Complications of Obesity I: Cancer

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• Is it a true phenomenon?
• Association or causality?
• What the mechanisms?
• What about prevention?
Obesity and Cancer

- Is it a true phenomenon?
- Association or causality?
- What the mechanisms?
- What about prevention?
Contribution of Overweight and Obesity to Mortality from Cancer in the United States


- Prostate (≥35) 1.34
- Non-Hodgkin’s lymphoma (≥35) 1.49
- All cancers (≥40) 1.52
- All other cancers (≥30) 1.68*
- Kidney (≥35) 1.70
- Multiple myeloma (≥35) 1.71
- Gallbladder (≥30) 1.76
- Colon and rectum (≥35) 1.84
- Esophagus (≥30) 1.91*
- Stomach (≥35) 1.94
- Pancreas (≥35) 2.61*
- Liver (≥35) 4.52

900,000 U.S. adults. FU: 16 yrs


900,000 U.S. adults. FU: 16 yrs
BMI AND RISK OF 22 SPECIFIC CANCERS: A POPULATION-BASED COHORT STUDY OF 5·24 MILLION UK ADULTS

Bhaskaran K et al, Lancet, 2014
The risk of developing certain cancers is increased at the highest BMI category

Relative risk of developing cancers with BMI $\geq 40$ kg/m$^2$ vs BMI 18.5–24.9 kg/m$^2$

*Post-menopausal

In 2014, approximately 631,000 persons in the United States received a diagnosis of a cancer associated with overweight and obesity, representing **40% of all cancers diagnosed**.
Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry

Hyuna Sung PhD, Rebecca L Siegel MPH, Philip S Rosenberg PhD, Ahmedin Jemal PhD
Emerging Cancer Trends among Young Adults in the USA: Analysis of a Population-based Cancer Registry


Sung H et al, Lancet PH, 2019
Obesity and Cancer

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Weight loss reduces the incidence of cancers in individuals with obesity

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Surgery group N=6596</th>
<th>Control group N=9442</th>
<th>Surgery vs control groups</th>
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<tbody>
<tr>
<td></td>
<td>N (rates/1000 person-years)</td>
<td>N (rates/1000 person-years)</td>
<td>HR (95% CI)</td>
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<td>All cancers: males and females combined</td>
<td>41 (0.50)</td>
<td>107 (0.94)</td>
<td>0.54 (0.37 ; 0.78)</td>
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<td>All cancers: males only</td>
<td>10 (0.12)</td>
<td>24 (0.21)</td>
<td>0.70 (0.34 ; 1.48)</td>
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<td>All cancers: females only</td>
<td>31 (0.38)</td>
<td>83 (0.73)</td>
<td>0.38 (0.23 ; 0.64)</td>
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<tr>
<td>Obesity-related cancers†</td>
<td>20 (0.24)</td>
<td>55 (0.48)</td>
<td>0.54 (0.32 ; 0.90)</td>
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<td>Non-obesity-related cancers‡</td>
<td>21 (0.25)</td>
<td>52 (0.46)</td>
<td>0.53 (0.31 ; 0.91)</td>
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</table>

*Hazard ratios adjusted for age, sex and BMI. Prevalent cancers at baseline were excluded; †Obesity-related cancers included oesophageal adenocarcinomas, colorectal, pancreas, post-menopausal breast, corpus and uterus, kidney, non-Hodgkin’s lymphoma, leukaemia, multiple myeloma, liver and gallbladder; ‡All cancers that are not included as obesity-related cancers. BMI, body mass index; CI, confidence interval; HR, hazard ratio. p-values are unadjusted for multiple comparisons.
Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial
Obesity and Cancer

- Is it true?
- Association or causality?
- **What the mechanisms?**
- What about prevention?
Diet, Nutrition, Physical Activity and Cancer: a Global Perspective

- Summary of the Third Expert Report:
- figures and matrices
Effects of obesity on cellular microenvironments & links to cancer

WHO summary of the Third Expert Report on diet, nutrition, physical activity and cancer

DISEASE PROCESS

- No apparent abnormalities
- Borderline abnormalities
- T2 Diabetes Hypertension Dyslipidemia OSAS PCOS Osteoarthritis etc.
- AMI CHF Stroke etc
- End-stage Disability

Quality

EOSS Staging

Fat Mass (& distribution)
## SUMMARY OF STRONG EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND THE PREVENTION OF CANCER

To reference this table please use the following citation:

Abbreviation: SLR, systematic literature review.

