# **Obesity and cancer**



### Milken Institute School of Public Health

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# Obesity

- Defined as the presence of excess body fat
- Adipose tissue is metabolically active and critical to health
  - Storage of energy for periods of fasting
  - Cushioning to protect organs and bones from injury
  - Important for maintaining body temperature
  - Endocrine functions: production of hormones such as leptin, adiponectin, angiotensin, estradiol
  - Involved in production of other important proteins: aromatase, cytokines
- Not all body fat is equal: visceral fat may be more metabolically active than subcutaneous

# **Medical Complications of Obesity**

#### Pulmonary disease \

abnormal function obstructive sleep apnea hypoventilation syndrome

### Nonalcoholic fatty liver

#### disease

steatosis steatohepatitis cirrhosis

### Gall bladder disease

#### Gynecologic abnormalities

abnormal menses infertility polycystic ovarian syndrome

### Osteoarthritis

Skin

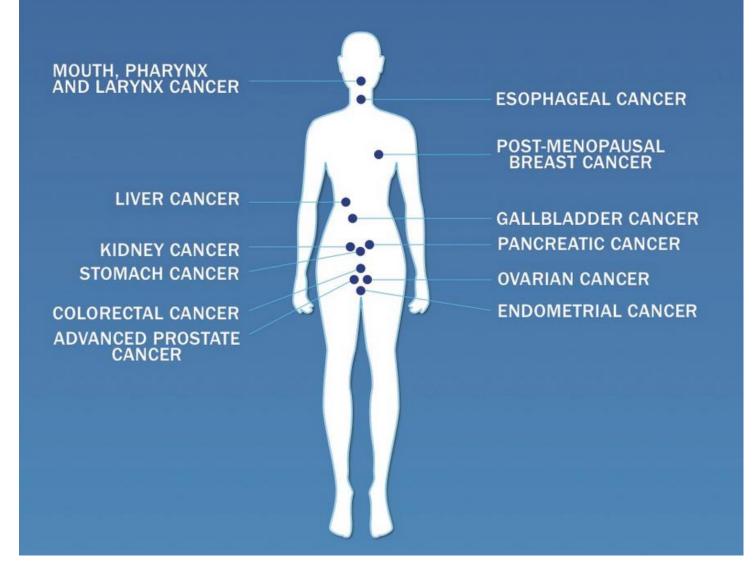
Gout

**Idiopathic intracranial** hypertension Stroke Cataracts **Coronary heart disease** Diabetes Dyslipidemia Hypertension Severe pancreatitis Cancer breast, endometrial, ovarian, prostate, colorectal, esophagus, pancreas, liver

Phlebitis venous stasis

kidney, gall bladder

## HAVING OVERWEIGHT AND OBESITY INCREASES RISK FOR 12 CANCERS



https://www.aicr.org/learn-more-about-cancer/infographics/infographic-obesity-and-cancer.html

# Possible biologic mechanisms

- Comorbid conditions such diabetes
- Inflammation
- Alterations in hormone, growth factor levels



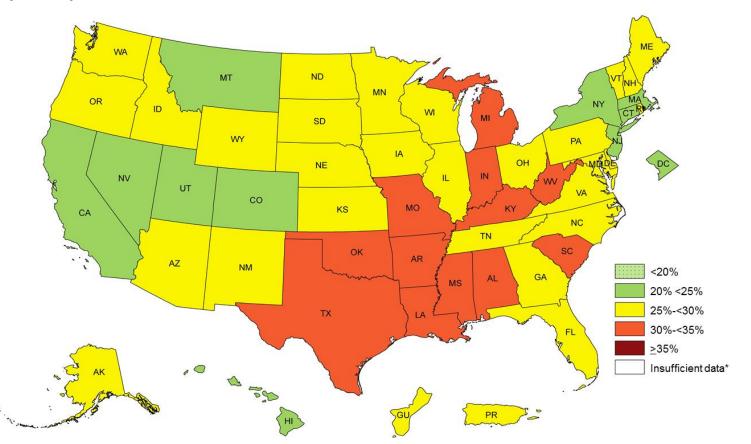
# Body Mass Index (BMI)

