## Underdiagnosis and undertreament of modifiable cardiovascular risk factors: a Childhood Cancer Survivor Study (CCSS) report

Background: Survivors of childhood cancer exposed to cardiotoxic therapies are at increased risk of heart disease. Hypertension, dyslipidemia, and diabetes are modifiable cardiovascular risk factors (CVRFs) that synergistically increase this risk. Therefore, we aimed to determine the prevalence of and predictors associated with CVRF underdiagnosis and undertreatment in this population.

Methods: CCSS participants at increased risk of heart disease due to prior cancer therapy were enrolled in an ongoing randomized intervention trial (NCT03104543) to improve CVRF identification and treatment. Participants completed a baseline survey (CVRF status, lifestyle habits, attitudes towards healthcare), anthropometry, and blood draw. Blood pressure, low density lipoprotein, triglyceride, glucose and Hgb A1c were measured and classified as normal/abnormal per standard clinical criteria. Multivariable logistic regression estimated odds ratios (OR [95% confidence intervals]) associated with predictors and risk of CVRF underdiagnosis and undertreatment.

Results: As of January 2020, 522 participants (43% male) were available for analysis (47% response), with a median age 38y (range 20-65) and 28y (18-49) from original cancer treatment (75% anthracycline, 47% chest radiation). With mean measured BMI 27.3±6.5 kg/m<sup>2</sup>, self-reported prevalence rates were hypertension 27%, dyslipidemia 33%, and diabetes 9%. While 90% of participants had a routine check-up ≤2y ago, 58% had a measured CVRF in the abnormal range. Specifically, among previously undiagnosed participants, we observed rates of abnormal blood pressure (26%), lipids (17%), and glucose tolerance (27%). Among those with pre-existing hypertension, dyslipidemia, and diabetes, 11%, 49%, and 54%, respectively, had measurements outside of the usual therapeutic target range. In multivariable analysis, BMI ≥25 kg/m<sup>2</sup> (vs <25) was associated with risk of underdiagnosis (OR 1.8 [1.2-2.8]). For undertreatment, significant adverse factors included older age (>35 vs ≤35y: OR 2.5 [1.2-5.1]), BMI ≥30 kg/m<sup>2</sup> (vs <25: OR 3.3 [1.7-6.4]), and greater perceived reliance on others for healthcare decisions (OR 1.7 [1.2-2.4]). Those with greater health-related self-efficacy were less likely to be undertreated (OR 0.5 [0.3-0.96]).

Conclusions: CVRF underdiagnosis and undertreatment among childhood cancer survivors at increased risk of heart disease was common. Greater awareness among survivors and primary care providers and more aggressive control of CVRFs may mitigate this risk.

Eric J. Chow<sup>1,2,3</sup> Yan Chen<sup>4</sup> Gregory T. Armstrong<sup>5</sup> Laura-Mae Baldwin<sup>6</sup> Todd M. Gibson<sup>7</sup> Melissa M. Hudson<sup>5,8</sup> Aaron McDonald<sup>5</sup> Paul C. Nathan<sup>9</sup> Karen Syrjala<sup>1,2</sup> Emily S. Tonorezos<sup>10</sup> Kevin C. Oeffinger<sup>11</sup> Yutaka Yasui<sup>4,7</sup> <sup>1</sup>Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle WA <sup>2</sup>Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle WA

<sup>3</sup>Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, WA

<sup>4</sup>University of Alberta, Edmonton, Alberta, Canada

<sup>5</sup>Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN

<sup>6</sup>Department of Family Medicine, University of Washington, Seattle, WA

<sup>7</sup>National Cancer Institute, Bethesda, MD

<sup>8</sup>Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN

<sup>9</sup>Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

<sup>10</sup>Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

<sup>11</sup>Department of Medicine, Duke University, Durham, NC