isoflavona	0,68 (0,55-0,82)	↓ 32%
Adesão a um padrão alimentar saudável	0,62 (0,44-0,88)	↓ 38%
Índice de alimentação saudável	0,49 (0,27-0,87)	↓ 51%
Padrão alimentar pouco saudável	1,44 (1,06-1,96)	↑ 44%
Consumo de álcool	1,75 (1,33-2,30)	↑ 75%

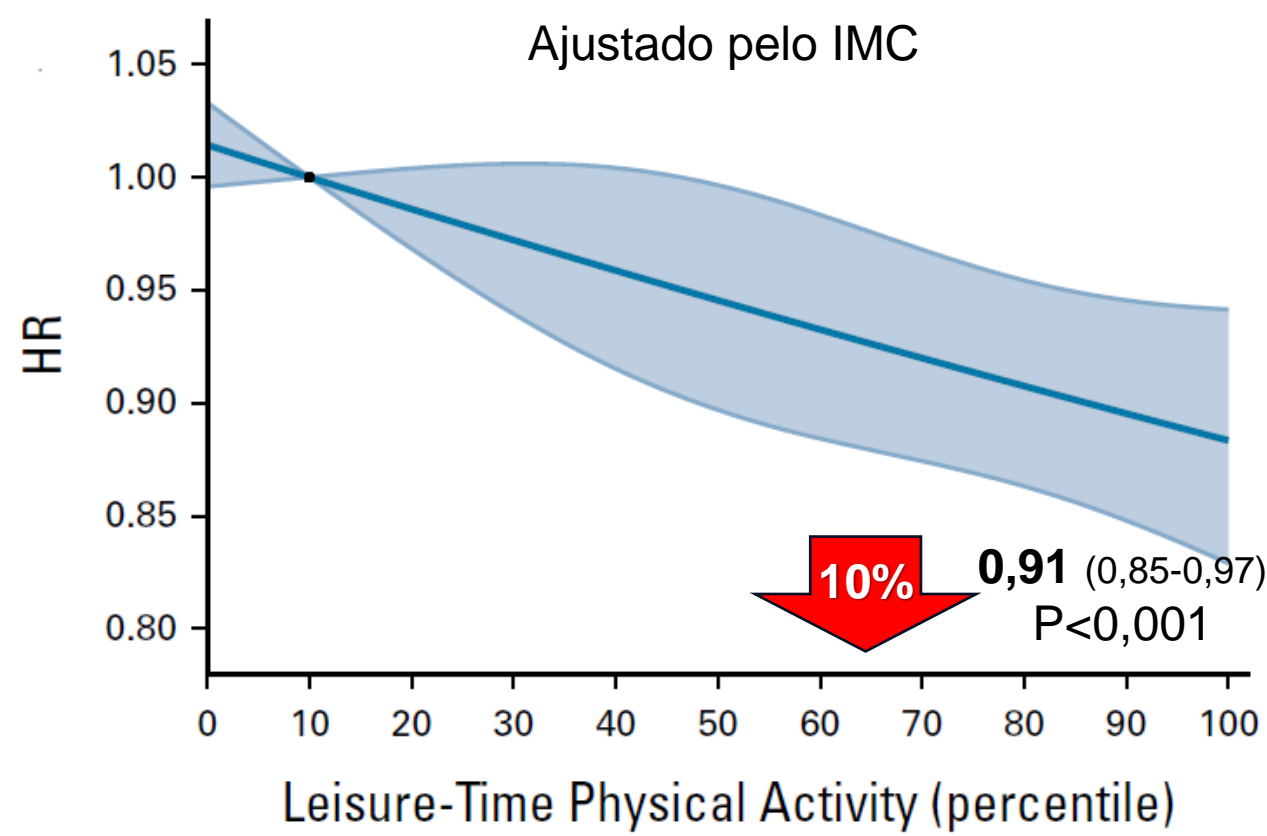
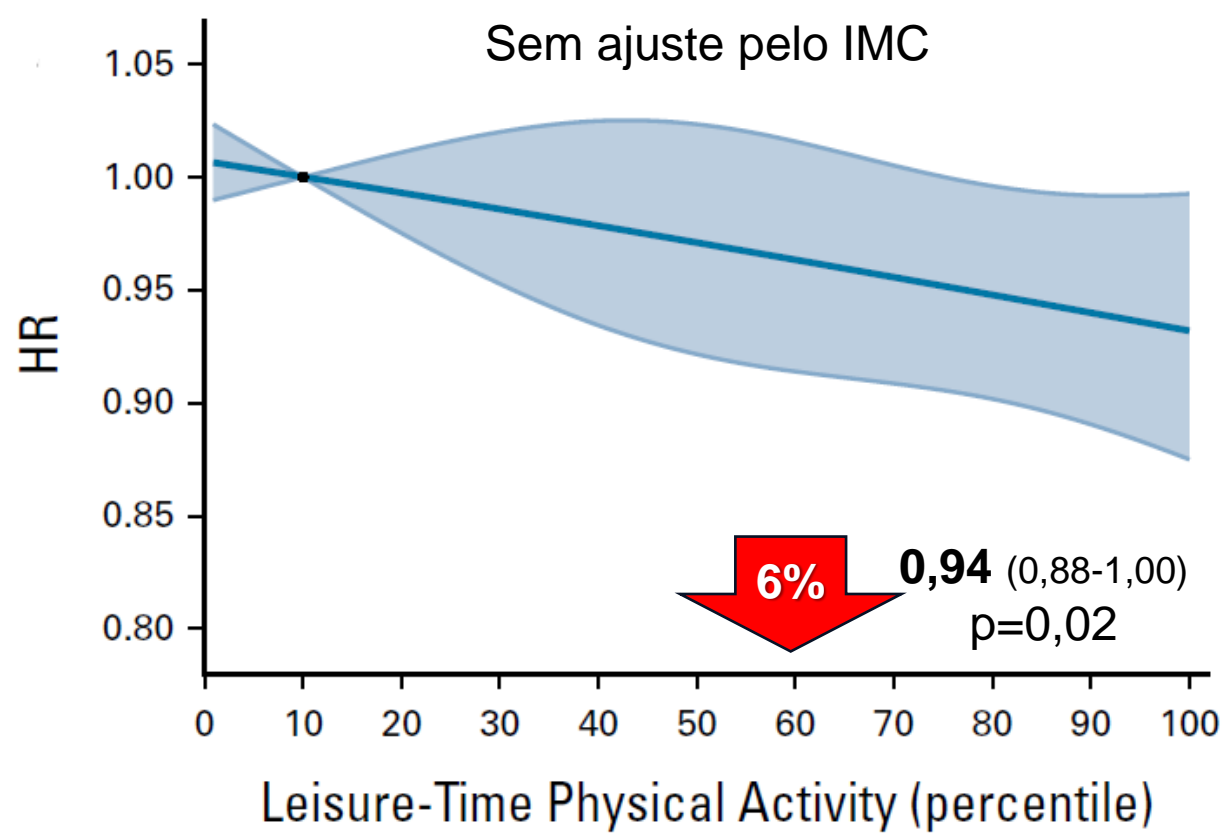
# Evidência entre atividade física e incidência de neoplasia

## Suficiente força de evidência em humanos

Sítio ou tipo de câncer	Redução do risco relativo (%)
Bexiga	15%
<b>Mama</b>	<b>12% - 21%</b>
Cólon	19%
Endométrio	20%
Esofago, adenocarcinoma	19%
Estômago	12%
Rim	21% - 25%

# International Pooled Analysis of Leisure-Time Physical Activity and Premenopausal Breast Cancer in Women From 19 Cohorts

547.601 ♀ na pré-menopausa, seguimento mediano 11,5 anos



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# Influência nos desfechos do tratamento

# Obesidade e desfechos do tratamento

## Neoplasia de mama

82 estudos (213.075 pacientes)

Obesas (BMI  $\geq 30$  kg/m<sup>2</sup>) versus Normal (BMI 18,5-24,9 kg/m<sup>2</sup>)

