

## Conclusions and levels of evidence for surveillance of cancer-related fatigue in childhood, adolescent and young adult cancer survivors

Who needs surveillance?	
<b>Prevalence of cancer-related fatigue (CRF) in childhood, adolescent and young adult (CAYA) cancer survivors [13-15, 17, 18, 32-54]</b>	
CAYA cancer survivors are at risk for CRF with prevalence ranging from 10 to 85%	Level A [13-15, 17, 18, 32-54]
Increased risk for fatigue in CAYA cancer survivors vs. controls There was a higher prevalence of CRF in survivors with a difference ranging from 5 to 20%	Level C [13, 14, 17, 33, 39, 44]
<b>Levels of CRF in CAYA cancer survivors [15, 16, 18, 33, 36, 37, 43, 44, 49, 52, 53, 55-73]</b>	
Higher levels of fatigue in CAYA cancer survivors vs. controls	Level B [15, 16, 33, 36, 43, 44, 55-66]
<b>Risk factors for CRF in CAYA cancer survivors [13-18, 41, 42, 45, 50, 53, 60, 61, 68, 70, 73]</b>	
<b>Treatment-related risk factors</b>	
Unclear risk after CNS/brain irradiation	Conflicting evidence [16, 17, 41, 42, 61]
Unknown risk after pulmonary radiation	No studies
Increased risk after radiotherapy (not further specified)	Level C [15-17, 53, 60]
No significant effect of total body irradiation	Level B [41, 61]
No significant effect of chemotherapy	Level B [15, 17, 41, 53, 60]
No significant effect of surgery	Level B [17, 41]
No significant effect of stem cell transplantation	Level B [17, 60]
No significant effect of duration of treatment	Level C [16]
No significant effect of treatment era	Level C [13]
<b>Clinical risk factors</b>	
Increased risk in survivors with psychological distress	Level A [13, 15, 16, 50, 53, 70]
Increased risk in survivors with a relapse	Level B [17, 18, 45]
Increased risk in survivors with late effects or health problems	Level B [16, 17, 50, 53, 60]
Increased risk in survivors who experience pain	Level B [18, 42, 50, 70]
Increased risk in survivors with sleep problems	Level C [18, 70]
Increased risk in survivors with neuro-cognitive impairment	Level C [18]
Increased risk in survivors with higher brain dysfunction	Level C [68]
Increased risk in survivors with a heart problem	Level C [15, 42]
Increased risk in survivors with exercise-induced symptoms	Level C [18]
Increased risk in survivors with lung fibrosis	Level C [15]
Increased risk in survivors with higher BMI or obesity	Level C [13, 15, 18, 42, 50, 53]
Decreased risk in survivors with better health-related quality of life	Level C [60]
Decreased risk with longer time since diagnosis	Level C [16, 17, 53, 60, 61]
No significant effect of age at diagnosis	Level B [15-17]
No significant effect of primary cancer diagnosis	Level B [13, 15-17, 42, 53, 60, 61]
No significant effect of thyroid status	Level B [13, 15]
No significant effect of amount of exercise	Level B [70, 73]
No significant effect of motility disturbance of limbs	Level C [68]
No significant effect of seizures	Level C [68]
No significant effect of ocular/vision impairment	Level C [68]
No significant effect of endocrine abnormality	Level C [68]

No significant effect of cytokine levels	Level C [42]
No significant effect of smoking	Level C [42]
No significant effect of happiness	Level C [60]
<b>Demographic risk factors</b>	
Increased risk with older age at follow-up	Level B [13, 14, 16, 17, 42, 53, 60, 61]
Increased risk in female survivors	Level C [13-17, 41, 42, 50, 53, 60, 61]
Increased risk in unmarried survivors	Level C [13-16, 18]
Increased risk in survivors with children	Level C [15, 18]
Decreased risk in employed survivors	Level B [14-16, 18, 50]
No significant effect of level of education, overall average grade and remedial education	Level B [13, 14, 16, 60]
No significant effect of household income	Level C [17]
No significant effect of ethnicity	Level C [17, 53]
No significant effect of receiving social benefits	Level C [14]

<b>At what frequency and for how long should surveillance be performed?</b>	
<b>Risk of CRF in CAYA cancer survivors[70, 73]</b>	
Unknown latency time to develop CRF	No studies
Unknown predictors for change over time	No studies
Risk of CRF does not change over time in the majority of survivors. However, in some survivors the risk of CRF increases or decreases over time.	Level B [70, 73]

<b>What surveillance modality should be used?</b>	
<b>Reliability and validity in CAYA cancer patients and survivors [37, 58, 61, 74-88]</b>	
In CAYA cancer patients, the <b>Fatigue Scale-Child (FS-C)</b> and <b>Fatigue Scale-Adolescent (FS-A)</b> with its proxy versions (Fatigue Scale-Parents, Fatigue Scale-Staff) is a valid and reliable instrument to measure CRF.	Level B [58, 74-78]
In CAYA cancer patients and survivors, the <b>PedsQL Multidimensional Fatigue Scale</b> (5-7 years, 8-12 years, 13-18 years, 18-25 years) with its proxy versions (parent versions 2-4 years, 5-7 years) is a valid and reliable instrument to measure CRF.	Level B [74, 79-81]
In CAYA cancer patients and survivors, the <b>PROMIS Pediatric Fatigue measures</b> (short form, and computerized adaptive testing) is a valid and reliable instrument to measure CRF.	Level B [82-85]
In CAYA cancer patients and survivors, other measuring instruments, such as the Multidimensional Fatigue Inventory, and the Turkish Scale for the Assessment of Fatigue in Pediatric Oncology Patients (versions 7-12 years, 13-18 years) are valid and reliable instruments to measure CRF.	Level C [61, 86-88]
In AYA brain tumor survivors, a single-item screening measure for CRF (Fatigue Thermometer) is not able to reliably identify clinically significant CRF.	Level C [37]

What should be done if abnormalities are identified?

**Effectiveness of CRF interventions in CAYA cancer patients and survivors [36, 89-95]**

No studies reported on the effect of individual physiotherapy as an intervention for CRF	No studies
No studies reported on the effect of a revalidation program as an intervention for CRF	No studies
Reduction in CRF after a physical activity intervention	Level B, existing guideline [36, 92-95]
Reduction in CRF after an education intervention	Level B [91, 94]
Reduction in CRF after a cognitive behavioral therapy intervention	Level C, existing guideline [89, 95]
Reduction in CRF after an adventure-based training	Level C [90]
Reduction in CRF after relaxation and mindfulness interventions	Level C, existing guideline [92, 95]
No significant effect of a combined physical activity plus psychosocial intervention	Level C [92]
The evidence is insufficient about the usefulness and safety of pharmacological interventions	Existing guideline [95]