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Prevention and Monitoring of Medication-Related Hearing Disability: A Cross-Sectional Analysis of Ototoxicity Trials Registered on ClinicalTrials.gov

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ABSTRACT: Medication-related hearing disability is a significant and potentially preventable consequence of various therapies. Although clinical trials are crucial for prevention, treatment, and screening strategies, it remains unclear how well they evaluate disability-related outcomes.

Objective: This study aimed to characterize ototoxicity studies on ClinicalTrials.gov and examine drug classes, clinical contexts, and outcome measures for medication-related hearing disability. **Methods:** A registry-based cross-sectional analysis used ClinicalTrials.gov (<http://www.clinicaltrials.gov>). The search and data export were performed on May 11, 2026, with the search term “ototoxicity.” Eligible records included interventional and observational studies on ototoxicity, hearing loss, tinnitus, vestibular issues, audiological, and rehabilitation outcomes related to hearing disabilities. After screening, 48 records were included. Variables extracted were study status, type, phase, age, region, drug/exposure, purpose, and hearing outcomes. Data were analyzed descriptively with frequencies and percentages.

Results: Of the 48 studies included in the analysis, 21 (43.8%) were completed, and 34 (70.8%) were interventional clinical trials. The most common clinical contexts were platinum-based chemotherapy and mixed cancer treatment exposures, accounting for 33 (68.8%) studies, followed by aminoglycoside and anti-infective therapy, with 10 (20.8%) studies. Most studies assessed the incidence, severity, or grade of hearing loss/ototoxicity (41, 85.4%), and objective audiometric or cochlear measures (33, 68.8%). Fewer studies included patient-reported hearing disabilities or hearing-related quality of life (22, 45.8%), tinnitus-related outcomes (18, 37.5%), vestibular or balance-related outcomes (12, 25.0%), rehabilitation or assistive-device outcomes (10, 20.8%), and speech perception outcomes (9, 18.8%). Trial purpose: 22 (45.8%) studies focused on prevention, eight (16.7%) focused on treatment/rehabilitation, and 18 (37.5%) focused on monitoring/screening.

Conclusion: Ototoxicity trials mainly focus on clinical grading and audiometric changes, with less consistent assessment of functional and patient-centered disability outcomes. Future studies should include hearing, communication, tinnitus, vestibular, quality-of-life, and rehabilitation outcomes to better reflect the real-world impact of medication-related hearing disability.

1. INTRODUCTION

Hearing disability is one of the most significant sensory-related causes of functional limitation worldwide [1]. Its impact extends beyond reduced auditory perception to include difficulties in communication, education, employment, social interaction,

emotional well-being, and independent living [2]. Individuals with hearing loss struggle to understand speech, especially in noisy environments, participate in conversations, follow medical instructions, maintain social relationships, and perform work or academic tasks that require verbal communication [3]. In children, hearing impairment can interfere with speech and language development, learning, school performance, and social integration [4]. In adults and older adults, it can contribute to social isolation, reduced productivity, dependence on others, and lower quality of life [5]. Given these consequences, hearing loss should be viewed not only as an impairment of the auditory system but also as a disability-related condition with clinical, psychosocial, educational, and economic implications [6]. The disability burden is especially important when hearing loss is preventable or medically induced [7]. Medication-related hearing loss is one such example, where exposure to necessary but potentially ototoxic therapies may cause permanent or progressive auditory damage [8]. This presents a significant challenge for healthcare systems: maintaining the therapeutic benefits of essential medicines while minimizing the risk of preventable hearing impairments. Therefore, research on hearing disability should focus on documenting changes in hearing thresholds and addressing the functional consequences of hearing impairment, including communication difficulties, tinnitus burden, speech perception problems, need for assistive devices, rehabilitation referrals, and hearing-related quality of life.

Ototoxicity is an injury to the cochlear or vestibular structures caused by exposure to certain therapeutic medications, resulting in hearing loss, tinnitus, dizziness, imbalance, or audiovestibular dysfunction [9]. Several drug classes have been linked to ototoxicity risk, but platinum-based chemotherapy and aminoglycoside antibiotics are the most clinically significant [10, 11]. Cisplatin is a highly effective anticancer medication for treating many solid tumors, including head and neck cancers, testicular cancer, bladder cancer, lung cancer, and pediatric malignancies [12]. However, cisplatin-related ototoxicity may cause bilateral sensorineural hearing loss, often irreversible [13]. This is particularly concerning for children who are cancer survivors, in whom even mild-to-moderate hearing loss can affect language development, educational progress, psychosocial adjustment, and long-term survivorship outcomes [14]. Aminoglycosides, such as gentamicin, amikacin, and tobramycin, treat severe bacterial infections, multidrug-resistant infections, neonatal sepsis, cystic fibrosis, and mycobacterial diseases [15]. However, aminoglycoside ototoxicity, including cochlear and vestibular toxicities, requires careful risk assessment and monitoring [16]. Other medication- or treatment-related factors may also contribute to hearing injury, including combined chemoradiotherapy, high cumulative drug doses, repeated treatment cycles, renal dysfunction, genetic susceptibility, noise exposure, and the co-administration of multiple ototoxic medications [17]. The resulting disability extends beyond hearing thresholds and includes tinnitus, difficulty understanding speech, balance impairment, communication-related fatigue, reduced participation in daily life, and the need for hearing rehabilitation. These features make medication-related hearing disabilities an important area for research and practice across disability, medication safety, oncology care, infectious disease management, audiology, pharmacy practice, and rehabilitation services.

