

Body mass index and risk of over 100 cancer forms and subtypes in 4.1 million individuals in Sweden: a pooled cohort study aiming to identify further obesity-related cancers

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Introduction: Obesity, assessed by body mass index (BMI), is an established risk factor for 13 cancers (1). The previous largest prospective studies on BMI and cancer risk recorded around 200,000 incident cancers during follow-up, categorized into 22 and 26 cancers respectively (2, 3). In a large, pooled prospective study, we aimed to identify further potential obesity-related cancers, and to quantify their association with BMI relative to that of established obesity-related cancers.

Methods: We investigated BMI in 4,142,349 individuals in Sweden (mean age 27 years) with risks of 124 cancers grouped according to topography and morphology. We fitted Cox regression models to calculate hazard ratios (HRs) of cancer and regarded previously unestablished obesity-related cancers with a positive HR at an α -level of 0.05 for either obesity

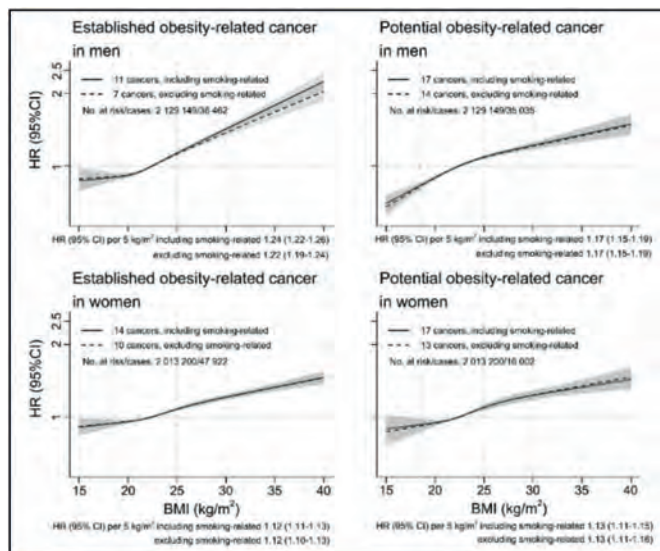
(BMI ≥ 30 kg/m²) vs. normal weight (BMI 18.5–24.9 kg/m²) or per 5 kg/m² higher BMI level as potentially obesity-related.

Results: After 100 million person-years of follow-up, 332,501 cancer cases were recorded. We identified many potential obesity-related cancers: several head and neck cancers, gastrointestinal tract cancers (gastric gastrointestinal stromal, small intestine, biliary tract), melanoma, genital cancers (vulva, cervical adenocarcinoma, penis), several endocrine cancers, connective tissue cancer, and haematological cancers (Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia). Amongst cancer subtypes, some were more strongly obesity-related such as small intestine neuroendocrine tumours and non-Hodgkin diffuse large B-cell lymphoma. The HR (95% confidence interval) of potential obesity-related cancers combined (n=51,037) per 5 kg/m² higher BMI level was 1.17 (1.15–1.20) in men and 1.13 (1.11–1.15) in women, as compared to 1.24 (1.22–1.26) and 1.12 (1.11–1.13), respectively, for established obesity-related cancers (n=84,384).

Conclusion: This study suggests a potentially large addition of obesity-related cancers to already established ones and provides further evidence for specific cancer subtypes driving some of the associations. Studies accounting for cancer-specific potential confounders are needed to confirm these findings.

References

- 1) Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body Fatness and Cancer-Viewpoint of the IARC Working Group. *N Engl J Med* 2016; 375: 794–8.
- 2) Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet* 2014; 384: 755–65.
- 3) Recalde M, Davila-Batista V, Diaz Y, et al. Body mass index and waist circumference in relation to the risk of 26 types of cancer: a prospective cohort study of 3.5 million adults in Spain. *BMC Med* 2021; 19: 10.



Established obesity-related cancers include cancer of the oesophagus-adenocarcinoma, stomach-cardia, colon, rectum, liver/intrahepatic bile ducts, gallbladder, pancreas, meningioma, thyroid, multiple myeloma and renal cell carcinoma for both men and women, and additionally includes cancer of the postmenopausal breast, endometrium, and ovary for women. Potential obesity-related cancers include cancer of the nasal and paranasal sinuses, gastric-gastrointestinal stromal (excluding gastric-cardia), small intestine, biliary tract (excluding gallbladder), pancreatic islets, adrenal glands, parathyroid gland, pituitary gland, connective tissue, Hodgkin lymphoma, non-Hodgkin lymphoma, and leukemia for both men and women, and additionally includes cancer of the lip, tongue, penis, melanoma, and head and neck-adenocarcinoma for men and cancer of the oral cavity, melanoma-thinner nodular, vulva, head and neck-squamous cell carcinoma, and cervical adenocarcinoma for women. Smoking-related cancers include cancer of the oesophagus-adenocarcinoma, stomach-cardia, liver/intrahepatic bile ducts, pancreas, oral cavity, nasal and paranasal sinuses, head and neck-adenocarcinoma, head and neck-squamous cell carcinoma, and Hodgkin lymphoma.

Fig. 1. Hazard ratios of established obesity-related cancers and potential obesity-related cancers according to BMI level, with 95% CIs.