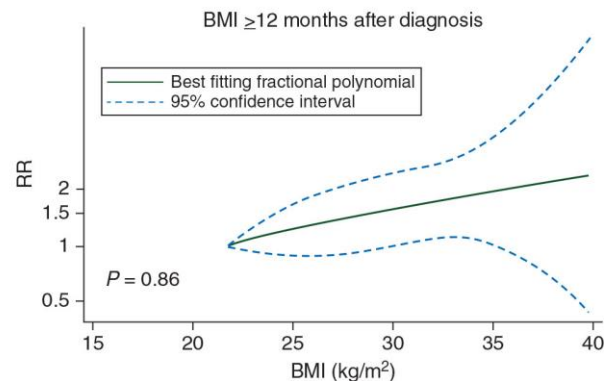
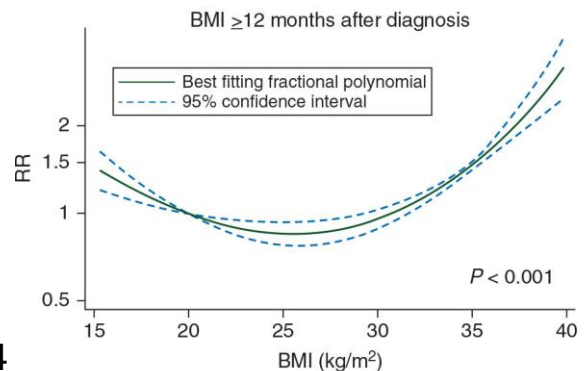
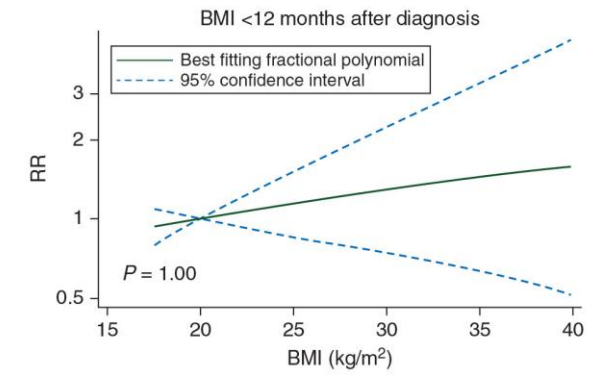
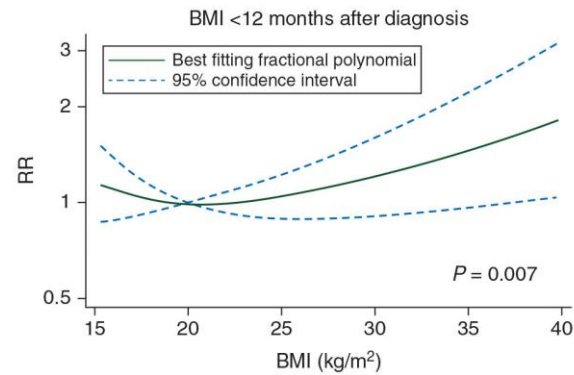
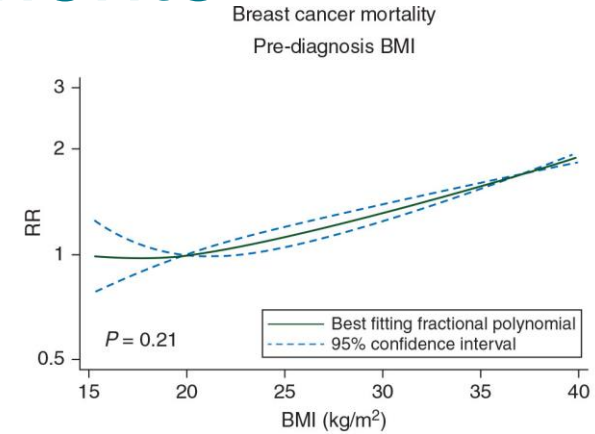
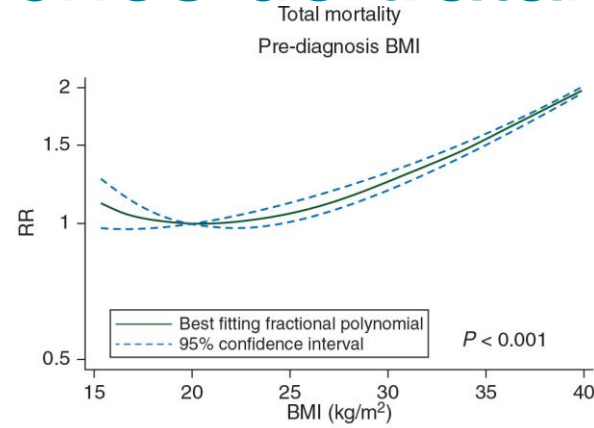
HR: 1,41 (IC95%: 1,29-1,53) – Mortalidade por todas as causas

HR: 1,35 (IC95%: 1,24-1,47) – Mortalidade por neoplasia de mama

A obesidade está associada a piores resultados tanto na pré como na pós menopausa

# Obesidade e desfechos do tratamento

## Neoplasia de mama



# Dieta e mortalidade por todas as causas em pacientes com câncer de mama

11 publicações (n=27.346 sobreviventes)

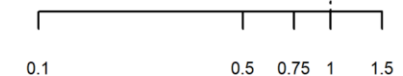
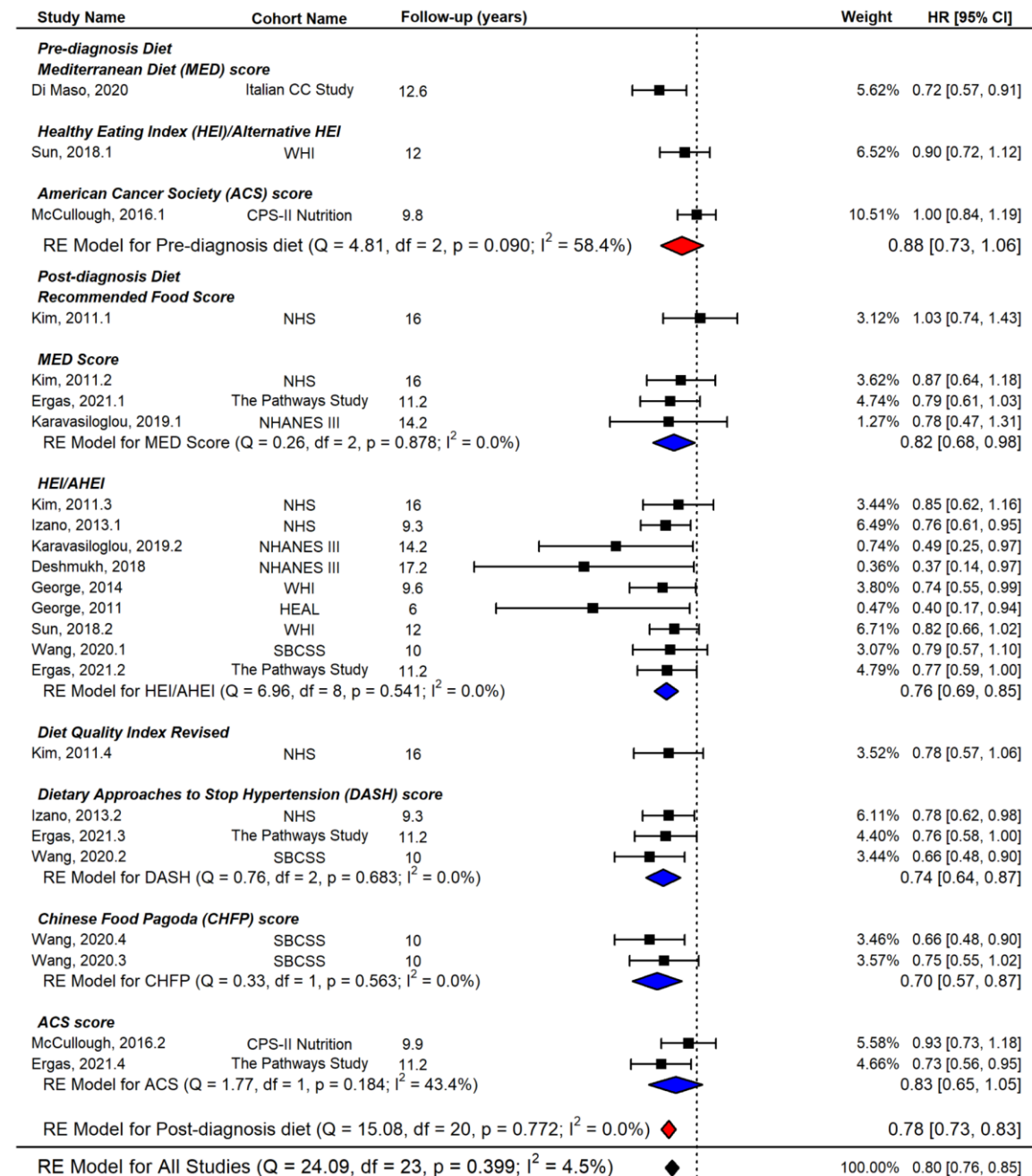
Qualidade da dieta pré diagnóstico

