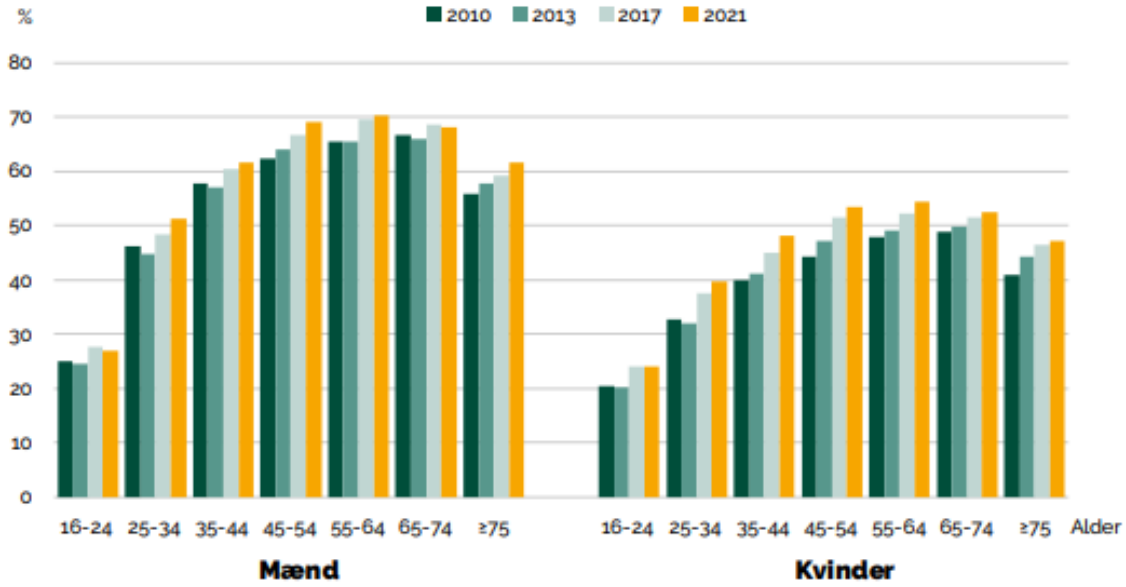
Professor, Forskningsgruppeleder Anne Tjønneland,
Danish Cancer Institute

Giver fedme kræft, eller er sandheden en anden?

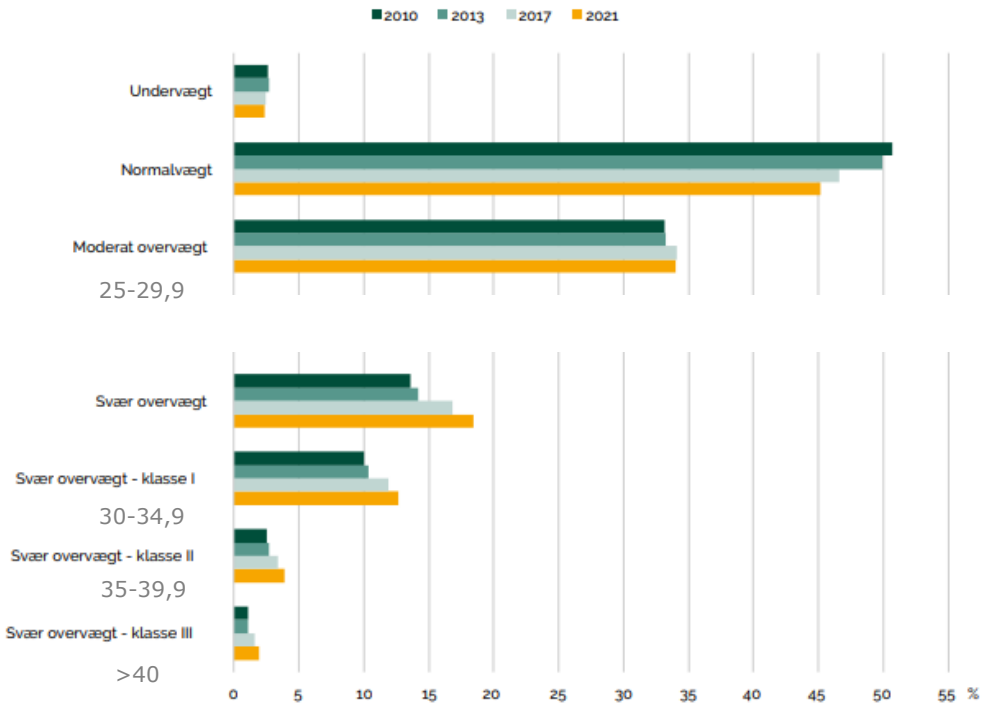
Overvægt/fedme prævalens baseret på BMI >25

Figur 3.5.4 Andel med moderat eller svær overvægt (BMI≥25) blandt mænd og kvinder i forskellige aldersgrupper. 2010, 2013, 2017 og 2021. Procent.

