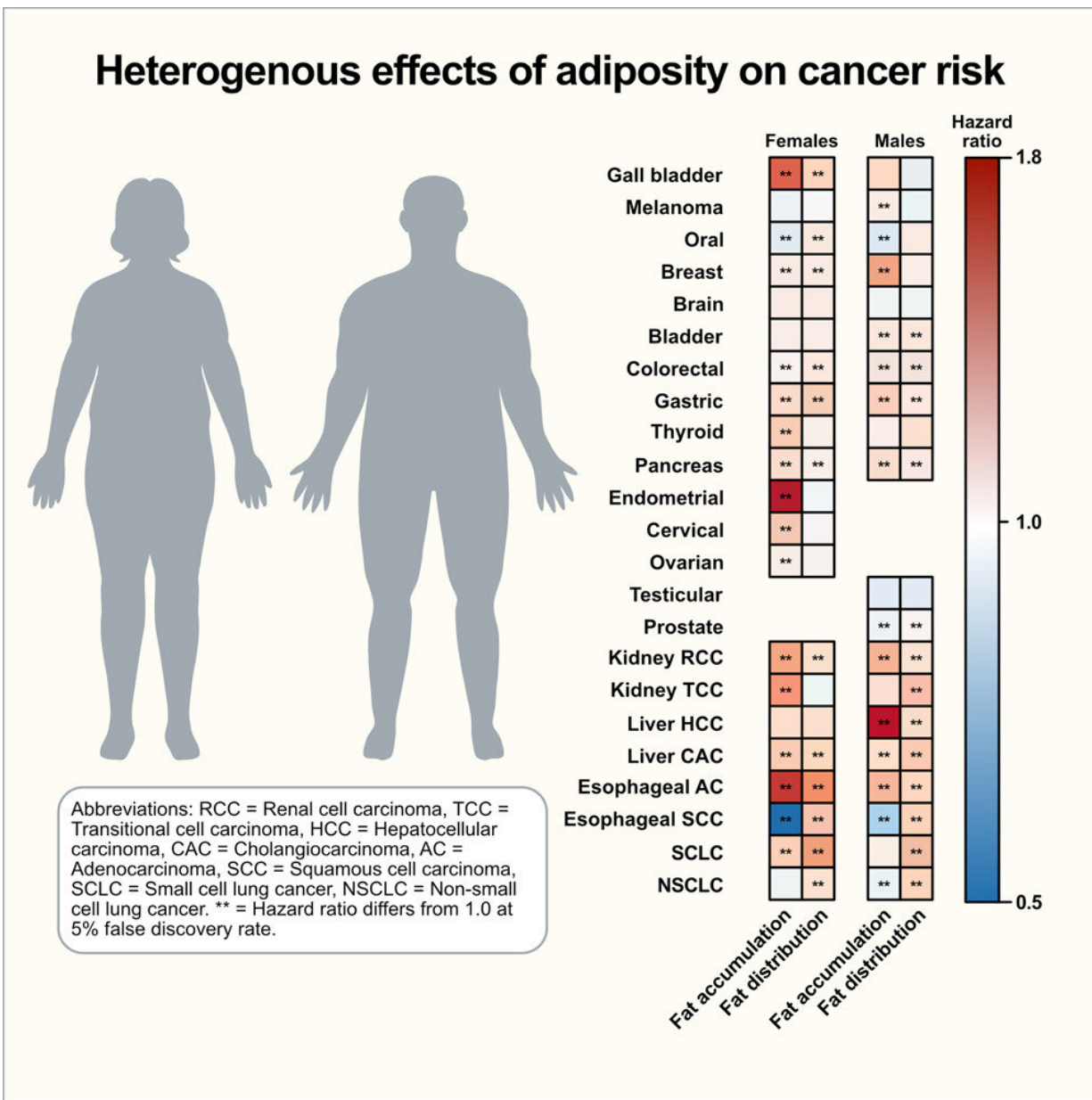


Cancer has an obesity-related risk factor, and it depends on sex and cancer type

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Graphical abstract. Credit: *Cancer Cell* (2023). DOI: 10.1016/j.ccell.2023.05.010

Obesity has been previously linked to an increased risk of cancer, but most studies have not differentiated the risks between male and female patients. A new study published June 12 in the journal *Cancer Cell* takes a closer look at this connection. The investigators report that both overall fat accumulation and fat distribution in different parts of the body confer different cancer risks depending on sex. Additionally, the risks vary across cancer types, like colorectal, esophageal, and liver cancer.

