

## Abstract

### Late Pulmonary Adverse Effects in Childhood and Adolescent Acute Lymphoblastic Leukaemia Survivors: A Cross-sectional ALL-STAR Lungs study

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#### Background

Acute lymphoblastic leukaemia (ALL) is the most common malignancy in children, with improved survival rates now reaching 95%. However, 25-50% of survivors experience significant treatment-related toxicities. This study investigates late pulmonary adverse effects, including respiratory symptoms and pulmonary function deficit (PFD), in children and adolescent ALL survivors included in the Acute Lymphoblastic Leukemia Survivor Toxicity And Rehabilitation study.

#### Methods

This Danish national cross-sectional study (February 2019 - May 2024) compared standard and novel pulmonary function measures and questionnaire-reported respiratory symptoms from 192 ALL survivors with 213 matched controls.

#### Results

Most ALL survivors exhibited pulmonary function comparable to controls. Overall, ALL survivors experienced a significantly higher prevalence of exertional dyspnoea (14% vs 3%). Prevalences of exertional dyspnoea were markedly elevated among groups of high-risk stratified ALL survivors, with the highest severity in 18% of survivors receiving high-risk chemotherapy (HR) and 26% of those receiving both high-risk chemotherapy and stem cell transplantation (HR-SCT). Pulmonary function tests indicated PFD by impaired mean z-scores in forced expiratory volume in the first second, diffusing capacity for carbon monoxide and diffusing capacity for nitric oxide, especially among HR and HR-SCT survivors.

#### Conclusions

Reassuringly, most ALL survivors demonstrated pulmonary function comparable to that of their peers. However, the findings emphasise the importance of enhanced follow-up recommendations with timely detection of PFD, including baseline pulmonary function tests, tailored monitoring and early management strategies to improve lung health outcomes for this vulnerable population, particularly in HR and HR-SCT survivors.