## Modifiable Lifestyle Factors and Risk for Subsequent Neoplasms in Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Lenat Joffe<sup>1</sup>, Sedigheh Mirzaei<sup>2</sup>, Shalini Bhatia<sup>2</sup>, Himani Darji<sup>2</sup>, Kirsten K. Ness<sup>3</sup>, Aron Onerup<sup>3,4</sup>, Elena J. Ladas<sup>5</sup>, Cindy Im<sup>6</sup>, Philip J. Lupo<sup>7</sup>, Kevin C. Oeffinger<sup>8</sup>, Danielle Novetsky Friedman<sup>9</sup>, Rebecca M. Howell<sup>10</sup>, Miriam R. Conces<sup>11</sup>, Michael A. Arnold<sup>12</sup>, Gregory T. Armstrong<sup>3</sup>, Joseph P. Neglia<sup>6</sup>, Yutaka Yasui<sup>3</sup>, Nina S. Kadan-Lottick<sup>13</sup>, Lucie M. Turcotte<sup>6</sup>

<sup>1</sup>Department of Pediatrics, Cohen Children's Medical Center, Northwell, New Hyde Park, NY, USA

<sup>2</sup> Department of Biostatistics, St Jude Children's Research Hospital, Memphis, TN, USA

<sup>3</sup> Department of Epidemiology and Cancer Control, St Jude Children's Research Hospital, Memphis, TN, USA

<sup>4</sup> Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

<sup>5</sup> Department of Pediatrics, Columbia University Irving Medical Center, New York, NY, USA

<sup>6</sup> Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA

<sup>7</sup> Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA

<sup>8</sup> Duke University School of Medicine and Duke Cancer Institute, Durham, NC, USA

<sup>9</sup> Memorial Sloan Kettering Cancer Center, New York, NY, USA

<sup>10</sup> Department of Radiation Physics, MD Anderson Cancer Center, Houston, TX, USA

<sup>11</sup> Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH, USA

<sup>12</sup> Department of Pathology and Laboratory Medicine, Children's Hospital Colorado, Aurora, CO, USA

<sup>13</sup> Departments of Oncology and Cancer Prevention and Control, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA

**Purpose**: High body mass index (BMI) and low physical activity (PA) levels are risk factors for adultonset cancers. Limited data exist on whether these factors increase subsequent neoplasm (SN) risk among survivors of childhood cancer.

**Methods**: Associations between time-varying self-reported BMI / maximum self-reported PA (metabolic task hours per week [MET-h/wk]) and SN risk were evaluated among five-year survivors, diagnosed 1970-1999 at <21 years old, enrolled in the Childhood Cancer Survivor Study. BMI/PA were assessed prior to SN development, first at cohort entry and up to six times thereafter. Cumulative incidence and relative risks (RRs), adjusted for demographic and clinical variables, were calculated for any, subtype (hematologic, solid organ, central nervous system [CNS], skin), and specific (breast, thyroid, colorectal, meningioma) SNs.

**Results**: Among 22,716 survivors, we identified 2,554 SNs among 2,156 individuals (57% female, median age at SN diagnosis: 37.35 years [range 13.7-63.3]). Survivors with lower PA had a higher 30-year SN cumulative incidence: 18.6% (95%CI 17.0-20.3) for 0 MET-h/wk versus 10.9% (95%CI 9.9-12.1) for 15-21 MET-h/wk. Obese BMI ( $\geq$ 30 kg/m<sup>2</sup>) was associated with increased risk for solid organ (RR, 1.22, 95%CI, 1.01-1.46), CNS (RR, 1.47, 95%CI 1.12-1.95), and skin (RR, 1.30, 95%CI 1.13-1.50) SNs, along with meningiomas (RR, 1.48, 95%CI 1.09-2.00) and thyroid carcinomas (RR, 1.64, 95%CI 1.15-2.34). Increased PA (15-21 MET-h/wk) was protective for any (RR, 0.61, 95%CI 0.53-0.71), solid organ (RR, 0.65, 95%CI 0.52-0.83), CNS (RR, 0.50, 95%CI 0.35-0.70), and skin (RR, 0.72, 95%CI 0.60-0.86) SNs, along with meningiomas (RR, 0.51, 95%CI 0.35-0.75) and thyroid carcinomas (RR, 0.53, 95%CI 0.34-0.83). BMI/PA were not associated with subsequent hematologic, breast, or colorectal cancers.

**Conclusions**: Childhood cancer survivors with high BMI are at increased risk for multiple types of SNs, while vigorous PA is protective for SN development. Modifiable lifestyle factor interventions should be included in future subsequent cancer investigations.