

Determinants of hearing outcomes in pediatric oncology: Insights from South Africa's public health context

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Abstract

Hearing loss is a major morbidity among pediatric cancer survivors, particularly in Low- And Middle-Income Countries (LMICs) such as South Africa, where platinum-based chemotherapy agents are widely used. Although prior research has described the prevalence of ototoxicity in this population, limited evidence exists on the determinants of hearing outcomes in resource-constrained health systems. This study investigated demographic, diagnostic, and treatment-related factors influencing hearing loss in children receiving platinum-based chemotherapy within South Africa's public healthcare context. A retrospective review of 47 records (ages 5–18) from two public hospitals (2018–2022) was conducted. Data included demographic (age, sex, race), diagnostic (cancer type, treatment duration), and treatment (cisplatin, carboplatin) variables. Audiological outcomes were determined using pure tone audiometry and otoacoustic emissions. Descriptive statistics, chi-square tests, ANOVA, and logistic regression were applied. Hearing loss occurred in 36.2% of patients. Younger age significantly predicted hearing loss ($p = .03$), and age effects on high-frequency thresholds were confirmed ($p < .05$). CNS cancers ($\chi^2 = 8.12$, $p = .004$), treatment duration beyond six months ($p < .01$), and cisplatin therapy ($p < .001$) were all associated with greater ototoxicity risk. Younger age, CNS malignancies, prolonged treatment, and cisplatin exposure are key determinants of ototoxicity in South African pediatric oncology. Strengthening ototoxicity monitoring through context-specific protocols, expanded audiological capacity, and interdisciplinary collaboration is essential to improve equitable care and long-term outcomes.

Keywords: Pediatric cancer, Ototoxicity, Cisplatin, Carboplatin, Hearing loss, South Africa, Audiology, Chemotherapy

Introduction

Childhood cancer in South Africa, though less common than adult cancers, remains a major public health concern with 800–1,000 new cases annually.¹ Treatment often requires aggressive chemotherapy with platinum-based drugs, notably cisplatin and carboplatin, which, while lifesaving, are highly ototoxic.^{2–5} Up to 70% of children treated with cisplatin may develop permanent hearing loss, influenced by cumulative dose, treatment duration, and age at treatment onset.⁶ In South Africa, these risks are amplified by resource limitations, uneven access to audiological monitoring, and broader social determinants of health, highlighting ototoxicity as both a clinical and public health challenge.

Chemotherapy-induced hearing loss typically presents as high-frequency sensorineural impairment, leading to speech and language delays, academic challenges, and social isolation.^{7–9} These impacts are often more severe in Low- And Middle-Income Countries (LMICs), where affected children

may lack access to hearing technology, specialized services, and educational support.^{10,11}

Platinum-related ototoxicity is mediated by oxidative stress and reactive oxygen species damaging cochlear outer hair cells.¹² Cisplatin is more ototoxic than carboplatin but remains indispensable for some aggressive childhood cancers such as medulloblastoma.^{6,13} International evidence identifies younger age, cumulative dose, and co-exposure to other ototoxic agents (e.g., aminoglycosides, loop diuretics) as principal risk factors.^{6,8,13} However, evidence from LMICs—where health system constraints and socioeconomic inequities may modify risk patterns—remains limited.

Previous research from this cohort has reported the prevalence and audiological profile of ototoxic hearing loss in South African pediatric oncology.¹⁴ To avoid duplication, this manuscript performs a secondary, inferential analysis of the same cohort and focuses on determinants of hearing outcomes

(demographic, diagnostic and treatment variables) and on practical implications for ototoxicity monitoring in South Africa's public hospitals. This approach contributes novel insight into the contextual drivers of hearing loss in a resource-constrained setting.

Age is a consistent predictor of ototoxic vulnerability, with younger children particularly vulnerable.⁸ In this study, children under 5 years were excluded because routine behavioral audiometry in that age group was not consistently recorded, reflecting a broader challenge in reliably monitoring very young pediatric patients with cancer in public settings. Findings on sex and race are inconsistent in the literature,^{15,16} but in South Africa racial categories often intersect with socioeconomic disadvantage and healthcare access, so demographic effects must be interpreted in context.¹⁷ Treatment characteristics - including drug type, dosing schedule, and multimodal therapies - further influence ototoxic risk.^{18,19} Cisplatin confers the greatest risk, especially at cumulative doses above 400 mg/m².^{6,8} When combined with cranial irradiation, the risk of auditory damage increases.⁹ In this cohort, documentation of radiotherapy and concurrent ototoxic co-medications was inconsistent, a common limitation of retrospective LMIC record reviews that highlights the need for improved clinical documentation.

