Conclusions and levels of evidence for metabolic syndrome surveillance for CAYA cancer survivors

Who needs surveillance?	
Risk of MetS[a] in CAYA cancer survivors	**GRADE level of evidence**
Increased risk of MetS in CAYA cancer survivors vs the normal population	⨁⨁⊖⊖ LOW [24-34]
Unknown risk of MetS related mortality in CAYA cancer survivors vs the normal population	No studies
Increased risk after C(S)RT vs no C(S)RT	⨁⨁⨁⊖ MODERATE [26, 29-31, 35-37, 39]
Unknown risk after radiotherapy to the HP axis	No studies
No significant effect of abdominal radiation vs no abdominal radiation	⨁⨁⊖⊖ LOW [29]
No significant effect of chest radiation vs no radiation	⨁⨁⊖⊖ LOW [29]
Unknown risk after higher doses of radiotherapy vs lower doses	No studies
Increased risk after a combination of HSCT and TBI vs no HSCT	⨁⨁⨁⊖ MODERATE [29, 31, 35, 37, 38]
No significant effect of HSCT without TBI vs chemo-only and age/sex-matched controls	⨁⨁⊖⊖ LOW [31, 37]
No significant effect of MetS after platinum agents	⨁⨁⊖⊖ LOW [29]
No significant effect of anthracyclines vs no anthracyclines	⨁⨁⨁⊖ MODERATE [29, 30]
No significant effect of anthracycline dose	⨁⨁⊖⊖ LOW [29, 30]
Increased risk after oral methotrexate vs no oral methotrexate	⨁⨁⊖⊖ LOW [30]
No significant effect of steroids	⨁⨁⨁⊖ MODERATE [30, 38]
Unknown risk after surgery	No studies
Increased risk in males vs females	⨁⊖⊖⊖ VERY LOW [29, 37-39]
No significant effect of age at diagnosis or HSCT	⨁⨁⊖⊖ LOW [29, 38]
Increased risk in testicular cancer survivors with lower but not necessarily abnormal total testosterone levels	⨁⨁⊖⊖ LOW [41, 42]
Unknown risk in survivors with thyroid hormone deficiency or excess	No studies
Increased risk in survivors with GH insufficiency vs without GH insufficiency	⨁⨁⊖⊖ LOW [26]
Unknown risk in survivors treated with hormonal replacement therapy	No studies
No significant effect of former/current smoking vs never smoking	⨁⨁⊖⊖ LOW [29]
Increased risk in survivors who have a sedentary lifestyle vs no sedentary lifestyle	⨁⨁⊖⊖ LOW [29, 43]
Increased risk in survivors who have a diet that does not resemble a Mediterranean diet vs a diet that highly resembles a Mediterranean diet	⨁⨁⊖⊖ LOW [43]
Increased risk in survivors that do not adhere to diet and physical activity guidelines vs survivors that adhere to diet and physical activity guidelines	⨁⨁⊖⊖ LOW [36]
Increased risk in survivors with a higher BMI vs lower BMI at primary cancer diagnosis	⨁⨁⨁⨁ HIGH [38-40]
Which surveillance modality should be used?	
Diagnostic tests to detect MetS in CAYA cancer survivors	**GRADE level of evidence**
Overweight or obesity: BMI and waist circumference	Existing guidelines [14-16, 20, 51]
Hypertension: blood pressure using a blood pressure monitor	Existing guidelines [14-16, 20, 51]

(pre)diabetes: fasting blood glucose	Existing guidelines [14-16, 20, 51]
Dyslipidemia: fasting lipid profile	Existing guidelines [14-16, 20, 51]
When should surveillance be initiated?	
Latency time of MetS in CAYA cancer survivors	**GRADE level of evidence**
Unknown latency time of developing MetS	No studies
At what frequency should surveillance be performed?	
Risk of MetS over time in CAYA cancer survivors	**GRADE level of evidence**
The cumulative incidence of MetS increases over time	⨁⨁⨁⨁ HIGH [26, 31, 39]
What should be done if abnormalities are identified?	
Risk of MetS after lifestyle interventions	**GRADE level of evidence**
Unknown risk in survivors after lifestyle interventions	No studies

Abbreviations: MetS = metabolic syndrome, CAYA = childhood, adolescent and young adult, C(S)RT = cranial or craniospinal radiotherapy, HP = hypothalamic pituitary, TBI = total body irradiation, HSCT = hematological stem cell transplantation, GH = growth hormone, BMI = body mass index, LTFU = long-term follow-up.

[a] The clustering of at least 3 cardiovascular risk factors. Definitions of MetS were as described in each eligible study.