Prevalence of Ototoxicity-Related Symptoms Among Chemotherapy Patients: A Systematic Review

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ABSTRACT

Chemotherapy-related ototoxicity can affect hearing, tinnitus, and vestibular or balance function, yet reported prevalence varies with treatment exposure, patient population, outcome definition, and assessment method. This systematic review examined the prevalence and clinical characteristics of ototoxicity-related outcomes among patients receiving systemic chemotherapy and explored audiometric patterns, treatment-related factors, and patient characteristics associated with risk. English-language observational studies of human cancer patients of any age or cancer type, published from 2019 to 31 May 2026, were eligible. PubMed/MEDLINE, Europe PMC, the Cochrane Library, and Google Scholar were last searched on 16–17 July 2026. The review was reported in accordance with PRISMA 2020, and methodological quality was appraised using design-specific JBI critical appraisal tools. Owing to substantial clinical and methodological heterogeneity, findings were synthesised narratively and no meta-analysis was performed. Twenty-three publications were included. Prevalence estimates for self-reported hearing loss ranged from approximately 30.5% to 59%, whereas audiometrically defined hearing loss ranged from 43.8% to 78%. Tinnitus was common where assessed, with occurrence estimates of 37.1%–68%, but was examined in only seven publications; vestibular or balance-related outcomes were examined in five. High-frequency sensorineural hearing loss was the most consistent audiometric pattern, and cisplatin dominated the evidence base. Greater cumulative exposure, treatment schedule, baseline hearing status, and selected patient-related factors were associated with ototoxic risk. Interpretation was limited by heterogeneous outcome definitions and sparse evidence outside cisplatin-treated populations. Overall, chemotherapy-related ototoxicity is heterogeneous, supporting more consistent outcome definitions, broader assessment across symptom domains, and risk-based audiological monitoring. The review was not prospectively registered.

Keywords: *chemotherapy, ototoxicity, hearing loss, tinnitus, vestibular dysfunction, cisplatin, audiological monitoring.*

INTRODUCTION

Chemotherapy remains one of the main treatment approaches used in the management of different types of cancer. Advances in cancer treatment have improved survival rates and allowed many patients to live longer after diagnosis. In the United States, the five-year relative survival rate across all cancers increased from 63% in the mid-1990s to 70% among patients diagnosed between 2015 and 2021 (Siegel et al., 2026). However, despite its therapeutic value, chemotherapy may also cause adverse effects that can continue during and after treatment. Among these complications, ototoxicity is an important concern, particularly in patients treated with platinum-based agents such as cisplatin and carboplatin, which have been associated with hearing loss, tinnitus, and other ototoxic effects in cancer survivors (Landier, 2016).

Ototoxicity refers to drug-induced damage to the auditory system and the vestibular structures of the inner ear. It encompasses cochleotoxicity, which affects hearing, and vestibulotoxicity, which affects balance. In patients receiving chemotherapy, it may present as hearing loss, tinnitus, dizziness, vertigo, or unsteadiness, with several symptoms often occurring together rather than in isolation (Paken et al., 2016).

The impact of ototoxicity extends beyond measurable changes in hearing thresholds. Hearing loss and tinnitus can make communication more difficult, particularly in noisy environments, and the additional effort required to listen may contribute to fatigue and reduced participation in conversations. Vestibular difficulties can also interfere with walking and increase the risk of falls. Together, these effects can limit everyday functioning, contribute to social withdrawal, and reduce overall quality of life (Phillips et al., 2023).

Among chemotherapeutic drugs, platinum-based agents are the most widely recognized causes of ototoxicity, with cisplatin being the main concern. Cisplatin-induced hearing loss is typically sensorineural, bilateral, progressive, and permanent (Landier, 2016). It usually begins at higher frequencies before gradually extending toward the frequencies that are important for speech. Because these early changes may fall outside the range assessed by conventional pure-tone audiometry, measurable hearing loss can develop before patients notice difficulties in everyday listening (Paken et al., 2016). The risk and severity of hearing loss generally increase with greater cumulative exposure to cisplatin, although individual susceptibility may also be influenced by patient- and treatment-related factors. Carboplatin can also cause ototoxicity, but its reported risk is usually lower than that associated with cisplatin-containing treatment (Dillard et al., 2022).

Although hearing loss has received the most attention in chemotherapy related ototoxicity research, tinnitus and vestibular symptoms are not always assessed consistently. Studies also differ in the methods used to identify and measure ototoxicity, including patient related symptoms, pure tone audiometry, high frequency audiometry, otoacoustic emissions, auditory brainstem response, and ototoxicity grading scales. In addition, differences in cancer type, chemotherapy agent, follow up duration, and patient characteristics make it difficult to estimate the true prevalence of ototoxicity related-

symptoms among chemotherapy patients (El Charif et al., 2019; Zhang et al., 2022).

These inconsistencies highlight the need for a systematic review that brings together recent evidence on ototoxicity related symptoms among patients receiving chemotherapy. Previous reviews have generally focused on individual aspects of chemotherapy-related ototoxicity, such as hearing loss, vestibular dysfunction, or its impact on quality of life (Dillard et al., 2022; Fleihan et al., 2024; Phillips et al., 2023). However, few have examined hearing loss, tinnitus, and vestibular symptoms together across different chemotherapy agents and cancer types. A clearer understanding of the prevalence of hearing loss, tinnitus, and vestibular symptoms is important for clinical practice, as early identification of ototoxicity may support timely audiological monitoring, counseling, hearing rehabilitation, and referral when needed. It may also help clinicians recognize patients who are at higher risk and may require closer follow up during and after chemotherapy.

Therefore, this thesis aims to systematically review the literature published between 2019 and 2026 on the prevalence of ototoxicity related symptoms among patients receiving chemotherapy, with a focus on hearing loss, tinnitus, and vestibular symptoms. It examines how frequently these symptoms occur, how they present, and which factors may influence their occurrence and severity. The scope of the review, based on the eligibility criteria described in the Methods, is defined as follows:

Population: Patients of any age receiving one or more systemic chemotherapeutic agents for cancer treatment, regardless of cancer type.

Exposure: Chemotherapeutic agents, with particular attention to platinum-based compounds and cumulative administered dose.

Outcomes: Hearing loss, tinnitus, dizziness, and other vestibular symptoms occurring during or after chemotherapy.

Main research question

What is the prevalence of hearing loss, tinnitus, and vestibular symptoms among patients receiving chemotherapy, and which factors are associated with their occurrence and severity?

Specific objectives

1. To determine the prevalence of hearing loss among patients receiving chemotherapy.
2. To determine the prevalence of tinnitus among patients receiving chemotherapy.
3. To determine the prevalence of dizziness and vestibular symptoms among patients receiving chemotherapy.
4. To describe the audiometric patterns reported in chemotherapy-related ototoxicity.
5. To examine the relationship between cumulative chemotherapy dose and the severity of ototoxicity-related symptoms and audiometric changes.
6. To identify the chemotherapeutic agents most strongly associated with ototoxicity-related symptoms.
7. To explore whether patient-related factors, including age, sex, and comorbidities, influence the

occurrence or severity of ototoxicity-related symptoms where sufficient data are available.

Need of the study

Routine audiological monitoring is still not consistently implemented across oncology settings. Even where monitoring programmes are available, they may be limited by staffing, equipment, and the clinical priorities of active cancer treatment (Ehlert et al., 2022; Gambacorta et al., 2023). In this context, decisions about which patients should be monitored, how frequently testing should occur, and which protocols should be used depend largely on identifying those at greatest risk. Clarifying the patients, chemotherapy agents, and dose levels most commonly associated with ototoxicity may therefore support more effective use of limited audiological resources.

This issue is also important from an audiological perspective. Much of the research on chemotherapy-related ototoxicity has been conducted within oncology and pharmacology, where auditory and vestibular effects are often recorded as treatment-related adverse events rather than examined as primary outcomes. As a result, audiological reporting is often inconsistent. Testing procedures may be described only briefly, extended high-frequency audiometry may not be included, and symptoms such as tinnitus or imbalance may be assessed through general adverse-event reporting rather than validated symptom-specific measures. Reviewing this evidence from an audiological standpoint allows consideration not only of the reported findings, but also of whether the methods used were sensitive enough to detect ototoxic changes.