What distinguishes the South African context are not only the biological risk factors but also systemic barriers to effective monitoring and mitigation.^{20,21} Public hospitals serving the majority of children face shortages of audiologists, limited access to high-frequency audiometry and inconsistent implementation of standardized monitoring protocols.²²⁻²⁵ International bodies such as the International Society of Pediatric Oncology recommend structured ototoxicity monitoring with validated grading systems,⁶ yet these are infrequently operationalized in LMICs practice. Consequently, hearing loss is often identified late and rehabilitation delayed.

By framing ototoxicity through both biological determinants and health-system constraints, this study adds analytic and contextual insight to the previously reported descriptive data. The aim is to identify predictors of hearing outcomes among

pediatric patients with cancer and to inform feasible, context-sensitive monitoring and policy responses for South Africa.

Methodology

Aim and objectives

This study aimed to explore factors influencing hearing outcomes in pediatric patients with cancer in South Africa. Specific objectives were to:

- Determine factors influencing overall hearing function in this population.
- Examine relationships between demographic factors (age, sex, race) and hearing outcomes.
- Assess diagnostic factors (cancer type, treatment duration) in relation to hearing outcomes.
- Evaluate treatment factors (cisplatin vs carboplatin) and their association with hearing outcomes.

Research design

Study design and setting

A descriptive, retrospective record review²⁶ was conducted at two tertiary public hospitals in Johannesburg: Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Both institutions serve predominantly low-income populations and provide oncology and audiology services for pediatric patients with cancer. Descriptive findings from this cohort have been reported previously.¹⁴ The current analysis uses the same dataset but extends the work through inferential analysis to identify demographic, diagnostic, and treatment-related predictors of hearing outcomes. The earlier paper presented prevalence and audiological characteristics, whereas this study focuses on determinants and contextual factors affecting ototoxicity risk in South Africa's public healthcare context.

Sampling and study population

A non-probability purposive sampling strategy²⁷ was used to identify patient records that met the inclusion criteria. Eligible participants were pediatric patients

aged 5–18 years, diagnosed with cancer and treated with platinum-based chemotherapy (cisplatin and/or carboplatin) at CHBAH or CMJAH between 2018 and 2022.

Inclusion criteria

- Age 5–18 years.
- Treatment with cisplatin and/or carboplatin.
- At least two audiological assessments recorded.

Exclusion criteria

- Children <5 years, due to reduced reliability of behavioral audiometry.
- Cognitive impairment affecting audiological test validity.
- Incomplete or missing audiological data (<2 assessments).

Data collection procedures

Ethical approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (M221128).

Data were extracted from hospital records using a structured form that captured:

1. *Demographics:* age, sex, race (as documented).
2. *Diagnostic factors:* cancer type and duration of treatment.
3. *Treatment factors:* chemotherapy agent (cisplatin/carboplatin). Where available, the number of cycles, cumulative dose, radiotherapy, and co-exposure to ototoxic drugs (aminoglycosides, loop diuretics) were recorded, though documentation was inconsistent.
4. *Audiological data:* hearing thresholds, tympanometry, distortion product otoacoustic emissions (DPOAEs), and pure-tone audiometry (PTA). Both conventional and high-frequency audiometry were included where available. Rehabilitation details (hearing aid referral, fitting, and educational support) were recorded if noted.

Ototoxicity grading

Where high-frequency audiometric thresholds (≥ 4 kHz) were available, the SIOP Boston/Chang (Brock) ototoxicity grading system⁶ was retrospectively applied. Records lacking adequate data were summarized descriptively.

Data analysis

Descriptive statistics were used to summarize demographic, diagnostic, treatment, and audiological variables. Inferential tests included²⁸:

- *Chi-square tests* for associations between categorical variables (e.g., sex and hearing loss).
- *ANOVA and t-tests* for differences across diagnostic or treatment groups.
- *Logistic regression* to assess predictors of hearing loss (independent variables: age, sex, race, cancer type, treatment type; dependent variable: hearing function).

