Who needs cardiomyopathy surveillance?	
Risk by anthracycline dose	
- Exponential increase in risk for *symptomatic* cardiomyopathy with increasing lifetime cumulative dose for all childhood cancer survivors	Level A
- Childhood cancer survivors treated with cumulative anthracycline dose ≥250 mg/m2 are at highest risk for *symptomatic* cardiomyopathy	Level A
- Increased risk for *asymptomatic* cardiomyopathy with increasing cumulative dose	Level A
Risk by age at anthracycline exposure	
- Increased risk for *symptomatic* cardiomyopathy with younger age at exposure	Conflicting evidence
- Increased risk for *asymptomatic* cardiomyopathy with younger age at exposure	Conflicting evidence
Risk by anthracycline derivatives (including mitoxantrone)	
- Cardiomyopathy has been associated with all anthracycline derivatives	Level A
- Daunorubicin is as cardiotoxic as doxorubicin when given at an equieffective dose	Level C
- Epirubicin is less cardiotoxic than doxorubicin when given at an equieffective dose	No evidence
- Idarubicin is more cardiotoxic than doxorubicin when given at an equieffective dose	No evidence
- Mitoxantrone is more cardiotoxic than doxorubicin when given at an equieffective dose	No evidence
Risk by chest radiation dose	
- Increased risk for *symptomatic* cardiomyopathy with increasing radiation dose to cardiac tissues	Level A
- Childhood cancer survivors treated with chest radiation dose ≥35 Gy are at highest risk for *symptomatic* cardiomyopathy	Level B
- Increased risk for *asymptomatic* cardiomyopathy with increasing radiation dose to cardiac tissues	Level B
Risk following anthracycline and chest radiation exposure	
- Increased risk after anthracycline and chest radiation exposure	Level B
Risk following conditioning with TBI	
- There is no increased risk following conditioning with TBI	Level B
Risk due to modifiable cardiovascular risk factors	
- Increased risk in anthracycline—or radiation, or both—exposed survivors who develop modifi able cardiovascular risk factors (hypertension, diabetes, dyslipidaemia, obesity)	Level B
What surveillance modality should be used?	
Diagnostic value of echocardiography	
- Good diagnostic value of two-dimensional echocardiography for detection of asymptomatic cardiomyopathy in childhood cancer survivors	Level B
Diagnostic value of cardiac magnetic resonance imaging (CMR)	
- Good diagnostic value of CMR for detection of asymptomatic LV systolic dysfunction in childhood cancer survivors	Level B
Diagnostic value of radionuclide angiography	
- Good diagnostic value for detection of asymptomatic LV systolic dysfunction in childhood cancer survivors	Level C
Diagnostic value of blood biomarkers of cardiac injury and remodeling	
- Poor diagnostic value of cardiac troponins (Troponin-T) for detection of asymptomatic LV systolic dysfunction in childhood cancer survivors	Level B
- Poor diagnostic value of cardiac troponins (Troponin-I) for detection of asymptomatic LV systolic dysfunction in childhood cancer survivors	Level C
- Poor diagnostic value of natriuretic peptides (BNP, NT Pro-BNP) for detection of asymptomatic LV systolic dysfunction in childhood cancer survivors	Level B
Cost-benefit of surveillance in *childhood cancer survivors*	
- Screening for asymptomatic LV systolic dysfunction using conventional imaging or blood biomarkers is cost-effective.	**No evidence**

Cost-benefit of surveillance in *other populations*	
- Screening for asymptomatic LV systolic dysfunction using conventional imaging or blood biomarkers is cost-effective.	Level B
At what frequency and for how long should surveillance for cardiomyopathy be performed?	
- High risk childhood cancer survivors have a more rapid rate of deterioration in cardiac function when compared to moderate/low-risk survivors	No evidence
- There is a more rapid rate of deterioration in cardiac function during puberty	No evidence
- Female childhood cancer survivors who have *asymptomatic* cardiomyopathy at the time of becoming pregnant are at risk for *symptomatic* cardiomyopathy during pregnancy/delivery	Level C
- Female childhood cancer survivors treated with anthracyclines or radiation who have normal LV systolic function at the time of becoming pregnant are not at increased risk for deterioration in cardiac function during pregnancy/delivery	Level C
- The risk for deterioration in cardiac function continues to increase with longer follow-up	Level B
What should be done when abnormalities are detected during surveillance?	
Use of medical interventions in *childhood cancer survivors*	
- ACE-inhibitors are effective for improving cardiac function in survivors with asymptomatic cardiomyopathy	No evidence
- Beta-blockers are effective for improving cardiac function in survivors with asymptomatic cardiomyopathy	No evidence
- Other interventions such as angiotensin II receptor blockers or placement of ICD can be effective for prevention of sudden arrhythmic cardiac death in survivors with asymptomatic cardiomyopathy	No evidence
Utility of medical interventions in *other populations*	
- ACE-inhibitors are effective for improving cardiac function in individuals with asymptomatic cardiomyopathy	Level A
- Beta-blockers are effective for improving cardiac function in individuals with asymptomatic cardiomyopathy	Level C
- Other interventions such as angiotensin II receptor blockers or placement of ICD can be effective for prevention of arrhythmic cardiac death in patients with asymptomatic cardiomyopathy	Level C
What are the limitations for physical activity?	
Role of physical activity in *childhood cancer survivors*	
- Regular physical exercise, as recommended by the AHA and ESC, is beneficial for childhood cancer survivors with *normal* LV systolic function	Level C
- Regular physical exercise, as recommended by the AHA and ESC, is beneficial for childhood cancer survivors with *asymptomatic* cardiomyopathy	No evidence
- Participation in high intensity exercise increases the risk for cardiac functional deterioration in childhood cancer survivors	No evidence
Role of physical activity in *other populations*	
- Regular physical exercise, as recommended by the AHA and ESC, is beneficial for individuals who have *normal* cardiac function	Level A
- Regular physical exercise, as recommended by the AHA and ESC, is beneficial for individuals who have *normal* cardiac function, but at risk for cardiomyopathy owing to genetic susceptibility	Level B
- Participation in high intensity exercise increases the risk for cardiac functional deterioration in individuals with asymptomatic cardiomyopathy	Level B

Level A=high level of evidence (ie, consistent evidence from well performed and high quality studies or systematic reviews with a low risk of bias, and direct, consistent and precise results). Level B=moderate-to-low level of evidence (ie, evidence from studies or systematic reviews with few important limitations). Level C=very low level of evidence (ie, evidence from studies with serious fl aws, only expert opinion or standards of care)

Abbreviations: Gy, Gray; LV, left ventricular; ACE, angiotensin converting enzyme; ICD, implantable cardioverter defibrillator; AHA, American Heart Association; ESC, European Society of Cardiology; TBI, total body irradiation.