

Ototoxicity Monitoring: Tinnitus

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Recommendations for ototoxicity surveillance for childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCare Consortium

Eva Clemens, Marry M van den Heuvel-Eibrink*, Renée L Mulder, Leontien C M Kremer, Melissa M Hudson, Roderick Skinner, Louis S Constine, Johnnie K Bass, Claudia E Kuehni, Thorsten Langer, Elvira C van Dalen, Edith Bardi, Nicolas-Xavier Bonne, Penelope R Brock, Beth Brooks, Bruce Carleton, Eric Caron, Kay W Chang, Karen Johnston, Kristin Knight, Paul C Nathan, Etan Orgel, Pinki K Prasad, Jan Rottenberg, Katrin Scheinemann, Andrica C H de Vries, Thomas Walwyn, Annette Weiss, Antoinette am Zehnhoff-Dinnesen, Richard J Cohn†, Wendy Landier† on behalf of the International Guideline Harmonization Group ototoxicity group‡*

At what frequency and for how long should surveillance be done?

Risk of hearing loss in children, adolescent, and young adult cancer survivors

Hearing function might deteriorate over time after platinum-based drugs (as a group); in some patients, hearing function improves or remains stable Level C^{32,33,51-55}

Hearing function might 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^{5,10,55-57}

Predictors for change of hearing function over time unknown No studies

Unknown likelihood of change of hearing loss over time after comedication, surgery involving the ear or cranial nerve VIII or after noise exposure No studies

Risk of tinnitus in children, adolescent, and young adult cancer survivors

Unknown likelihood of change of tinnitus over time No studies

Clemens E, et al. Recommendations for ototoxicity surveillance for childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCare Consortium, *Lancet Oncol*, 2019, 20(1):e29-e41.

AAO-HNS Foundation Clinical Practice Guidelines: Tinnitus

- Primary Tinnitus
 - Idiopathic & may or may not be associated with SNHL
 - Alternative term for subjective tinnitus
- Secondary Tinnitus
 - Associated with a specific underlying cause (other than SNHL) or an identifiable organic condition
 - Alternative term for objective tinnitus

Tunkel DE, Bauer CA, Sun GH, et al. Clinical practice guidelines: tinnitus, Otolaryngol Head Neck Surg, 2014, 151(2 Suppl):S1–40.



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AAO-HNS Foundation Clinical Practice Guidelines: Assessment

- Ask about tinnitus as part of medical history
- Essential if patient is on ototoxic medications

Table 6. Key Details of Medical History in the Tinnitus Patient.^a

Key Issue	Significance	Implication
Medications and potential ototoxic exposures	Some medications such as salicylates are associated with tinnitus; ototoxins can cause hearing loss and tinnitus. Interactions between medications have unknown effects and can exacerbate tinnitus symptoms.	Counseling regarding medication use, etiology of tinnitus is facilitated; patients can be provided list of known ototoxic medications as part of counseling; comprehensive audiologic assessment

Tunkel DE, Bauer CA, Sun GH, et al. Clinical practice guidelines: tinnitus, Otolaryngol Head Neck Surg, 2014, 151(2 Suppl):S1–40.



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American Academy of Audiology

POSITION STATEMENT ON PROVISION OF OTOTOXIC MONITORING BY AUDIOLOGISTS

Audiological Interests in Ototoxicity Monitoring

Audiologic monitoring for ototoxicity is primarily performed for two purposes: (1) early detection of changes to hearing status presumably attributed to a drug/treatment regime so that changes in the drug regimen may be considered, and (2) audiologic intervention when handicapping hearing impairment has occurred. These clinical goals are differentiated in the following.

The term “ototoxicity monitoring” is generally taken to express the principle of early identification, yet the concept also embraces the principle of early intervention. For example, when changes are detected early, the physician can be alerted so that alternative treatment protocols, possibly with less ototoxic medications, may be considered. Furthermore, when clinically significant changes occur, especially hearing deterioration that has migrated into the speech frequencies, the purpose of a monitoring program becomes to assist the patient and/or patient’s family to maintain effective communication, especially as hearing loss progresses. Unfortunately, this degree of hearing impairment may be unavoidable even with proactive ototoxicity monitoring, as the priority is effective treatment of the disease via the given drug therapy.

Durrant J, Campbell K, Fausti S, et al. American Academy of Audiology Position Statement and Clinical Practice Guidelines Ototoxicity Monitoring, Oct 2009, 1-25.



