

# Survivors of childhood leukemia with Down syndrome have unique health risks, benefits

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Doctors have long recognized that children with Down syndrome are significantly more susceptible to leukemia, and have believed that they also were at higher risk of treatment-related chronic conditions. Now, new research led by UCSF Benioff Children's Hospital San Francisco, with data from the Childhood Cancer Survivor Study, challenges this belief and offers fresh insights into survivorship.

In their investigation, researchers found that, among survivors of [childhood leukemia](#), those with Down [syndrome](#) had treatment-related chronic [conditions](#) at generally the same rate as survivors without the genetic disorder.

They did find that those with Down syndrome had an increased risk of severe or multiple conditions, including cataracts, hearing loss and thyroid dysfunction. However, when the researchers looked at the onset of these conditions, they determined that they appeared to be less likely related to [leukemia](#) treatment, and more likely related to the natural consequences of Down syndrome.

They also found that those in the study with Down syndrome had a significantly decreased risk of second cancers related to their leukemia treatment.

The findings were published in the journal *Cancer* on Nov. 3, 2017.

The researchers, led by Robert Goldsby, MD, of UCSF Benioff

Children's Hospital San Francisco, tracked the outcomes of 154 pediatric leukemia survivors with Down syndrome, a disorder caused by an extra copy of chromosome 21. They compared them with 581 non-Down syndrome survivors, matched by age at diagnosis, race, gender and treatment. Both groups had a minimum of five years' survivorship. Approximately two-thirds of survivors had been diagnosed with leukemia between the ages of 1 and 4, and the majority were aged between 10 and 29 at the time of last follow-up.

The study participants had been diagnosed with [acute lymphoblastic leukemia](#) (ALL), the most common pediatric [cancer](#), or [acute myeloid leukemia](#) (AML), which together make up about 30 percent of all childhood cancers.

## **Risks May Be 'Natural History' of Down Syndrome**

The overall survival at 25 years post-diagnosis was similar in both groups: 88 percent for those with Down syndrome, versus 84 percent for those without.

While survivors with Down syndrome were at higher risk of certain [chronic health conditions](#), these had been apparent prior to or in the early years following diagnosis, suggesting they may reflect the "natural history" of Down syndrome. When the researchers looked at chronic conditions occurring at least five years after diagnosis, the rates were similar for both groups: 20 percent for the Down syndrome group, versus 16.5 percent for the non-Down syndrome group.

The researchers noted that, historically, the risks of chronic conditions for the Down syndrome survivors may have been inflated. "The patients' chronic health conditions were usually reported by their parents," said Goldsby of the UCSF Department of Pediatric Hematology/Oncology. "We know from previous studies that parents are more concerned about

future health and late effects than patients, and are more likely to over-report events."

"Nevertheless, we cannot exclude the possibility that treatment for childhood leukemia might exacerbate or increase the risk for some of these conditions," said senior author Wendy Leisenring, ScD, of the Fred Hutchinson Cancer Research Center in Seattle. "It is possible that children with Down syndrome and underlying heart disease may not have survived the required five years to be eligible for the study."

Regarding the incidence of second cancers in the Down syndrome survivors, the researchers found a single case (0.6 percent), versus 26 cases (4.3 percent) in the non-Down syndrome group.

"The lower risk of second cancers may indicate a potential protective effect of one or more chromosome 21-localized genes," said Goldsby, who is the medical director of the UCSF Childhood Cancer Survivors Program. "Studies assessing genetic and environmental modifiers that may influence these risks are warranted."

## **Kids with Down Syndrome Twice as Likely to Survive AML**

Previous studies have shown that Down syndrome patients are less likely to survive ALL than non-Down syndrome patients, but are more than twice as likely to survive AML – approximately 80 percent, compared with 35 percent – due to a genetically distinct form of AML that may be more sensitive to chemotherapy. Down syndrome survivors of both types of leukemia are more likely to suffer from acute toxicities relating to chemotherapy, such as mucositis, sepsis and pulmonary complications.

Children with Down syndrome face a 2-3 percent overall risk of

developing AML or ALL, according to the American Cancer Society. Among the general pediatric population in the United States, approximately 3,500 are diagnosed with leukemia each year, or about a 0.0052 percent rate overall.

**More information:** Robert E. Goldsby et al. Long-term sequelae in survivors of childhood leukemia with Down syndrome: A childhood cancer survivor study report, *Cancer* (2017). [DOI: 10.1002/cncr.31065](https://doi.org/10.1002/cncr.31065)

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