Hearing loss classification followed established pediatric norms.²⁹ Pure-tone thresholds >20 dB HL at any frequency (0.5–8 kHz; up to 12 kHz when high-frequency data were available) were considered abnormal. Both ear-specific thresholds and the better-ear four-frequency pure-tone average (0.5, 1, 2, 4 kHz) were calculated. Hearing loss was recorded if either ear exceeded 20 dB HL at one or more frequencies, to capture early high-frequency losses. Where possible, severity was classified using the SIOP Boston/Chang system.⁶ Significance was set at $p < 0.05$. Statistical analyses were performed with IBM SPSS v26.0.²⁸

Reliability and validity measures

Validity was supported by strict inclusion/exclusion criteria and by requiring at least two audiological assessments per patient. Audiological procedures conformed to HPCSA standards,²⁹ ensuring data accuracy. Reliability was maintained through standardized testing across both hospitals, structured data collection, and data quality checks.

Ethical considerations and data management

Ethical approval was granted (M221128). As a

retrospective record review, informed consent was waived under national guidelines permitting use of anonymized data. Each patient was assigned a unique study code. Data were stored on password-protected, access-controlled systems, with regular verification for accuracy. Upon study completion, anonymized data were archived according to University of the Witwatersrand retention policies for potential secondary analysis.

Results

Demographic profile of the sample

Records from 47 pediatric patients were reviewed. The sample showed an approximately equal sex distribution and diverse racial composition reflective of Johannesburg's population (Table 1). The mean age at diagnosis was 12.3 years (SD = 3.1; range 5–18 years).

Table 1: Demographic profile of participants

Variable	N = 47	%
Sex		
Male	26	55.30%
Female	21	44.70%
Race		
Black	31	66.00%
White	8	17.00%
Mixed Race	6	12.80%
Other	2	4.30%

Most diagnoses occurred between ages 10 and 15 (59.6%), followed by 5–9 years (23.4%) and 16–18 years (17.0%) (Table 2).

Table 2: Age distribution of pediatric patients with cancer

Age Group (years)	Number of Patients	Percentage (%)
5–9	11	23.4
10–15	28	59.6
16–18	8	17
Total	47	100

The predominance of patients aged 10–15 likely reflects increased incidence of certain cancers in early adolescence and greater exposure to intensive treatment protocols in this developmental phase — a relevant consideration for ototoxicity vulnerability.

Audiological findings

Hearing loss was identified where pure-tone thresholds exceeded 20 dB HL at any test frequency (0.5–8 kHz; extended to 12 kHz where available), in accordance with HPCSA guidelines. Severity was graded using the SIOP Boston/Chang scale when data permitted. Overall, 36.2% (n = 17) of patients exhibited hearing loss, predominantly bilateral high-frequency sensorineural loss (42.6%).

Table 3: Proportion of hearing loss by frequency range

Frequency Range	Number of Patients with Hearing Loss	Percentage (%)
High Frequency	14	82.4
Low-to-Mid Frequency	3	17.6
Total	17	100

High-frequency hearing loss predominated (82.4% of affected patients), consistent with the typical ototoxic profile of platinum-based agents.

Objective 1: Factors Influencing Hearing Function

Logistic regression analysis examined the effects of age, sex, and race on hearing loss. Age was a significant predictor, $\chi^2(3, N = 47) = 10.68, p < .05$, with younger patients showing higher risk ($p = .03$). Neither sex nor race showed significant associations ($p > .05$) (Table 4).

Table 4: Logistic regression results for factors influencing hearing loss

Predictor	B	SE	OR	p-value
Age	0.91	0.42	2.5	0.03*
Sex	-0.22	0.51	0.81	0.64
Race	0.13	0.32	1.14	0.72

*Significant at $p < .05$

Although age-related susceptibility was evident, interpretation should be cautious given the modest sample size.

Objective 2: Demographic Factors and Hearing Outcomes

ANOVA confirmed a significant effect of age on high-frequency thresholds ($F = 4.67, p < .05$), indicating younger children were more affected. No statistically

significant differences were observed by sex or race ($p > .05$). These findings align with international reports suggesting that younger age increases ototoxic vulnerability, while demographic variables such as sex and race play minimal direct roles but may intersect with structural inequities.

Objective 3: Relationship Between Diagnostic Factors and Hearing Function

Children with central nervous system (CNS) cancers exhibited a greater prevalence of hearing loss than those with other cancer types. A significant association was observed between CNS cancer and hearing loss ($\chi^2(1, N = 47) = 8.12, p = .004$). Treatment duration also influenced outcomes: patients treated for more than six months had higher hearing loss prevalence (52.9%) compared to those treated for shorter durations (21.7%) ($t = 3.45, p < .01$) (Table 5).