Previous reviews have addressed separate aspects of the problem. Dillard et al. (2022) focused on chemotherapy-related hearing loss, Fleihan et al. (2024) examined vestibulotoxicity, and Phillips et al. (2023) explored the impact of ototoxicity on quality of life. However, hearing loss, tinnitus, and vestibular symptoms have rarely been considered together across different chemotherapy agents and cancer types. By bringing together recent evidence on these outcomes and examining how ototoxicity was defined and measured, this review addresses a gap left by more narrowly focused syntheses. Its findings may support clinicians involved in the audiological care of patients receiving chemotherapy and help researchers identify areas in which greater methodological consistency and standardization are needed.

METHOD

Design

This study was conducted as a systematic review with narrative synthesis and was reported in accordance with PRISMA 2020 (Page et al., 2021). Narrative synthesis was specified in the approved research proposal and retained after study selection because the included publications differed substantially in cancer population, chemotherapy exposure, outcome definition, assessment method, and follow-up. These differences made statistical pooling inappropriate. The review was not prospectively registered and no separate protocol was published; the approved proposal served as the prespecified methodological framework.

Eligibility Criteria

Eligible reports were English-language, peer-reviewed quantitative observational studies published from January 2019 to 31 May 2026. Participants were patients of any age with cancer who were receiving or had previously received systemic chemotherapy. Eligible designs included descriptive or analytical cross-sectional studies, cohort studies, and case-control studies. A report had to provide patient-level information on the occurrence, prevalence, incidence, severity, or development of at least one review outcome: hearing loss, tinnitus, dizziness, vertigo, imbalance, falls related to balance disturbance, or objective vestibular dysfunction.

Outcomes could be measured by patient report, conventional or extended high-frequency audiometry, otoacoustic emissions, speech-in-noise testing, vestibular assessment, or a recognised ototoxicity grading system. Chemoradiotherapy studies were eligible when systemic chemotherapy was an essential component of treatment and the relevant auditory or vestibular outcomes were reported. No age restriction was applied.

Animal and laboratory studies, case reports, reviews, editorials, letters, study protocols, conference-only publications, radiotherapy-only studies, non-systemic chemotherapy studies, and reports describing monitoring practice without patient-level outcomes were excluded. Studies designed primarily to test an intervention intended to prevent or treat ototoxicity were also excluded. When publications arose from the same or an overlapping cohort, they were linked and used only for the distinct information they contributed rather than counted as independent populations.

Information Sources and Search Strategy

An initial search was undertaken in May 2026. Because the source-level documentation from that search was incomplete, a formal updated search was subsequently conducted to verify the earlier retrieval and identify additional potentially eligible reports. PubMed/MEDLINE, Europe PMC, and the Cochrane Library were searched on 16 July 2026, and ten supplementary Google Scholar searches were conducted through Publish or Perish on 17 July 2026. The eligibility cut-off remained fixed at 31 May 2026, so later publications were not included.

Search strategies combined terms for chemotherapy and antineoplastic treatment with cancer terms and auditory or vestibular outcomes. Concepts included cisplatin, carboplatin, platinum-based chemotherapy, taxanes, ototoxicity, hearing loss, tinnitus, dizziness, vertigo, imbalance, audiometry, extended high-frequency audiometry, otoacoustic emissions, auditory brainstem response, VEMP, and vHIT. Controlled vocabulary was used where available together with free-text terms, and syntax was adapted for each source. Reference lists of relevant studies and reviews were also examined. Full executed strategies, search dates, and yields are provided in Appendix A.

The executed information sources differed from those specified in the approved proposal: Scopus, Web of Science, and ScienceDirect were not searched, whereas Europe PMC was added. Grey-literature databases and trial registries were not searched, and eligibility was restricted to

English-language publications. These deviations were retained transparently and considered when interpreting the completeness of the evidence base.

Study Selection Process

All records were combined in Microsoft Excel and deduplicated using DOI, PMID, normalised title, author names, publication year, and URL information where available. ChatGPT (OpenAI) was used to assist bibliographic processing, duplicate detection, and a conservative rule-based first screening pass. Records were classified as potentially eligible, unclear, or ineligible; when eligibility could not be established confidently from the available title and abstract, the record was retained for further assessment rather than automatically excluded.

A targeted high-sensitivity audit was then used to re-examine records judged more vulnerable to false-negative automated classification. The author made final article-level eligibility decisions and reassessed unclear cases, with thesis-advisor discussion when necessary. After deduplication, 2,475 unique records entered screening, 29 reports were sought for full-text assessment, and 23 publications were included. Appendix B contains the complete screening arithmetic, operational rules, and audit trail; Appendix C lists the full-text exclusions, and the PRISMA diagram summarises the overall process.

Data Extraction

Data were extracted by the author using a structured study-level framework. ChatGPT (OpenAI) assisted with organisation and preliminary extraction, but the author determined the final recorded values. Extracted information included country, design, sample size and population, cancer type, chemotherapy agent and regimen, cumulative exposure and treatment schedule, follow-up, audiological or vestibular assessment methods, outcome definitions, prevalence or treatment-emergent findings, frequency-specific threshold changes, otoacoustic-emission or vestibular-test results, associated risk factors, and study limitations.

When a study reported several follow-up points, relevant timepoints were retained. Patient-reported symptoms and objective findings were recorded separately when both were available, and original grading systems or study-specific definitions were preserved rather than converted to a common scale. Missing or unclear information was recorded as not reported and was not inferred; study authors were not contacted. Detailed characteristics of the included publications are presented in Table 1 (Results).

Risk of Bias Assessment

Methodological quality was assessed by the author using the Joanna Briggs Institute (JBI) critical appraisal tool appropriate to each design: the prevalence checklist (Munn et al., 2020), analytical cross-sectional tool (Barker et al., 2026), cohort tool (Barker et al., 2025), and case-control checklist (Moola et al., 2020). Appraisal considered domains such as participant selection, exposure and outcome measurement, confounding, statistical analysis, and completeness of follow-up where applicable. Item-level judgements were retained and were not converted into numerical JBI quality scores.

For interpretive purposes, each publication was additionally classified as low methodological concern, some concerns, or

high concern according to whether limitations affected critical domains such as selection, outcome ascertainment, confounding, or follow-up. These were review-defined qualitative categories rather than JBI scores. No study was excluded solely because of appraisal findings; instead, studies with limitations directly relevant to a result were given less interpretive weight. Full item-level judgements are presented in Appendix D.

Data Synthesis

Findings were synthesised narratively under seven prespecified themes: hearing loss and audiological findings, tinnitus, vestibular and balance outcomes, audiometric patterns, chemotherapy agents, cumulative dose and other treatment-related factors, and patient-related risk factors. Prevalence measured at a defined assessment point was distinguished from incidence or other treatment-emergent change because these measures describe different epidemiological quantities. Patient-reported symptoms were also kept separate from objectively measured abnormalities.

When longitudinal studies reported multiple follow-up assessments, all relevant timepoints were retained during extraction; the longest follow-up was used only when one estimate was required for a cross-study description. Multiple ototoxicity grading systems were not harmonised retrospectively, and frequency-specific outcomes were interpreted within the test range used by each study. Chemoradiotherapy cohorts were synthesised with particular attention to concurrent cochlear radiation, so their findings were not used to support chemotherapy-specific causal attribution when the treatment effects could not be separated.

Publications from overlapping Platinum Study populations were treated as linked reports rather than independent samples. Potential reporting bias was considered qualitatively, especially where tinnitus or vestibular outcomes were not assessed or not reported; absence of measurement was not treated as evidence that an outcome was absent. No meta-analysis, funnel-plot analysis, formal sensitivity analysis, or GRADE assessment was undertaken because of the clinical and methodological heterogeneity across the included evidence.

Results

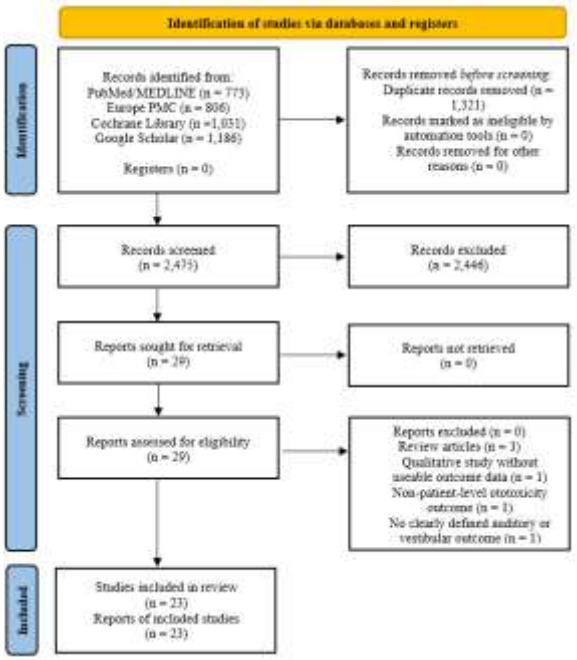
Study Selection

The searches identified 3,796 records; after removal of 1,321 duplicates, 2,475 unique records entered title-and-abstract screening. Twenty-nine reports proceeded to full-text assessment and 23 publications met the eligibility criteria. Six full-text reports were excluded, and no additional eligible publications were identified through reference-list screening.