 $BMI = weight (kg) / height (m^2)$ 

NHLBI BMI Calculator: https://bit.ly/29ubNRk

Weight status category	BMI
Under weight	< 18.5
Healthy weight	18.5 – 24.9
Overweight	25.0 - 29.9
Obese I	30.0 - 34.9
Obese II	35.0 – 39.9
Extreme obesity	≥ 40.0

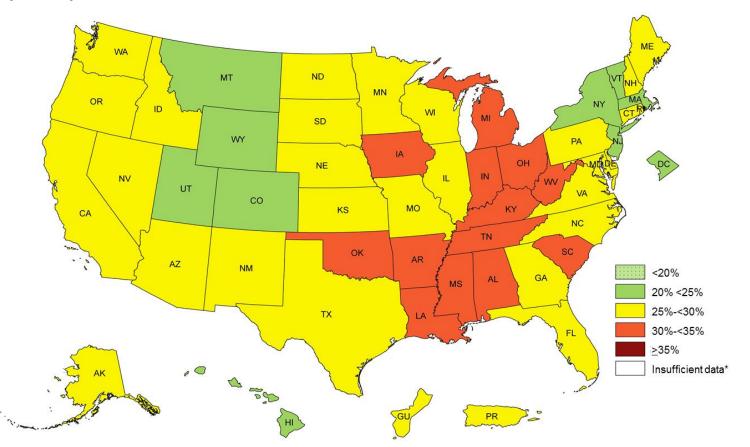
<sup>1</sup> Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



\*Sample size <50 or the relative standard error (dividing the standard error by the prevalence)  $\geq$  30%.

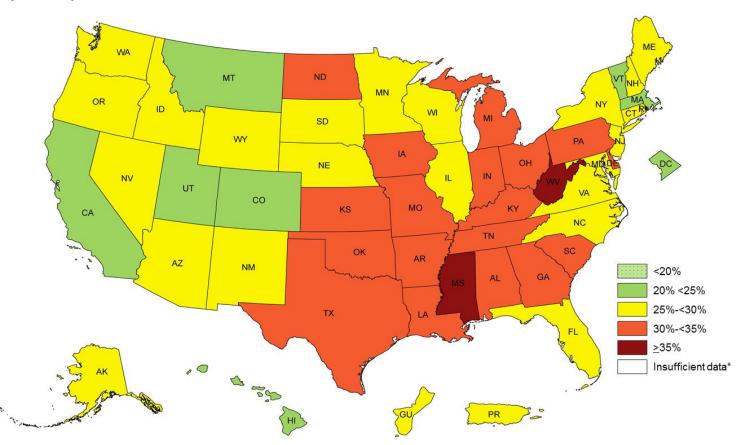


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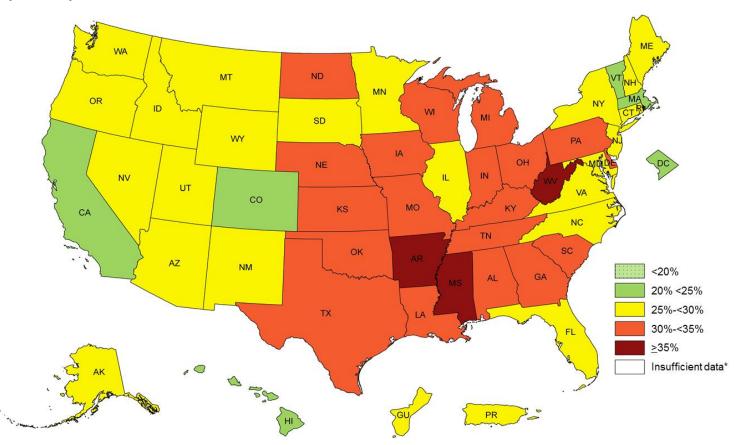