Table 5: Hearing loss prevalence by cancer type and treatment duration

Cancer Type	Hearing Loss (%)	Duration (>6 months)	Hearing Loss (%)
CNS	67%	Yes	52.90%
Non-CNS	21%	No	21.70%

Extended treatment duration likely reflects cumulative ototoxic exposure, though this may also be confounded by multimodal therapies and incomplete dosing data.

Objective 4: Relationship Between Treatment Factors and Hearing Function

Cisplatin-treated patients demonstrated substantially higher hearing loss rates than those receiving carboplatin (53.8% vs. 15.8%; Table 6). The difference was statistically significant ($t = 5.22, p < .001$), confirming cisplatin's stronger ototoxic profile.

Table 6: Hearing loss prevalence by treatment type

Treatment Type	Hearing Loss (n)	% of Group with Hearing Loss
Cisplatin	14	53.80%
Carboplatin	3	15.80%

This pattern reinforces international evidence of cisplatin's dose-related cochleotoxicity. Limited high-

frequency testing in public sector settings may, however, underestimate early ototoxic effects.

Discussion

Unlike the earlier report on prevalence within this cohort,¹⁴ the present study provides a secondary inferential analysis examining determinants of ototoxicity. This analytic extension enables contextual interpretation of hearing outcomes in relation to demographic, diagnostic, and treatment variables, offering insights relevant to risk stratification and health system strengthening in South Africa.

The findings highlight that young age, cancer type, treatment duration, and chemotherapy agent were key determinants of hearing outcomes. Rather than reiterating well-established risk factors, this study situates them within South Africa's public healthcare system, where ototoxicity monitoring remains inconsistent and constrained by limited resources.^{22,23} The results thus advance understanding of how structural and contextual factors amplify biological vulnerabilities.

Age emerged as a significant determinant of hearing loss, with children under ten showing greater susceptibility.^{8,17} Their developing auditory systems are more vulnerable to high-frequency damage from platinum compounds.⁶ The exclusion of children under five, due to limited audiometric reliability, is acknowledged as a weakness that future work should address through objective measures such as auditory brainstem response. No associations were found between hearing outcomes and sex or race, consistent with Brooks and Knight.¹³ However, in the South African context, "race" reflects socioeconomic disparities that shape access to care. Hendricks et al.³⁰ have shown that socioeconomic status—rather than race per se—drives childhood cancer outcomes, underscoring the need to disentangle biological from structural contributors to ototoxicity risk.

Diagnostic variables also played a role. Children with CNS cancers were more likely to experience hearing loss, aligning with Tillmanns et al.⁹ and Brock et al.⁶ This may relate to the frequent use of cisplatin in CNS protocols and potential exposure to cranial radiotherapy, which was not consistently captured here. Treatment duration exceeding six months was

also associated with poorer hearing outcomes. Duration served as a proxy for cumulative exposure due to incomplete dosing data, though this is confounded by multimodal regimens. Future studies in South Africa should systematically record cumulative doses (mg/m^2) to improve dose–toxicity modelling. These findings are consistent with global evidence that extended exposure to platinum agents heightens auditory risk. In South Africa, longer treatment courses may also increase delays in audiological follow-up, reflecting systemic barriers to continuity of care.^{20,22,23}

Cisplatin was again confirmed as the most ototoxic agent, with significantly higher rates of hearing loss compared with carboplatin.⁶ A key contextual insight is that high-frequency audiometry—critical for early detection—is seldom available in South African public hospitals.^{22,23} As a result, ototoxicity is typically identified only when it affects speech frequencies, delaying rehabilitation. Implementation of HPCSA guidelines²⁹ remains inconsistent due to shortages of audiologists, limited equipment, and competing clinical priorities. Practical solutions could include adoption of portable audiometry, mobile health tools for community-based screening, and integration of ototoxicity monitoring within oncology care pathways through stronger oncologist–audiologist collaboration.

The observed hearing loss prevalence of 36.2% aligns with findings from LMICs such as Richard and Andrea’s Tanzanian study¹⁷ but exceeds many high-income country (HIC) estimates.⁶ This reflects inequities in monitoring infrastructure. In HICs, baseline and follow-up testing are routine; in LMICs, detection often occurs only after communication difficulties arise, leading to underestimation of true prevalence. Clinically, reducing cumulative ototoxic exposure remains a priority. Adhering to antibiotic stewardship can limit aminoglycoside use in febrile neutropenia, and substituting furosemide with less ototoxic diuretics could mitigate risk. Randomized trials and international guidelines have shown that sodium thiosulfate effectively reduces cisplatin-induced hearing loss, with promising real-world uptake.^{9,17,31–35} Even where thiosulfate is unavailable, these context-sensitive strategies are feasible and impactful.