Clinical trials play an important role in developing strategies to prevent, detect, monitor, and manage medication-related hearing disabilities. Trials in this field assess otoprotective drugs, alternative dosing strategies, monitoring protocols, audiological screening tools, biomarkers of ototoxic susceptibility, pharmacogenetic approaches, tinnitus interventions, hearing rehabilitation, and assistive hearing technologies [18, 19]. However, these studies may differ in how they defined and measured hearing disabilities. Some studies have focused primarily on audiometric threshold shifts, otoacoustic emissions, or ototoxicity grading systems. In contrast, others include more patient-centered outcomes such as tinnitus burden, speech perception, hearing-related quality of life, vestibular symptoms, hearing-aid use, and rehabilitation needs. This distinction is important because objective hearing changes do not always reflect the full functional impact of patients' experiences in communication, education, work, social participation, and daily living. ClinicalTrials.gov offers an opportunity to examine how ototoxicity-related studies are designed and which outcomes are prioritized. A registry-based cross-sectional analysis can identify the main drug classes and clinical contexts linked to hearing disability; determine whether studies focus on prevention, treatment/rehabilitation, or monitoring/screening; and assess the extent to which disability-relevant outcomes are included. Therefore, this study aimed to characterize ototoxicity-related studies registered at ClinicalTrials.gov and examine the drug classes, clinical contexts, and outcome measures used to assess medication-related hearing disability.

2. MATERIALS AND METHODS

2.1 Study Design and Data Source

This study was designed as a registry-based cross-sectional analysis of ototoxicity-related clinical studies that were registered at ClinicalTrials.gov. This manuscript does not report a clinical trial conducted by the authors; rather, it presents a secondary

registry-based cross-sectional analysis of publicly available ClinicalTrials.gov study records. This study followed the relevant items of the STROBE checklist for cross-sectional studies, adapted for publicly available registry-level data. This study focused on medication-related hearing disabilities and examined how clinical trials address the prevention, treatment/rehabilitation, and monitoring/screening of ototoxic hearing injuries. ClinicalTrials.gov search and data export were conducted on May 11, 2026. This design was selected because ClinicalTrials.gov provides structured information on registered clinical studies, including study status, study type, intervention, phase, eligibility criteria, outcome measures, sponsor information, location, and availability of posted results. Therefore, this study provides an overview of current and past clinical research activities in medication-related hearing disabilities, including studies that may not yet be published. This study followed a disability-focused framework. Hearing disability was broadly defined to include not only hearing loss or audiometric threshold shifts, but also tinnitus, speech-perception difficulties, vestibular or balance-related impairments, hearing-related quality of life, functional communication problems, use of hearing aids or cochlear implants, and the need for rehabilitation. This approach is important because medication-related ototoxicity may extend beyond cochlear injury, affecting communication, education, employment, social participation, and daily functioning. No separate study protocol was registered for this registry-based cross-sectional study.

Data were obtained from ClinicalTrials.gov by using an ototoxicity-focused search strategy. The primary search term used was “ototoxicity.” The search included all registered studies regardless of recruitment status, study design, intervention type, population age group, geographic region, or trial phase. The exported ClinicalTrials.gov file includes study identifiers, titles, URLs, recruitment status, summaries, conditions, interventions, outcome measures, eligibility criteria, enrollment, sponsor and collaborator information, study type, study design, phase, dates, locations, and result-posting status. The search was not restricted by year, country, participant’s age, sex, or study status. This broad approach was used to capture the full registry landscape of ototoxicity-related studies and to avoid excluding early-phase, observational, diagnostic, monitoring, or rehabilitation studies that may be relevant to medication-related hearing disability. After exporting, all records were manually reviewed to confirm eligibility and remove invalid entries. All exported records were manually reviewed against the study title, summary, intervention, condition, and outcome fields to confirm their relevance to ototoxicity or medication-related hearing disabilities.

2.2 Eligibility Criteria

Studies were eligible if they were registered on ClinicalTrials.gov and addressed ototoxicity, hearing loss, hearing impairment, tinnitus, vestibular dysfunction, or audiovestibular outcomes in relation to medication- or treatment-related exposures. The eligible studies included interventional clinical trials, observational studies, diagnostic studies, prevention studies, treatment or rehabilitation studies, and monitoring or screening studies. Studies were included if they met at least one of the following criteria: evaluated the prevention or reduction of ototoxic hearing loss, hearing disability associated with platinum-based chemotherapy, aminoglycosides, or other ototoxic medications; examined audiological, vestibular, tinnitus-related, speech-perception, or hearing-related quality-of-life outcomes; and evaluated monitoring, screening, biomarkers, genetic susceptibility, electrophysiological assessment of ototoxicity, or addressed rehabilitation or assistive-device outcomes related to hearing or audiovestibular disability.

2.3 Data Extraction

The following variables were extracted from each eligible ClinicalTrials.gov record: NCT number, study title, study URL, acronym, recruitment status, summary, availability of study results, condition, intervention, primary outcome measures, secondary outcome measures, other outcome measures, sponsor, collaborators, sex eligibility, age eligibility, phase, enrollment, funder type, study type, study design, start date, primary completion date, completion date, first posted date, last updated date, and study location. Study status was classified using ClinicalTrials.gov, including recruiting, not yet recruiting, completed, terminated, withdrawn, active not recruiting, suspended, and unknown. Study type was classified as interventional or observational. Age eligibility was coded as child, adult, or older adult based on the categories reported in ClinicalTrials.gov. These age categories were treated as non-mutually exclusive, because a single study could include multiple age groups. Sex eligibility was coded as male, female, or both based on whether male or female participants were eligible. The study phase was recorded as reported in the registry and included Early Phase 1, Phase 1, Phase 2, Phase 3, Phase 4, not applicable, or missing/not reported. The selected study locations were used to determine the geographic regions. Studies with locations in more than one country or region were coded for all applicable regions. The regions were grouped into Africa, Europe, North America, Asia, South America, and other regions. The funder type was recorded according to the ClinicalTrials.gov

classification, where available. The second reviewer independently verified the extracted variables and classifications. The reviewers resolved disagreements through discussion and review of the original ClinicalTrials.gov records.