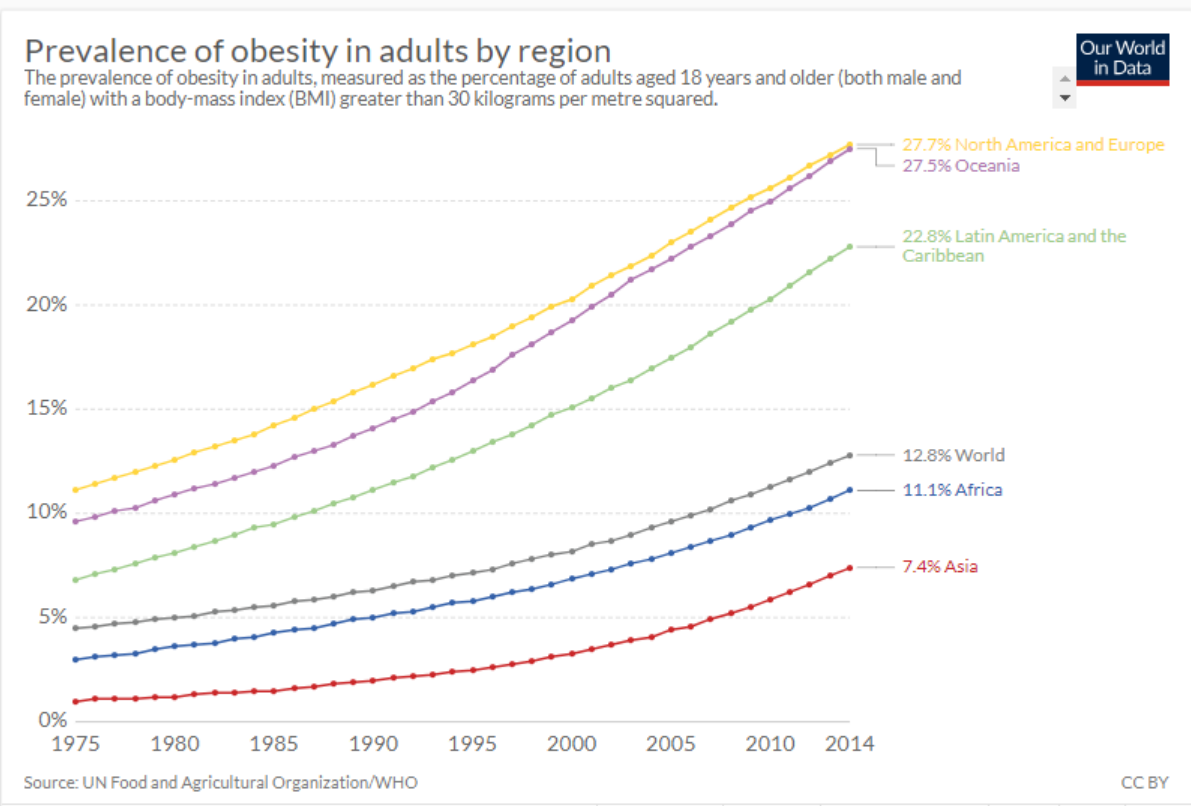


Danskernes Sundhed 2021, BMI grupper

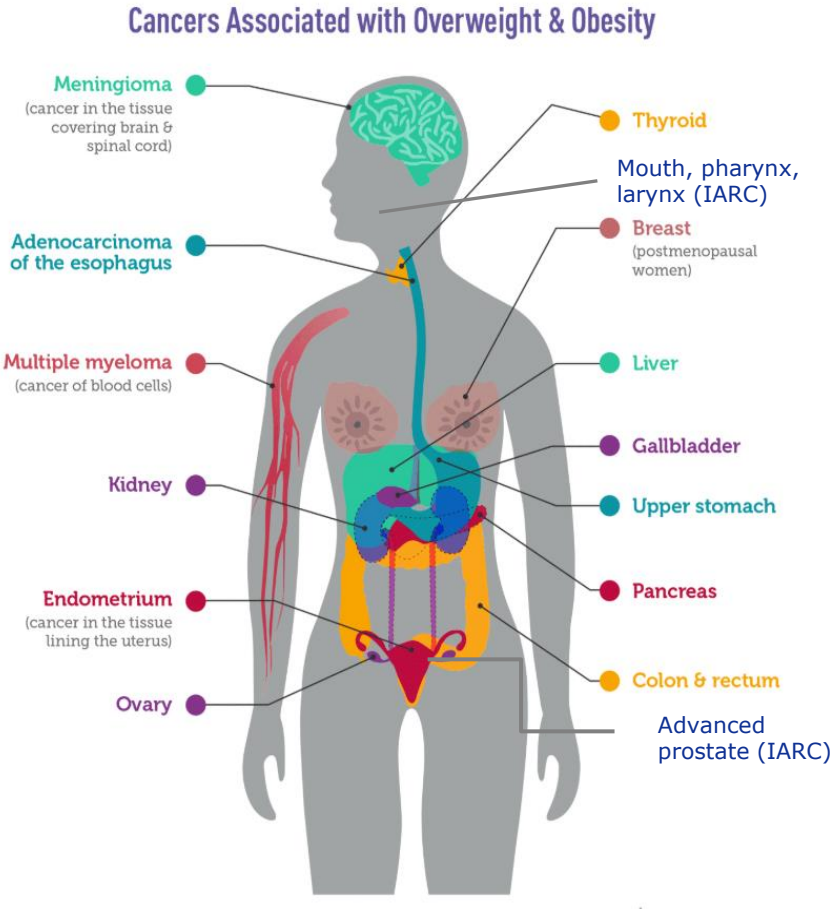
Figur 3.5.1 Udvikling i vægtgrupper. 2010, 2013, 2017 og 2021. Procent .