The detailed machine-assisted screening and audit arithmetic is provided in Appendix B. Six included publications involved cisplatin-based chemoradiotherapy; these were retained because systemic chemotherapy was an essential treatment component, with concurrent radiation considered during interpretation.

The study-selection process is presented in Figure 1.

Figure 1.
PRISMA 2020 flow diagram of the study-selection process



Characteristics of Included Studies

The review included 23 publications from 13 countries: seven cross-sectional studies, 15 cohort studies, and one case-control study. Sample sizes ranged from 20 to 1,680 participants; most populations were adults, with three publications including paediatric or mixed younger populations.

Cisplatin-based treatment dominated the evidence, while carboplatin, other platinum agents, taxanes, and mixed chemotherapy exposures were less frequently represented. Five publications arose from related Platinum Study cohorts and were therefore interpreted as linked evidence rather than independent prevalence samples. Detailed study characteristics are provided in Table 1.

Table 1.
Characteristics of the 23 included publications

Study / design	Population / exposure	Assessment / key findings
Sanchez et al. (2023) United States; cross-sectional	145 testicular cancer survivors Exposure: Cisplatin	Validated hearing/tinnitus questionnaires Tinnitus 68%; hearing loss 59%; both 52%. Risk increased with age, dose and cardiovascular factors.
Sanchez et al. (2024) United States; longitudinal cohort	100 testicular cancer survivors; ≥3.5-year interval Exposure: Cisplatin	Audiometry 0.25–12 kHz; speech-in-noise Hearing loss 78% at follow-up; progression exceeded ageing expectations and was dose-associated.
Prayuenyong, Kasbekar, et al. (2021) United Kingdom; cross-sectional	65 adult cisplatin survivors Exposure: Cisplatin	Symptoms, balance tests, vHIT Balance symptoms 17%; vHIT normal. Neuropathy associated with symptoms.
El Charif et al. (2019) United States/Canada; cross-sectional	762 testicular cancer survivors Exposure: Cisplatin	Tinnitus questionnaires; clinical/genetic analyses Moderate/severe tinnitus associated with age and cumulative dose; >400 mg/m² increased risk.
Moke et al. (2021) Canada/United States; cohort	1,481 patients aged 0–39; 1,414 audiograms Exposure: Cisplatin	SIOP Boston audiogram review Moderate/severe hearing loss 43.8%; younger age, dose intensity and vincristine increased risk.
Zand et al. (2024) Iran; retrospective cohort	20 children, 6–17 years Exposure: Cisplatin	Extended high-frequency audiometry EHF loss 45%; more likely with ≥7 courses and >400 mg/m².
Cheung et al. (2023) United States; cross-sectional	273 adult cancer survivors Exposure: Platinum, taxane, or both	Self-report; audiometry 0.25–16 kHz Audiometric loss 52.3%–71.4%; tinnitus 37.1%–40.0%; no significant group differences.

Study / design	Population / exposure	Assessment / key findings
Funt et al. (2023) United States; retrospective cohort	115 germ-cell tumour patients Exposure: High-dose carboplatin-containing chemotherapy	Pre/post audiometry; ASHA criteria 66% developed moderate–profound speech-frequency loss; baseline high-frequency loss predicted severity.
Ehlert et al. (2025) South Africa; prospective cohort	32 mixed-cancer patients Exposure: Platinum agents	Audiometry, vHIT, VEMPs, DVA Cochleotoxic change in 50%; objective vestibular change occurred without reported symptoms.
Voruz et al. (2023) Switzerland; retrospective cohort	401 adults Exposure: Cisplatin	Baseline + symptom-triggered audiometry Symptomatic confirmed hearing loss 20%, mainly 4–8 kHz; 60% of affected patients developed tinnitus.
Paken et al. (2023) South Africa; prospective cohort	82 women with cervical cancer Exposure: Weekly cisplatin + radiotherapy	Serial conventional/EHF audiology Progressive bilateral high-frequency loss; severity increased with dose and was greater with HIV.
Halani et al. (2022) India; prospective cohort	80 adults Exposure: Cisplatin ± other treatment	Serial audiometry; WHO grading Ototoxicity 30% by three months; higher dose and baseline impairment increased risk.
Burger et al. (2024) Netherlands; retrospective cohort	129 head-and-neck cancer patients Exposure: Weekly vs triweekly cisplatin + radiotherapy	Speech/EHF audiometric averages Speech-frequency loss 19% weekly vs 42% triweekly; EHF loss remained common in both.
Basheer et al. (2025) India; prospective cohort	59 cisplatin-treated patients Exposure: Cisplatin	Audiometry to 20 kHz, DPOAE, speech-in-noise EHF thresholds, DPOAEs and speech-in-noise worsened; dose associations were non-significant.
Piper et al. (2024) Denmark; cross-sectional	200 adults ≥65 with gastrointestinal cancer Exposure: Systemic chemotherapy	Dizziness/balance questionnaire Dizziness 54%, impaired balance 48%, falls 11%; neuropathy associated with symptoms.
Musio et al. (2022) Italy; prospective cohort	35 head-and-neck cancer patients Exposure: Cisplatin chemoradiotherapy	Serial audiometry; cochlear dosimetry Hearing loss 37.1%; higher cochlear radiation dose increased risk.
Hülse et al. (2022) Germany; prospective cohort	45 head-and-neck cancer patients Exposure: Cisplatin chemoradiotherapy	Audiometry, vHIT, VEMPs Objective vestibular measures changed without dizziness; pure-tone thresholds did not change significantly.
Gamez et al. (2024) United States; retrospective cohort	96 head-and-neck cancer patients Exposure: Weekly vs triweekly cisplatin + IMRT	Serial audiology; CTCAE v5 Severe ototoxicity 13% weekly vs 56% triweekly; schedule remained independently associated.
Lee et al. (2024) Canada; case-control	201 HPV-positive oropharyngeal cancer patients Exposure: Weekly or high-dose cisplatin chemoradiotherapy	Audiometry; CTCAE v5 Ototoxicity 56.2%; high-dose cisplatin, cochlear radiation, smoking and age increased risk.
Kameo et al. (2021) Brazil; retrospective cohort	181 women with breast cancer Exposure: Systemic chemotherapy	Medical records; CTCAE tinnitus grading Tinnitus 49.2%; weak associations with neuropathy severity and completed cycles.
Okada and Kitagawa (2023) Japan; prospective cohort	96 evaluable adults with mixed cancers Exposure: Cisplatin ± chemoradiotherapy	Serial audiometry; CTCAE v4 Grade ≥2 hearing impairment 28.1%; ≥300 mg/m² associated with greater risk.
Ardeshirrouhanifard et al. (2022) United States/Canada/UK; cross-sectional	1,410 testicular cancer survivors Exposure: Cisplatin	Audiometry 0.25–12 kHz; ASHA; questionnaires Self-reported loss 34.8%; EHF loss often under-recognised. Age, dose and hypertension increased severity.

Study / design	Population / exposure	Assessment / key findings
Zhang et al. (2022) United States/Canada/UK ; cross-sectional	1,680 testicular cancer survivors Exposure: Cisplatin	Clinical/lifestyle and genetic analyses Hearing loss, tinnitus and neuropathy interrelated; lifestyle/metabolic and exploratory genetic associations identified.

Note. Design labels are harmonised with Appendix D. Related Platinum Study publications were retained separately for distinct outcomes but were not treated as independent populations.

Risk of Bias Findings

All 23 publications were appraised using the design-appropriate JBI tool. Four were classified as low methodological concern, 17 as having some concerns, and two as high concern. The strongest profiles were observed in El Charif et al. (2019), Paken et al. (2023), Ardeshirrouhanifard et al. (2022), and Zhang et al. (2022).