2.4 Classification of drug classes and clinical contexts

Each study was classified according to primary drug or treatment exposure associated with hearing disabilities. The primary exposure categories were platinum-based chemotherapy and mixed cancer-treatment exposures; aminoglycoside and anti-infective therapy; radiation- or radiosurgery-related hearing risk; COVID-19 treatment- or vaccine-related exposure; surgical antiseptic or chemical exposure; and antihypertensive medication-related context. Platinum-based chemotherapy and mixed cancer treatment exposure included studies involving cisplatin, carboplatin, platinum salts, or platinum-based chemoradiotherapy. Studies on aminoglycoside and anti-infective therapy have included amikacin, gentamicin, tobramycin, or aminoglycoside-related ototoxicity. Radiation- or radiosurgery-related studies were retained because some ototoxicity-related records reported hearing preservation or hearing loss outcomes in cancer treatment contexts, even when exposure was not purely medication-based. These studies were coded separately to preserve transparency and to distinguish medication-related ototoxicity from broader treatment-related hearing risks. As shown in Table 2, each study was assigned to a single dominant drug/exposure class based on the title, intervention, condition, and study summary. For comparative analyses, clinical contexts were coded as indicator variables, allowing multiple contexts to be assigned when a study involved overlapping exposures or outcomes.

2.5 Classification of trial purpose

Each study was categorized into one of the three main trial-purpose groups: prevention, treatment/rehabilitation, or monitoring/screening. Prevention trials were defined as those primarily designed to prevent, reduce, or alleviate ototoxic hearing loss before or during exposure to a potentially ototoxic medicine, including trials of otoprotective agents, preventive pharmacological interventions, or approaches intended to reduce treatment-related hearing damage. Treatment/rehabilitation trials were defined as studies addressing existing hearing or vestibular disability, tinnitus, balance impairment, or functional consequences of ototoxicity, including studies on hearing aids, cochlear implants, vestibular implants, tinnitus interventions, hearing rehabilitation, or treatment strategies for established audiovestibular impairment. Monitoring/screening trials were defined as studies that focused on detecting, measuring, predicting, or monitoring ototoxicity or hearing disability, including diagnostic studies, observational studies, screening programs, biomarker studies, genetic susceptibility studies, electrophysiological assessments, audiological monitoring protocols, and risk assessment studies. This classification was used because the relevance of disability to ototoxicity research varies depending on whether the study aims to prevent hearing loss, manage existing disabilities, or improve early detection and monitoring.

2.6 Classification of hearing-disability outcomes

Outcome measures were extracted from the primary, secondary, and other outcome-measure fields and classified into predefined hearing disability categories. These categories are not mutually exclusive because a single study could include more than one outcome type. The categories included the incidence or severity of hearing loss/ototoxicity, objective audiometric or cochlear measures, patient-reported hearing disability or hearing-related quality of life, tinnitus-related outcomes, vestibular or balance-related outcomes, hearing rehabilitation or assistive-device outcomes, speech perception or speech-in-noise outcomes, biomarker/genetic/electrophysiological outcomes, and screening or monitoring implementation outcomes. Records with no clearly reported hearing- or ototoxicity-related endpoints were classified as having no direct hearing disability. The primary outcome was the type and frequency of hearing disability outcomes reported in the registered ototoxicity-related studies. Secondary outcomes included the distribution of studies by drug/exposure class, clinical context, trial purpose, study status, study type, age, eligibility, region, and availability of posted results.

2.7 Statistical analysis

The data were descriptively analyzed. Categorical variables are summarized as frequencies and percentages. Percentages were calculated using the final analytic sample of 48 valid ClinicalTrials.gov records as the denominator unless otherwise stated. Data cleaning, coding, and descriptive analyses were conducted using Microsoft Excel. For subgroup comparisons among the prevention, treatment/rehabilitation, and monitoring/screening trials, percentages were calculated within each trial-purpose category. Subject demographics were limited to registry-reported eligibility characteristics, including age group and sex; individual-level demographic data, such as exact age, weight, or participant-level sex distribution, were not available. Because

several categories were not mutually exclusive, especially age eligibility, geographic region, clinical context, and outcome type, the totals could exceed 100% in those sections. This is clearly indicated in the table footnotes. The analysis emphasized descriptive interpretation over hypothesis testing because the sample size was modest and the study aimed to characterize the clinical trial landscape rather than estimate treatment effects. A priori power analysis or sample size calculation was not performed because the objective was descriptive rather than hypothesis testing, and the final analytic sample included all eligible ototoxicity-related ClinicalTrials.gov records identified using the predefined search strategy. The comparative table examined differences across the three trial-purpose groups in terms of study status, study type, intervention/exposure type, clinical context, age eligibility, results availability, and hearing-disability outcome categories. No meta-analysis was conducted because this study did not analyze individual participant data, treatment effects, or published efficacy outcomes. Missing or unclear registry fields were retained as “missing/not reported” categories when applicable; no imputation was performed. As this was a registry-based cross-sectional analysis of study records rather than a participant-level clinical trial, no participant recruitment, allocation, randomization, blinding, or follow-up was performed. Therefore, participant attrition and loss to follow-up were not possible. No a priori power calculation was conducted because the study included all eligible ototoxicity-related records retrieved from ClinicalTrials.gov using a predefined search strategy. Age and sex were extracted as registry-reported eligibility categories, rather than individual participant demographics. No custom statistical code was generated, and data cleaning, coding, and descriptive analyses were performed using Microsoft Excel. Participant attrition and loss to follow-up were not applicable because this study analyzed ClinicalTrials.gov registry records rather than the recruited participants or individual-level longitudinal data.