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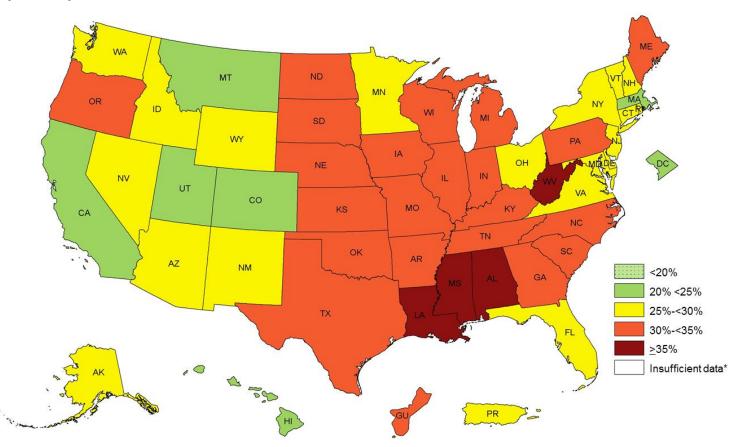
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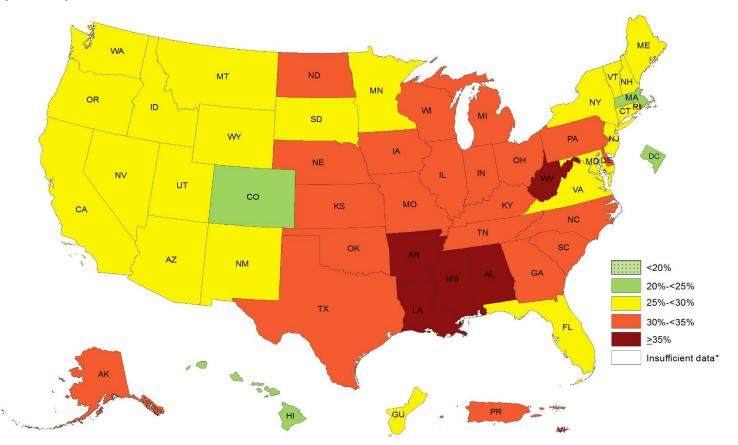
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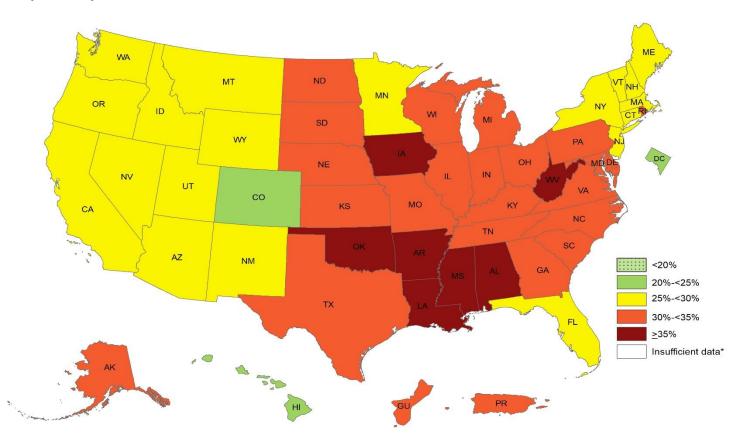
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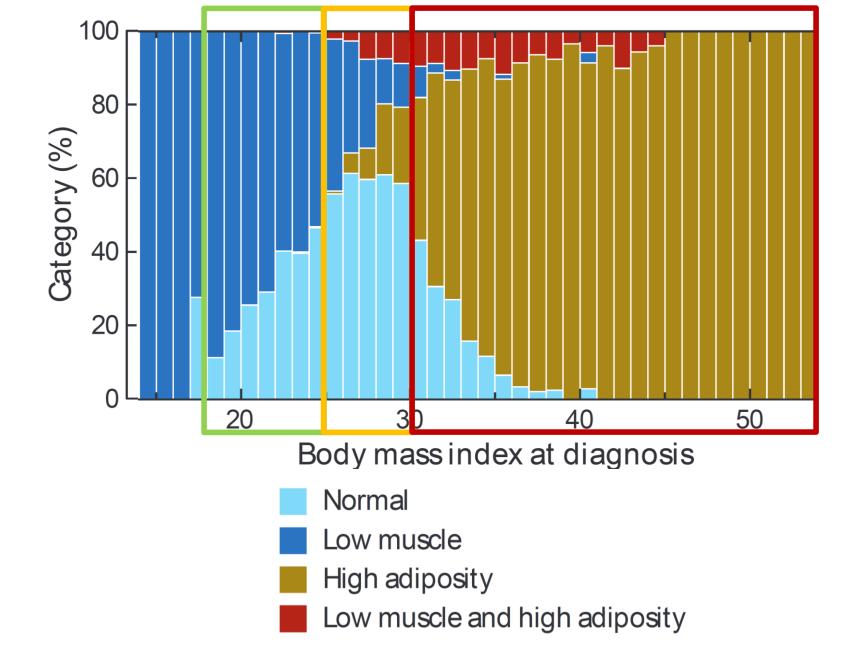
# Body Mass Index (BMI)

### **Strengths**

- Provides a more accurate measure of total body fat compared with the assessment of body weight alone.
- Inexpensive, easily calculated
- Most practical method of assessing body composition in the clinic, and for large research studies.