Fedme prævalens baseret på BMI >30



Status for evidens til kræft, 2022



- Baseret på WCRF/AICR og IARC/WHO er der samlet set nu stærk evidens for sammenhæng mellem overvægt og udvikling af 15 forskellige kræfttyper

- European Obesity Report, 2022: … it is predicted that obesity will overtake smoking as the main risk factor for preventable cancer in the coming decade in some countries…..

Article

https://doi.org/10.1038/s41467-023-39282-y

Longitudinal body mass index and cancer risk: a cohort study of 2.6 million Catalan adults

nature communications

Received: 12 April 2022

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Martina Recalde[1,2,3,7], Andrea Pistillo[2,7], Veronica Davila-Batista[1,4] ✉, Michael Leitzmann[5], Isabelle Romieu[6], Vivian Viallon[1], Heinz Freisling[1,8] ✉ & Talita Duarte-Salles[2,8] ✉

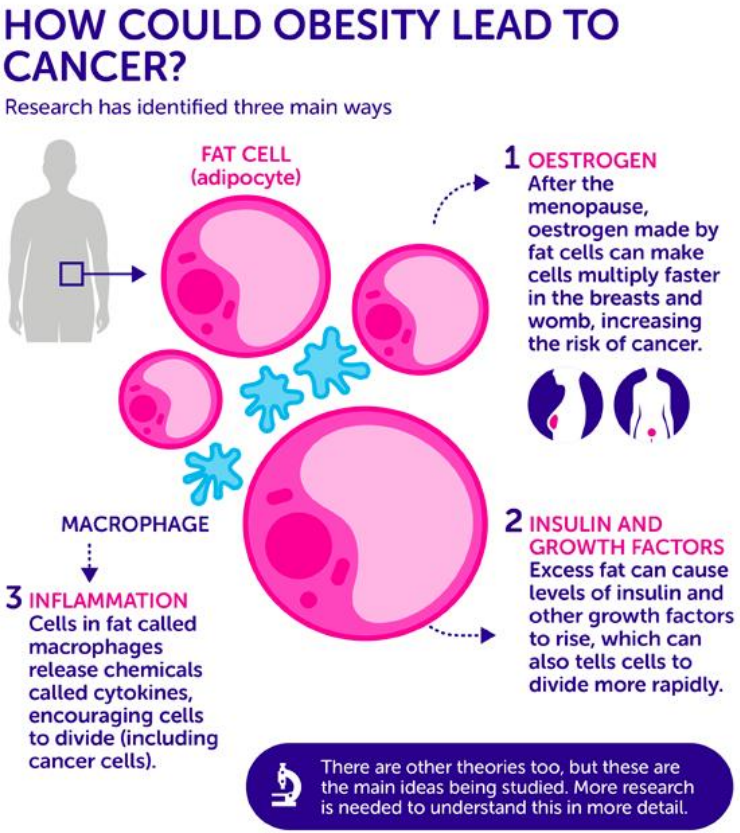
Obesity now linked to 18 cancers

Overweight and obesity during early adulthood could increase the risk of developing 18 cancers according to new research funded by Wereld Kanker Onderzoek Fonds, our network charity in the Netherlands.

The study found that the following factors related to overweight and obesity were associated with an increased risk of developing 18 cancers:

- longer length of time
- greater degree
- younger age of onset

Biologiske mekanismer, der kan forklare sammenhænge mellem overvægt og kræft?



Ikke alle overvægtige har en øget risiko for tarmkræft, i EPIC

Model	Metabolic-Health-Defined Body Size Phenotype			
	Metabolic Health/BMI Definition			
	Metabolically Healthy/Normal Weight	Metabolically Healthy/ Overweight	Metabolically Unhealthy/ Normal Weight	Metabolically Unhealthy/ Overweight
Colorectal cancer				
N cases/ controls	101/131	93/121	158/133	385/352
Model 1	1.00	0.95 (0.65–1.40)	1.58 (1.11–2.25)	1.47 (1.07–2.00)
Model 2	1.00	0.96 (0.65–1.42)	1.59 (1.10–2.28)	1.40 (1.01–1.94)
Model 3	—	0.69 (0.49–0.96)	—	1.00

PLOS Medicine
DOI:10.1371/journal.pmed.1001988 April 5, 2016

Samme fund i relation til postmenopausal brystkræft og endometrie cancer i EPIC

Received: 24 October 2022 | Revised: 6 March 2023 | Accepted: 23 March 2023

DOI: 10.1002/cam4.5886

RESEARCH ARTICLE

Cancer Medicine — WILEY

Metabolically defined body size and body shape phenotypes and risk of postmenopausal breast cancer in the European Prospective Investigation into Cancer and Nutrition