→ Sem impacto na mortalidade

Qualidade da dieta pós diagnóstico

↓ 21% a mortalidade por todas as causas

(HR = 0,79, IC95% = 0,70-0,89, I<sup>2</sup> = 16.83%, n = 7)



# Dieta e mortalidade por câncer de mama

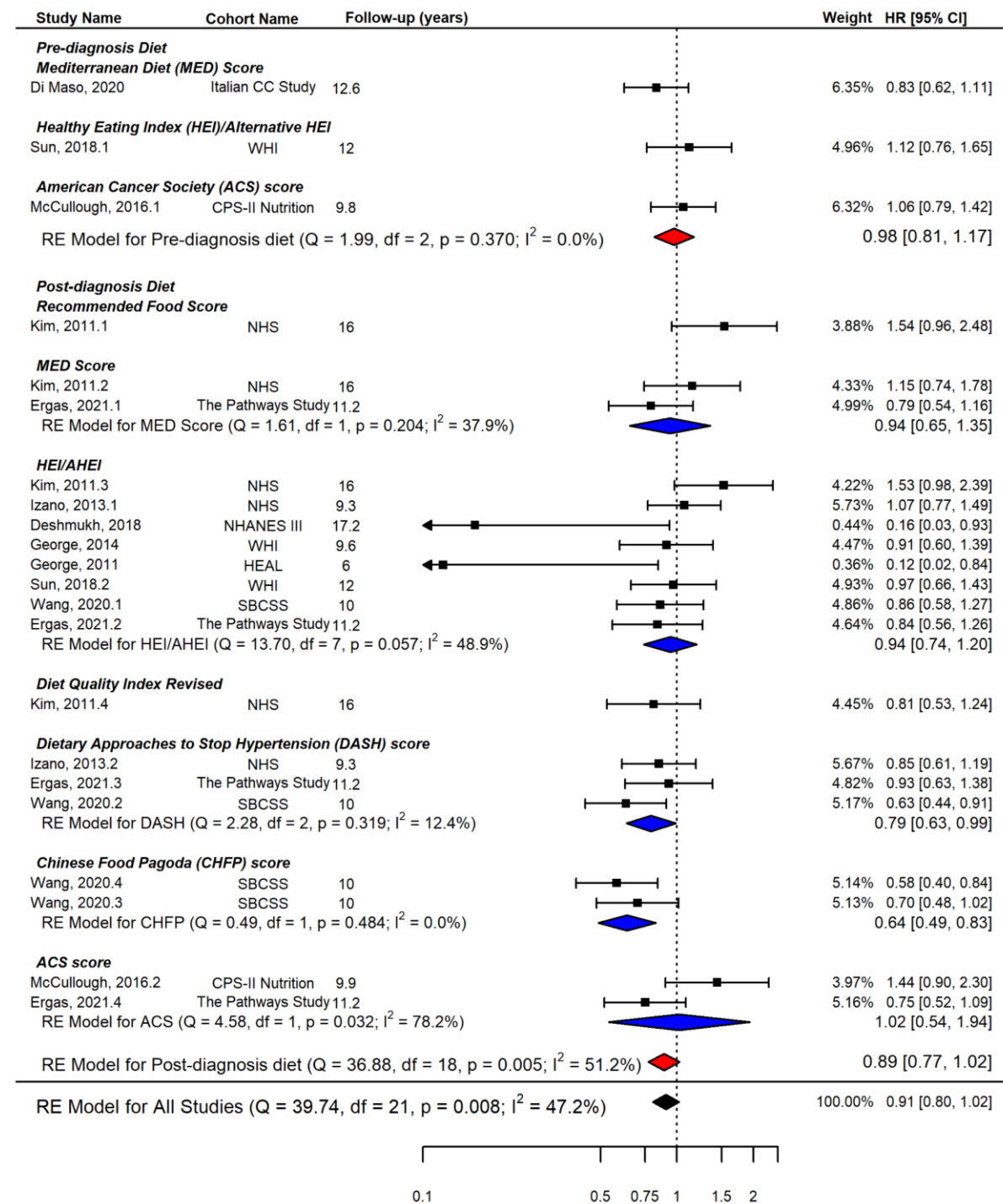
Qualidade da dieta pré diagnóstico

→ Sem impacto na mortalidade

Qualidade da dieta pós diagnóstico

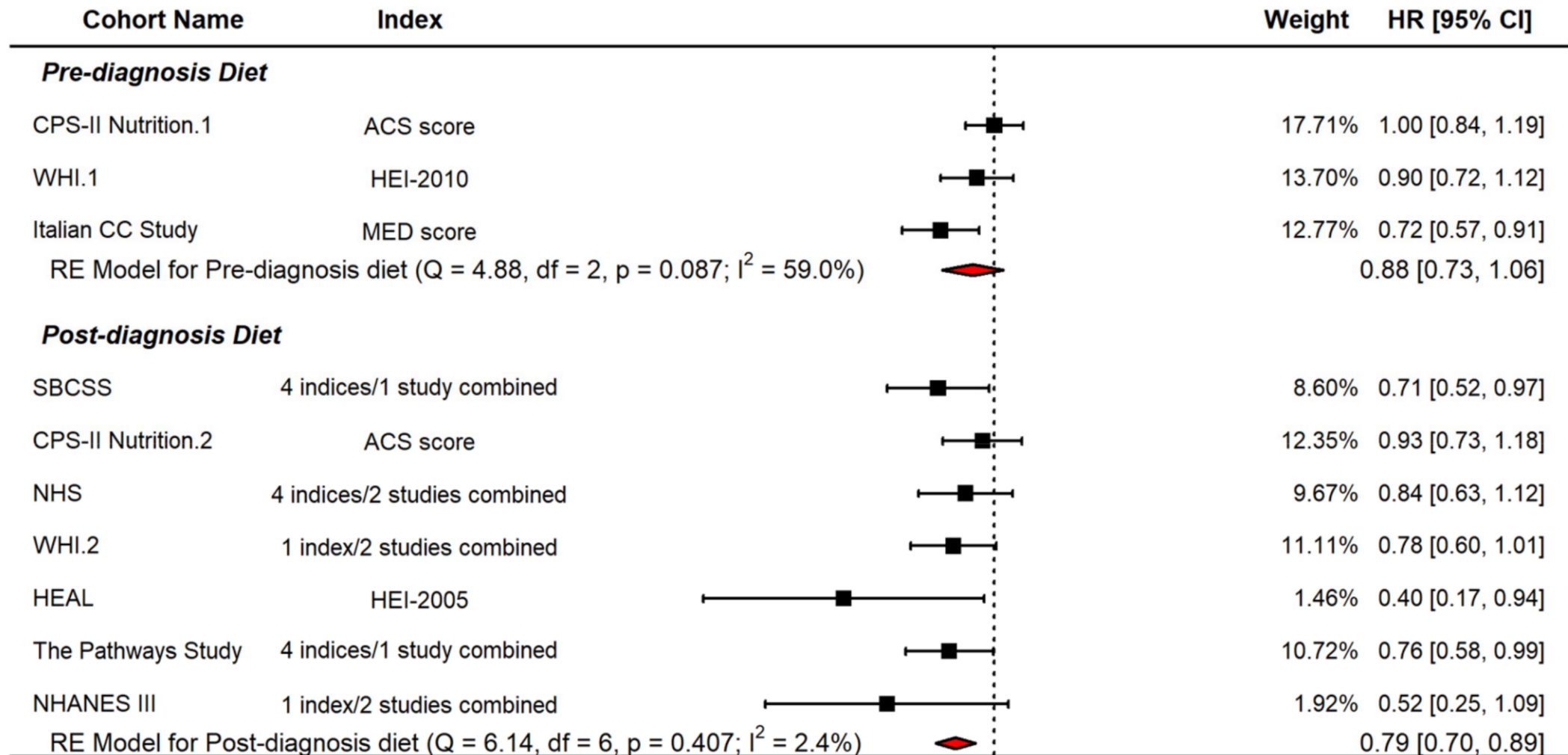
↓ 15% a mortalidade por câncer de mama

(HR = 0,85, IC95% = 0,62-1,18, I<sup>2</sup> = 57.4%, n = 7)

