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**Title:** Symptom Phenotypes, Physical Inactivity and Smoking among Long-term Survivors of the Childhood Cancer Survivor Study (CCSS)

**Limit=300 words, not counting title, currently= 296**

**Background:** The aims of this study were to examine physical and psychological symptom burden patterns among childhood cancer survivors and their associations with risky health behaviors.

**Methods:** CCSS participants (N=17,231; Mean age=27.4 [5.98]; 79% non-Hispanic white; 48% female) self-reported sensory, motor, cardiac, respiratory, pain, gastrointestinal, fatigue, memory, depression, and anxiety symptoms at baseline; latent class analysis identified symptom-pattern classes. Self-reported smoking status (current, former, never) and physical activity (Inactive: metabolic equivalents [METs]<450; Active: METs≥450) were assessed a median of 6.3 years after baseline. Logistic regression examined associations between symptom-pattern class membership and health behaviors at follow-up, adjusting for sex, age, health insurance, and global chronic health conditions (CHCs) at baseline.

**Results:** Five classes of symptom patterns were identified: 1) elevated across all symptoms (Global; 7.7%); 2) emotional distress and pain (Distress-Pain; 13.3%); 3) neurologic and pain (Neuro-Pain; 10.6%); 4) cardiopulmonary and pain (Cardio-Pain; 5.3%); 5) non-elevated symptoms (Norm; 63.1%). Compared to the Norm class, almost all other classes were associated with greater risk for physical inactivity (Cardio-Pain, OR=1.18 [1.07,1.31]; Neuro-Pain, OR=1.16 [1.07, 1.25]; Global, OR= 1.11 [1.01, 1.23]), and being a current smoker (Distress-Pain, OR=1.81 [1.54, 2.13]; Cardio-Pain, OR=1.91 [1.49, 2.46]; Neuro-Pain, OR =1.35 [1.11, 1.66]; Global, OR =3.25 [2.67, 3.96]). These classes were also associated with higher likelihood of being a former smoker.

**Conclusion:** Adjusting for insurance, CHCs, age, and sex, self-reporting of physical and psychological symptoms at baseline were associated with future inactivity, previous smoking behaviors, and future smoking behaviors among CCSS participants. Ongoing symptom burden may be preventing survivors from engaging in health optimizing behaviors or alternatively risky health behaviors may be used to cope with symptom burden (e.g., smoking to reduce distress). Of note, pain was prevalent in all elevated symptom-pattern classes, which suggests an important intervention target for improving health behaviors.