<table>
<thead>
<tr>
<th>Sub-site</th>
<th>Tobacco</th>
<th>Alcohol</th>
<th>High-carbohydrate diet</th>
<th>Meat</th>
<th>Processed meat</th>
<th>Red meat</th>
<th>Fish</th>
<th>Ultra-processed foods</th>
<th>Physical inactivity</th>
<th>Other</th>
<th>Smoking (adults)</th>
<th>Alcohol consumption</th>
<th>Physical activity</th>
<th>Weight loss</th>
<th>Obesity (adults)</th>
<th>Physical activity (children)</th>
<th>Smoking (children)</th>
<th>Alcohol consumption (children)</th>
<th>Physical activity (children)</th>
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<td>Risk of weight gain, overweight or obesity 2018</td>
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- **Coordinating increases risk**
- **Probably decreases risk**
- **Probable increases risk**
- **Coordinating increases risk**
- **Substantial effect on risk unlikely**
stromal cell-derived factor-1 (SDF-1) metallo proteinase (MMP)

ADIPOSE TISSUE AND CANCER RISK

Interactions between tumour cells and cells within the obese adipose tissue microenvironment

Quail et al., Nature Reviews Endocrinology 2019
Liver
- Lipogenesis
- Inflammation
- Insulin resistance

Pancreas
- Hyperglycemia
- Hyperinsulinemia

Adipose tissue
- Adiponectin \( \downarrow \)
- Leptin \( \uparrow \)
- Inflammatory cytokines \( (IL-\beta, \text{TNF-}\alpha) \uparrow \)
- NEFA \( \uparrow \)

Colon
- Dysbiosis
- Permeability
- LPS

Systemic tumor promotion by obesity

↑ NEFA
↑ Insulin
↑ Glucose
↑ Leptin
↓ Adiponectin
↑ Inflammatory cytokines
Specific microbiota derived metabolites
The calcium–cancer signalling nexus

Gregory R. Monteith1–3, Natalia Prevarskaya4 and Sarah J. Roberts-Thomson1

Abstract | The calcium signal is a powerful and multifaceted tool by which cells can achieve specific outcomes. Cellular machinery important in tumour progression is often driven or influenced by changes in calcium ions; in some cases this regulation occurs within spatially defined regions. Over the past decade there has been a deeper understanding of how calcium signalling is remodelled in some cancers and the consequences of calcium signalling on key events such as proliferation, invasion and sensitivity to cell death. Specific calcium signalling pathways have also now been identified as playing important roles in the establishment and maintenance of multidrug resistance and the tumour microenvironment.
Obesity and Cancer

• Is it a true phenomenon?
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• **What about prevention?**
OUR CANCER PREVENTION RECOMMENDATIONS

- Limit consumption of red and processed meat
- Limit consumption of sugar sweetened drinks
- Limit alcohol consumption
- Eat a diet rich in wholegrains, vegetables, fruit and beans
- Be physically active
- Be a healthy weight
- Do not use supplements for cancer prevention
- For mothers: breastfeed your baby, if you can
- After a cancer diagnosis: follow our recommendations, if you can

Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk. Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases.
Obesity and Cancer

• Is it a true phenomenon?
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• **What about treatment?**
The Surprisingly Positive Association Between Obesity and Cancer Immunotherapy Efficacy

Murphy WJ, JAMA 2009