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Title: Physical performance and health-related quality of life in adult survivors of childhood cancer

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**Background:** Survivors of childhood cancer may have limitations in physical performance. Limitations in physical performance may interfere with role participation and impact health-related quality of life (HRQOL). The aims of these analyses were to evaluate the association between physical performance and HRQOL among adult survivors of childhood cancer and compare HRQOL between survivors and siblings. **Methods:** Participants included 7147 adult (mean age 33 years; mean survival time 23 years) members of the childhood cancer survivor study (CCSS) and 388 randomly selected siblings of the cancer survivors. Participants completed the Medical Outcomes Survey Short Form 36 (SF-36) as part of a follow-up survey. Information related to original diagnosis was abstracted from medical records. Physical performance was measured by summing participant answers to six physical activity questions. Executive functioning was measured with the Very BRIEF scale and emotional performance with the Brief Symptom Inventory. Normative scores on sub- and summary scales of the SF-36 were compared between survivors, overall and by diagnosis group, and siblings in generalized linear mixed models. The associations between physical performance (dichotomized so that poor performance corresponded to scores in lowest 10th% of the siblings) and SF-36 normative scores were evaluated in linear regression models. **Results:** Overall and mental component summary (MCS) normative scores did not differ by more than 5 points (1/2 standard deviation) among survivors and siblings on the SF-36. Only brain and bone tumor survivors had a mean physical component score (PCS) more than 5 points lower than siblings (45 vs. 53,  $p < 0.001$ ). Bone and brain tumor survivors scored at least 5 points lower than siblings on the physical function and role physical subscales (all  $p$  values  $< 0.001$ ). Hodgkin's disease survivors scored lower than siblings on the general health subscale (46 vs. 53,  $p < 0.001$ ). Among survivors, after adjusting for age, gender, executive and emotional functioning, poor physical performance was associated with a mean decreases in PCS, physical function, role physical, bodily pain, and general health scales of 5-8 points ( $p < 0.001$ ). **Conclusions:** On average, adult survivors of childhood cancer report similar HRQOL when compared to siblings. Bone and brain tumor survivors report meaningful, significantly lower scores than siblings on SF-36 summary and sub-scales associated with physical health. Impaired physical performance is associated with lower scores on scales that reflect physical health. Research is needed on interventions that target physical performance limitations and may improve HRQOL.