The most frequent limitations were inadequate control of confounding and incomplete follow-up. Confounding concerns were identified in 11 of 21 analytical studies, particularly in chemoradiotherapy cohorts, and follow-up concerns occurred in 9 of 15 cohort studies. Outcome-ascertainment limitations were especially relevant to symptom-triggered audiometry in Voruz et al. (2023), questionnaire-only balance outcomes in Piper et al. (2024), and retrospective tinnitus documentation in Kameo et al. (2021).

Kameo et al. (2021) and Voruz et al. (2023) were classified as high concern. Three of the four low-concern publications were derived from the related Platinum Study population, so methodological strength did not imply independent replication. Full item-level judgements are presented in Appendix D.

Narrative Synthesis

Hearing Loss and Audiological Findings

Hearing loss was the most frequently reported ototoxic outcome. Among studies reporting survivor prevalence or hearing status at a defined follow-up, self-reported hearing loss ranged from approximately 30.5% to 59% (Cheung et al., 2023; Sanchez et al., 2023). Ardeshirrouhanifard et al. (2022) reported self-perceived hearing loss in 34.8% of 1,410 cisplatin-treated testicular cancer survivors. In the related Platinum Study population, Sanchez et al. (2023) reported self-reported hearing loss in 59% and concurrent hearing loss with tinnitus in 52%.

Audiometrically defined prevalence was generally higher. Sanchez et al. (2024) found hearing loss in 78% of 100 survivors at longitudinal follow-up using full-spectrum audiometry to 12 kHz. Moke et al. (2021) reported moderate or severe cisplatin-induced hearing loss in 43.8% of 1,414 children, adolescents, and young adults with audiometry at latest follow-up. Cheung et al. (2023) reported audiogram-confirmed hearing loss in 71.4% of the platinum-only group, 52.3% of the taxane-only group, and 59.0% of the combined-treatment group, with no significant between-group difference.

Several studies reported new or worsened hearing loss from a defined baseline rather than prevalence. Zand et al. (2024) identified extended high-frequency loss in 9 of 20 children (45%) after cisplatin. Ehlert et al. (2025) found cochleotoxic change in 16 of

32 participants (50%) receiving platinum agents. Funt et al. (2023) reported that 66% of patients with normal-to-mild baseline hearing in the speech frequencies developed moderate-to-profound loss after high-dose carboplatin-containing chemotherapy, and 22% of those not already using hearing aids were subsequently recommended amplification.

In cisplatin cohorts, Halani et al. (2022) reported ototoxicity in 30% within three months, Musio et al. (2022) reported significant hearing loss in 37.1%, and Okada and Kitagawa (2023) reported CTCAE grade 2 or greater hearing impairment in 28.1%. Paken et al. (2023) documented progressive deterioration across serial assessments rather than a single comparable prevalence estimate, while Basheer et al. (2025) reported progressive changes across extended high-frequency thresholds, DPOAEs, and speech-in-noise performance.

Schedule-specific chemoradiotherapy studies showed marked differences according to cisplatin delivery. Burger et al. (2024) reported clinically relevant speech-frequency hearing loss in 42% of the triweekly group and 19% of the weekly group. Gamez et al. (2024), using a more severe outcome threshold, reported grade 3 or greater ototoxicity in 56% and 13%, respectively, and Lee et al. (2024) reported CTCAE grade 2 or greater ototoxicity in 56.2% overall. Voruz et al. (2023) found symptomatic audiometrically confirmed hearing loss in 20% of 401 patients; because follow-up audiometry was symptom-triggered, this estimate did not represent systematic detection of asymptomatic threshold change.

Tinnitus

Tinnitus findings were available from seven of the 23 included publications. Sanchez et al. (2023) reported tinnitus in 68% of cisplatin-treated testicular cancer survivors, exceeding the frequency of self-reported hearing loss in the same sample. Cheung et al. (2023), using a criterion requiring tinnitus awareness for at least 10% of waking hours, reported tinnitus in 37.1%–40.0% across platinum-only, taxane-only, and combined-treatment groups, with no significant difference between groups.

El Charif et al. (2019) provided severity information within the Platinum Study: 25.8% reported mild tinnitus and 15.0% moderate or severe tinnitus, while 59.1% reported none. Kameo et al. (2021) recorded tinnitus in 49.2% of women receiving chemotherapy for breast cancer, most commonly grade 1, but baseline tinnitus status was not clearly established. Okada and Kitagawa (2023) reported tinnitus awareness in 33.3% of evaluable patients receiving cisplatin-containing treatment.

Voruz et al. (2023) reported new-onset tinnitus in 60% of the subgroup who developed symptomatic audiometrically confirmed hearing loss; this proportion therefore applied to the affected subgroup rather than the full treated cohort. Zhang et al. (2022) examined tinnitus mainly through clinical, lifestyle, and genetic associations and did not provide a single prevalence estimate for cross-study comparison. Because Sanchez et al., El Charif et al., and Zhang et al. arose from related Platinum Study populations, their tinnitus findings were treated as complementary rather than independent prevalence observations.

Vestibular and Balance-Related Findings

Only five publications contributed eligible vestibular or balance findings. Prayuenyong, Kasbekar, et al. (2021) reported balance-related symptoms after cisplatin in 17% of 65 survivors, including vertigo in 9.2%. Clinical histories in the vertigo subgroup were consistent with BPPV, peripheral neuropathy was associated with balance symptoms, and all vHIT measurements were normal. Abnormal functional balance testing was limited to the participants who reported falls.

Piper et al. (2024) reported substantially more frequent symptoms among 200 adults aged 65 years or older receiving chemotherapy for gastrointestinal cancer: dizziness affected 54%, impaired walking balance 48%, neuropathy 32%, and falls 11%. Neuropathy was associated with both dizziness and impaired walking balance. The study relied on structured patient report and did not include laboratory vestibular testing, so the findings represented dizziness and functional balance impairment rather than confirmed peripheral vestibular dysfunction.

Ehlert et al. (2025) and Hülse et al. (2022) showed the opposite symptom-test pattern. Both identified treatment-related changes on objective vestibular measures, including vHIT and VEMP findings, despite an absence of reported vestibular symptoms. In Hülse et al., no participants reported dizziness during follow-up. El Charif et al. (2019) also found a strong association between moderate/severe tinnitus and persistent dizziness or vertigo but did not provide a population-level prevalence estimate for the vestibular symptom.

Audiometric Patterns

Across frequency-specific studies, the most consistent configuration was high-frequency or extended high-frequency involvement. Paken et al. (2023) and Halani et al. (2022) described predominantly bilateral high-frequency sensorineural deterioration. Voruz et al. (2023) and Lee et al. (2024) observed the greatest changes in the upper conventional range, principally from 4 to 8 kHz, although Voruz et al. assessed follow-up only in symptomatic patients.

Extended high-frequency testing revealed a larger burden than speech-frequency averages in several cohorts. Burger et al. (2024) reported loss at 8, 10, and 12.5 kHz in 74%–75% of patients, while loss at the 1, 2, and 4 kHz average occurred in 19%–42% depending on schedule. Ehlert et al. (2025) found the largest baseline-to-exit changes between 4 and 16 kHz, and Zand et al. (2024) identified post-treatment loss specifically above 8 kHz in children with normal baseline hearing.

Ardeshirrouhanifard et al. (2022) demonstrated that patient report did not reliably identify isolated extended high-frequency impairment: self-reported hearing difficulty increased as audiometric loss extended from the 10–12 kHz range into conventional frequencies. Funt et al. (2023) found that baseline high-frequency impairment was associated with subsequent speech-frequency loss and a greater likelihood of hearing-aid recommendation. Basheer et al. (2025) extended assessment to 20 kHz and documented parallel deterioration in extended high-frequency thresholds, DPOAE responses, and speech-in-noise performance. Hülse et al. (2022), in contrast, found no significant pure-tone deterioration over three months.

Chemotherapy Agents Associated with Ototoxicity

Cisplatin or cisplatin-based treatment was the principal exposure in 18 of the 23 publications, including several chemoradiotherapy cohorts. These studies contributed the majority of hearing-loss, tinnitus, and frequency-specific findings and most of the available dose-response analyses. The concentration of studies on cisplatin reflected the composition of the evidence base rather than a head-to-head ranking of chemotherapy agents.