The implications of this study are twofold: first, it

provides inferential evidence on ototoxicity determinants among South African pediatric oncology patients; second, it highlights systemic gaps in monitoring and intervention capacity. Addressing these requires national policy commitment, integration of ototoxicity screening into standard oncology care, workforce development for audiologists, and cross-sector partnerships to enhance access to equipment and services.

Study limitations include its retrospective design, reliance on incomplete clinical records, and small sample size ($n = 47$) from two hospitals, which limits generalizability. Variations in audiological procedures may have influenced consistency of results. Missing data on radiotherapy, concurrent ototoxic medications, and genetic susceptibility represent additional constraints. Prospective studies with larger cohorts, precise dose documentation, and genomic analyses within African populations are needed to strengthen predictive modelling and inform contextually appropriate interventions.^{8,14}

Conclusion

This study identified younger age, CNS cancers, prolonged treatment duration, and cisplatin exposure as key determinants of hearing loss among South African children with cancer. Its contribution lies in framing these risks within the realities of South Africa’s under-resourced public health system, where structured ototoxicity monitoring is rarely standardized. These findings reinforce the need for locally adapted guidelines, expanded audiology capacity, and integrated multidisciplinary care. Future research should include cumulative dose and radiotherapy data and explore genetic susceptibility to inform equitable, evidence-based ototoxicity prevention and monitoring strategies for African pediatric oncology settings.

Brief points

What is already known on this topic

- Platinum-based chemotherapy agents, particularly cisplatin, are effective in pediatric oncology but highly ototoxic.
- Younger children are more vulnerable to chemotherapy-induced hearing loss, often presenting with high-frequency

sensorineural loss.

- Standardized ototoxicity monitoring protocols exist in high-income countries but are inconsistently applied in low- and middle-income countries (LMICs).

What this paper adds

- Provides the first analysis of demographic, diagnostic, and treatment-related factors influencing hearing outcomes in pediatric patients with cancer in South Africa.
- Highlights the absence of standardized ototoxicity monitoring protocols in South Africa's public healthcare system and the systemic barriers to their implementation.
- Offers context-specific recommendations for improving ototoxicity monitoring in LMICs, including integration of audiology into oncology care and feasible strategies to reduce additional ototoxic exposures.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was granted by the University of the Witwatersrand's Medical Human Research Ethics Committee (Protocol Number: M221128). As this was a retrospective record review, informed consent was not required. The need for consent was waived by the Committee in accordance with National Ethics Guidelines which permits the use of de-identified patient records for research without individual consent. All data were anonymized to maintain confidentiality.

Clinical trial number: not applicable.

Funding: The study was self-funded.

Consent to publish'

Consent to publish was not necessary as no participant images and/or identifying information is used in the manuscript.

Availability of data and materials

Data supporting the findings of this study are available within the paper and the rest of the data that support the findings of this study are not openly

available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TNC and KKS co-conceptualized the study. TNC performed all data collection and conducted data capturing with KKS supervising. TNC and KKS analyzed and interpreted the data. Both authors read and approved the final manuscript.

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References

1. National Cancer Registry. *Childhood Cancer Registry 2019 Annual Report*. 2023. <https://www.nicd.ac.za/wp-content/uploads/2023/04/The-National-Childhood-Cancer-Incidence-Report-2019.pdf>
2. Yancey A, Harris MS, Egbelakin A, Gilbert J, Pisoni DB, Renbarger J. Risk factors for cisplatin-associated ototoxicity in pediatric oncology patients. *Pediatric blood & cancer*. 2012; 15;59(1):144-8.
3. da Silva AM, de Oliveira MD, Cristofani LM, Odone Filho V. The prevalence of hearing loss in children and adolescents with cancer. *Brazilian Journal of Otorhinolaryngology*. 2007; 1;73(5):608-14.
4. Strebel S, Mader L, Jörger P, Waespe N, Uhlmann S, von der Weid N, Ansari M, Kuehni CE. Hearing loss after exposure to vincristine and platinum-based chemotherapy among childhood cancer survivors. *EJC Paediatric Oncology*. 2023 1; 1:100017.
5. Skalleberg J. Long-term ototoxicity after cisplatin-based chemotherapy-A study of long-term hearing loss and tinnitus in patients after

