**Title:** Neuromuscular dysfunction and associated health/socioeconomic outcomes: A report from the Childhood Cancer Survivor Study

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**Background:** Childhood cancer survivors are at risk for neuromuscular dysfunction. We estimated the prevalence and cumulative incidence of neuromuscular dysfunction in a cohort of childhood cancer survivors and examined associations with treatment exposures and health/socioeconomic outcomes.

**Methods:** CCSS participants ≥5 years from cancer diagnosed between 1970-1999 (n=25,583, 46.5% female, median [range] age 54.4 [15.1-57.6] years) and siblings (n=5,044, 52.3% female, median [range] age 54.1 [32.5-57.0] years) were included. Neuromuscular dysfunction was identified by self-report of 1) motor dysfunction: impaired balance, tremor, or extremity weakness; 2) sensory dysfunction: impaired touch sensation. Multivariable analyses examined predictors of dysfunction by diagnosis.

**Results:** Cumulative incidence of neuromuscular dysfunction was elevated at 20 years from diagnosis in survivors (24.3%, 95% CI 23.8-24.8; motor 18.2%, sensory 13.5%) versus siblings (8.9%, 95% CI 8.1-9.7). In survivors five years from diagnosis, motor dysfunction was associated with exposure to cytarabine (OR=1.39, 95% CI 1.10-1.77) and spinal radiation (OR=2.11, 95% CI 1.31-3.41) in acute lymphoblastic leukemia/non-hodgkin lymphoma (ALL/NHL), vinca alkaloids (OR 1.29, 95% CI 1.03-1.60) and brain radiation (OR=1.58, 95% CI 1.35-1.85) in central nervous system tumors, and cytarabine (OR=3.73, 95% CI 1.62-8.57) and non-brain/spine radiation (OR=1.84, 95% CI 1.42-2.40) in bone/soft tissue tumors. Sensory dysfunction was associated with exposure to vinca alkaloids (OR=3.45, 95% CI 1.06-11.22) in ALL/NHL, and platinum agents (OR=1.31, 95% CI 1.03-1.67) and spinal radiation (OR=3.71, 95% CI 1.24-11.11) in bone/soft tissue tumors. Survivors with neuromuscular dysfunction were at increased risk for adverse health/socioeconomic outcomes (Table).

**Conclusions:** Neuromuscular dysfunction is a prevalent morbidity in childhood cancer survivors, associated with specific therapies within a particular diagnosis. Interventions are needed to identify
and improve neuromuscular dysfunction given its association with adverse health/socioeconomic outcomes.

**Table:** Health/socioeconomic outcomes in survivors with neuromuscular dysfunction compared with those without dysfunction

<table>
<thead>
<tr>
<th>Health/socioeconomic outcomes</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>College or Higher Degree</td>
<td>0.72</td>
<td>0.67 – 0.78</td>
</tr>
<tr>
<td>Ever Employed</td>
<td>0.46</td>
<td>0.37 - 0.56</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.76</td>
<td>2.40 - 3.18</td>
</tr>
<tr>
<td>Depression</td>
<td>2.27</td>
<td>2.02 - 2.55</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.15</td>
<td>1.06 - 1.24</td>
</tr>
</tbody>
</table>

Model adjusted for sex, race/ethnicity, age, presence of any grade 3/4 chronic condition.