

Conclusions of evidence from the systematic literature search and expert opinion for ototoxicity surveillance for CAYA cancer survivors

Who needs surveillance?	
Risk of hearing loss in CAYA cancer survivors	
Increased risk after cisplatin vs. no cisplatin	Level B ¹⁻³
Increased risk after higher cisplatin dose vs. lower dose	Level A ^{1,2,4-9}
Unknown risk after longer cisplatin administration duration vs. shorter duration	No studies
Increased risk after carboplatin	Expert opinion* ¹⁰⁻¹⁶
Unknown risk after higher carboplatin dose vs. lower dose	No studies
Unknown risk after longer carboplatin administration duration vs. shorter duration	No studies
Unknown risk after oxaliplatin vs. no oxaliplatin	No studies
Unknown risk after higher oxaliplatin dose vs. lower dose	No studies
Unknown risk after longer oxaliplatin administration duration vs. shorter duration	No studies
Increased risk after cranial radiotherapy vs. no cranial radiotherapy	Expert opinion* ¹⁷⁻¹⁹
Increased risk after higher cranial radiotherapy dose vs. lower dose	Level B ^{3,20}
Increased risk after combination of platinum chemotherapy and cranial radiotherapy	Level C ¹⁷
Increased risk after co-treatment with furosemide or aminoglycosides vs. no furosemide or aminoglycosides	Level C ^{2,21}
Decreased risk after co-treatment with sodium thiosulfate vs. no sodium thiosulfate	Level C ^{22,23}
Decreased risk after co-treatment with amifostine vs. no amifostine	Level C ^{18,24}
Increased risk after younger age at cancer treatment vs. older age	Level B ^{2,6-9,19,20,25,26}
No significant effect of sex	Level B ^{5,8,19,21,27}
Unknown association between timing of administration of platinum agents and cranial radiation	No studies
Increased risk after cerebrospinal fluid (CSF) shunts vs. no CSF shunts	Level B ^{5,17,20}
Unknown risk after posterior fossa tumor surgery	No studies
Unknown risk after surgery involving the ear or cranial nerve VIII	No studies
Risk of tinnitus in CAYA cancer survivors	
Increased risk after platinum agents as a group vs. no platinum agents	Level C ²⁸
Unknown risk after higher dose of platinum agents as a group vs. lower dose	No studies
Unknown risk after longer platinum agent administration duration vs. shorter duration	No studies
Increased risk after high-dose cranial radiotherapy ≥30 Gy vs. no cranial radiotherapy	Level C ²⁸
Unknown risk after higher cranial radiotherapy dose vs. lower dose	No studies
Unknown risk after co-treatment with furosemide or aminoglycosides	No studies
Unknown risk after co-treatment with sodium thiosulfate or amifostine	No studies
Unknown risk of age at cancer treatment	No studies
Unknown risk of sex	No studies
Unknown risk of cerebrospinal fluid (CSF) shunts	No studies
Unknown risk after posterior fossa tumor surgery	No studies
Unknown risk after surgery involving the ear or cranial nerve VIII	No studies
At what frequency and for how long should surveillance be performed?	
Risk of hearing loss in CAYA cancer survivors	
Hearing function may deteriorate over time after platinum agents (as a group); in some patients hearing function improves or remains stable	Level C ^{8,9,29-33}
Hearing function may deteriorate over time after cranial radiotherapy (also in combination with platinum or CSF shunts); in some survivors hearing function improves or remains stable	Level C ^{17,20,32,34,35}
Predictors for change of hearing function over time unknown	No studies
Unknown likelihood of change of hearing loss over time after co-medication, surgery involving the ear or cranial nerve VIII, or after noise exposure	No studies
Risk of tinnitus in CAYA cancer survivors	
Unknown likelihood of change of tinnitus over time	No studies
What surveillance modality should be used?	
Testing methods to detect abnormalities in CAYA cancer survivors	
Behavioural testing: a measure of hearing sensitivity	
Visual reinforcement audiometry: survivors between 5-24 months of age	Existing guidelines ³⁶⁻⁴⁵
Conditioned play audiometry: survivors between 2-5 years of age	
Pure tone conventional audiometry: survivors ≥5 years of age	

Speech audiometry: survivors >6 months of age (in addition to visual reinforcement audiometry also provides information on phoneme detection abilities to word recognition) Auditory brainstem response: an electrophysiological test to assess the cochlea/auditory nerve/lower brainstem structure function Distortion-product otoacoustic emission: a measure to evaluate cochlear outer hair cell function Tympanometry: a measure to assess middle ear function)	
Agreement testing methods to detect abnormalities in CAYA cancer survivors	
Agreement between pure tone audiometry and distortion product otoacoustic emission	Level B ^{16,46-48}
High frequency audiometry detects more abnormalities than pure tone audiometry	Level C ⁴⁶
Unknown agreement between pure tone audiometry and high frequency audiometry	No studies
Unknown agreement between pure tone audiometry and speech audiometry in noise	No studies
Pure tone audiometry detects more abnormalities than auditory brainstem response	Level C ⁴⁹
Unknown agreement between pure tone audiometry and frequency-specific auditory brainstem response	No studies
Unknown agreement between distortion product otoacoustic emission and frequency specific auditory brainstem response	No studies
What should be done when abnormalities are identified?	
Use of medical devices in CAYA cancer survivors with hearing loss or tinnitus	
Hearing aids are effective for improving disabilities, difficulties with hearing speech, spatial location and speech distortion in survivors with hearing loss	Level C ⁵⁰
Cochlear implants are effective for improving hearing function in survivors with hearing loss	Level C ⁵¹
Use of teaching/education/assistance in CAYA cancer survivors with hearing loss	
Education, amplification or hearing-assistive technology can be used for patients with hearing loss	Existing guideline ⁵²
Cochlear implantation, hearing aids, tactile aids, FM system, communication approaches, intervention programs can be used for patients with hearing loss	Existing guidelines ⁵³⁻⁵⁵
Use of teaching/education/assistance in CAYA cancer survivors with tinnitus	
Sound therapy, counseling/education, intervention/management, education about management strategies, hearing aid, cognitive behavioral therapy can be used for patients with tinnitus	Existing guideline ⁵⁶
Unknown use of environmental changes in CAYA cancer survivors with hearing loss or tinnitus	No studies

Abbreviations: CAYA, childhood, adolescent and young adult

*Expert opinion based on studies of the supplemental literature search that did not fulfill the inclusion criteria and/or very low quality of evidence

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