### Limitations

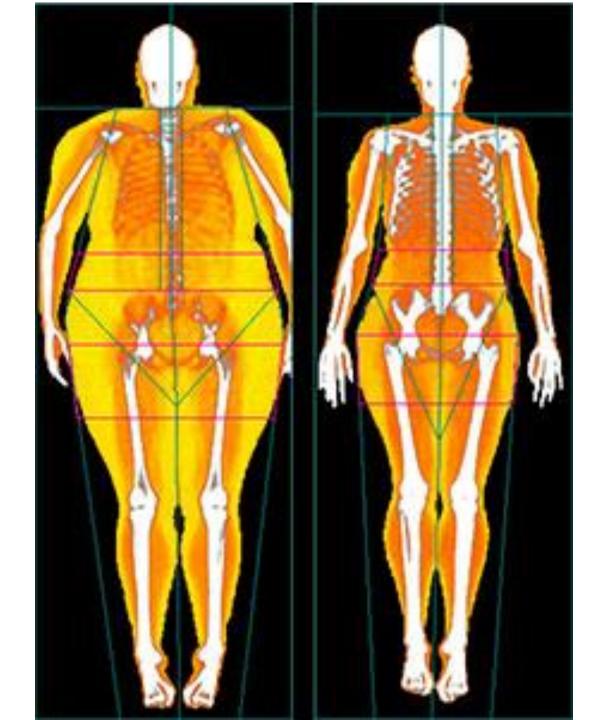
- Cannot differentiate between adipose (fat) tissue and lean (muscle) tissue.
  - Overestimates body fat in persons who are very muscular.
  - Underestimates body fat in persons who have lost muscle mass (example: many elderly)



Cespedes Feliciano EM, Kroenke CH, Caan BJ. The Obesity Paradox in Cancer: How Important Is Muscle? Annu Rev Nutr 2018;38:357-379. PMID: 29727593

# Other methods of measuring body composition (primarily used in research)

Method	Strengths	Limitations
Computed tomography (CT)	Can quantify adipose vs. lean body mass	Expensive Limited availability
Magnetic resonance imaging (MRI)	Can quantify adipose vs. lean body mass	Expensive Limited availability
Dual X-ray absorptiometry (DEXA)	Can quantify adipose vs. lean body mass	Moderately expensive Limited availability

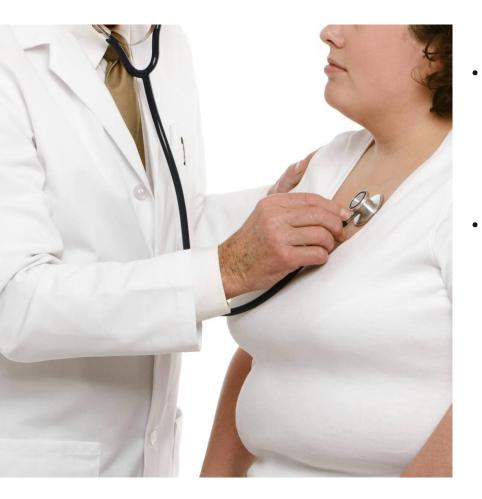


# **Body fat percentage**

	Women	Men
Essential fat	10–13%	3–5%
Athletes	14–20%	6–13%
Fitness	21–24%	14–17%
Average	25–31%	18–24%
Obese	32%+	25%+

https://www.acefitness.org/education-and-resources/lifestyle/tools-calculators/percent-body-fat-calculator

# Impact of obesity on cancer treatment and outcomes



- People who are obese are less likely to participate in cancer screening programs or preventive testing
- Obesity can alter the accuracy of cancer diagnostic testing, such as hemodilution of tumor biomarkers and reduced imaging quality