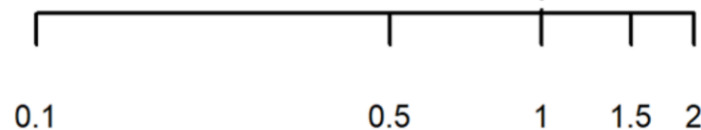




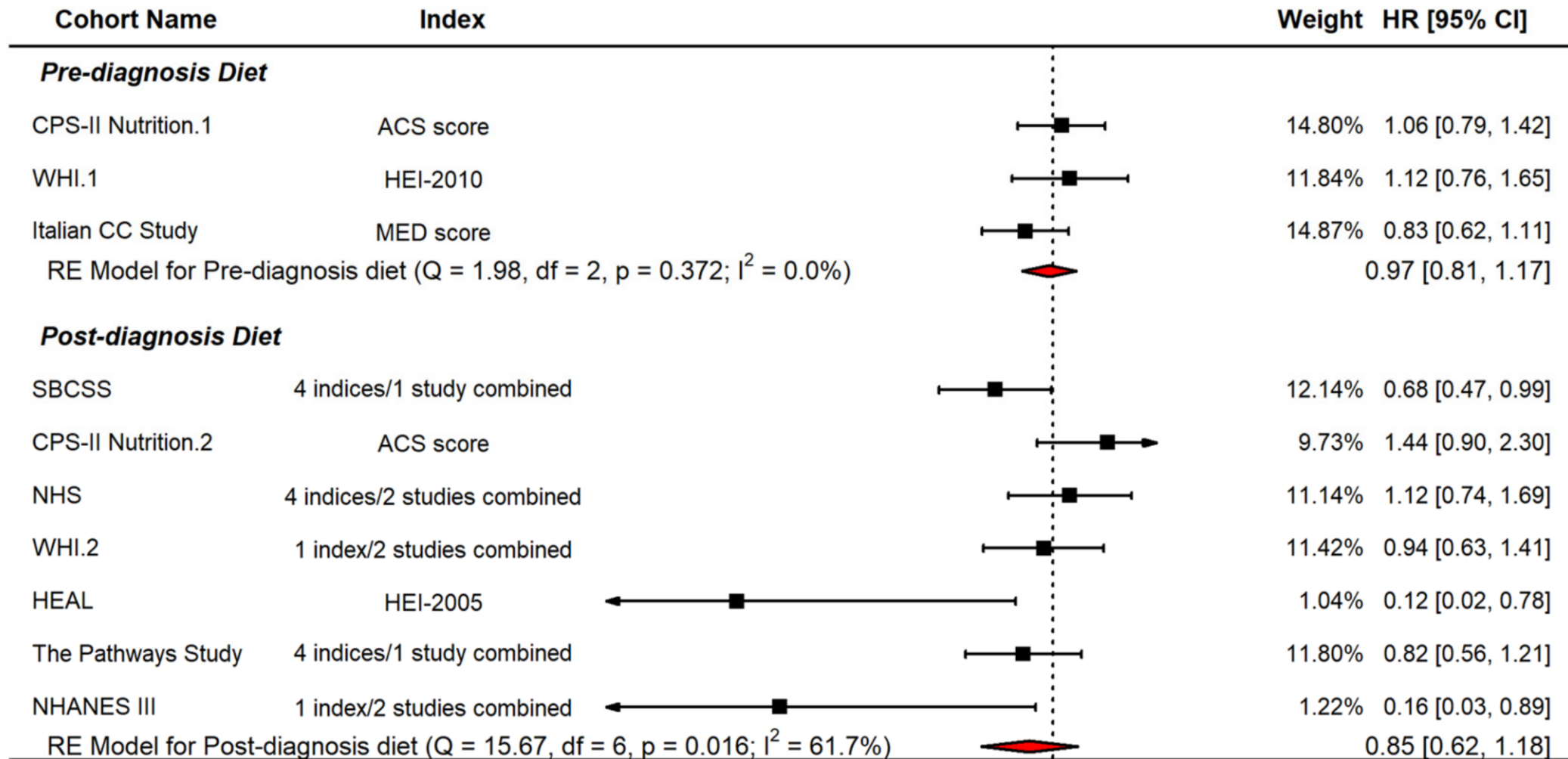
# Dieta e mortalidade por todas as causas



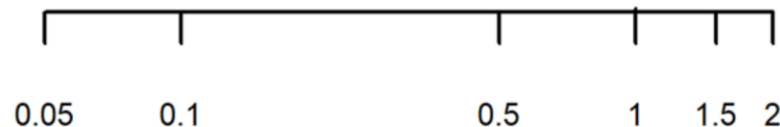
↓ 21% a mortalidade por todas as causas  
 (HR = 0,79, IC95% = 0,70-0,89, I<sup>2</sup> = 2.4%)



# Dieta e mortalidade por câncer de mama



↓ 15% a mortalidade por todas as causas  
 (HR = 0,85, IC95% = 0,62-1,18, I<sup>2</sup> = 61.7%)



Best Prognosis



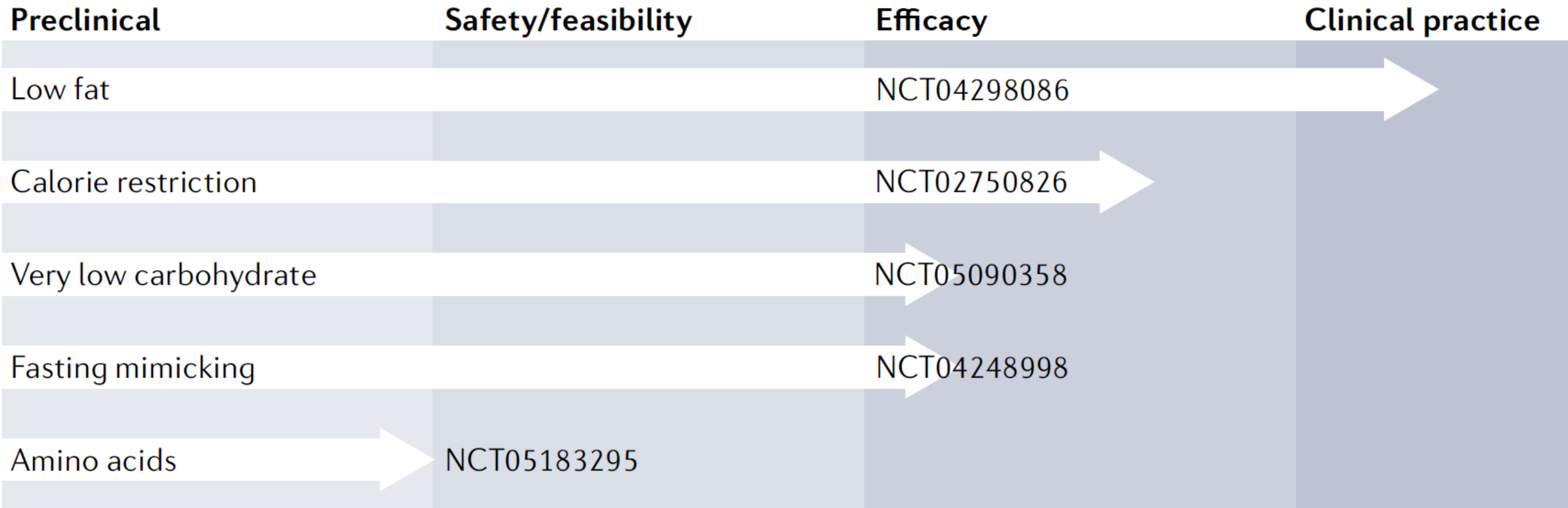
Worse Prognosis

<b>Luminal A (~24%)</b> HR+ (ER+ and/or PGR+), HER2-	<b>Luminal B (~50%)</b> HR+ (ER+ and/or PGR+), HER2+/-	<b>HER2-Enriched (~10-15%)</b> HR- (ER- and PGR-), HER2+	<b>Triple Negative (~15%)</b> HR- (ER- and PGR-), HER2-
<ul style="list-style-type: none"><li>• 1.78 fold increased risk of breast cancer mortality (Blair et al., 2019)</li><li>• Increased late recurrence and mortality (Jiralerspong &amp; Goodwin, 2016)</li><li>• Increased risk of postmenopausal breast cancer, decreased risk of premenopausal breast cancer (Jiralerspong &amp; Goodwin, 2016)</li></ul>	<ul style="list-style-type: none"><li>• 2.16 fold increased risk of breast cancer mortality (Blair et al., 2019)</li><li>• Increased late recurrence and mortality (Jiralerspong &amp; Goodwin, 2016)</li><li>• Increased risk of postmenopausal breast cancer, decreased risk of premenopausal breast cancer (Jiralerspong &amp; Goodwin, 2016)</li></ul>	<ul style="list-style-type: none"><li>• No evidence for mortality association (Blair et al., 2019)</li><li>• Pretrastuzumab era: worse overall survival and distant metastases compared to normal-weight patients (Jiralerspong &amp; Goodwin, 2016)</li><li>• Trastuzumab era: evidence varies making relationship unclear (Jiralerspong &amp; Goodwin, 2016)</li><li>• Limited and inconsistent evidence on breast cancer outcome (Lohmann et al., 2021)</li></ul>	<ul style="list-style-type: none"><li>• Evidence is limited and inconsistent; varies across publications</li><li>• No evidence for mortality association (Blair et al., 2019)</li><li>• Increased risk of premenopausal breast cancer; unclear relationship in terms of survival (Jiralerspong &amp; Goodwin, 2016)</li><li>• Limited and inconsistent evidence on breast cancer outcome (Lohmann et al., 2021)</li><li>• Higher incidence for all women in areas with higher prevalence of obesity (Moss et al., 2020)</li></ul>

