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## **ABSTRACT**

Longitudinal Symptoms Predict Future Clinically Assessed Chronic Health Conditions (CHCs) in Adult Survivors of Childhood Cancer: A Follow-Up Study Over Two Decades

**Background:** Childhood cancer survivors experience a high burden of CHCs. However, clinical validity of using self-reported symptoms to predict future CHCs has not been examined in this population.

**Methods:** 735 adult survivors of childhood cancer completed symptom surveys at 3 timepoints from 1994 to 2018, via participation in both the Childhood Cancer Survivor Study and the St Jude Lifetime Cohort Study. Ten symptom domains (sensory, cardiac, pulmonary, musculoskeletal, memory, pain, fatigue, nausea, anxiety, depression) were self-reported. Using latent class analyses, survivors were classified into 4 groups: 1) high physical & psychological symptoms, 2) moderate-high physical & psychological symptoms, 3) moderate-high physical symptoms alone, or 4) low physical & psychological symptoms. Hypertension/dyslipidemia, respiratory, endocrine, peripheral neuropathy, and musculoskeletal CHCs were clinically assessed and graded using modified CTCAE criteria. Poisson regression explored associations of latent classes with new onset (grades 2-4 vs. 0-1) and/or worsened CHCs that occurred after symptom reports.

**Results:** At each survey timepoint, survivors' mean ( $\pm$ SD) ages were 27 $\pm$ 5, 36 $\pm$ 7 and 40 $\pm$ 7 years; mean years from diagnosis were 18 $\pm$ 5 years at clinical assessment. Survivors were mostly female (51%), Caucasian (90%) and treated for leukemia (46%). Compared to survivors with low physical & psychological symptoms at baseline, those with moderate-high physical & psychological symptoms at baseline had elevated risk of new onset and/or worsened hypertension/dyslipidemia (RR 1.31, 95% CI 1.06-1.63); those with high physical & psychological symptoms at baseline had greater risk of new onset and/or worsened respiratory (RR 1.39, 95% CI 1.04-1.86), musculoskeletal (RR 1.93, 95% CI 1.26-2.95) and peripheral neuropathy (RR 3.89, 95% CI 2.44-6.22) CHCs. Improvement of symptoms over time significantly decreased the risk of developing peripheral neuropathy (RR 0.53, 95% CI 0.36-0.79) and respiratory (RR 0.69, 95% CI 0.55-0.87) CHCs. However, associations of symptoms with these CHCs were not attenuated when adjusting for the influence of age, sex, treatment and smoking status.

**Conclusions:** Routine symptom screening may identify survivors at risk for new onset and/or worsened chronic health conditions, beyond the known risk factors (e.g., demographic, cancer therapy and smoking status), which would permit clinicians the opportunity for early or preventative intervention strategies.

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