Carboplatin was represented most clearly by Funt et al. (2023), in which high-dose carboplatin-containing chemotherapy was followed by clinically important speech-frequency hearing loss. Ehlert et al. (2025) included cisplatin, carboplatin, oxaliplatin, or combinations of platinum agents, but outcomes were reported for the mixed platinum cohort and could not be separated by drug. Cheung et al. (2023) directly compared platinum, taxane, and combined-treatment survivor groups and found no significant differences in hearing loss or tinnitus despite numerical variation. Evidence for individual non-cisplatin agents was otherwise too limited or insufficiently separated from mixed regimens for reliable agent-specific estimates.

Cumulative Dose and Treatment-Related Factors

Cumulative cisplatin exposure was repeatedly associated with auditory outcomes, but the relevant thresholds varied according to the outcome being measured. Ardeshirrouhanifard et al. (2022) associated exposure above 300 mg/m² with greater audiometric hearing-loss severity, and Sanchez et al. (2024) found greater longitudinal progression above this exposure range. Okada and Kitagawa (2023) and Halani et al. (2022) also identified increased hearing-loss risk at cumulative doses around or above 300 mg/m². El Charif et al. (2019), in contrast, reported an increased risk of moderate or severe tinnitus at doses above 400 mg/m²; this threshold concerned tinnitus rather than the same hearing-loss outcome.

Zand et al. (2024) found greater extended high-frequency loss among children receiving at least seven cisplatin courses and cumulative exposure above 400 mg/m². Paken et al. (2023) also found increasing ototoxicity severity with greater cisplatin exposure during follow-up. These study-specific dose categories were retained as reported and were not combined into one universal threshold.

Treatment intensity and schedule contributed information beyond total cumulative dose. Moke et al. (2021) found that higher daily dose and dose per cycle remained associated with cisplatin-induced hearing loss after cumulative exposure was considered, and vincristine exposure was an additional independent treatment factor. Gamez et al. (2024), Burger et al. (2024), and Lee et al. (2024) each reported greater ototoxicity with high-dose or triweekly cisplatin than with weekly treatment. In Gamez et al., the schedule association remained after adjustment for cumulative dose and cochlear radiation.

Concurrent radiation also influenced auditory outcomes in combined-treatment cohorts. Lee et al. (2024) found increasing cochlear radiation dose independently associated with ototoxicity, and Musio et al. (2022) reported a dose-dependent relationship between cochlear radiation exposure and hearing loss. Basheer et al. (2025) did not find statistically significant

associations between cumulative cisplatin dose and the audiological changes measured, and Voruz et al. (2023) found no significant treatment-related predictors of symptomatic confirmed hearing loss.

Patient-Related Risk Factors

Age was repeatedly examined but showed different patterns across clinical populations. Moke et al. (2021) reported the greatest cisplatin-induced hearing-loss burden among children younger than five years, whereas increasing age was associated with poorer auditory outcomes in adult cohorts reported by Sanchez et al. (2023), Ardeshirrouhanifard et al. (2022), and Lee et al. (2024). Sex could not be evaluated consistently across the review because several major populations involved sex-specific cancers.

Pretreatment hearing status was a prominent predictor of later impairment. Halani et al. (2022) found baseline hearing loss independently associated with post-treatment ototoxicity, while Funt et al. (2023) found baseline high-frequency impairment associated with later speech-frequency loss and hearing-aid recommendation. These findings came from different treatment contexts but both linked reduced baseline auditory reserve with greater subsequent clinical impact.

Cardiovascular, metabolic, and lifestyle variables were associated with outcomes in several survivor analyses. Hypertension and hypercholesterolaemia were linked to hearing outcomes in the Platinum Study reports; Zhang et al. (2022) also identified associations involving BMI, tobacco use, noise exposure, and hypercholesterolaemia, and Lee et al. (2024) identified smoking as an independent correlate of ototoxicity. Paken et al. (2023) reported greater ototoxicity severity among participants living with HIV.

For balance-related outcomes, peripheral neuropathy was associated with symptoms in both Prayuenyong, Kasbekar, et al. (2021) and Piper et al. (2024), despite major differences in population and assessment. El Charif et al. (2019) and Zhang et al. (2022) also reported exploratory genetic associations related to tinnitus or hearing loss; because these findings arose from related survivor populations and were not independently replicated in the other included studies, they were retained as exploratory rather than established clinical predictors.

Discussion

Principal Findings and Interpretation

The central finding of this review is that chemotherapy-related ototoxicity is heterogeneous in both presentation and detection. Hearing loss was the most consistently investigated manifestation, tinnitus was frequent when actively assessed, and vestibular or balance outcomes were comparatively sparse. This pattern is compatible with earlier syntheses that concentrated on platinum-related hearing loss or identified comparatively limited assessment of tinnitus and balance outcomes (Dillard et al., 2022; Phillips et al., 2023; Fleihan et al., 2024). The variation between the included studies was not explained only by different chemotherapy regimens; it also reflected differences in outcome definition, frequency range, follow-up, and whether assessment relied on patient report or objective testing.

This distinction is clinically important because the different measures did not identify identical patient groups. Audiometrically defined hearing loss was often more common than perceived hearing difficulty, particularly when impairment was confined to extended high frequencies (Ardeshirrouhanifard et al., 2022; Cheung et al., 2023). At the same time, tinnitus could be prominent even when hearing loss was not the principal complaint (Sanchez et al., 2023). Hearing loss and tinnitus should therefore be considered related but distinct outcomes, and neither should be used as a complete proxy for the other.

The review also reinforces the importance of distinguishing prevalence from treatment-emergent change. Cross-sectional survivor estimates describe the proportion affected at a later assessment, whereas serial studies capture new or progressive change from a defined baseline (Paken et al., 2023; Sanchez et al., 2024). Combining these measures into a single range would obscure both the timing of ototoxicity and the influence of baseline status. The results are therefore more informative when interpreted within their original assessment design rather than reduced to one overall prevalence figure.

The present findings can also be placed directly against the pooled estimate reported by Dillard et al. (2022). Their systematic review and meta-analysis estimated objectively measured ototoxic hearing loss at 43.17% among patients exposed to cisplatin and/or carboplatin. The lower end of the audiometrically defined prevalence range in the present review was similar, while several individual cohorts were substantially higher. This is not necessarily a disagreement: Dillard et al. pooled heterogeneous populations to estimate an overall burden, whereas the present review retained study-level estimates because the included populations, regimens, definitions, and follow-up periods were not sufficiently comparable for meta-analysis. The contrast is even clearer for carboplatin. Dillard et al. reported a pooled 13.47% prevalence for carboplatin-only treatment, whereas Funt et al. (2023) found that 66% of patients with normal-to-mild baseline speech-frequency hearing developed moderate-to-profound loss after high-dose carboplatin-containing chemotherapy. Funt et al. was published after Dillard et al. and therefore could not have contributed to that pooled estimate. The difference illustrates why agent-level averages should not be assumed to represent risk under a specific high-dose regimen.

Auditory and Vestibular Interpretation

The repeated concentration of auditory deterioration at high and extended high frequencies is one of the most consistent patterns across otherwise heterogeneous studies (Paken et al., 2023; Halani et al., 2022; Burger et al., 2024). This supports the clinical expectation that early chemotherapy-related cochlear change may occur beyond the conventional speech-frequency range. It also explains part of the mismatch between patient perception and audiometric findings: impairment restricted to the upper frequencies may be measurable before it produces obvious communication difficulty (Ardeshirrouhanifard et al., 2022).

Extended high-frequency testing is therefore potentially valuable for early detection, but it should not be treated as a complete monitoring solution. Measurable upper-frequency limits vary with age, equipment, and baseline hearing, and conventional frequencies remain essential for determining functional impact and rehabilitation needs.

The parallel extended high-frequency, DPOAE, and speech-in-noise changes reported by Basheer et al. (2025) further suggest that ototoxicity can affect cochlear function and everyday listening in ways that are not fully represented by a conventional pure-tone threshold shift alone.

Vestibular findings were less coherent and should be interpreted with greater caution. Symptom-test discordance occurred in both directions: patients could report dizziness or imbalance despite normal vHIT (Prayuenyong, Kasbekar, et al., 2021), while objective vestibular changes could occur without reported symptoms (Ehlert et al., 2025; Hülse et al., 2022). Peripheral neuropathy and probable BPPV were plausible alternative or additional explanations in symptomatic cohorts. Consequently, dizziness during chemotherapy should not automatically be attributed to direct vestibular toxicity, and absence of dizziness should not be considered proof of preserved vestibular function.