**Across all subtypes:**

- Increased likelihood of being diagnosed with stage 3/4 disease, metastases, and stage 3/4 tumors (Blair et al., 2019)
- 2-fold increased likelihood of having  $\geq 2$  comorbidities and 1.5 fold increase likelihood of receiving chemotherapy (Blair et al., 2019)
- 1.63 fold increased risk overall of breast cancer-specific mortality (Blair et al., 2019)
- Increased risk of early and late distant, but not local, recurrences and death (Jiralerspong & Goodwin, 2016)
- Larger tumors, higher grade tumors, increased lymph node metastases (Jiralerspong & Goodwin, 2016)
- Associated with worse disease free survival and overall survival (Lohmann et al., 2021)
- Higher body mass index and waist-to-hip ratio associated with increased incidence of breast cancer (Bunnel et al., 2022)

# Tipo de dieta



**Exercícios físicos**



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# F.I.T.T. PRINCIPLE

---

FREQUENCY | INTENSITY | TYPE | TIME

**F** Frequency

**I** Intensity

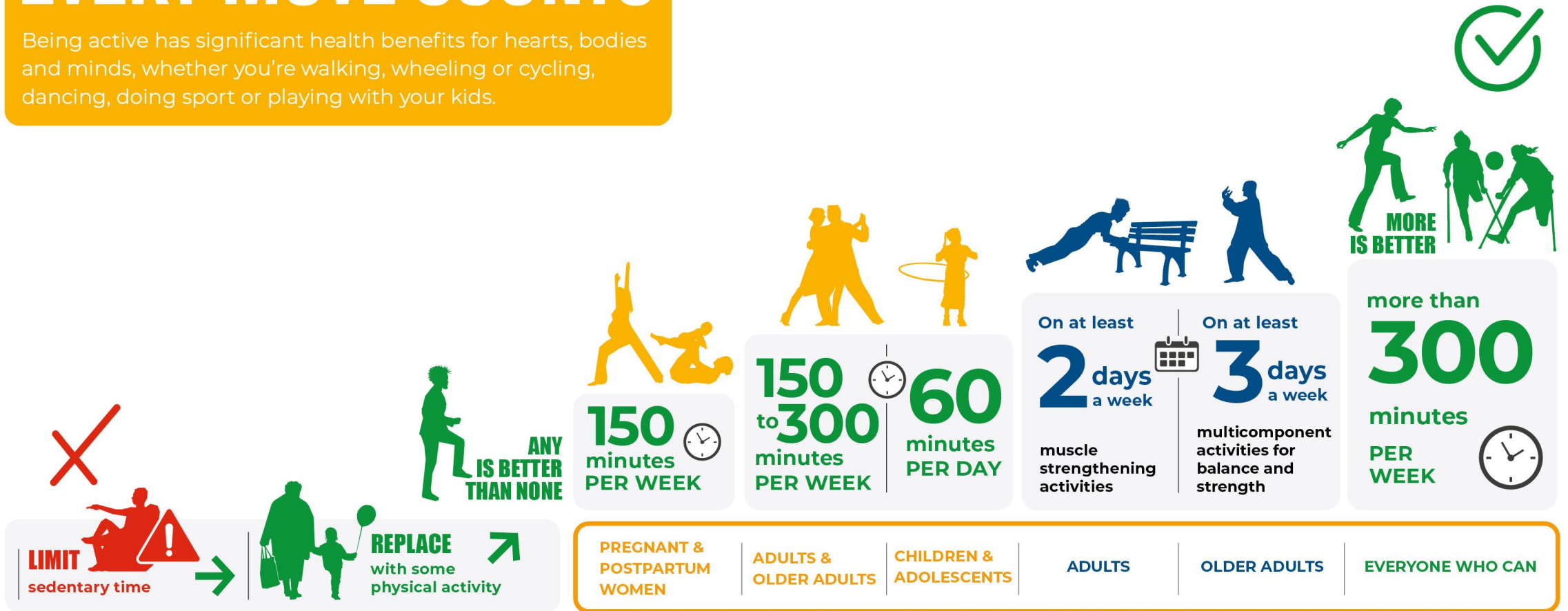
**T** Time

**T** Type



# EVERY MOVE COUNTS

Being active has significant health benefits for hearts, bodies and minds, whether you're walking, wheeling or cycling, dancing, doing sport or playing with your kids.



WHO guidelines on physical activity and sedentary behaviour (2020).

For more information, visit: [www.who.int/health-topics/physical-activity](http://www.who.int/health-topics/physical-activity)






# Clinical Practice Guidelines

Share



“Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.”(*Institute of Medicine, 1990*)

## Oncology

- [Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment \(\*CA: A Cancer Journal for Clinicians\*\)](#)
- [Clinical Practice Guidelines on the Use of Integrative Therapies as Supportive Care in Patients Treated for Breast Cancer \(\*Journal of the National Cancer Institute Monographs\*\)](#)
- [Exercise Guidelines for Cancer Survivors](#)  (*Medicine & Science in Sports & Exercise*)



# Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline

Jennifer A. Ligibel, MD<sup>1</sup>; Kari Bohlke, ScD<sup>2</sup>; Anne M. May, PhD<sup>3</sup>; Steven K. Clinton, MD, PhD<sup>4</sup>; Wendy Demark-Wahnefried, PhD, RD<sup>5</sup>; Susan C. Gilchrist, MD, MS<sup>6</sup>; Melinda L. Irwin, PhD, MPH<sup>7</sup>; Michele Late<sup>8</sup>; Sami Mansfield, BA<sup>9</sup>; Timothy F. Marshall, PhD, MS<sup>10</sup>; Jeffrey A. Meyerhardt, MD, MPH<sup>1</sup>; Cynthia A. Thomson, PhD, RD<sup>11</sup>; William A. Wood, MD, MPH<sup>12</sup>; and Catherine M. Alfano, PhD<sup>13</sup>

## Recommendations

**Question 1:** *Does exercise during cancer treatment safely improve outcomes related to QoL, treatment toxicity, or cancer control?*

**Recommendation 1.1.** Oncology providers should recommend aerobic and resistance exercise during active treatment with curative intent to mitigate side effects of cancer treatment (Type: evidence based, benefits outweigh harms; Evidence quality: moderate to low; Strength of recommendation: strong).

Note: Exercise interventions during active treatment reduce fatigue; preserve cardiorespiratory fitness, physical functioning, and strength; and in some populations, improve QoL and reduce anxiety and depression. In addition, exercise interventions during treatment have low risk of adverse events. Evidence was not sufficient to recommend for or against exercise during treatment to improve cancer control outcomes (recurrence or survival) or treatment completion rates.

**Recommendation 1.2.** Oncology providers may recommend preoperative exercise for patients undergoing surgery for lung cancer to reduce length of hospital stay and postoperative complications (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

SPECIAL COMMUNICATIONS

# Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable

CAMPBELL, KRISTIN L.; WINTERS-STONE, KERRI M.; WISKEMANN, JOACHIM; MAY, ANNE M.; SCHWARTZ, ANNA L.; COURNEYA, KERRY S.; ZUCKER, DAVID S.; MATTHEWS, CHARLES E.; LIGIBEL, JENNIFER A.; GERBER, LYNN H.; MORRIS, G. STEPHEN; PATEL, ALPA V.; HUE, TRISHA F.; PERNA, FRANK M.; SCHMITZ, KATHRYN H.

[Author Information](#) 

*Medicine & Science in Sports & Exercise* 51(11):p 2375-2390, November 2019. | DOI:

10.1249/MSS.00000000000002116

Kathryn Schmitz, et al. *Med Sci Sports Exerc* 2010. 42 (7): 1409-26

Kristin L Campbell, et al. *Med Sci Sports Exerc* 2019. 51 (11): 2375-90

EBO

ESCOLA  
BRASILEIRA  
DE ONCOLOGIA



**RECOMENDAÇÕES DE ATIVIDADE  
FÍSICA DURANTE E APÓS  
TRATAMENTO ONCOLÓGICO**

DISTRIBUIÇÃO  
VENDA PROIBIDA  
GRATUITA



Mais informações e dicas sobre como incorporar a atividade física no dia a dia podem ser encontradas no [Guia de Atividade Física para a População Brasileira](#) e nas [Recomendações para gestores e profissionais de saúde](#).