Y. Mahamat-Saleh[1] | S. Rinaldi[1] | R. Kaaks[2] | C. Biessy[1] | E. M. Gonzalez-Gil[1] | N. Murphy[1] | C. Le Cornet[2] | M. Guevara[8,9,10] | J. M. Huerta[3,4] | K. Overvad[11] | S. Sieri[5] | A. Tjønneland[6,7] | L. Mellemkjær[6] | L. Padroni[13] | V. Simeon[14] | A. Perez-Cornago[12] | S. Tin Tin[12] | M. Gunter[1] | G. Masala[15] | A. May[16] | E. Monninkhof[16] | S. Christakoudi[17,18] | A. K. Heath[17] | K. Tsilidis[17] | A. Agudo[19,20] | M. B. Schulze[21,22] | J. Rothwell[23] | C. Cadeau[23] | S. Severi[23] | E. Weiderpass[1]

[1]International Agency for Research on Cancer, Lyon, France
[2]Division of Cancer Epidemiology, German Cancer Research Center (DFKZ), Heidelberg, Germany
[3]Department of Epidemiology, Murcia Regional Health Council, Murcia, Spain
[4]CIBER Epidemiología y Salud Pública (CIBERESP), 28029, Madrid, Spain
[5]Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, 20133, Milan, Italy
[6]Danish Cancer Society Research Center, Copenhagen, Denmark
[7]Department of Public Health, University of Copenhagen, Copenhagen, Denmark
[8]Navarra Public Health Institute, 31003, Pamplona, Spain
[9]Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), 28029, Madrid, Spain
[10]Navarra Institute for Health Research (IdiSNA), 31008, Pamplona, Spain
[11]Department of Public Health, Section for Epidemiology, Aarhus University, Aarhus, Denmark
[12]Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK
[13]Department of Clinical and Biological Sciences, University of Turin, Turin, Italy
[14]Dipartimento di Salute Mentale e Fisica e Medicina Preventiva, Università degli Studi della Campania 'Luigi Vanvitelli', 80121, Naples, Italy
[15]Institute for Cancer Research, Prevention and Clinical Network (ISPRO), Florence, Italy
[16]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
[17]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
[18]Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece
[19]Unit of Nutrition and Cancer, Catalan Institute of Oncology – ICO, L'Hospitalet de Llobregat, Spain
[20]Nutrition and Cancer Group, Epidemiology, Public Health, Cancer Prevention and Palliative Care Program, Bellvitge Biomedical Research Institute – IDIBELL, L'Hospitalet de Llobregat, Spain
[21]Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany
[22]Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany
[23]Paris-Saclay University, UVSQ, Inserm, Gustave Roussy, "Exposome and Heredity" team, CESP, Villejuif, France

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CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | RESEARCH ARTICLE

Metabolically Defined Body Size Phenotypes and Risk of Endometrial Cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC)

Nathalie Kilemann[1], Romain Ould Ammar[2], Carine Biessy[1], Audrey Gicquiau[1], Verena Katzke[2], Anne Tjønneland[3,4], Sandar Tin Tin[5], Anja Olsen[4,5], Maria-Jose Sánchez[6,7,8], Marta Crous-Bou[9,10], Aurora Perez-Cornago[11], Dagfinn Aune[12,13,14], Sofia Christakoudi[14,15], Heinz Freisling[1], Rudolf Kaaks[2], Sandra M. Colorado-Yohar[6,16,17], Anne M. May[18], Elisabete Weiderpass[1], Hanna Sartor[19], Fabrizio Pasanisi[20], Gianluca Severi[21], Guri Skeie[22], Heinz Freisling[1], Alicia K. Heath[14], Sabina Rinaldi[1], Neil Murphy[1], Inge Huybrechts[1], Laure Dossus[1], and Marc J. Gunter[1]

ABSTRACT

Background: Obesity is a risk factor for endometrial cancer but whether metabolic dysfunction is associated with endometrial cancer independent of body size is not known.

Methods: The associations of metabolically defined body size phenotypes with endometrial cancer risk were investigated in the European Prospective Investigation into Cancer and Nutrition (EPIC), a prospective cohort study (817 cases; 817 controls) within EPIC. Concentrations of C-peptide were used to define insulin sensitivity. Healthy (H) and unhealthy (U) states among the combined participants with normal weight (NW), overweight (OW), and obesity (OB) were defined using body mass index (BMI) and waist circumference (WC) or waist-to-hip ratio (WHR) as follows: (i) NW, OW, and OB: BMI<25 kg/m^2 or WC<80 cm or WHR<0.8; (ii) MetNW: BMI≥25 kg/m^2 or WC≥80 cm or WHR≥0.8 and HOMA-IR<2.5; (iii) MetOW: BMI≥25 kg/m^2 or WC≥80 cm or WHR≥0.8 and HOMA-IR≥2.5; (iv) MetOB: BMI≥30 kg/m^2. Cox regression was used to estimate HRs and 95% CIs for endometrial cancer risk compared with MetNW individuals, adjusting for potential confounders.