The limited vestibular evidence also mirrors earlier reviews. Phillips et al. (2023) found that 12 of 13 quantitative studies assessed hearing loss whereas only three assessed balance, corroborating the imbalance observed in the present review. Fleihan et al. (2024) likewise concluded that human evidence for cisplatin-related vestibular dysfunction remains variable and highlighted the limited use of comprehensive vestibular assessment. Taken together, these comparisons suggest that the small vestibular evidence base should not be interpreted as evidence that vestibular toxicity is necessarily uncommon; it also reflects how infrequently and inconsistently balance and vestibular outcomes have been investigated.

Treatment and Patient Susceptibility

Cisplatin has the strongest documented association with ototoxicity in this review because it dominated the included literature, consistent with the emphasis of the broader platinum-ototoxicity evidence base (Dillard et al., 2022). That concentration should not be interpreted as a definitive ranking showing that other agents are clinically unimportant. Carboplatin, taxane, oxaliplatin, and mixed-regimen evidence was much smaller and often arose from treatment contexts that were not comparable with cisplatin cohorts (Cheung et al., 2023; Funt et al., 2023). The available comparative evidence was insufficient to assign reliable relative risks across drug classes.

The dose findings argue against a single universal ototoxic threshold. Cumulative exposure was repeatedly associated with risk, but the relevant dose differed according to whether the outcome was hearing loss, tinnitus, or progression (El Charif et al., 2019; Okada & Kitagawa, 2023; Sanchez et al., 2024). In addition, dose per administration and dosing schedule remained important after total exposure was considered in several cohorts (Moke et al., 2021; Gamez et al., 2024; Burger et al., 2024). In chemoradiotherapy, cochlear radiation represented a separate contributor (Lee et al., 2024; Musio et al., 2022). These findings indicate that treatment intensity and context may be as important as cumulative dose alone when identifying patients who require closer monitoring.

Patient susceptibility was likewise multifactorial. Baseline hearing impairment is especially actionable because patients who

begin therapy with reduced auditory reserve can reach functionally important hearing loss after a smaller additional decline (Funt et al., 2023; Halani et al., 2022). Age, cardiovascular and metabolic conditions, smoking, noise exposure, HIV status, and neuropathy were associated with outcomes in particular populations (Ardeshirrouhanifard et al., 2022; Paken et al., 2023; Zhang et al., 2022), but the pattern was not sufficiently consistent to define one universal high-risk patient profile. Risk stratification is therefore better conceptualised as the combination of treatment exposure, baseline audiological status, and relevant clinical factors.

Methodological Quality, Strengths and Limitations

The methodological appraisal supports narrative synthesis but not a pooled prevalence estimate. Studies used multiple ototoxicity grading systems, different frequency ranges, varied symptom measures, and substantially different follow-up periods. Confounding was a recurrent concern, especially in chemoradiotherapy where chemotherapy and radiation effects could not always be separated (Musio et al., 2022; Lee et al., 2024). Incomplete follow-up was also common and is particularly important because delayed progression may be missed when only treatment-completion outcomes are available, as illustrated by later progression documented in longitudinal survivorship assessment (Sanchez et al., 2024).

A further issue is the concentration of methodologically strong evidence within related Platinum Study cohorts (El Charif et al., 2019; Ardeshirrouhanifard et al., 2022; Zhang et al., 2022; Sanchez et al., 2023, 2024). These publications provide detailed information on cisplatin-treated testicular cancer survivors, but they do not constitute independent replication and they limit generalisability to women, children, older adults, other malignancies, and different treatment regimens. Conversely, some studies with broader clinical populations had smaller samples or greater confounding. Confidence is therefore strongest for recurring clinical patterns observed across different methods rather than for isolated estimates from a single cohort.

The review itself has several strengths: it considered hearing, tinnitus, and vestibular/balance outcomes together; separated prevalence from treatment-emergent change; preserved original definitions instead of imposing artificial harmonisation; used design-specific JBI appraisal; and explicitly accounted for overlapping cohorts. Review-level limitations include single-reviewer screening, extensive machine-assisted first-pass exclusion, restriction to English-language publications, lack of prospective registration, and deviation from the planned database strategy because Scopus, Web of Science, and ScienceDirect were not searched. The targeted audit improved the screening process but cannot eliminate the possibility that eligible records were missed.

Clinical Implications and Future Research

For clinical practice, the findings support establishing a pretreatment audiological reference whenever feasible. A baseline is necessary to distinguish treatment-emergent change from pre-existing loss and is particularly important in patients who already have high-frequency impairment (Funt et al., 2023; Paken et al., 2023). Monitoring should not depend solely on the patient reporting noticeable hearing

difficulty, because early audiometric change may occur before functional complaints become obvious (Ardeshirrouhanifard et al., 2022). Conventional audiometry remains essential, while extended high-frequency testing can add sensitivity where equipment, age, and reliability permit (Burger et al., 2024; Basheer et al., 2025).

Tinnitus should be asked about directly rather than assumed to accompany hearing loss, and balance symptoms should prompt a differential assessment that considers vestibular dysfunction, BPPV, neuropathy, and other contributors (Sanchez et al., 2023; Prayuenyong, Kasbekar, et al., 2021). Where audiology resources are limited, prioritising patients with poorer baseline hearing or greater and more intensive cisplatin exposure is consistent with the risk patterns identified in this review (Funt et al., 2023; Moke et al., 2021). Selected patients may also require post-treatment follow-up because ototoxic change can progress during survivorship rather than ending with chemotherapy (Sanchez et al., 2024).

Future studies should use clearly specified ototoxicity definitions and report the underlying frequency-specific data whenever possible so that results can be compared across grading systems. Tinnitus and vestibular outcomes should be assessed prospectively rather than appearing only as incidental adverse events, a need also identified in previous reviews (Phillips et al., 2023; Fleihan et al., 2024). Vestibular studies in particular should combine symptom history with objective and functional measures instead of relying on a single questionnaire or laboratory test.

Research is also needed in populations and treatments that are currently under-represented. Comparative cohorts should include non-cisplatin agents, women, children, older adults, and patients with a wider range of cancers and comorbidities; the current evidence is heavily weighted toward cisplatin and selected survivor populations (Dillard et al., 2022; Sanchez et al., 2023). Longer predefined follow-up would clarify delayed progression and persistence. In chemoradiotherapy, cochlear radiation exposure should be reported and modelled alongside chemotherapy dose, dose intensity, and schedule so that the contribution of each treatment component can be interpreted more accurately (Gamez et al., 2024; Lee et al., 2024).

Greater consistency in monitoring protocols would also improve the link between research and practice. Future studies should state when baseline testing occurred, which frequencies were measurable, how missing or non-responsive extended high-frequency thresholds were handled, and whether post-treatment assessments were scheduled routinely or triggered by symptoms. The contrast between systematic serial monitoring and symptom-triggered follow-up in the included evidence shows how surveillance intensity can alter what is detected (Paken et al., 2023; Voruz et al., 2023). Reporting these details would help distinguish true differences in ototoxic risk from differences created by surveillance intensity and allow clinicians to judge which components of a monitoring protocol are most informative for specific patient groups.

CONCLUSION

This systematic review found that chemotherapy-related ototoxicity varies substantially according to treatment exposure, patient population, outcome

definition, and assessment method. Hearing loss was the most consistently studied manifestation, and high or extended high frequencies showed the clearest recurring vulnerability. Tinnitus was frequent where it was measured but was assessed much less consistently, while vestibular and balance outcomes were sparse and demonstrated poor correspondence between symptoms and objective test findings.

Cisplatin had the largest evidence base. Greater cumulative exposure, dose intensity or schedule, baseline hearing status, and selected clinical factors were associated with risk in individual studies, but these relationships did not support one universal dose threshold or patient-risk profile. Heterogeneous grading systems, chemoradiotherapy confounding, overlapping survivor cohorts, uneven follow-up, and limited evidence for non-cisplatin agents prevented meaningful statistical pooling.

The findings support baseline and risk-based audiological monitoring that does not rely solely on spontaneous hearing complaints. Extended high-frequency assessment can improve sensitivity where feasible, tinnitus should be assessed directly, and balance symptoms should be evaluated using a differential approach rather than assumed to represent vestibulotoxicity. More standardised outcome definitions, systematic tinnitus and vestibular assessment, diverse comparative cohorts, and longer post-treatment follow-up are needed to strengthen future evidence and make monitoring recommendations more precise. Until stronger comparative evidence is available, monitoring decisions should therefore be adapted to the treatment regimen, baseline auditory status, and clinical context rather than based on a single prevalence estimate.