# Impact of obesity on cancer treatment and outcomes

- Obesity increases risk of complications following surgical resection
- Unclear how to dose chemotherapy and radiation for overweight and obese patients
- Obesity is associated with increased risk of thromboembolism in individuals receiving chemotherapy
- People who are obese often have co-morbid health conditions



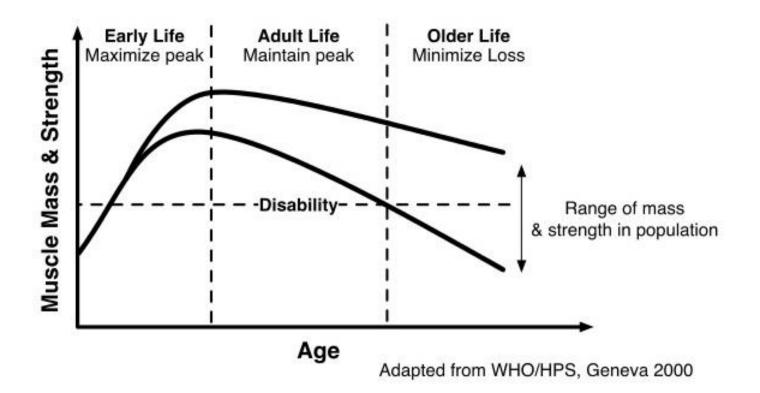
# Weight/body composition changes during cancer treatment



- Not all patients lose
  weight during cancer
  treatment, some
  treatment regimens are
  associated with weight
  gain
- Body composition may also change – such as increased adiposity and decreased muscle

# Sarcopenia

Degenerative loss of skeletal muscle mass, quality and strength typically associated with aging.



Cancer and/or its treatment may contribute to accelerated aging (Hurria *et al*, 2018, PMID: 30372283)

# **During cancer treatment**

Nutrition\*

- Prevent nutrient deficiencies
- Consume enough dietary protein to maintain/build muscle
- Minimize the impact of treatment-related side effects

Physical activity\*

Try to move every day

\* Specific plans should be tailored to the individual's needs and abilities.



# After cancer treatment is completed

Goals: Achieve (or maintain) a healthy weight and muscle mass

Nutrition\*

- Watch portion sizes
- Eat a variety of fruits, vegetables, whole grains to prevent nutrient deficiencies

### Physical activity\*

- Move more and sit less throughout the day!
- Do at least 150 minutes (2 hours and 30 minutes) a week of moderate-intensity aerobic exercise
- Muscle-strengthening resistance exercise at least 2 days per week.

\* Specific plans should be tailored to the individual's needs and abilities.





World Cancer Research Fund

wcrf.org/cancer-prevention-recommendations



dietandcancerreport.org

Analysing research on cancer prevention and survival



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#### Welcome to the NAP Challenge DC!



#### Take the New American Plate Challenge and you will:

- Lower your risk of cancer and chronic diseases like type 2 diabetes and heart disease
- · Make lifestyle changes to support a healthy weight
- · Have more energy and feel better
- · Gain more strength, flexibility and endurance

#### Take the Challenge if you want to:

- · Learn to eat a healthy, flexible plant-based diet
- · Become more physically active
- · Model a healthy lifestyle for your family
- · Complement your current healthy weight/ lifestyle program

#### Here's how it works:

· One weekly eat smart or move more challenge for 12 weeks

http://napchallengedc.org OR http://napchallenge.org/



# Body fatness & weight gain

# Body fatness and weight gain and the risk of cancer

🛓 View available downloads

https://www.wcrf.org/dietandcancer/exposures/body-fatness

## ASCO

# Obesity & Cancer

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ASCO is committed to informing oncology providers regarding the existing data linking obesity, inactivity and poor diet to poor outcomes in patients with cancer. In addition, the Society provides educational materials for patients regarding the role of weight management and healthy lifestyle behaviors in cancer. See below to learn about obesity clinical practice guidelines and obesity coverage and reimbursement.

