

Genetics weigh heavy on childhood cancer survivors' risk of developing obesity

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Researchers at St. Jude Children's Research Hospital combined genetic and clinical risk factors to create a method to predict which childhood cancer patients are most likely to develop severe or "morbid" obesity as adults. The tool will give physicians and survivors the information to help motivate positive lifestyle changes. The research was published today in *Nature Medicine*.

Childhood [cancer](#) survivors are at a high risk of developing many chronic illnesses. Of particular concern are conditions that can affect the heart, because certain cancer therapies can cause long-term cardiac damage. Adult survivors of [childhood cancer](#) have high rates of [obesity](#), which is a major risk factor for cardiac disease.

St. Jude scientists developed a method to predict, at diagnosis, which children with cancer are at the highest risk of developing severe obesity as adults. Using the tool, researchers calculated that survivors with the highest genetic risk [score](#) were at 53 times greater risk of obesity compared to survivors with the lowest genetic risk score. The risk of obesity was independent of other general

risk factors. The National Institutes of Health defines severe or "morbid" obesity as having a body mass of 40 kg/m² or higher.

The St. Jude method provides an opportunity for targeted interventions for children and their families to adopt healthy lifestyles early in life to prevent obesity in adulthood. This research is one of the first studies to show the contribution of genetics and treatment-related risk factors to increased risk of developing obesity and related traits that survivors experience compared to the general population.

"It is important for [childhood](#) cancer survivors to know if they are at risk for developing various chronic conditions," said first and co-corresponding author Yadav Sapkota, Ph.D., St. Jude Department of Epidemiology and Cancer Control. "We have developed a prediction model that can help healthcare providers identify which survivors are likely to develop severe obesity."

"In the future as this type of genetic testing becomes more clinically available, this knowledge will provide clinicians with the opportunity to intensify efforts to promote healthy weight maintenance in survivors at high risk for severe obesity," said Melissa Hudson, M.D., co-author and co-leader of the St. Jude Cancer Control and Survivorship Program. "Good nutrition and regular physical activity are important for all [cancer patients](#) but are particularly important for those with genetic and treatment risks associated with obesity," she said.

Obesity risk scores

The obesity risk score is based on clinical, lifestyle and [genetic factors](#). It can be calculated when the patient is diagnosed with childhood cancer.

The scientists applied their genetic risk models to more than 4,000 St. Jude childhood cancer

survivors enrolled in the St. Jude Lifetime Cohort Study (St. Jude LIFE). Participants have had whole genome sequencing of their germline (inherited) DNA. St. Jude LIFE participants return to St. Jude throughout their adult lives for regular health screenings.

Researchers checked to see how their tool performed in the [survivor](#) health data, predicting adult obesity in St. Jude LIFE childhood cancer survivors of European ancestry. The genetic risk score is an aggregate score derived from approximately 2.1 million common genetic variants associated with [body mass](#) index developed in individuals of European ancestry in the general population.

When investigators applied the same method to a different cohort of adult survivors of childhood cancer, they found a slightly weaker signal, but the score still predicted [severe obesity](#). The Childhood Cancer Survivor Study (CCSS) provided the second cohort of 6,064 survivors. CCSS is a retrospective analysis of cancer survivors at least five years post-therapy treated at one of 31 institutions in the U.S. and Canada.

"This is a really important advance for the care of survivors," said co-corresponding author Yutaka Yasui, Ph.D., St. Jude Department of Epidemiology and Cancer Control. "We can identify the highest risk survivors with this method—a genetic method. We can know which childhood cancer patients are high risk for severe or other obesity early on in life, so we can give personalized advice to them."

An ancestry problem

While the findings hold tremendous value for [childhood cancer survivors](#) of European ancestry, the genetic risk score was not predictive of obesity in people of African ancestry in either cohort. The researchers addressed this by developing a different genetic risk score customized for people of African ancestry.

"Populations of non-European ancestry are understudied," Sapkota said. "That's why genomic studies often don't apply directly to them. The number of genetic studies of African ancestry and

obesity is very small, but we still explored them to create a separate, ancestry-specific risk score. When we did that, we were able to predict obesity with statistical significance in [survivors](#) of African ancestry. That means, to better predict a risk of a given disease by using genetic variables, we need to consider the findings from within shared ancestries."

More information: Yadav Sapkota, Genetic risk score enhances the risk prediction of severe obesity in adult survivors of childhood cancer, *Nature Medicine* (2022). [DOI: 10.1038/s41591-022-01902-3](#). www.nature.com/articles/s41591-022-01902-3

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