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APPENDIX

Appendix A: Information Sources and Electronic Search Strategies

The executed review searched PubMed/MEDLINE, Europe PMC, the Cochrane Library, and Google Scholar. PubMed/MEDLINE, Europe PMC, and the Cochrane Library were searched on 16 July 2026; supplementary Google Scholar searches were completed on 17 July 2026. The electronic searches used a 2019–2026 search range, while the predefined eligibility cut-off of 31 May 2026 was applied during screening. Scopus, Web of Science, and ScienceDirect were specified in the approved proposal but were not searched.

Table A1.

Executed information sources and search yield

Source	Date last searched	Search Scope	Records identified	Notes
PubMed/MEDLINE	16 July 2026	2019–2026; English-language eligibility	773	Formal structured search
Europe PMC	16 July 2026	2019–2026; TITLE_ABS structured search	809	Formal structured search
Cochrane Library	16 July 2026	2019–2026	1,031	CENTRAL 1,024; Reviews 6; Clinical Answers 1
Google Scholar	16 July 2026	2019–2026; relevance ordering	1,186	Ten supplementary queries via Publish or Perish

Note. The four executed sources produced 3,796 records before cross-source deduplication. Google Scholar produced 1,186 gross records; 445 duplicate occurrences were removed within that source, leaving 741 Google Scholar records for the combined file. Across all sources, 1,321 duplicate occurrences were removed and 2,475 unique records remained for screening.

A1. PubMed/MEDLINE

The strategy combined chemotherapy and antineoplastic-agent terms with auditory and vestibular outcome terms. The retained strategy documentation contains the following core syntax:

```
(

"Antineoplastic Agents"[Mesh] OR
chemotherap*[tiab] OR
chemoradiotherap*[tiab] OR
chemoradiation[tiab]

OR antineoplastic*[tiab] OR "anticancer
agent*"[tiab] OR "anti-cancer
agent*"[tiab]

OR "cytotoxic drug*"[tiab] OR
cisplatin[tiab] OR carboplatin[tiab] OR
oxaliplatin[tiab]

OR "platinum-based chemotherap*"[tiab] OR
"platinum compound*"[tiab] OR
taxane*[tiab]

OR paclitaxel[tiab] OR docetaxel[tiab] OR
vincristine[tiab] OR vinblastine[tiab]

OR doxorubicin[tiab] OR
cyclophosphamide[tiab] OR
methotrexate[tiab] OR bleomycin[tiab]

OR etoposide[tiab]

)

AND

(

"Ototoxicity"[Mesh] OR "Hearing
Loss"[Mesh] OR "Tinnitus"[Mesh] OR
"Dizziness"[Mesh]

OR "Vertigo"[Mesh] OR "Vestibular
Diseases"[Mesh] OR "Postural
Balance"[Mesh]

OR ototoxic*[tiab] OR cochleotoxic*[tiab]
OR vestibulotoxic*[tiab]
```

```
OR "hearing loss"[tiab] OR "hearing impairment"[tiab] OR "auditory dysfunction"[tiab]

OR "sensorineural hearing loss"[tiab] OR "threshold shift*"[tiab] OR tinnitus[tiab]

OR dizziness[tiab] OR vertigo[tiab] OR imbalance[tiab] OR unsteadiness[tiab]

OR "balance impairment"[tiab] OR "postural balance"[tiab] OR "walking balance"[tiab]

OR falls[tiab] OR "gait instability"[tiab] OR "vestibular dysfunction"[tiab]

OR audiometr*[tiab] OR audiolog*[tiab] OR "high-frequency audiometry"[tiab]

OR "extended high-frequency audiometry"[tiab] OR "otoacoustic emission*"[tiab]

OR DPOAE[tiab] OR "auditory brainstem response"[tiab] OR VEMP[tiab] OR vHIT[tiab]

OR "video head impulse test"[tiab] OR caloric*[tiab]

)

AND english[lang]
```

A2. Europe PMC

The retained search screenshot confirms that the final Europe PMC search used the TITLE_ABS field and returned 806 records on 16 July 2026. The surviving search log describes it as the final chemotherapy/cancer/auditory-vestibular query. The beginning and conceptual structure can be reconstructed from the retained screenshot and search documentation as follows:

```
TITLE_ABS:(

  (chemotherap* OR chemoradiotherap* OR chemoradiation OR antineoplastic*

   OR cisplatin OR carboplatin OR oxaliplatin OR "platinum-based chemotherapy"

   OR taxane* OR paclitaxel OR docetaxel OR vincristine OR doxorubicin)

  AND

  (cancer* OR neoplasm* OR tumor* OR tumour* OR malignan* OR oncolog*)

  AND

  (ototoxic* OR cochleotoxic* OR vestibulotoxic* OR "hearing loss"

   OR "hearing impairment" OR "sensorineural hearing loss" OR tinnitus

   OR dizziness OR vertigo OR imbalance OR "balance impairment"

   OR "vestibular dysfunction" OR "vestibular symptom*"

   OR audiometr* OR audiolog* OR "high-frequency audiometry"

   OR "extended high-frequency audiometry" OR "otoacoustic emission*"

   OR DPOAE OR "auditory brainstem response" OR VEMP OR vHIT)

)
```

Note. This is a reconstruction of the documented search structure, not a verbatim copy of the complete executed Europe PMC string. The exact full interface string was not preserved in the retained export or workbook. The execution date (16 July 2026), TITLE_ABS field, 2019–2026 scope, and retrieval count (806) are documented.

A3. Cochrane Library

The Cochrane Search Manager strategy combined antineoplastic/chemotherapy terms, auditory and vestibular outcome terms, and a cancer-population block.

```
#1 MeSH descriptor: [Antineoplastic Agents] explode all trees

#2 (chemotherap* OR chemoradiotherap* OR chemoradiation OR antineoplastic* OR cisplatin

   OR carboplatin OR oxaliplatin OR "platinum-based chemotherap*" OR taxane*

   OR paclitaxel OR docetaxel OR vincristine OR vinblastine OR doxorubicin

   OR cyclophosphamide OR methotrexate OR bleomycin OR etoposide):ti,ab,kw

#3 #1 OR #2

#4 MeSH descriptor: [Ototoxicity] explode all trees

#5 MeSH descriptor: [Hearing Loss] explode all trees
```

```
#6 MeSH descriptor: [Tinnitus] explode all trees

#7 MeSH descriptor: [Dizziness] explode all trees

#8 MeSH descriptor: [Vertigo] explode all trees

#9 MeSH descriptor: [Vestibular Diseases] explode all trees

#10 MeSH descriptor: [Postural Balance] explode all trees

#11 (ototoxic* OR cochleotoxic* OR vestibulotoxic* OR "hearing loss" OR "hearing impairment"

    OR tinnitus OR dizziness OR vertigo OR imbalance OR unsteadiness OR "balance impairment"

    OR "postural balance" OR "walking balance" OR falls OR "gait instability"

    OR "vestibular dysfunction" OR audiometr* OR audiolog* OR "high-frequency audiometry"

    OR "extended high-frequency audiometry" OR "otoacoustic emission*" OR DPOAE

    OR "auditory brainstem response" OR VEMP OR vHIT OR "video head impulse test"

    OR caloric*):ti,ab,kw

#12 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

#14 MeSH descriptor: [Neoplasms] explode all trees

#15 (cancer* OR neoplasm* OR tumor* OR tumour* OR malignan* OR oncolog*):ti,ab,kw

#16 #14 OR #15

#17 #3 AND #12 AND #16
```

A4. Google Scholar

Ten supplementary Google Scholar searches were conducted through Publish or Perish using the 2019–2026 custom range and relevance ordering.

Table A2.

Google Scholar supplementary search queries

Search ID	Exact Query	Records Exported
GS01	"chemotherapy" ototoxicity	200
GS02	cisplatin "hearing loss" audiometry	200
GS03	cisplatin tinnitus prevalence	100
GS04	chemotherapy dizziness vestibular	106
GS05	chemotherapy imbalance "postural balance"	108
GS06	platinum chemotherapy "otoacoustic emissions"	200
GS07	carboplatin ototoxicity hearing	90
GS08	taxane chemotherapy hearing tinnitus	120
GS09	cisplatin chemoradiation ototoxicity	59
GS10	cisplatin chemoradiation vestibular VEMP vHIT	3

Appendix B: Title-and-abstract screening rules, decision logic, and false-negative audit

The machine-assisted first pass applied predefined conservative eligibility rules; uncertain records were retained for further review.

Table B1.

