Title: Patterns and predictors of psychological distress in adult survivors of childhood cancer: A Childhood Cancer Survivor Study (CCSS)

Background: Screening for psychological distress is an important part of comprehensive survivorship care. While elevated symptoms of depression and anxiety have been reported, patterns of emotional comorbidity have not been examined. The aims of this study are to identify clusters of distress symptoms and to examine disease, treatment and demographic predictors.

Methods: Latent profile analysis was conducted using 3 domains (depression, anxiety, somatization) from the Brief Symptom Inventory – 18 in siblings (N=3085) and 5+ year survivors (N= 16032) from the CCSS. High distress was defined using t-score >63. Bayesian information criterion and Lo-Mendell-Rubin adjusted certainty were used to select the optimal cluster number. Multinomial logistic regression was used among survivors to identify disease, treatment and demographic predictors of cluster membership stratified by sex.

Results: Four latent clusters were identified: low distress on all 3 domains (well-adjusted); high distress on all 3 domains (global distress); high somatization relative to anxiety and depression (somatic distress); high anxiety and depression relative to somatization (affective distress). Compared to siblings, fewer survivors were well-adjusted (62% *v*. 74%) and more had global distress (11% *v*. 5%), both p's<0.0001. Diagnosis-specific patterns of distress were identified (leukemia and bone cancer: global distress, CNS: affective distress, Hodgkin lymphoma and neuroblastoma: somatic distress). More male (66%) than female (58%) survivors were well-adjusted, but more females reported somatic (17% vs 10%) and global (12% vs 9%) distress, all p's<0.0001. Among females, fair/poor perceived health (OR 30.9, 95% CL 19.4-49.1; compared to excellent health), headache (OR 2.69, 95% CL 2.24-3.24), and antimetabolite chemotherapy (OR 1.31, 95% CL 1.10-1.55) were associated with global distress. Perceived health and pain were associated with global distress in males.

Conclusion: Results support the conceptual distinction between physical (somatic) versus affective (anxiety and depression) symptoms of distress and highlight sex differences and health-related predictors of distress.