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Read ASCO's obesity-related position statements and resources to learn about the links between obesity and cancer and the important role of weight management in cancer prevention and care.

https://www.asco.org/practice-guidelines/cancer-care-initiatives/preventionsurvivorship/obesity-cancer



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# **Certified Specialist in Oncology Nutrition (CSO)**



- Specialty certification administered by the Commission on Dietetic Registration
- Board certification is granted to registered dietitians in recognition of documented oncology practice experience and successful completion of an examination in oncology nutrition
- Provides potential employers, oncology patients and caregivers with a tool to evaluate the expertise of the dietetics professional providing oncology nutrition service
- There are currently 750 CSOs in the United States and Canada (16 in Maryland!)

https://www.cdrnet.org/certifications/board-certification-as-a-specialist-in-oncology-nutrition

# Other methods of measuring body composition (primarily used in research)

Method	Strengths	Limitations
Hydrostatic (underwater) weighing	Considered the gold standard	Limited availability Burdensome/traumatic for participants
Computed tomography (CT)	Can quantify composition in specific body parts	Expensive Limited availability
Magnetic resonance imaging (MRI)	Can quantify composition in specific body parts	Expensive Limited availability
Dual X-ray absorptiometry (DEXA)	Can quantify composition in specific body parts	Moderately expensive Limited availability
Bioelectric impedence analysis (BIA)	Portable	Somewhat expensive Highly dependent on hydration status, time of day
BodPod	Low participant burden	Moderately expensive Limited availability
Skin fold measurements	Relatively inexpensive Portable	Not very accurate Significant variation between operators

# Cancer risk associated with 5 unit change in BMI

Cancer	Increment	RR of increased body fatness (95% CI)	Report date
Kidney	5 kg/m <sup>2</sup>	1.30 (95% Cl 1.25-1.35)	2015
Gallbladder	5 kg/m <sup>2</sup>	1.25 (1.15-1.37)	2015
Liver	5 kg/m <sup>2</sup>	1.30 (1.16-1.46)	2015
Advanced prostate cancer	5 kg/m <sup>2</sup>	1.08 (1.04-1.12)	2014
Ovarian	5 kg/m <sup>2</sup>	1.06 (1.02-1.11)	2014
Endometrial	5 kg/m <sup>2</sup>	1.50 (1.42-1.59)	2013
Pancreatic	5 kg/m <sup>2</sup>	1.10 (1.07-1.14)	2012
Colorectal	1 kg/m <sup>2</sup>	1.02 (1.02-1.03)	2011
Postmenopausal breast cancer	2 kg/m <sup>2</sup>	1.05 (1.03-1.07)	2010

http://wcrf.org/int/cancer-facts-figures/link-between-lifestyle-cancer-risk/cancers-linked-greater-body-fatness

# Cancer preventability estimates for body fatness

Cancer	USA		UK		BRAZIL		CHINA	
	Male	Female	Male	Female	Male	Female	Male	Female
Oesophagus (adenocarcinoma)	32	38	29	33	20	26	14	20
Pancreas <sup>(1)</sup>	17	20	14	16	8	13	5	10
Gallbladder <sup>(2)</sup>	11	28	8	21	3	15	2	10
Liver <sup>(3)</sup>	27	28	22	19	11	13	6	7
Colorectum <sup>(4)</sup>	17	15	15	13	10	11	8	9
Breast <sup>(2)</sup> (postmenopausal)	-	17	-	16	-	14	-	12
Ovary <sup>(5)</sup>	-	5	-	4	-	3	-	1
Endometrium <sup>(6)</sup>	-	50	-	38	-	29	-	17
Prostate <sup>(7)</sup> (advanced)	11	-	9	-	5	-	4	-
Kidney <sup>(2)</sup>	20	28	17	21	10	16	6	10
Total for these cancers combined	21	21	16	17	9	14	6	10

http://wcrf.org/int/cancer-facts-figures/preventability-estimates/cancer-preventability-estimates-body-fatness



## Obesity, physical activity and cancer

There is a strong link between being overweight or obese & an **increased risk** of 10 cancers:

- ♦ Liver
- Advanced prostate
- Ovarian
- Gallbladder
- Kidney
- Colorectal (bowel)
- Oesophageal\*
- Postmenopausal breast
- Pancreatic
- Endometrial (womb)

1.9 billion adults worldwide are overweight or obese. This exceeds the population of China