Eligibility rules applied during title-and-abstract screening

Include/retain when the title or abstract indicates	Exclude when the title or abstract clearly indicates
1. Original human research involving cancer patients receiving systemic chemotherapy, alone or as part of combined treatment.	1. Animal, laboratory, histopathology, mechanistic, or other preclinical research without eligible patient outcomes.
2. Publication year from 2019 through 2026 and English-language full text or sufficient English record for initial screening.	2. Case reports, reviews, meta-analyses, guidelines, editorials, letters, perspectives, book chapters, protocols without results, or conference abstracts without eligible full text.

Include/retain when the title or abstract indicates	Exclude when the title or abstract clearly indicates
3. At least one chemotherapy-associated auditory or vestibular outcome: hearing loss, tinnitus, dizziness, vertigo, imbalance, vestibular dysfunction, or related ototoxicity.	3. No systemic chemotherapy exposure, radiotherapy-only exposure, or symptoms attributable to malignancy rather than chemotherapy.
4. Relevant objective or graded assessment such as conventional/high-frequency audiometry, OAEs, ABR, VEMP, vHIT, caloric testing, vestibular assessment, or an ototoxicity grading scale.	4. No eligible auditory or vestibular ototoxicity outcome, or balance/falls studied only as general neurotoxicity without vestibular attribution.
5. Prevalence, incidence, longitudinal change, severity, dose relationship, risk factors, or patient-level audiological/vestibular findings that can inform the review objectives.	5. Pre-treatment-only assessment, qualitative/service/practice research without patient-level prevalence or audiological outcome data, non-English publication, or publication before 2019.

Table B2

First-pass classification logic

Classification	Operational rule
Potentially eligible	Clearly or probably eligible from the title and abstract; retain for further assessment.
Unclear	Eligibility cannot be resolved confidently from the title and abstract; retain for manual review and, where necessary, full-text assessment.
Ineligible	At least one exclusion criterion is clearly met; exclude and record one primary exclusion reason.

False-negative audit procedure

The first pass retained 180 records and excluded 2,295. A targeted, non-random audit reviewed 171 potentially vulnerable exclusions, restored 11 records, and produced a corrected retained set of 191. Manual review then excluded 162 records, leaving 29 reports for full-text assessment.

Table B3.

Outcome of the targeted false-negative audit

Audit Stage	Number of records
Unique records entering title/abstract screening	2,475
Retained after initial machine-assisted pass	180
Initially classified as ineligible	2,295
Initially excluded records selected for targeted audit	171
Audit records that remained excluded	160
Audit records restored to the eligibility queue	11
Corrected title/abstract exclusions	2,284
Corrected eligibility/full-text queue	191
Records excluded by automation without individual audit	2,124
Records excluded during manual review of the retained set	162
Reports sought for retrieval	29

Note. The audit workbook preserves the reviewed records and decision rationales, but the exact programmatic rule used to generate the targeted audit set was not retained. The audit is therefore described as targeted and non-random. The PRISMA total excluded before retrieval comprises 2,284 post-audit exclusions plus 162 manual exclusions.

Appendix C: Reports excluded from the curated full-text synthesis and reasons for exclusion

The curated 23-publication synthesis was developed from a 29-article full-text set. Six reports were excluded from the primary synthesis and retained only as background sources. The reports and primary reasons for exclusion are listed below.

Table C1.

Reports excluded following full-text assessment

Report	Article Title	Primary reason of exclusion	Status
Dillard et al. (2022)	Global burden of ototoxic hearing loss associated with platinum-based cancer treatment: A systematic review and meta-analysis	Systematic review and meta-analysis; not original primary research.	Background source only
Fleihan et al. (2024)	Cisplatin vestibulotoxicity: a current review	Review article; not original primary research.	Background source only
Lacey et al. (2026)	Identifying Gaps and Opportunities to Improve Ototoxicity Management in Veterans With Cancer: Evidence From a Retrospective Cohort and Oncology Provider Survey	Focuses on audiology service use and management practices rather than patient-level ototoxicity prevalence or clinical outcomes.	Background source only
Phillips et al. (2023)	The long-term impacts of hearing loss, tinnitus and poor balance on the quality of life of people living with and beyond cancer after platinum-based chemotherapy: a literature review	Literature review; not original primary research.	Background source only
Pearson et al. (2022)	The impact of chemotherapy-induced inner ear damage on quality of life in cancer survivors: a qualitative study	Qualitative study without prevalence, incidence, or objective clinical outcome data.	Background source only
McNeish et al. (2023)	Executive function is associated with balance and falls in older cancer survivors treated with chemotherapy: A cross-sectional study	Examines cognition, fall risk, and functional balance rather than a clearly defined auditory or vestibular ototoxicity outcome.	Background source only

Note. All six excluded reports are included in the thesis reference list so that the full-text exclusion decisions can be verified.

Appendix D: JBI Critical Appraisal of the Included Publications

Methodological quality was assessed using design-appropriate JBI critical appraisal tools. Individual items were rated Yes, No, Unclear, or Not Applicable (N/A). Overall categories were review-defined qualitative judgements used to support interpretation and were not numerical JBI scores.

Table E1.

JBI appraisal item key

Tool/Code	Appraisal Item	Domain
Prevalence — P1	Was the sample frame appropriate to address the target population?	Selection
Prevalence — P2	Were study participants sampled in an appropriate way?	Selection
Prevalence — P3	Was the sample size adequate?	Statistical precision / coverage
Prevalence — P4	Were the study subjects and the setting described in detail?	Reporting / external validity
Prevalence — P5	Was the data analysis conducted with sufficient	Selection / analysis

Tool/Code	Appraisal Item	Domain
	coverage of the identified sample?	
Prevalence — P6	Were valid methods used for the identification of the condition?	Outcome measurement
Prevalence — P7	Was the condition measured in a standard, reliable way for all participants?	Outcome measurement
Prevalence — P8	Was there appropriate statistical analysis?	Statistical conclusion validity
Prevalence — P9	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Selection / response
Analytical cross-sectional — X1	Were the criteria for inclusion in the sample clearly defined?	Selection
Analytical cross-sectional — X2	Were the study subjects and the setting described in detail?	Reporting / external validity
Analytical cross-sectional — X3	Was the exposure measured in a valid and reliable way?	Exposure measurement
Analytical cross-sectional — X4	Were objective, standard criteria used for measurement of the condition?	Outcome measurement
Analytical cross-sectional — X5	Were confounding factors identified?	Confounding
Analytical cross-sectional — X6	Were strategies to deal with confounding factors stated?	Confounding
Analytical cross-sectional — X7	Were the outcomes measured in a valid and reliable way?	Outcome measurement
Analytical cross-sectional — X8	Was appropriate statistical analysis used?	Statistical conclusion validity
Cohort — C1	Were the two groups similar and recruited from the same population?	Selection and allocation
Cohort — C2	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Exposure classification
Cohort — C3	Was the exposure measured in a valid and reliable way?	Exposure measurement
Cohort — C4	Were confounding factors identified?	Confounding
Cohort — C5	Were strategies to deal with confounding factors stated?	Confounding
Cohort — C6	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Temporal precedence
Cohort — C7	Were the outcomes measured in a valid and reliable way?	Outcome measurement
Cohort — C8	Was the follow-up time reported and sufficient to be long enough for outcomes to occur?	Follow-up duration
Cohort — C9	Was follow-up complete, and if not, were the reasons for loss to follow-up described and explored?	Participant retention
Cohort — C10	Were strategies to address incomplete follow-up utilised?	Participant retention
Cohort — C11	Was appropriate statistical analysis used?	Statistical conclusion validity
Case-control — CC1	Were the groups comparable other than the presence of	Selection

Tool/Code	Appraisal Item	Domain
	disease/outcome in cases and absence in controls?	
Case-control — CC2	Were cases and controls matched appropriately?	Selection / matching
Case-control — CC3	Were the same criteria used for identification of cases and controls?	Outcome classification
Case-control — CC4	Was exposure measured in a standard, valid and reliable way?	Exposure measurement
Case-control — CC5	Was exposure measured in the same way for cases and controls?	Exposure measurement
Case-control — CC6	Were confounding factors identified?	Confounding
Case-control — CC7	Were strategies to deal with confounding factors stated?	Confounding
Case-control — CC8	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Outcome measurement
Case-control — CC9	Was the exposure period of interest long enough to be meaningful?	Temporal relationship
Case-control — CC10	Was appropriate statistical analysis used?	Statistical conclusion validity