Results: In a multivariable-adjusted conditional logistic regression model, compared with MetNW individuals, endometrial cancer risk was higher among those classified as MetUNW (OR, 1.65; 95% CI, 1.05–2.58) and MetOW (OR, 2.38; 95% CI, 1.68–3.37) and MetOB (OR, 3.03; 95% CI, 1.89–4.85). Risk was also higher among individuals with normal metabolic dysfunction (MetNW, MetOW, MetOB) compared with healthy individuals (OR, 1.94; 95% CI, 1.32–2.84). MetUNW individuals had a higher risk of endometrial cancer compared with MetNW individuals (OR, 1.83; 95% CI, 1.23–2.70). MetUOW individuals had a higher risk of endometrial cancer compared with MetNW individuals (OR, 2.49; 95% CI, 1.73–3.57). MetUOB individuals had a higher risk of endometrial cancer compared with MetNW individuals (OR, 3.04; 95% CI, 1.91–4.84). Associations were similar for endometrial cancer risk compared with MetNW individuals.

Conclusions: Women with metabolic dysfunction appear to have higher risk of endometrial cancer regardless of their body size. However, OW status raises endometrial cancer risk compared with women with normal insulin levels, suggesting that obesity-related pathways are relevant for the development of this cancer beyond insulin.

Impact: Classifying women by metabolic health may be of greater utility in identifying those at higher risk for endometrial cancer than anthropometry *per se*.

Introduction

Endometrial cancer is the second most common gynecological cancer worldwide, with 604,127 new cases and 341,831 deaths reported in 2020 (1). Higher body mass index (BMI≥25 kg/m^2) is a well-established risk factor for endometrial cancer (2–5). A meta-analysis of prospective studies has shown that every 5 kg/m^2 increase in BMI is associated with a 60% increase in endometrial

[1]International Agency for Research on Cancer, Lyon, France. [2]Division of Cancer Epidemiology, German Cancer Research Center (DKFZ), Heidelberg, Germany. [3]Danish Cancer Society Research Center, Copenhagen, Denmark. [4]Department of Public Health, University of Copenhagen, Copenhagen, Denmark. [5]Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy. [6]Navarra Public Health Institute, Pamplona, Spain. [7]Navarra Institute for Health Research (IdiSNA), Pamplona, Spain. [8]Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain. [9]Department of Epidemiology, Murcia Regional Health Council, IMIB-Arrixaca, Murcia, Spain. [10]Research Group on Demography and Health, National Faculty of Public Health, University of Antioquia, Medellín, Colombia. [11]Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy. [12]Department of Nutrition, Norwegian Institute of Public Health, Oslo, Norway. [13]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK. [14]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK. [15]Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK. [16]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands. [17]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK. [18]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK. [19]Department of Clinical and Biological Sciences, University of Turin, Turin, Italy. [20]Dipartimento di Salute Mentale e Fisica e Medicina Preventiva, Università degli Studi della Campania 'Luigi Vanvitelli', Naples, Italy. [21]Institute for Cancer Research, Prevention and Clinical Network (ISPRO), Florence, Italy. [22]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands. [23]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK. [24]Unit of Nutrition and Cancer, Catalan Institute of Oncology – ICO, L'Hospitalet de Llobregat, Spain. [25]Nutrition and Cancer Group, Epidemiology, Public Health, Cancer Prevention and Palliative Care Program, Bellvitge Biomedical Research Institute – IDIBELL, L'Hospitalet de Llobregat, Spain. [26]Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany. [27]Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany. [28]Paris-Saclay University, UVSQ, Inserm, Gustave Roussy, "Exposome and Heredity" team, CESP, Villejuif, France.

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Marc J. Gunter, International Agency for Research on Cancer, 150 Cours Albert Thomas, CEDEX 08, Lyon, France. Phone: 33-4-72-73-84-92; Fax: 33-4-72-73-83-19; E-mail: gunterm@iarc.fr.

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Hvordan definerer vi metabolisk usunde?

Metabolisk syndrom:

En samling af risikofaktorer for diabetes,

hjertekarsygdomme, stroke, etc.:

- **Abdominal fedme**
- **Højt blodtryk**
- **Højt fasteglucose**
- **Højt triglycerid**
- **Lavt HDL kolesterol**

3 af disse faktorer

88% af amerikanere har mindst en af disse!

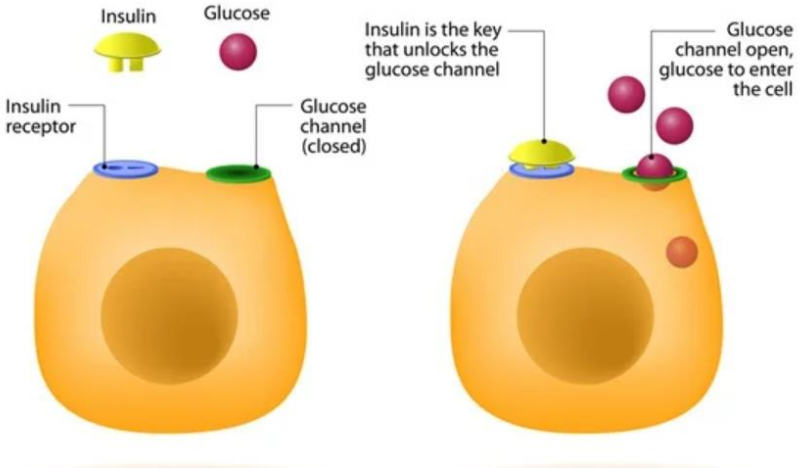
Insulinresistens/hyper insulinæmi

Grundlæggende årsag til metabolisk syndrom - kronisk forhøjede niveauer af insulin