# Contra indicações

Presença de infecções, incluindo celulites;

Hérnia ou infecção relacionada à ostomia;

Febre, dor intensa ou qualquer dor no peito ainda não investigada.

Pessoas com sintomas de desequilíbrio devem evitar atividade física mais intensa e de maior risco de queda.

Pessoas com metástase óssea, osteoporose ou ostomia devem evitar atividades de contato físico (futebol, handebol e basquetebol, por exemplo).

# Atividade física pós-diagnóstico

Meta-análise de 6 estudos, 12.108 pacientes

Reduz a mortalidade por câncer de mama em 34%

HR=0,66; IC<sub>95%</sub>: 0,57-0,77; p<0,00001

Reduz a mortalidade por todas as causas em 41%

HR=0,59; IC<sub>95%</sub>: 0,53-0,65; p<0,00001

Reduz a taxa de recidiva da doença em 24%

HR=0,76; IC<sub>95%</sub>: 0,66-0,87; p=0,00001

Benefícios restrito às pacientes com RE positivo

# Atividade física pós diagnóstico na recorrência (mama)

Meta-análise de 5 estudos prospectivos de coorte

10.094 pacientes com câncer de mama, 1.561 com recidiva (10 a 156 meses)

## Atividade física recreacional (rPA)

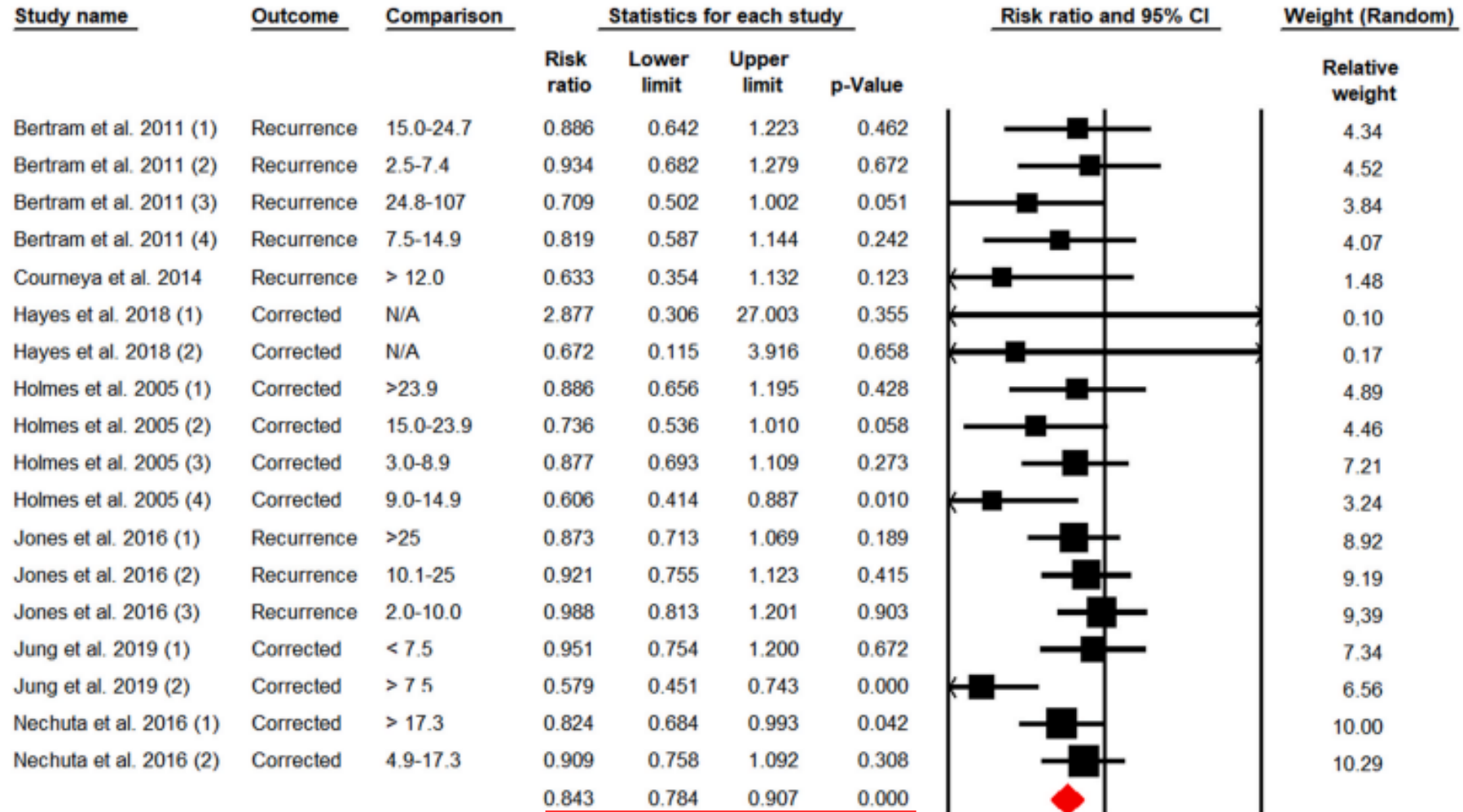
rPA  $\geq 7,5$  vs. 0-3 equivalentes metabólicos (MET-h/week)

**Redução de 35% no risco de recidiva**

HR: 0,65 (0,58-0,73);  $p < 0,00001$ ;  $I^2 = 0\%$

# Atividade física recreacional (Neoplasia de mama)

## Atividade pós diagnóstico e Recorrência



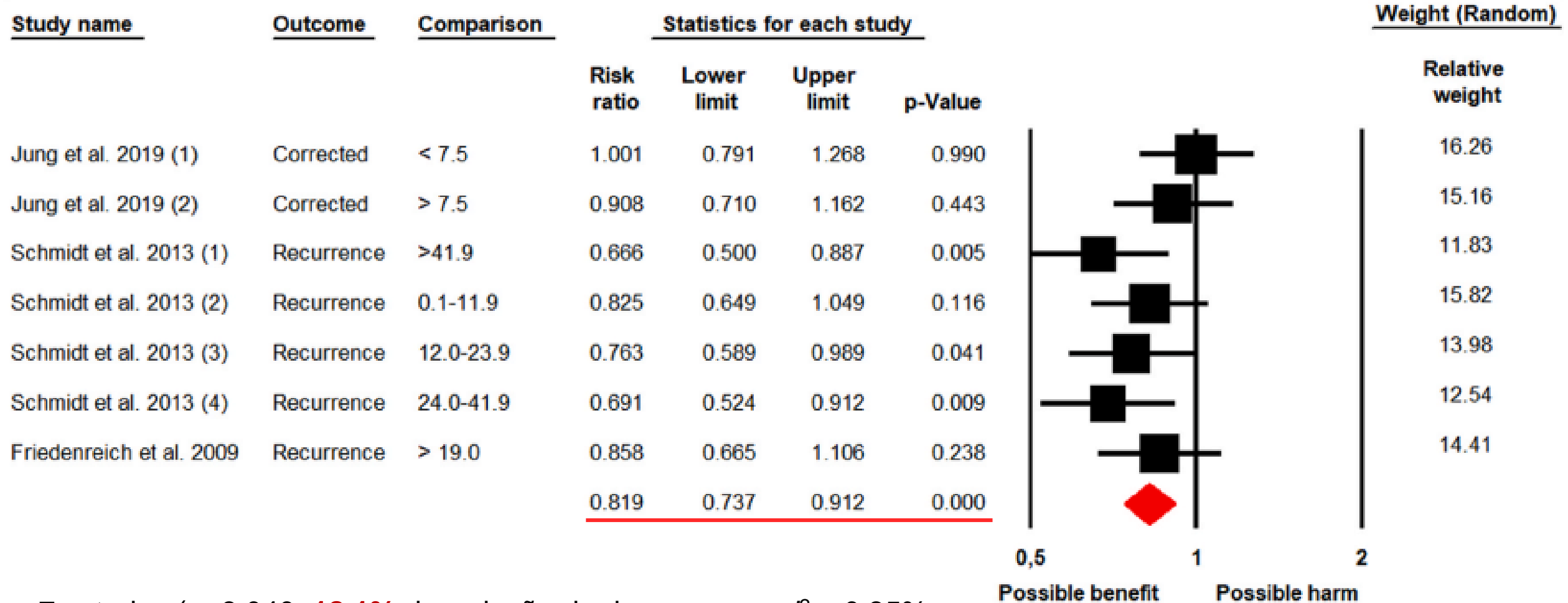
18 estudos (n=20.686): **15,7%** de redução de risco  $I^2 = 0,15\%$

