

## Survivors of childhood cancer are at great risk of heart problems in adulthood

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Survivors of childhood cancer are at increased risk of suffering prematurely from cardiovascular disease in adulthood, according to a study published today (Friday) in the *European Heart Journal*.

In the first study to investigate the long-term health of <u>childhood cancer</u> <u>survivors</u> by means of systematic and comprehensive clinical evaluation of their health in comparison to the general population, researchers in Germany found that as adults these people were at increased risk of having <u>high blood pressure</u> and dyslipidaemia (abnormal, usually high, levels of cholesterol and other fats in the blood). These conditions occurred six and eight years earlier respectively when compared with the general population.

In addition, childhood cancer survivors had a nearly two-fold increased risk of cardiovascular diseases such as <u>congestive heart failure</u> and venous thromboembolism. Cardiovascular disease was found in 4.5% of survivors and occurred in the majority before they reached the age of 40, nearly eight years earlier than in the general population.

Between October 2013 and February 2016, a total of 951 adult longterm survivors of childhood cancer, who were part of the "Cardiac and vascular late sequelae in long-term survivors of childhood cancer" (CVSS) study, underwent a clinical examination that included assessing factors that might put them at higher risk of <u>cardiovascular disease</u>, such as high blood pressure and dyslipidaemia. The researchers also checked their medical history, whether or not they smoked and whether there was



any family history of cardiovascular disease. Their ages ranged from 23 to 48 at the time of this follow-up. The results were compared with over 15,000 people selected from the general population.

Professor Joerg Faber, head of the Department of Paediatric Haematology / Oncology / Haemostaseology at the University Medical Centre of the Johannes Gutenberg University Mainz, one of the three principal investigators, said: "Our results show that these survivors of childhood cancer have a substantially elevated burden of prematurely occurring traditional <u>cardiovascular risk factors</u> and cardiovascular diseases."

Professor Wild, who is head of the Department of Preventive Cardiology and Preventive Medicine at the University Medical Centre of the Johannes Gutenberg University Mainz and principal investigator of the German Centre for Cardiovascular Research (DZHK), added: "In particular, the premature onset of high blood pressure and blood lipid disorders may play an important role in the development of severe cardiovascular conditions, such as heart disease and stroke in the long term.

"We also found that a remarkable number attended their clinical examination for this study with previously unidentified cardiovascular risk factors and cardiovascular disease. For example, only 62 out of 269 were aware of having dyslipidaemia. Consequently, 207, approximately 80%, were only diagnosed at that point. This applies to high blood pressure in the arteries as well."

High blood pressure and dyslipidaemia were the most common cardiovascular risk factors identified in the childhood cancer survivors, 23% and 28% respectively, whereas diabetes was only found in two per cent. These conditions occurred earlier than in the general population; 17% and 25% had high blood pressure or dyslipidaemia respectively



before the age of 30, and 39% and 38% by the age of 45.

At least one cardiovascular disease was identified in 4.5% of the survivors; venous thromboembolism was the most common (2%), followed by congestive heart failure (1.2%), stroke or peripheral artery disease (0.5% for each), atrial fibrillation (0.4%) and coronary heart disease (0.3%). These conditions occurred in 31 out of 43 people who were younger than 40.

The researchers say that these findings show that survivors of childhood cancer have a considerably greater risk of cardiovascular disease - a risk that continued to increase with age rather than levelling off - and this meant that, in the longer term, they may be more likely to die earlier than the general population.

However, it might be possible to prevent this, said Professor Wild. "Early systematic screening, particularly focusing on blood pressure and lipid measurements, might be suggested in all childhood cancer survivors irrespective of the type of cancer or treatment they had had. This might help to prevent long-term cardiovascular diseases by intervening early, for instance by modifying life styles and having treatment for high blood pressure."

Professor Faber added: "Usually survivors are followed for only five to ten years after completion of therapy, and this is focused on the risk of the cancer returning and the acute adverse effects of their treatment, rather than on other conditions. Current guidelines recommend cardiovascular assessments only for sub-groups known to be at risk, such as for patients who were treated with anthracycline therapy and / or radiation therapy. However, further investigations are needed to answer questions about the best follow-up care."

Treatments for childhood cancer include chemotherapy and



radiotherapy, both of which can affect the heart, causing temporary or sometimes permanent damage to heart cells and blood vessels. The mechanisms for this are not all fully understood, particularly for longterm chronic effects, but certain genetic factors seem to increase the probability of adverse effects on the heart.

In an accompanying editorial, Dr John Groarke, a cardiovascular medicine specialist at Brigham and Women's Hospital Heart and Vascular Centre, Boston, USA, who was not involved in the research, writes: "The prospective and systematic phenotyping of survivors and comparison with control cohorts are welcome strengths of this study. Previous reports on the burden of CV <u>disease</u> in childhood cancer survivors have mostly relied on patient-reported outcomes and/or failed to consider relevant controls..."

He points out that treatments for childhood cancer have improved since the 1980s. "Refinements in radiation protocols and reductions in cumulative anthracycline exposure are succeeding in reducing late mortality among 5-year survivors of childhood cancer." He concludes: "There is a pressing need for research to inform practice guidelines for screening, prevention and management. There are now sufficient observational data that childhood cancer survivors represent a high-CV risk cohort that warrant more comprehensive care systems to improve CV outcomes. It is time to progress from risk observation to risk modification."

**More information:** "Burden of cardiovascular risk factors and cardiovascular disease in childhood cancer survivors: data from the German CVSS-study", by J. Faber et al. *European Heart Journal*. DOI: 10.1093/eurheartj/ehy026

"Cardiovascular vulnerability of childhood cancer survivors: time to progress from risk observation to risk modification", by John D.



## Groarke. European Heart Journal. DOI: 10.1093/eurheartj/ehy099

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