Review of the key results from the Swedish Obese Subjects (SOS) trial – a prospective controlled intervention study of bariatric surgery

L. Sjöström

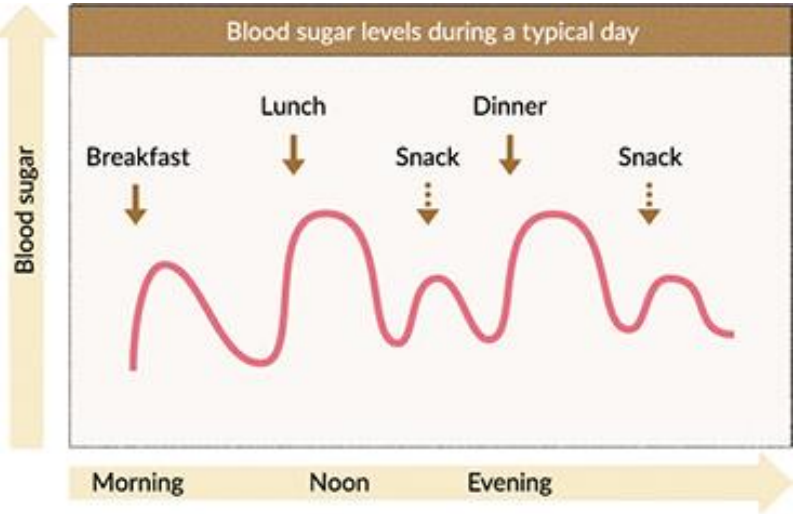
BMI thus did not predict the effect of surgery on any of these endpoints. By contrast, insulin predicted the treatment effect with respect to mortality (P for interaction = 0.013) [35], cardiovascular events ($P < 0.001$) [37] and incidence of diabetes ($P = 0.007$) [38]



Årsager til hyper insulinæmi:

Højt og hyppigt indtag af raffinerede kulhydrater

Manglende motion og dermed lav muskelmasse



Insulin Resistance and Cancer-Specific and All-Cause Mortality in Postmenopausal Women: The Women's Health Initiative

Kathy Pan, Rebecca A. Nelson, Jean Wactawski-Wende, Delphine J. Lee, JoAnn E. Manson, Aaron K. Aragaki, Joanne E. Mortimer, Lawrence S. Phillips, Thomas Rohan, Gloria Y. F. Ho, Nazmus Saquib, Aladdin H. Shadyab, Rami Nassir, Jinnie J. Rhee, Arti Hurria, Rowan T. Chlebowski

Results: During a median of 18.9 years of follow-up, 1820 cancer deaths and 7415 total deaths occurred. Higher HOMA-IR quartile was associated with higher cancer-specific mortality (Q4 vs Q1, HR = 1.26, 95% CI = 1.09 to 1.47; $P_{trend} = .003$) and all-cause mortality (Q4 vs Q1, HR = 1.63, 95% CI = 1.51 to 1.76; $P_{trend} < .001$). A sensitivity analysis for diabetes status did not change findings. Among women with body mass index less than 25 kg/m^2, higher HOMA-IR quartile was associated with higher cancer mortality (Fine and Gray, P = .004).

Conclusions: High insulin resistance, as measured by HOMA-IR, identifies postmenopausal women at higher risk for cancer-specific and all-cause mortality who could potentially benefit from early intervention.

JNCI J Natl Cancer Inst (2020) 112(2): djz069

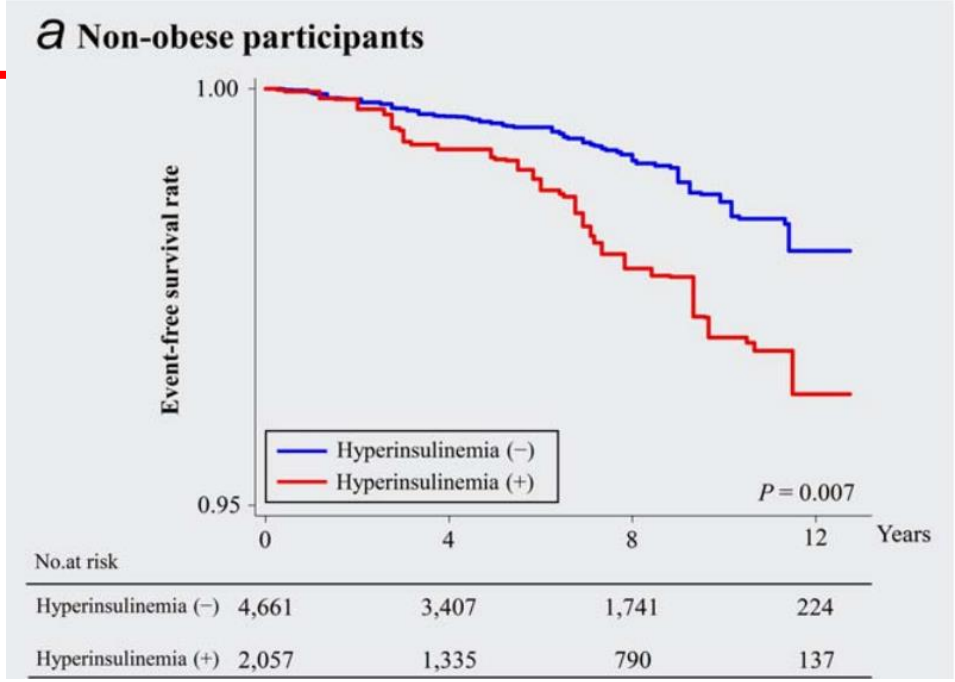
Considering that non-obese people with hyperinsulinemia were at higher risk of cancer mortality than those without hyperinsulinemia, improvement of hyperinsulinemia may be an important approach for preventing cancer regardless of the presence or absence of obesity

