

Prospective Prediction of Improved Health-Related Quality of Life (HRQL) Among Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

Madeline R. Horan, PhD^{1,*}; Fiona Schulte, PhD^{2,*}; Yan Chen, MSc³; Yutaka Yasui, PhD¹; Wendy Leisenring, ScD⁴; Paul Nathan, MD⁵; Kevin C. Oeffinger, MD⁶; Leslie L. Robison, PhD¹; Melissa M. Hudson, MD^{1,7}; Gregory T. Armstrong, MD, MSCE¹; Kevin R. Krull, PhD⁸; I-Chan Huang, PhD¹

¹ Department of Epidemiology & Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee, U.S.A.

² Department of Oncology, University of Calgary, Calgary, Alberta, Canada

³ Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada

⁴ Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, U.S.A.

⁵ Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, Ontario, Canada

⁶ Department of Medicine, Duke University, Durham, North Carolina, U.S.A.

⁷ Department of Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee, U.S.A.

⁸ Department of Psychology & Biobehavioral Sciences, St. Jude Children's Research Hospital, Memphis, Tennessee, U.S.A.

* Co-first authors with equal contribution

Word count: 2,969/3,000 characters (including space)

Background/Purpose: Risk factors (e.g., poor lifestyle, chronic health conditions, emotional distress, and neurocognitive dysfunction) for predicting longitudinal decline in HRQL in adult survivors of childhood cancer have been previously identified (Schulte et al., JAMA Network Open, 2022). However, factors predicting improved HRQL over time have not been examined.

Methods: Study participants were 371 and 583 adult childhood cancer survivors with suboptimal Physical and Mental Component Summaries (PCS, MCS) of HRQL, respectively, from the CCSS who completed baseline (T0 around 1994) and two follow-up surveys (T1 around 2003, T2 around 2014). Sociodemographic, lifestyle, and emotional factors and chronic health conditions (CHCs) were assessed at T0 and T1. Chronic health conditions were considered present if Common Terminology Criteria for Adverse Events (CTCAE) grades of any CHCs within a specific organ system were 2, 3, or 4 (i.e., moderate to life-threatening). Neurocognitive function was assessed at T1. The SF-36 assessed PCS and MCS at T1 and T2, with scores classified as optimal (≥ 40) or suboptimal (< 40). Improved HRQL was defined as a change from suboptimal at T1 to optimal at T2. The cohort was randomly split into training (80%) and test (20%) datasets for model development and validation. Among survivors in the training dataset with suboptimal HRQL at T1, multivariable logistic regression identified factors at T0,

T1, and/or changes in factors from T0-T1 predicting improved HRQL (vs. persistently suboptimal HRQL from T1-T2 as the reference) using backward variable selection (stopping at $p < 0.05$). Area under the receiver operating curve (AUC) evaluated model performance in the test dataset.

Results: 191 and 362 survivors had improved PCS and MCS, respectively, from T1 to T2. The mean \pm SD age at T0, T1, and T2 were 24.5 \pm 7.6, 32.2 \pm 7.4, and 43.8 \pm 7.4 years, and 55.2% of the survivors were female. T0 factors predicting improved PCS were male sex (OR 2.0, 95% CI 1.1-3.6) and family income \geq \$60,000 (OR 2.9, 95% CI 1.2-7.1). Having no cardiovascular (OR 2.3, 95% CI 1.3-4.0), musculoskeletal (OR 2.7, 95% CI 1.3-5.6), or neurologic (OR 3.9, 95% CI 2.0-7.1) CHCs at T1 predicted improved PCS, and so did higher educational attainment from T0 to T1 (OR 2.2, 95% CI 1.1-4.3). Most of the factors predicting improved MCS were from T1, including lack of neurologic CHCs (OR 2.2, 95% CI 1.4-3.6), no anxiety (OR 2.2, 95% CI 1.5-3.3), and no deficits in task efficiency (OR 1.8, 95% CI 1.2-2.6). The test-set AUC of improved PCS was 0.73 (95% CI 0.62-0.83) and improved MCS was 0.72 (95% CI 0.63-0.81).

Conclusions: We found that maintaining good physical and mental health conditions post-cancer therapy is associated with improved HRQL in childhood cancer survivors. Our findings emphasize the potential benefits of long-term follow-up care that facilitates prevention and remediation of chronic health conditions and promotes mental health.