"Doctors and scientists are aware that obesity increases [cancer risk](#), but this connection is less well known to members of the public," says first author Mathias Rask-Andersen, a researcher at Uppsala University in Sweden. "These observations are important for [risk assessment](#) and to gain a deeper understanding of adiposity-related disease risks."

"An important aspect of obesity-associated disease risk is the distribution of fat in different compartments of the body," says senior author Åsa Johansson, also of Uppsala University. "Fat stored in the abdomen is considered more pathogenic compared to [subcutaneous fat](#). In addition, the amount of fat stored in different compartments, as well as the rates of most cancers, is known to differ between females and males. These facts motivated a careful sex-stratified analysis of adiposity-related cancer risk."

The investigators used data from the UK Biobank, a cross-sectional cohort of 500,000 U.K. residents aged between 37 and 73 who were recruited between 2006 and 2010 and then followed for a mean time of 13.4 years. Among the data collected from participants in the database were details about the distribution of fat in their bodies and whether they developed cancer.

The researchers used Cox proportional hazards modeling to identify the associations between the levels and distribution of fat in the participants' bodies at the time of the initial assessment and their later rates of cancer. The team found that all [cancer types](#) except brain, cervical, and testicular cancers are associated with at least one obesity-related trait.

In [female patients](#), the strongest links between overall fat accumulation and cancer were in gallbladder cancer, endometrial cancer, and esophageal adenocarcinoma. In males, the strongest links between overall fat accumulation and cancer were in [breast cancer](#), [hepatocellular carcinoma](#), and renal cell carcinoma. In terms of fat accumulation and distribution, there were differential effects between sexes on colorectal, esophageal, and [liver cancer](#). For instance, a larger proportion of fat stored in the abdomen was associated with esophageal squamous cell carcinoma in females, but not in males. Additionally, body fat accumulation was associated with a high risk for hepatocellular carcinoma in males, an effect that was not present in females.

"We were surprised to see that there appeared to be a difference in the effect of obesity on cancer risk, not only between males and females, but also between post- and pre-menopausal females," Johansson says. "Most remarkable, obesity is only a risk factor for breast cancer after menopause, probably due to the change in estrogen production in association with menopause."

The investigators note limitations to this study, especially that it was limited largely to British White participants, which make up almost 95% of the UK Biobank. They explain that their findings may differ from or may not be applicable to other ethnicities. They also say that because participants were older, the results are likely not directly transferable to younger populations.

They plan to do additional studies to help develop a complete

understanding of the molecular mechanisms underlying these findings. Future work will also focus on genetic and environmental [risk factors](#) for cancer, which are not static but differ across a person's lifespan. This includes taking a closer look at the variation in the effects of obesity before and after menopause.

"Given the rapidly increasing rates of obesity globally, obesity is now the fastest-growing risk factor for overall cancer risk," Rask-Andersen says. "Measures to prevent and reduce the occurrence of [obesity](#) and being overweight are therefore highly motivated. However, it is important to consider that reducing weight does not eliminate the risk of cancer. There are still many individual risk factors that play a much larger impact on specific types of cancer, such as smoking for lung cancer and exposure to sun for skin cancer."

More information: Mathias Rask-Andersen, Adiposity and sex-specific cancer risk, *Cancer Cell* (2023). [DOI: 10.1016/j.ccell.2023.05.010](#)

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