Int. J. Cancer: **141**, 102–111 (2017) © 2017

Association between hyperinsulinemia and increased risk of cancer death in nonobese and obese people: A population-based observational study

Tetsuro Tsujimoto[1], Hiroshi Kajio[1] and Takehiro Sugiyama[2,3]

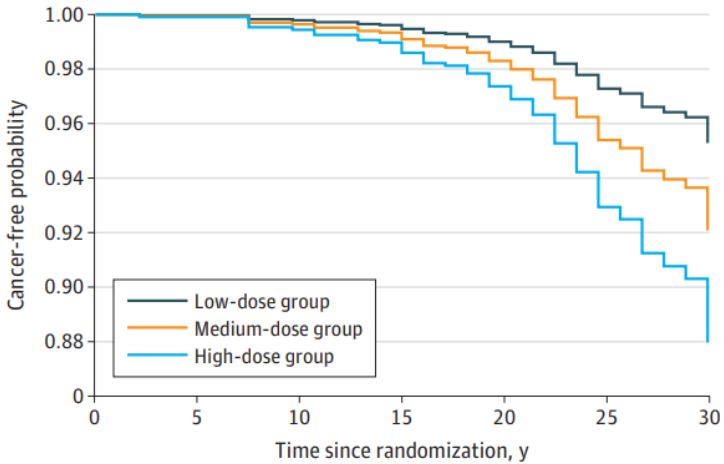
[1] Department of Diabetes, Endocrinology, and Metabolism, Center Hospital, National Center for Global Health and Medicine, Tokyo, Japan
[2] Diabetes and Metabolism Information Center, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan
[3] Department of Public Health/Health Policy, the University of Tokyo, Tokyo, Japan



Type1 diabetes og insulin doser og cancer

JAMA Oncology September 2022 Volume 8, Number 9

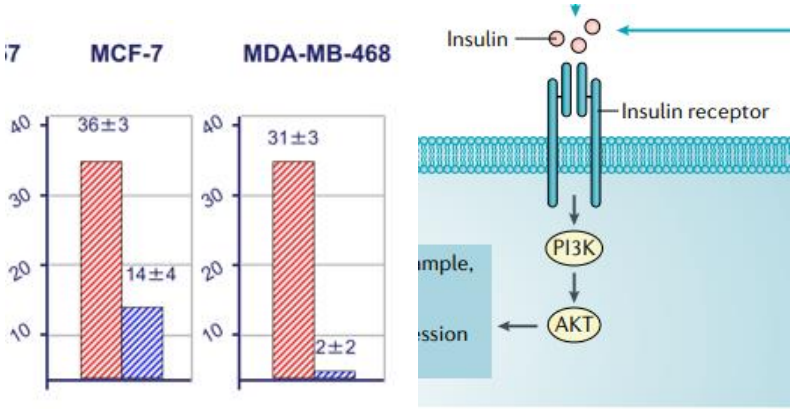
Figure. Cancer-Free Probability by Daily Insulin Dose Over 28 Years of Follow-up



No. at risk							
Low-dose group	221	221	220	218	215	124	0
Medium-dose group	832	831	828	825	813	494	0
High dose-group	250	250	249	245	240	157	0

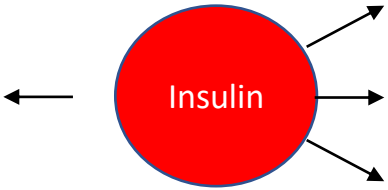
Hvorfor forårsager hyperinsulinæmi fedme og cancer?