3. RESULTS AND DISCUSSION

3.1 Study Selection

ClinicalTrials.gov export yielded 48 records. All percentages were calculated using these 48 records as the denominator unless otherwise stated. Of the included studies, 21 (43.8%) were completed, 10 (20.8%) were recruited, 9 (18.8%) had unknown status, 3 (6.3%) were not yet recruited, and 2 (4.2%) were active but not recruited. One study was terminated, withdrawn, or suspended. Most studies were interventional clinical trials (34, 70.8%), whereas 14 (29.2%) were observational studies. Most studies included adult participants (45, 93.8%), followed by older adults (37, 77.1%) and children (10, 20.8%). North America was the most common study location (20, 41.7%), followed by Europe (14, 29.2%), Asia (seven, 14.6%), Africa (three, 6.3%), South America (three, 6.3%), and other regions (one, 2.1%). As some studies included more than one region or age group, these categories were not mutually exclusive. The study phase was most commonly classified as not applicable (23, 47.1%), followed by phase 2 (14, 29.2%) (Table 1).

Table 1. Table 1: General characteristics of ototoxicity-related studies registered in ClinicalTrials.gov

Status	N (%)
Recruiting	10 (20.8)
Not yet recruiting	3 (6.25)
Enrolling by invitation	0
Completed	21 (43.75)
Terminated	1 (2.08)
Withdrawn	1 (2.08)
Active, not recruiting	2 (4.16)
Approved for market	0
Suspended	1 (2.08)
Unknown	9 (18.75)
Sex eligibility	

All sexes	48 (100)
Female	47 (97.91)
Male	48 (100)
Age	
Child (birth - 17)	10 (20.8)
Adult (18 - 64)	45 (93.75)
Older adult (65+)	37 (77.08)
Study type	
Interventional (Clinical Trial)	34 (70.83)
Observational	14 (29.16)
Region	
Africa	3 (6.25)
Europe	14 (29.16)
North America	20 (41.66)
Asia	7 (14.58)
South America	3 (6.25)
Others	1 (2.08)
Study Phase	
Early Phase 1	1 (2.08)
Phase 1	3 (6.25)
Phase 2	14 (29.16)
Phase 3	5 (10.41)
Phase 4	2 (4.16)
Not applicable (Describes trials without FDA-defined phases, including trials of devices or behavioral interventions.)	23 (47.08)

Platinum-based chemotherapy and mixed cancer treatment exposures were the largest categories of ototoxicity-related studies, accounting for 33 (68.8%).

These studies commonly involved cisplatin, carboplatin, platinum salts, or platinum-based chemoradiotherapy in adult or pediatric cancer settings. Aminoglycoside and anti-infective therapies were the second most common category (10, 20.8%), including studies involving amikacin, gentamicin, tobramycin, or aminoglycoside-related ototoxicity.

Radiation- or radiosurgery-related hearing risk was identified in two (4.2%) studies, whereas COVID-19 treatment/vaccine-related exposure, surgical antiseptic/chemical exposure, and antihypertensive medication-related context were each reported in one (2.1%) study. These categories indicated that most registered ototoxicity-related studies were concentrated in cancer treatment contexts, particularly in platinum-based chemotherapy (Table 2).

Table 2. Drug classes and clinical contexts associated with hearing disability in ototoxicity-related ClinicalTrials.gov studies (Values are presented as n (%). Percentages were calculated using 48 valid ClinicalTrials.gov records as the denominator. Each study was assigned to one dominant drug/exposure class based on the title, condition, intervention, and summary)

Drug/exposure class	Main ototoxic agent or exposure	Main clinical context	Hearing-disability relevance	n (%)
Platinum-based chemotherapy and mixed cancer treatment exposures	Cisplatin, carboplatin, platinum salts, platinum-based chemoradiotherapy	Adult and pediatric cancer treatment, including head and neck cancers, childhood cancers, osteosarcoma, liver cancer, testicular cancer, and solid tumors	Sensorineural hearing loss, ototoxic hearing loss, tinnitus, hearing-related quality of life, hearing screening, and hearing preservation	33 (68.8)
Aminoglycoside and anti-infective therapy	Amikacin, tobramycin, gentamicin, aminoglycosides, anti-infective therapy $\pm$ vancomycin	Nontuberculous mycobacterial infection, cystic fibrosis, neonatal infection, peritoneal dialysis-related infection, and aminoglycoside-associated vestibular dysfunction	Drug-induced hearing loss, ototoxicity monitoring, cochlear toxicity, hearing impairment, and audiotestibular disability	10 (20.8)
Radiation or radiosurgery-related hearing risk	Stereotactic radiosurgery, intensity-modulated radiation therapy, 3-dimensional conformal radiation therapy	Vestibular schwannoma and head/neck tumor treatment without a clear primary medication exposure	Hearing preservation, radiation-induced ototoxicity, hearing loss, and quality-of-life impact	2 (4.2)
COVID-19 treatment/vaccine-related exposure	Medications used for COVID-19 treatment and COVID-19 vaccine exposure	Assessment of hearing after COVID-19 treatment or vaccination	Hearing changes and ototoxicity assessment	1 (2.1)
Surgical antiseptic/chemical exposure	Chlorhexidine scrub	Facial cutaneous surgery	Potential ocular or ear toxicity, including ototoxicity risk	1 (2.1)
Antihypertensive medication-related context	Ototoxic drugs used for arterial hypertension	Tinnitus and arterial hypertension	Tinnitus severity and hearing loss in relation to medication exposure	1 (2.1)

