

## Impact of Exercise on Psychological Burden, Quality of Life, and Cognitive Dysfunction in Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)

Emily S. Tonorezos, MD MPH;<sup>1,2</sup> Jennifer S. Ford, PhD;<sup>1,2</sup> Linwei Wang, MS;<sup>3</sup> Kirsten K. Ness, PT PhD;<sup>4</sup> Yutaka Yasui, PhD;<sup>4</sup> Wendy Leisenring, ScD;<sup>5</sup> Charles A. Sklar, MD;<sup>1</sup> Leslie L. Robison, PhD;<sup>4</sup> Kevin C. Oeffinger, MD;<sup>6</sup> Paul C. Nathan, MD MSc;<sup>7</sup> Gregory T. Armstrong, MD; MSCE,<sup>4</sup> Kevin Krull, PhD;<sup>4\*</sup> Lee W. Jones, PhD<sup>1,2\*</sup>

<sup>1</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA

<sup>2</sup>Weill Cornell Medical College, New York, NY USA

<sup>3</sup>BC Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada

<sup>4</sup>St. Jude Children's Research Hospital, Memphis, TN, USA

<sup>5</sup>Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA, USA

<sup>6</sup>Duke Cancer Institute, Duke University, Durham, NC USA

<sup>7</sup>The Hospital for Sick Children and University of Toronto, Toronto, Canada

\*Denotes equal contribution

**Background:** Adult survivors of childhood cancer are at risk for adverse psychological outcomes. Whether exercise can attenuate this risk is unknown.

**Methods:** Using a longitudinal design, 6199 CCSS participants (median [range] age 34 years [22-54] and median [range] age at diagnosis 10 years [0-21]) completed a baseline questionnaire assessing vigorous exercise, medical and psychological conditions. Psychological outcomes were evaluated in a subsequent questionnaire a median of 7.8 years later (range 0.1-10). Primary outcome was overall psychological burden, defined as: symptom level above the 90<sup>th</sup> percentile of population norms on the Brief Symptom Inventory-18 for depression, anxiety, or somatization ; cancer-related pain; cognitive impairment; or poor quality of life. Log-binomial regression estimated associations between exercise [total metabolic equivalent-hrs wk<sup>-1</sup> (MET-hrs wk<sup>-1</sup>)] and these outcomes adjusting for cancer diagnosis/treatment, demographics, and baseline medical/psychological illness.

**Results:** The prevalence of overall psychological burden at follow-up was 71.3%. The prevalence of depression was 11.4%, anxiety 7.4%, and somatization 13.9%. Among those not engaged in vigorous exercise, the prevalence of overall psychological burden was 75.9%, compared to 68.6% in those who exercised  $\geq 3$  MET-hrs wk<sup>-1</sup> ( $p < 0.001$ ). Compared to 0 MET-hrs wk<sup>-1</sup> of vigorous exercise, the adjusted prevalence ratio (PR) for overall psychological burden was 0.98 (95% CI, 0.95-1.01) for 3-6 MET-hrs wk<sup>-1</sup>, 0.93 (95% CI, 0.90-0.96) for 9-12 MET-hrs wk<sup>-1</sup>, and 0.94 (95% CI, 0.90-0.98) for 15-21 MET-hrs wk<sup>-1</sup>. Compared to not reporting vigorous exercise, 9 to 12 MET-hrs wk<sup>-1</sup> was associated with an adjusted PR of 0.76 (95% CI, 0.62-0.93;  $p = 0.004$ ) for depression and 0.79 (95% CI, 0.66-0.94;  $p = 0.003$ ) for somatization. Vigorous exercise was associated with higher cognitive function in domains of task completion, organization, and working memory ( $p$ 's  $< 0.05$ ) but was not associated with cancer pain or quality of life.

**Conclusions:** Vigorous exercise is associated with lower psychological burden and less cognitive impairment in long-term survivors of childhood cancer.