Cancer



Vækstfaktor

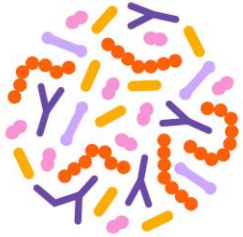
Fedme/overvægt



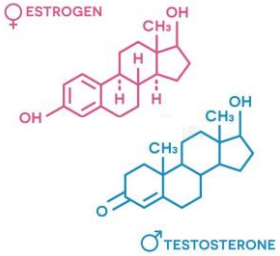
- Blokerer nedbrydning af fedt
- Blokerer fedtforbrænding
- Stimulerer lagring af fedt fra glucose

Genes

Food

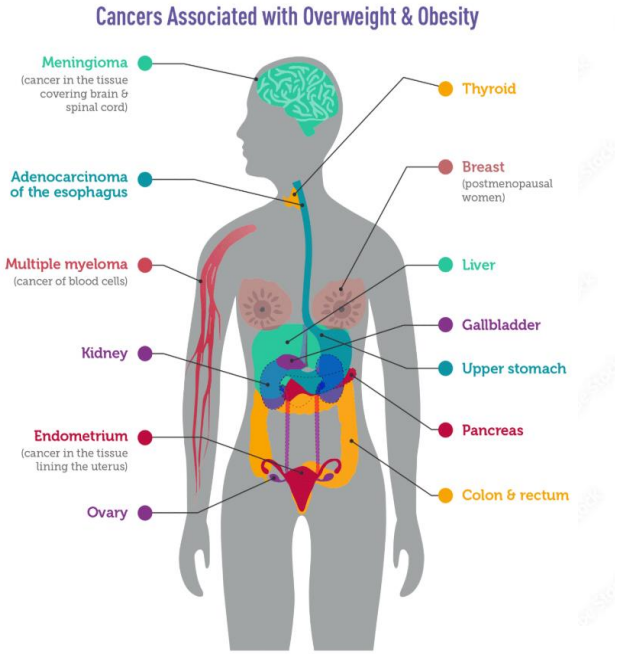


Gut microbiome

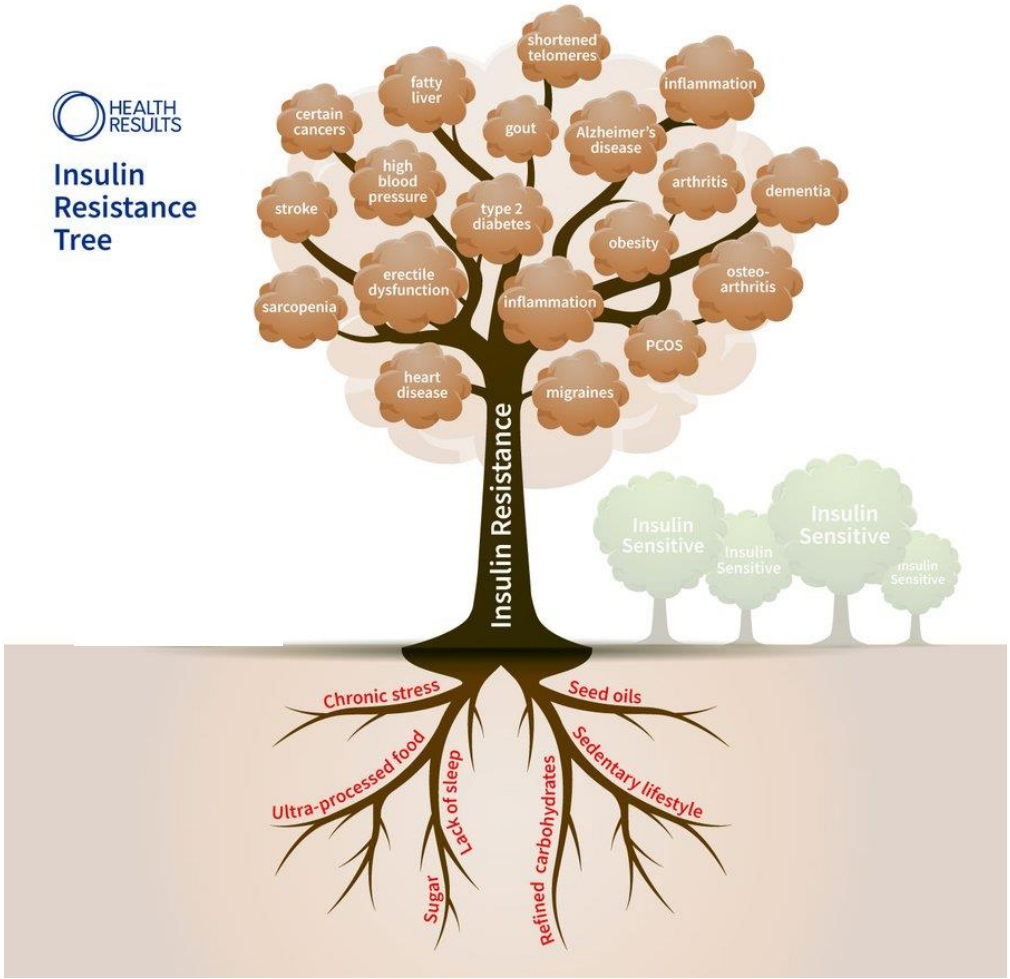


Hormones

Medication



Exercise



Forebyggelse på alle niveauer:

Primær forebyggelse
Sekundær forebyggelse
Under kræftbehandling

Studier med måling af Insulin niveauer

Raffinerede kulhydrater
Ultraforarbejdede fødevarer
Manglende fysisk aktivitet

Søvn mangel
Kronisk stress
Olier baseret på frø

Tak for opmærksomheden