3.2 Outcome measures used to assess hearing disability

Most studies reported outcomes related to the incidence, severity, or grade of hearing loss/ototoxicity (41, 85.4%). Objective audiometric or cochlear measures were also common (33, 68.8%), including pure-tone audiometry, extended high-frequency audiometry, hearing thresholds, otoacoustic emissions, and other measures of cochlear function. Studies included patient-reported hearing disabilities or hearing-related quality-of-life outcomes in 22 (45.8%) studies. Tinnitus-related outcomes were reported in 18 (37.5%) studies, whereas vestibular or balance-related disability outcomes were included in 12 (25.0%) studies. Outcomes related to hearing rehabilitation or assistive device use were reported in 10 studies (20.8%). Speech perception or speech-in-noise outcomes and biomarker/genetic/electrophysiological outcomes were reported in 9 (18.8%) studies. Only 5 (10.4%) studies reported screening or monitoring implementation outcomes. Three studies (6.3%) did not report direct hearing disability or ototoxicity-related outcomes. Overall, studies used clinical and audiometric outcomes more frequently than patient-

centered, functional, rehabilitation, or implementation outcomes (Table 3). It provides an overview of the included studies, the main clinical contexts, trial purposes, and hearing-disability outcomes assessed (Figure 1).

Table 3. Types of outcomes used to measure hearing disability in ototoxicity-related ClinicalTrials.gov studies (Values are presented as n (%). Categories are not mutually exclusive because a single study could include more than one outcome type)

Outcome type	Examples of measures or indicators	n (%)
Incidence, severity, or grade of hearing loss/ototoxicity	Hearing loss incidence, ototoxicity grade, ASHA ototoxic shift criteria, Brock grading, CTCAE ototoxicity, and hearing preservation	41 (85.4)
Objective audiometric or cochlear measures	Pure-tone audiometry, extended high-frequency audiometry, audiogram, hearing thresholds, DPOAE, otoacoustic emissions, cochlear function	33 (68.8)
Patient-reported hearing disability or hearing-related quality of life	Speech, Spatial and Qualities of Hearing Scale, hearing-related quality of life, hearing-related fatigue, questionnaires, TOMI, Tinnitus Handicap Inventory	22 (45.8)
Tinnitus-related outcomes	Tinnitus incidence, tinnitus severity, Tinnitus Functional Index, Tinnitus Handicap Inventory, SOMA-LENT tinnitus grading	18 (37.5)
Vestibular or balance-related disability outcomes	Vestibular symptoms, vertigo, balance, Dynamic Gait Index, vestibulo-ocular reflex, video head impulse test	12 (25.0)
Hearing rehabilitation or assistive-device outcomes	Hearing aid use, hearing prosthesis, cochlear implant, hearing rehabilitation, referral for hearing support	10 (20.8)
Speech perception or speech-in-noise outcomes	Speech audiometry, speech perception in noise, Digits-in-Noise test, words-in-noise test, consonant identification, sentence test	9 (18.8)
Biomarker, genetic, or electrophysiological outcomes	Plasma/serum biomarkers, electrophysiological tests, genetic susceptibility, pharmacogenomics	9 (18.8)
Screening or monitoring implementation outcomes	Hearing screening completion, ototoxicity monitoring programs, audiology screening tools, tablet/web-based audiometry, referral or follow-up indicators	5 (10.4)
No direct hearing-disability outcome stated	No outcome measures reported or outcomes not directly related to hearing disability	3 (6.3)

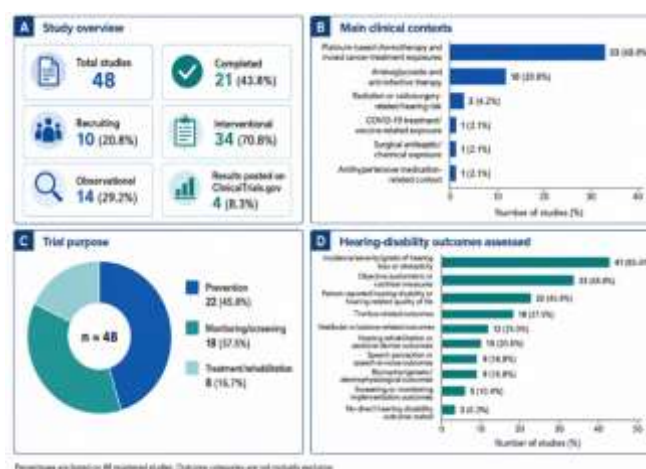


Figure 1. Overview of ototoxicity-related ClinicalTrials.gov studies. This figure summarizes the general characteristics, main clinical contexts, trial purposes, and hearing-disability outcomes assessed among 48 ototoxicity-related studies registered in ClinicalTrials.gov. Percentages are based on 48 registered studies. Outcome categories are not mutually exclusive.