0,5 1 2  
Possible benefit Possible harm



# Atividade física recreacional (neoplasia de mama)

## Atividade pré diagnóstico e recorrência

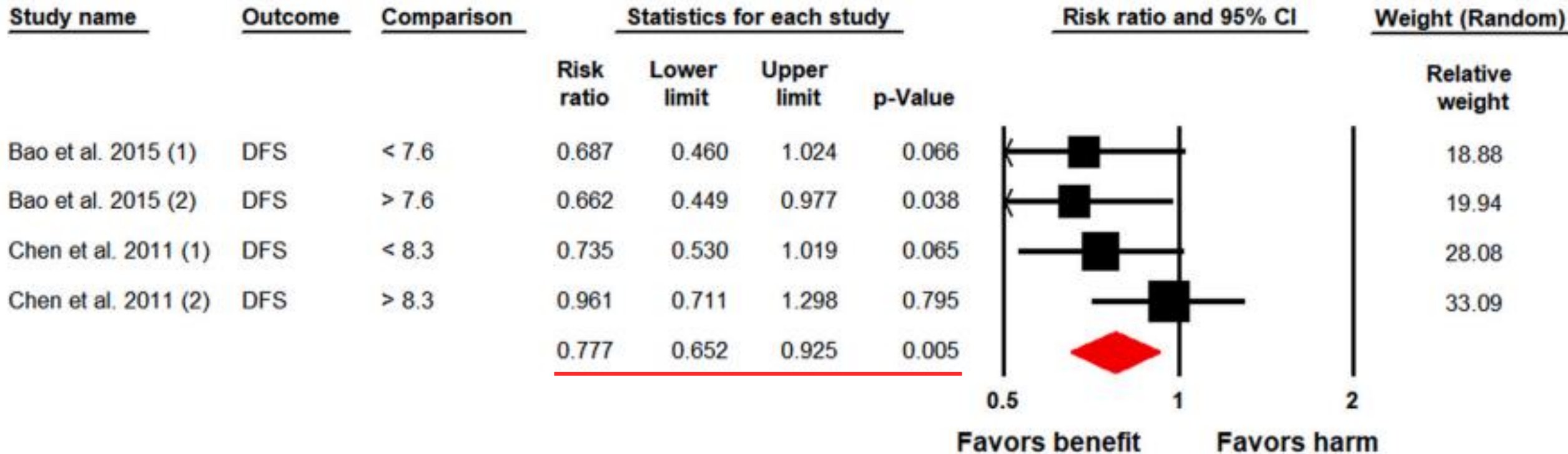


7 estudos (n=6.040: **18,1%** de redução de risco

$I^2 = 0,35\%$

# Atividade física recreacional (Neoplasia de mama)

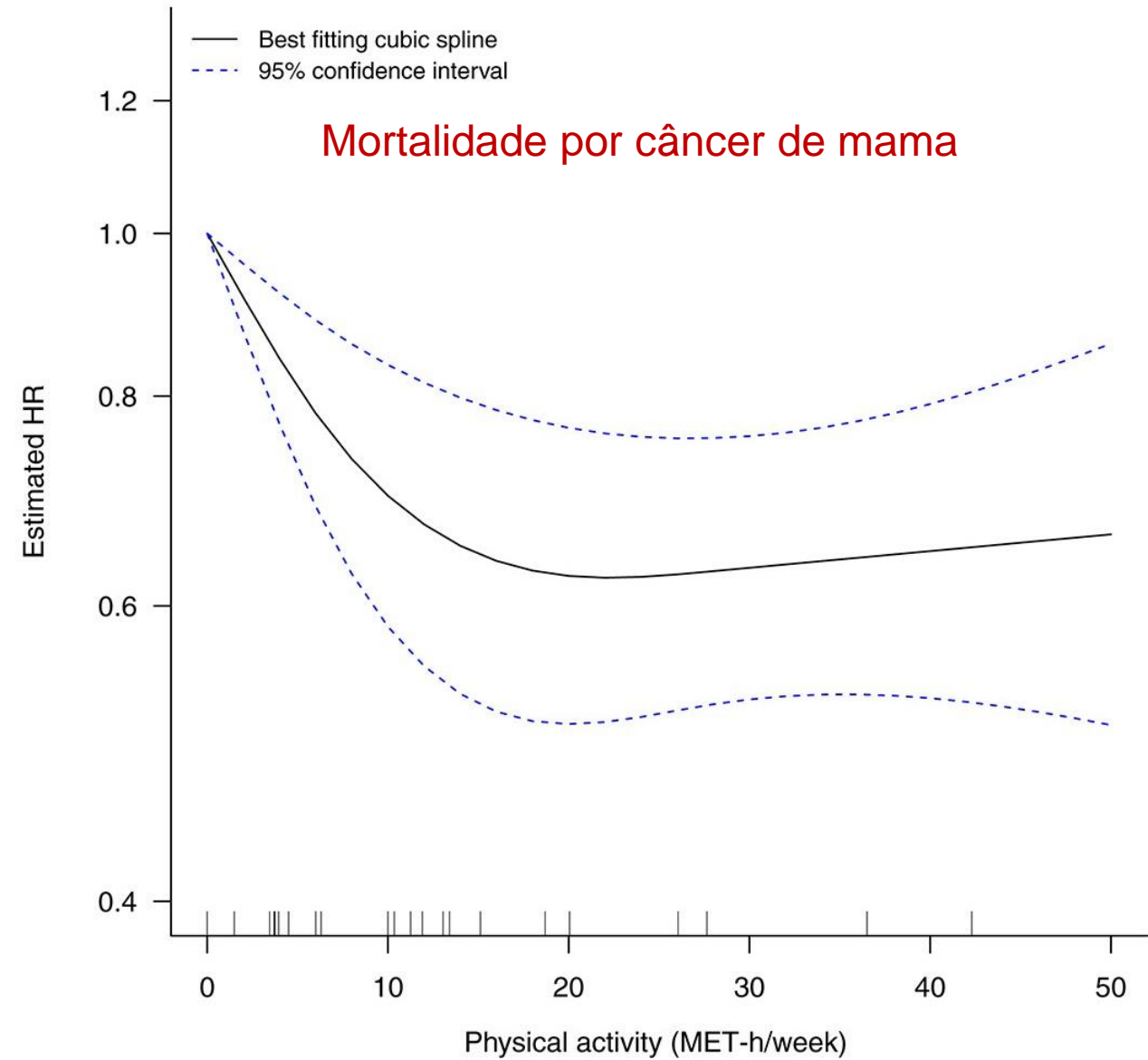
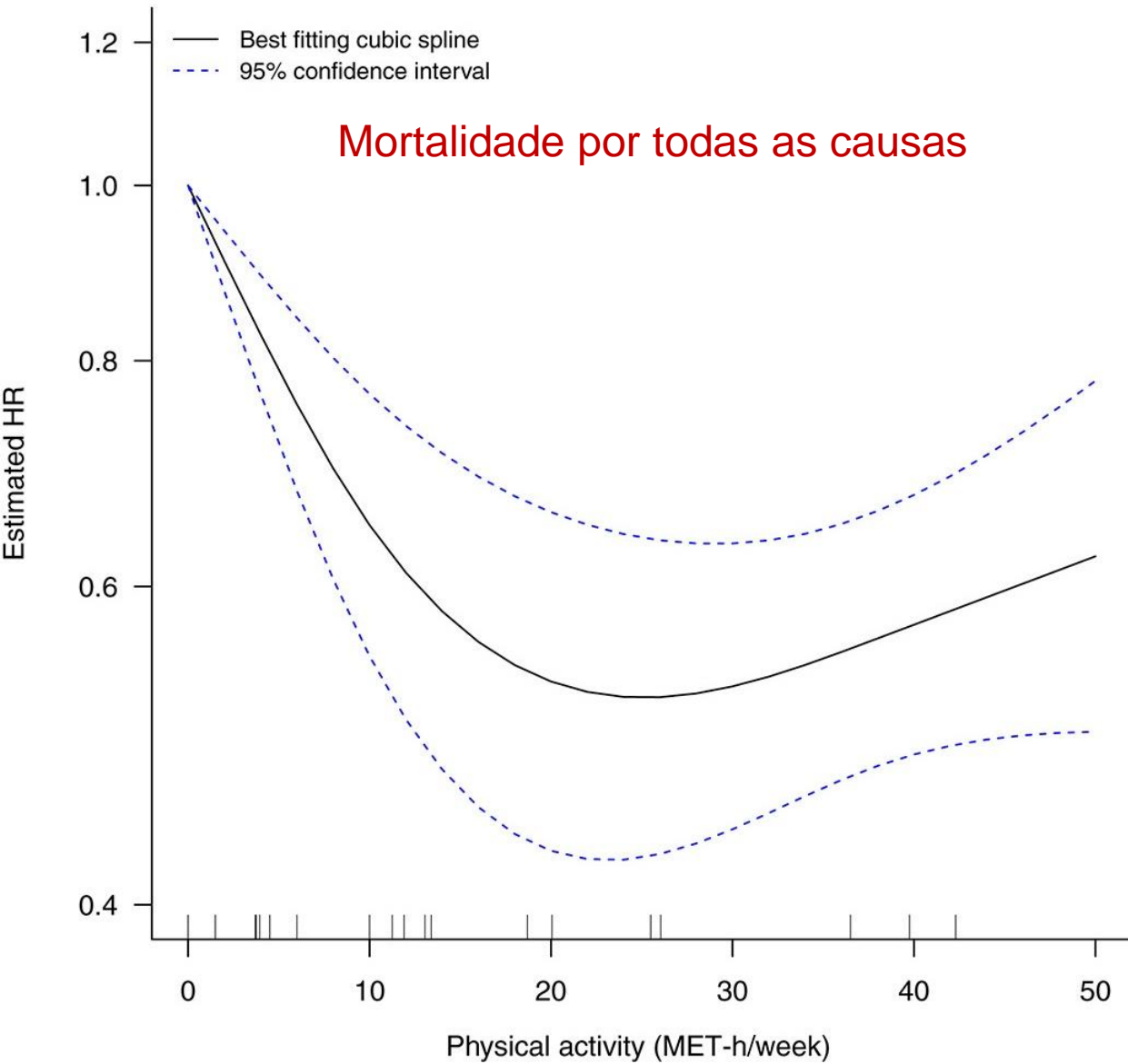
Atividade pós diagnóstico e recorrência / mortalidade específica pela doença