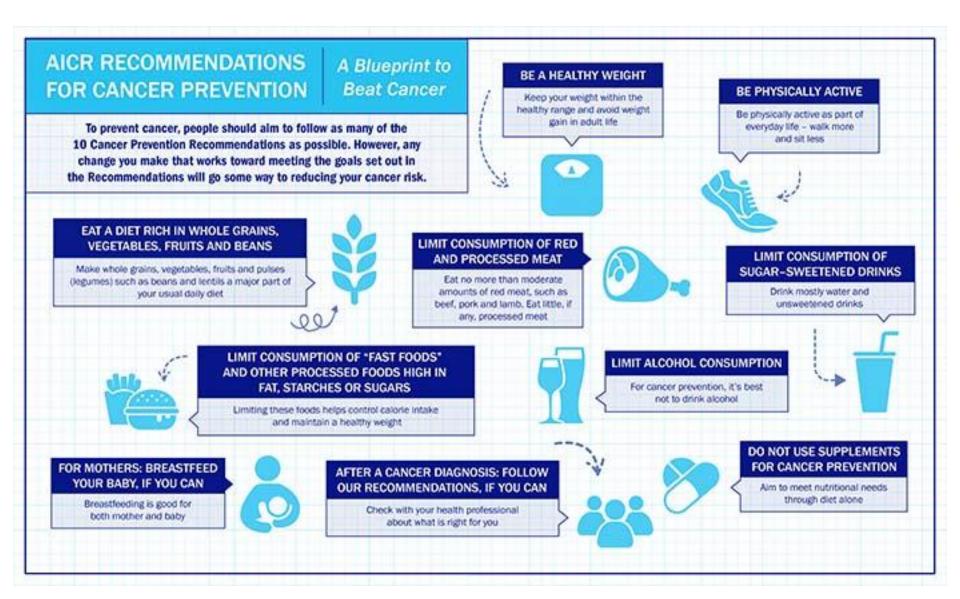
Physical inactivity is the 4th leading cause of death worldwide There is a strong link between being physically active & a **decreased risk** of 3 cancers:

- Postmenopausal breast
- Colorectal (bowel)
- Endometrial (womb)

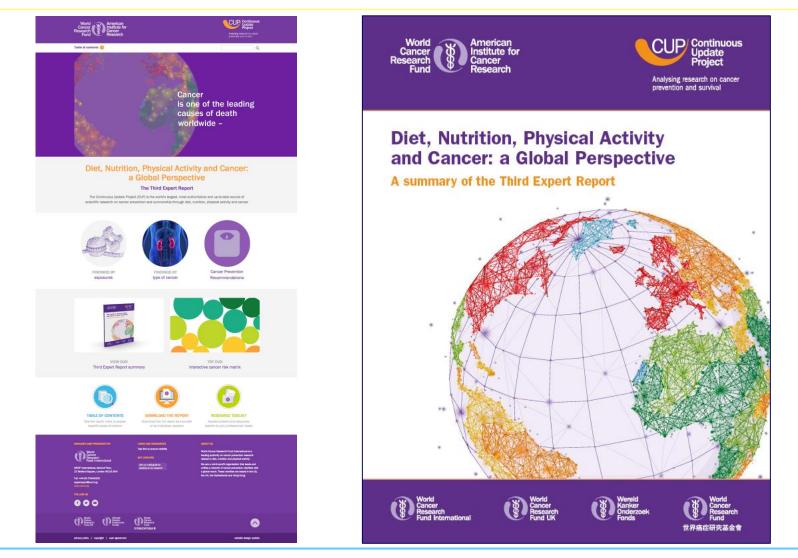
Top 10 countries\* with the highest % of overweight or obese adults

- Mexico 71.3%
- United States 68.6%
- Chile 64.5%
- New Zealand 63.8%
- Australia 63.4%
- Israel 62.2%
- United Kingdom 61.9%
- Hungary 61.6%
- Ireland 61%
- Finland 59.2%
- Luxembourg 59.2%

#### www.wcrf.org



## **The Third Expert Report: Online access**





dietandcancerreport.org

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Analysing research on cancer prevention and survival DIET AND PHYSICAL ACTIVITY AND WEIGHT GAIN, OVERWEIGHT AND OBESITY IN ADULTS AND CHILDREN<sup>1</sup>: A SUMMARY MATRIX