3.3 Comparison by trial purpose

When studies were classified by primary purpose, 22 (45.8%) were prevention trials, eight (16.7%) were treatment/rehabilitation trials, and 18 (37.5%) were monitoring/screening trials. Among the prevention trials, 11 (50.0%) were completed, and 9 (40.9%) were unknown, terminated, withdrawn, or suspended. In contrast, most treatment/rehabilitation trials were active, recruiting, or not yet recruiting ($n = 6$, 75.0%). Monitoring/screening trials included nine (50.0%) completed studies, and seven (38.9%) were active, recruiting, or not yet recruiting.

All prevention and treatment/rehabilitation trials were interventional, whereas most monitoring/screening trials had observational or other non-interventional designs (14, 77.8%). Drug interventions were most common in prevention trials (21, 95.5%), less common in treatment/rehabilitation trials (three, 37.5%), and rare in monitoring/screening trials (one, 5.6%). Cancer/platinum-related contexts were common in prevention (19, 86.4%) and monitoring/screening trials (13, 72.2%), whereas aminoglycoside/anti-infective contexts were more prominent in treatment/rehabilitation trials (5, 62.5%). Only four (8.3%) studies had results posted on ClinicalTrials.gov, including three (13.6%) prevention trials and one (5.6%) monitoring/screening trial; no treatment/rehabilitation trials had posted results (Table 4). This registry-based analysis summarizes the major findings and research gaps (Figure 2).

Table 4. Comparison between prevention, treatment/rehabilitation, and monitoring/screening trials

Characteristic	Prevention trials $n = 22$	Treatment/rehabilitation trials $n = 8$	Monitoring/screening trials $n = 18$	Total $N = 48$
Study status				
Completed	11 (50.0)	1 (12.5)	9 (50.0)	21 (43.8)
Active/recruiting/not yet recruiting	2 (9.1)	6 (75.0)	7 (38.9)	15 (31.3)
Unknown/terminated/withdrawn/suspended	9 (40.9)	1 (12.5)	2 (11.1)	12 (25.0)
Study type				
Interventional	22 (100.0)	8 (100.0)	4 (22.2)	34 (70.8)
Observational/other	0 (0.0)	0 (0.0)	14 (77.8)	14 (29.2)
Main intervention/exposure type				
Drug intervention	21 (95.5)	3 (37.5)	1 (5.6)	25 (52.1)
Device, diagnostic, behavioral, genetic, procedure, radiation, or other intervention	4 (18.2)	5 (62.5)	13 (72.2)	22 (45.8)

Clinical context				
Cancer/platinum-related context	19 (86.4)	3 (37.5)	13 (72.2)	35 (72.9)
Aminoglycoside/anti-infective context	2 (9.1)	5 (62.5)	3 (16.7)	10 (20.8)
Radiation/radiosurgery-related context	1 (4.5)	1 (12.5)	4 (22.2)	6 (12.5)
Age eligibility				
Child participants eligible	5 (22.7)	0 (0.0)	5 (27.8)	10 (20.8)
Adult and/or older adult participants are eligible	22 (100.0)	8 (100.0)	16 (88.9)	46 (95.8)
Results availability				
Results posted on ClinicalTrials.gov	3 (13.6)	0 (0.0)	1 (5.6)	4 (8.3)
Hearing-disability outcome type				
Incidence, severity, or grade of hearing loss/ototoxicity	21 (95.5)	3 (37.5)	17 (94.4)	41 (85.4)
Objective audiometric/cochlear outcome	21 (95.5)	1 (12.5)	11 (61.1)	33 (68.8)
Hearing-related quality of life or patient-reported outcome	8 (36.4)	6 (75.0)	8 (44.4)	22 (45.8)
Tinnitus-related outcome	6 (27.3)	7 (87.5)	5 (27.8)	18 (37.5)
Vestibular or balance-related outcome	4 (18.2)	5 (62.5)	3 (16.7)	12 (25.0)
Rehabilitation or assistive-device outcome	0 (0.0)	5 (62.5)	5 (27.8)	10 (20.8)
Speech perception or speech-in-noise outcome	4 (18.2)	1 (12.5)	4 (22.2)	9 (18.8)

Biomarker, genetic, or electrophysiological outcome	5 (22.7)	1 (12.5)	3 (16.7)	9 (18.8)
Screening or monitoring implementation outcome	0 (0.0)	0 (0.0)	5 (27.8)	5 (10.4)
No direct hearing-disability outcome stated	1 (4.5)	1 (12.5)	1 (5.6)	3 (6.3)