4 estudos (n=2.870: **22,3%** de redução de risco

$I^2 = 0\%$

# Atividade física recreacional e prognóstico (mama)



Metabolic Equivalent of Task (MET)-h/week

# Evidência entre atividade física e mortalidade

## Em sobreviventes do câncer

Sítio ou tipo de câncer	Redução do risco relativo (%)
<b>Mortalidade por todas as causas</b>	
Mama	48%
Colorretal	42%
Próstata	37%-49%
<b>Mortalidade causa específica</b>	
Mama	38%
Colorretal	38%
Próstata	38%



**Falta de profissionais especializados**



PÓS-GRADUAÇÃO MÉDICA  
**NUTROLOGIA  
ESPORTIVA**  
2022 - 2º SEM.



# CÂNCER E ESTILO DE VIDA

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REALIZAÇÃO



APOIO CIENTÍFICO



# Contextualizar as recomendações

Dieta do mediterrâneo, “plant-based”, etc.

Em quem não tem acesso ao básico

Pratica regular de atividade física

Em quem faz dupla jornada de trabalho



1  
7  
3  
3  
5  
5  
7  
75 KVA

CP 1186

RLX  
0A14





FALIA

SUPERQUEIMA  
MÁRIO

motorolaone  
REVEL

# Fator psicológico

Ansiedade em lidar com a incerteza

Fatores “impalpáveis”

Dieta e exercício dão alguma sensação de controle

mas também podem causar culpa

→ Sucesso na mídia!

O QUE O SR.  
RECOMENDA ?



FAÇA EXERCÍCIOS,  
PARE DE BEBER,  
FAÇA DIETA E  
DURMA CEDO.



CONTRA  
CASPA ?



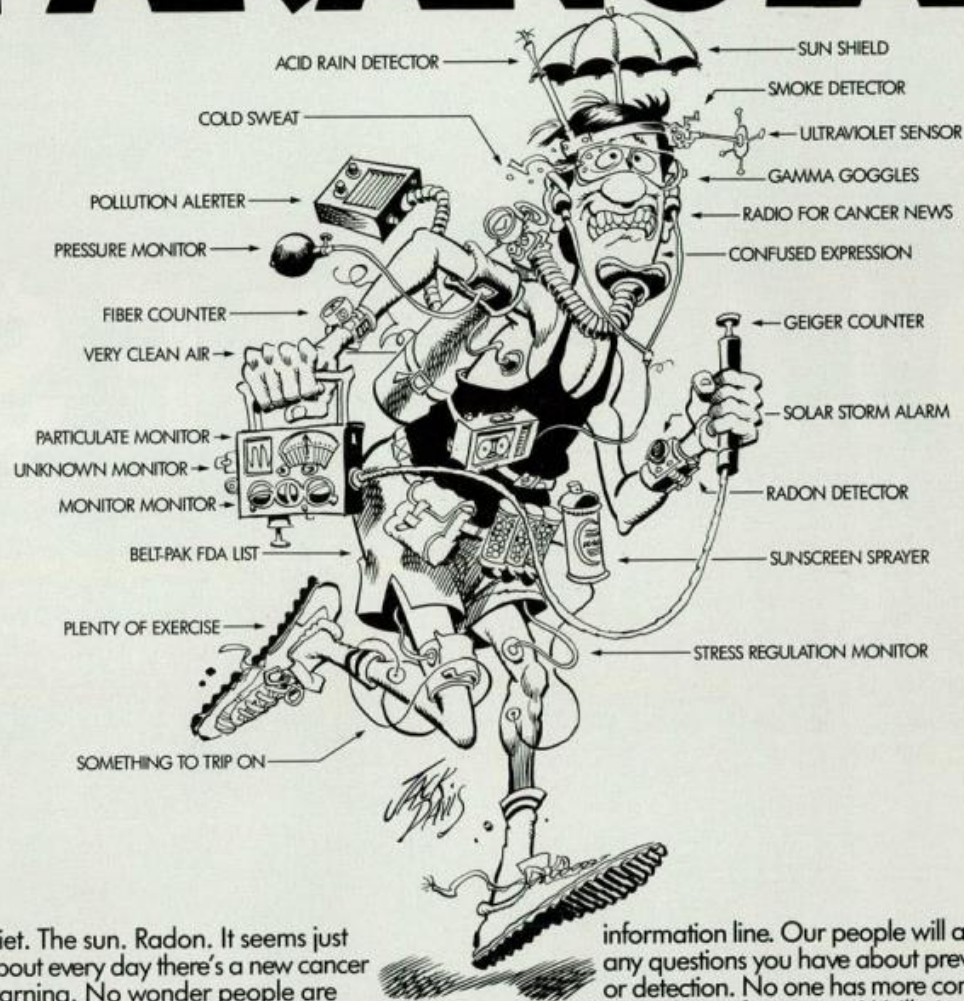
BEM, MAL  
NÃO IRIA  
FAZER !





American  
Cancer  
Society®

# CANCER PARANOIA?



Diet. The sun. Radon. It seems just about every day there's a new cancer warning. No wonder people are getting a little crazy. But there is a simple way to take control of the situation. And your life.

Call the American Cancer Society's toll-free

information line. Our people will answer any questions you have about prevention or detection. No one has more complete and up-to-date information. We'll give you the truth. The facts. The personal guidance to do what's right.

*Special tips for*

# EVERYDAY CANCER PREVENTION

*Less of these & More of these*

PROCESSED MEATS  
**BACON**  
HOT DOGS · SAUSAGES

*Avoid excessive radiation from*  
**TANNING BEDS**  
*or*  
**SUN EXPOSURE**

DO NOT SMOKE OR CHEW  
**TOBACCO**

LIMIT SUGARS · WHITE BREAD  
GRILLED OR PAN-FRIED FOODS  
ALCOHOL & SUGARY DRINKS

MAINTAIN A HEALTHY WEIGHT : ENJOY REGULAR  
**EXERCISE**

*Eat more* **FRESH FRUIT**

**VEGETABLES**

**WHOLE GRAINS**

*Remember:* ALL THINGS IN  
**MODERATION**

# Conclusões

Controle de peso não é mais um luxo, é uma necessidade

Dieta e exercícios = Melhor sobrevida & qualidade de vida

Baixo custo = Alto QALY!

Adesão é o principal obstáculo



**OSWALDO CRUZ**  
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