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Methods to Screen for Tinnitus

- Questionnaires
 - Tinnitus Screener, Tinnitus Handicap Inventory-Screener, etc.
- Rating Scales
 - Verbal Rating Scale, Numeric Rating Scale, Visual Analog Scale
- Single Question (NHANES*)
 - “In the past 12 months, have you been bothered by ringing, roaring, buzzing in your ears or head that lasts for 5 minutes or more?”
 - Note: Chronic defined in this survey as > 3 months

*National Health and Nutrition Examination Survey
<https://www.cdc.gov/nchs/nhanes/index.htm>

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Example Ototoxicity Monitoring Questions for Tinnitus Surveillance

1. Did you have tinnitus, *ringing, buzzing, humming or other sounds in your ears or head*, prior to starting chemotherapy?
 YES
 NO, but I have **NEW** tinnitus that started since my first chemotherapy treatment
 NO, tinnitus before NO tinnitus now (**STOP you have completed necessary questions**)
2. Have you noticed changes to your tinnitus?
 YES, WORSE NO CHANGE
3. Have you experienced any tinnitus since your last treatment?
 YES NO
4. Has your tinnitus gone back to normal?
 YES NO UNSURE
5. Where is your tinnitus located?
 RIGHT ear LEFT ear BOTH ears In my head UNSURE
6. When you are in a quiet room is the sound(s) always there? YES NO (it seems to come and go)

Challenges with Defining Tinnitus

- Multiple Definitions Exist
 - Inconsistent definitions means cannot easily compare across data-sets or studies
 - Possibly over- or under-estimating condition
 - To assess change over time, must be consistent in how you ask about tinnitus
 - Use same definition and question wording at each time point

Do you have tinnitus? vs. Do you have *bothersome* tinnitus?

Questionnaires are Helpful Clinical Tools

- Tinnitus Screener
 - Categorizes how often tinnitus is experienced
- Tinnitus and Hearing Survey
 - Differentiates tinnitus-related from hearing-related problems
- Tinnitus Functional Index
 - Quantifies degree of tinnitus impact
- Can be helpful to administer more than one questionnaire (Theodoroff, 2020 in press)



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Theodoroff SM. Tinnitus Questionnaires for Research and Clinical Use. In: Jinsheng Zhang and Grant Searchfield (Eds.), *The Behavioral Neuroscience of Tinnitus*, Springer-Nature CTBN series, 2020, in press

Tinnitus Screener and Clinical Recommendations

Clinical Recommendations for Primary Tinnitus According to Temporal Characteristics of Tinnitus^a

Primary Tinnitus	Frequency of Occurrence	Symptoms/Duration	Clinical Implications
Spontaneous (transient ear noise)	Random	Sudden tone in 1 ear, usually accompanied by sense of ear fullness and hearing loss All symptoms resolve within 2-3 minutes	Normal physiological event experienced by almost everyone Recommend: No referral indicated. Reassure patient this is normal and not a sign of pathology.
Temporary	Follows tinnitus-inducing event—usually noise exposure but also some medications and chemicals	May accompany temporary change in hearing—can be a warning sign that temporary hearing loss has occurred Can last 1 or more days	Indicates possible damage to inner ear Recommend: Educate about hearing conservation (eg, use hearing protection, reduce exposure to hazardous noise, get periodic hearing test) and monitor symptoms
Occasional	Less than weekly	Lasts at least 5 minutes	Referral not indicated unless there are otologic complaints Recommend: Educate about hearing conservation and monitor symptoms
Intermittent	At least daily or weekly	Lasts at least 5 minutes	Recommend: (1) Refer for clinical audiologic examination and brief tinnitus assessment; (2) Counsel re: hearing conservation
Constant	Always audible in quiet	Continuous sound	Recommend: Same as for intermittent tinnitus

^a See text for description of the different types of primary tinnitus.

Adapted from the document “Tinnitus: Guidance for DoD Primary Care Providers” developed by the Tinnitus Working Group, consisting of researchers and clinicians from the U.S. Departments of Defense and Veterans Affairs.

Henry JA, McMillan L, Manning C. Multidisciplinary tinnitus care, *The Journal for Nurse Practitioners*, 2019, 15:671-675.



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Tinnitus Severity Questionnaires

Many to choose from, here are two options:

- Tinnitus Functional Index

- Request permission prior to use:

<https://apps.ohsu.edu/research/tech-portal/technology/view/1004796>

- Tinnitus Handicap Inventory

- Public domain: <https://www.entnet.org/content/otology-outcome-tool-thi>

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Tinnitus Management

- Step One: Perform Needs Assessment
 - Gain insight into the patient’s perspective
 - Tells you how the patient’s tinnitus impacts their daily functioning
 - Tells you about the patient’s motivation and readiness
- Step Two: Management Options
 - Assessing patient’s needs will direct appropriate care path and treatment recommendations
 - e.g., sound therapy, behavioral counseling, hybrid approach
 - Ask: “What situation is your tinnitus most bothersome?”

Patient's Perspective

“This video introduces you to Brian, a 40-year-old Veteran with bothersome tinnitus that he describes as ‘hell,’ an ‘invisible disability’ that ‘affects [his] well-being and way of life.’” (Theodoroff & Konrad-Martin, 2020, pp 545).

<https://www.ncrar.research.va.gov/PatientVoices/Index.asp>

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Summary

- Ototoxicity monitoring is not standardized
- Various types and definitions of tinnitus exist
- Need to distinguish tinnitus as a symptom vs. having bothersome tinnitus
- Perform needs assessment for a patient-centered approach to tinnitus management

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