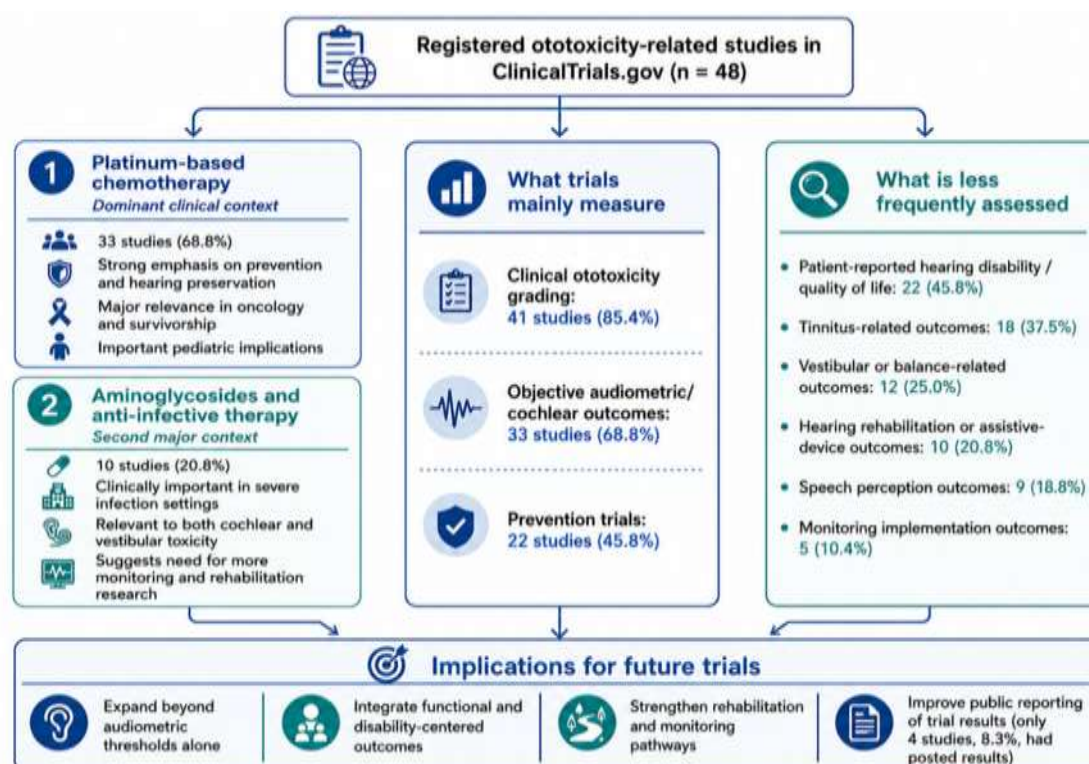


Figure 2. Major findings and research gaps in medication-related hearing disability trials.

This figure summarizes the dominant clinical contexts, commonly assessed outcomes, less frequently assessed disability-centered outcomes, and future research implications from the registry-based analysis of ototoxicity-related ClinicalTrials.gov studies.

3.4 Hearing-disability outcomes by trial purpose

The distribution of hearing disability outcomes varied across trial-purpose groups. Prevention trials most often assessed the incidence, severity, or grade of hearing loss/ototoxicity (21, 95.5%), and objective audiometric or cochlear outcomes (21, 95.5%). However, fewer prevention trials included patient-reported hearing disabilities or quality-of-life outcomes (8, 36.4%), tinnitus-related outcomes (6, 27.3%), speech perception outcomes (4, 18.2%), and vestibular/balance-related outcomes (4, 18.2%). None of the prevention trials included screening or monitoring of implementation outcomes. Treatment/rehabilitation trials have exhibited different patterns. Six (75.0%) studies reported patient-reported hearing disability or quality-of-life outcomes, seven (87.5%) reported tinnitus-related outcomes, five (62.5%) reported vestibular or balance-related outcomes, and five (62.5%) reported rehabilitation or assistive-device outcomes. However, only 3 (37.5%) treatment/rehabilitation trials reported the incidence or severity of hearing loss/ototoxicity, and only 1 (12.5%) reported objective audiometric or cochlear outcomes. Monitoring/screening trials commonly reported the incidence, severity, or grade of hearing loss/ototoxicity (17,

94.4%), and objective audiometric or cochlear outcomes (11, 61.1%). Patient-reported hearing disability or quality-of-life outcomes were reported in eight (44.4%) monitoring/screening trials, while tinnitus-related outcomes were reported in five (27.8%) trials. The monitoring/screening group reported implementation outcomes in only five trials (27.8%). Across all trial-purpose groups, disability-centered outcomes, such as speech perception, rehabilitation or assistive-device use, vestibular/balance disability, and implementation outcomes, were reported less frequently than clinical ototoxicity grades or audiometric outcomes (Table 4).

3.5 DISCUSSION

This registry-based cross-sectional study characterized ototoxicity-related clinical studies registered on ClinicalTrials.gov, focusing on medication-related hearing disabilities. The current trial landscape centers on two ototoxic drugs: platinum-based chemotherapy and aminoglycoside or anti-infective therapy. Platinum-based chemotherapy was the primary clinical context, whereas aminoglycoside-related studies formed a smaller, but clinically important group. Among these studies, ototoxicity was most often assessed using clinical grading systems and audiometric measures, whereas functional and disability-centered outcomes were reported less consistently. This suggests that registered ototoxicity trials focus more on detecting auditory injury than on capturing the broader real-world consequences of medication-related hearing disabilities.

Several studies have shown that platinum-based chemotherapy, particularly with cisplatin, is strongly associated with permanent sensorineural hearing loss [20-22]. This explains why most studies have focused on platinum-based chemotherapy and combined cancer treatment. Previous studies indicated that cisplatin-related ototoxicity is often bilateral, progressive, and irreversible, making hearing preservation an important concern in oncology [13, 23]. Therefore, the strong representation of platinum-related trials reflects the clinical importance of preventing hearing damage in patients receiving essential anticancer therapies. However, the findings also show that many of these trials continue to prioritize audiometric threshold changes and ototoxicity grades over outcomes that reflect communication, participation, rehabilitation, and QoL. The impact of platinum-induced ototoxicity on disability is significant in pediatric oncology. Several studies have reported that cisplatin-related hearing loss in children may affect speech and language development, educational performance, social participation, and long-term survivorship outcomes [24, 25]. Therefore, pediatric platinum-related trials should not only evaluate hearing thresholds, but also assess speech perception, classroom communication, hearing-aid use, rehabilitation needs, and hearing-related quality of life. However, in the present study, disability-centered outcomes were less common than the objective hearing measures. This suggests that the current evidence may underestimate the long-term functional burden associated with platinum-induced hearing disability.