WCRF/AICR GRADING		DECREASES RISK OF WEIGHT GAIN, OVERWEIGHT AND OBESITY	INCREASES RISK OF WEIGHT GAIN, OVERWEIGHT AND OBESITY				
Convincing		Walking	Screen time (children) <sup>2</sup> Sugar sweetened drinks <sup>3</sup>				
STRONG EVIDENCE	Probable	Aerobic physical activity Foods containing dietary fibre 'Mediterranean type' dietary pattern <sup>4</sup> Having been breastfed <sup>5</sup>	Screen time (adults) <sup>2</sup> 'Fast foods' <sup>6</sup> 'Western type' diet <sup>7</sup>				
	Limited – suggestive	Wholegrains <sup>8</sup> Fruit and vegetables Lactation (mother)	Sedentary behaviours <sup>9</sup> Refined grains <sup>8</sup>				
LIMITED EVIDENCE	Limited – no conclusion	Vegetarian or vegan diets, adherence to dietary guidelines, dietary variety, eating breakfast, family meals, eating in the evening, eating frequency, snacking, pulses (legumes), nuts, fish, dairy, confectionery, water, artificially sweetened drinks, fruit juice, coffee and tea, alcoholic drinks, total carbohydrate, glycaemic load, total protein, caffeine, catechins, strength training, energy density, sleep					
STRONG Evidence	Substantial effect on risk unlikely	None identified					

The factors identified in the matrix as increasing or decreasing risk of weight gain, overweight or obesity do so by promoting excess energy intake (positive energy balance, increased risk) relative to the level of energy expenditure (in particular physical activity), or appropriate energy balance (decreased risk), through a complex interplay of physiological, psychological and social influences.<sup>10</sup>

https://www.wcrf.org/sites/default/files/energy-balance-and-body-fatness.pdf



Please see the matrix in the report for footnotes relating to each exposure and explanation of the grading criteria.

\*NCDs, non-communicable diseases \*\*ICL, Imperial College London; NICE, National Institute for Health and Care Excellence; USDA DGAC, United States Department of Agriculture Dietary Guidelines Advisory Committee.

https://www.wcrf.org/sites/default/files/Energy-Balance-Graphical-Abstract-WEB.pdf

### Appropriate Chemotherapy Dosing for Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline

Jennifer J. Griggs, Pamela B. Mangu, Holly Anderson, Edward P. Balaban, James J. Dignam, William M. Hryniuk, Vicki A. Morrison, T. May Pini, Carolyn D. Runowicz, Gary L. Rosner, Michelle Shayne, Alex Sparreboom, Lara E. Sucheston, and Gary H. Lyman

See related articles in *J Oncol Pract* doi: 10.1200/JOP.2012.000623 and doi: 10.1200/ JOP.2012.000606

A B S T R A C T

#### **Purpose**

To provide recommendations for appropriate cytotoxic chemotherapy dosing for obese adult patients with cancer.

#### Methods

The American Society of Clinical Oncology convened a Panel of experts in medical and gynecologic oncology, clinical pharmacology, pharmacokinetics and pharmacogenetics, and biostatistics and a patient representative. MEDLINE searches identified studies published in English between 1996 and 2010, and a systematic review of the literature was conducted. A majority of studies involved breast, ovarian, colon, and lung cancers. This guideline does not address dosing for novel targeted agents.

#### Results

Practice pattern studies demonstrate that up to 40% of obese patients receive limited chemotherapy doses that are not based on actual body weight. Concerns about toxicity or overdosing in obese patients with cancer, based on the use of actual body weight, are unfounded.

#### Recommendations

The Panel recommends that full weight–based cytotoxic chemotherapy doses be used to treat obese patients with cancer, particularly when the goal of treatment is cure. There is no evidence that short- or long-term toxicity is increased among obese patients receiving full weight–based doses. Most data indicate that myelosuppression is the same or less pronounced among the obese than the non-obese who are administered full weight–based doses. Clinicians should respond to all treatment-related toxicities in obese patients in the same ways they do for non-obese patients. The use of fixed-dose chemotherapy

is rarely justified, but the Panel does recommend fixed dosing for a few select agents. The Panel recommends further research into the role of pharmacokinetics and pharmacogenetics to guide appropriate dosing of obese patients with cancer.

J Clin Oncol 30:1553-1561. © 2012 by American Society of Clinical Oncology