Aminoglycosides represented the second major medication-related context in this analysis. It is well established that aminoglycosides such as gentamicin, amikacin, and tobramycin can cause cochlear and vestibular toxicity [26, 27]. Aminoglycosides remain critically important because they treat severe infections, neonatal sepsis, cystic fibrosis, resistant gram-negative infections, and mycobacterial diseases. Several studies have shown that aminoglycoside ototoxicity may involve both the hearing and balance systems, leading to hearing loss, tinnitus, dizziness, imbalance, and reduced daily functioning [28-30]. Therefore, aminoglycoside-induced ototoxicity should be regarded as an audiovestibular disability, rather than merely a hearing threshold. The relatively small number of aminoglycoside-related studies indicates an important research gap. Unlike platinum chemotherapy, which is typically administered in specialized oncology settings, aminoglycosides are used in a wide range of clinical settings, including hospitals, neonatal units, infectious disease services, and outpatient antimicrobial programs. This makes monitoring and follow-up challenging. Therefore, future aminoglycoside-related trials should include outcomes related to vestibular function, balance, tinnitus, speech perception, therapeutic drug monitoring, genetic susceptibility, audiology referral, and access to rehabilitation services. Such outcomes are necessary to fully understand the burden of disability associated with aminoglycoside exposure.

A key finding of this study is the gap between clinical detection and disability assessment. Most studies have assessed ototoxicity using incidence, severity, grading systems, or objective audiometric outcomes [31, 32]. These measures are scientifically important because they provide standardized indicators of auditory injuries. However, audiometric findings alone may not fully capture a patient's lived experience of hearing disability [33]. Patients may experience difficulty understanding speech in noise, communication fatigue, tinnitus distress, balance problems, social withdrawal, and reduced quality of life [34]. Therefore, trials that focus primarily on audiograms may fail to capture outcomes most relevant to patients' daily lives. This issue applies to both platinum-based chemotherapy and aminoglycoside therapy. In patients treated with platinum, hearing loss may affect cancer

survival, school performance, employment, and social participation. In patients treated with aminoglycosides, vestibular injury may limit balance, mobility, and independence. Despite this, rehabilitation and implementation outcomes related to speech perception, vestibular function, and balance were reported less frequently than audiometric outcomes. This finding supports the need for a broader, disability-centered outcome framework for ototoxicity trials.

Prevention trials were also the most common trial purpose, especially in platinum-related contexts. This is because preventing ototoxicity before permanent hearing damage occurs is clinically important, especially when ototoxic drugs are essential for cancer treatment. However, prevention measures alone are insufficient. Despite preventive strategies, some patients still develop hearing or vestibular disabilities. Therefore, additional studies are needed on treatment, rehabilitation, tinnitus management, vestibular rehabilitation, assistive hearing technologies, and long-term follow-up after ototoxic injuries. Monitoring and screening are essential during platinum-based chemotherapy and aminoglycoside therapy. Several studies have emphasized the importance of early ototoxicity identification to enable timely dose review, audiology referral, counseling, and rehabilitation planning. However, in the present analysis, the implementation outcomes were rare. This matters because a monitoring protocol has limited value if it is not feasible, incomplete, or not linked to clinical action. Future trials should assess not only whether ototoxicity can be detected, but also whether monitoring improves referral rates, follow-up, access to rehabilitation, patient counseling, and the prevention of long-term disability. Another important finding was the limited availability of the posted results on ClinicalTrials.gov. Although many studies were completed, only a small proportion of their results were posted in the registry. This limits transparency and reduces clinicians', researchers', and policymakers' ability to use existing trial evidence. For platinum-based chemotherapy and aminoglycosides, where treatment decisions require balancing the therapeutic benefits against the risk of long-term disability, timely public reporting is especially important. Improved reporting would support evidence synthesis, reduce duplication, and strengthen medication safety and ototoxicity monitoring guidelines.

This study had several limitations. The analysis depends on ClinicalTrials.gov records, which may be incomplete, inconsistently updated, or less detailed than the full protocols or published articles. The search strategy focused on the term “ototoxicity,” so relevant studies on cisplatin, aminoglycosides, hearing loss, tinnitus, or vestibular toxicity may have been missed if they did not use ototoxicity-related terminology in the registry. This may have introduced selection bias, and reliance on registry-reported descriptions and outcome fields may have introduced a reporting or misclassification bias. Finally, this study analyzed registry records rather than individual participant data; therefore, it could not evaluate treatment effectiveness, incidence rates, or the actual severity of hearing disability among the enrolled participants.

4. CONCLUSION

This study found that registered ototoxicity studies are primarily focused on platinum-based chemotherapy, with fewer addressing aminoglycoside-related audiovestibular toxicities. Current trials frequently assess clinical ototoxicity grades and audiometric changes, but are less consistent in measuring the functional and patient-centered consequences of medication-related hearing disability. Future studies on platinum and aminoglycoside medications should integrate audiometric, speech perception, tinnitus, vestibular, quality of life, rehabilitation, and implementation outcomes. This broader approach would better reflect the real-world burden of ototoxicity and support more effective prevention, monitoring, and rehabilitation strategies for patients at risk of medication-related hearing disabilities.

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AUTHOR CONTRIBUTIONS

Not Applicable

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

ETHICS STATEMENT

This study used publicly available registry data from ClinicalTrials.gov and did not involve individual-level patient data, direct contact with participants, or access to private identifiable information. Therefore, institutional review board approval was not required for this study. Informed consent was not applicable because the study did not involve direct contact with participants, delivery of interventions, or analysis of individually identifiable participant data.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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