- receiving cisplatinbased chemotherapy.2021.
- 6.Brock PR, Knight KR, Freyer DR, Campbell KC, Steyger PS, Blakley BW, Rassekh SR, Chang KW, Fligor BJ, Rajput K, Sullivan M. Platinum-induced ototoxicity in children: a consensus review on mechanisms, predisposition, and protection, including a new International Society of Pediatric Oncology Boston ototoxicity scale. *Journal of Clinical Oncology*. 2012, 1;30(19):2408-17.
 - 7.Dillard LK, Lopez-Perez L, Martinez RX, Fullerton AM, Chadha S, McMahon CM. Global burden of ototoxic hearing loss associated with platinum-based cancer treatment: A systematic review and meta-analysis. *Cancer epidemiology*. 2022, 1;79:102203.
 - 8.Knight KR, Kraemer DF, Neuwelt EA. Ototoxicity in children receiving platinum chemotherapy: underestimating a commonly occurring toxicity that may influence academic and social development. *Journal of Clinical Oncology*. 2005 Dec 1;23(34):8588-96.
 - 9.Tillmanns A, Lanvers-Kaminsky C, Parfitt R, Meijer A, Tóth M, Münscher A, Beck JD, van den Heuvel-Eibrink M, am Zehnhoff-Dinnesen A. Ototoxicity After Childhood Cancer. Late Treatment Effects and Cancer Survivor Care in the Young: From Childhood to Early Adulthood. 2021:27-48.
 - 10.Khoza-Shangase K, Kanji A, Maluleke NP. Communication and school readiness abilities of children with hearing impairment in South Africa: A retrospective review of early intervention preschool records. *South African Journal of Communication Disorders*. 2019 Jan 1;66(1):1-7.
 - 11.Casoojee A, Khoza-Shangase K, Kanji A. A comparative study of learning outcomes for hearing-impaired foundation phase learners. *South African Journal of Childhood Education*. 2024 Feb 29;14(1):1419.
 - 12.Sheth S, Mukherjee D, Rybak LP, Ramkumar V. Mechanisms of cisplatin-induced ototoxicity and otoprotection. *Frontiers in cellular neuroscience*. 2017 Oct 27; 11:338.
 - 13.Brooks B, Knight K. Ototoxicity monitoring in children treated with platinum chemotherapy. *International journal of audiology*. 2018 Aug 24;57(sup4):S62-8.
 - 14.Chauke TN, Khoza-Shangase K. Investigating Hearing Function in Paediatric Patients with Cancer in South Africa. *Indian Journal of Otolaryngology and Head & Neck Surgery*. 2025 Mar;77(3):1238-47.
 - 15.Li Y, Womer RB, Silber JH. Predicting cisplatin ototoxicity in children: the influence of age and the cumulative dose. *European Journal of Cancer*. 2004 Nov 1;40(16):2445-51.
 - 16.Ross CJ, Visscher H, Rassekh SR, Castro-Pastrana LI, Shereck E, Carleton B, Hayden MR. Pharmacogenomics of serious adverse drug reactions in pediatric oncology. *J Popul Ther Clin Pharmacol*. 2011 Mar 21;18(1):134-51.
 - 17.Richard E, Andrea A. Hearing Loss among Children Treated with Chemotherapy at Paediatric Oncology Department in Tanzania. *East African Journal of Health and Science*. 2023 Aug 25;6(1):335-45.
 - 18.Waters GS, Ahmad M, Katsarkas A, Stanimir G, McKay J. Ototoxicity Due to Cis-diamminedichloro-platinum in the treatment of ovarian cancer: influence of dosage and schedule of administration. *Ear and hearing*. 1991 Apr 1;12(2):91-102.
 - 19.Ganesan P, Schmiedge J, Manchaiah V, Swapna S, Dhandayutham S, Kothandaraman PP. Ototoxicity: a challenge in diagnosis and treatment. *Journal of audiology & otology*. 2018 Apr;22(2):59.
 - 20.Khoza-Shangase K. Confronting realities to early hearing detection in South Africa. *Early detection and intervention in audiology: An African perspective*. 2021 Feb 1:66-8.
 - 21.Pillay M, Tiwari R, Kathard H, Chikte U. Sustainable workforce: South African audiologists and speech therapists. *Human Resources for Health*. 2020 Dec; 18:1-3.
 - 22.Khoza-Shangase K, Masondo N. In pursuit of preventive audiology in South Africa: Scoping the context for ototoxicity assessment and management. *Journal of Pharmacy and Bioallied Sciences*. 2021 Jan 1;13(1):46-60.
 - 23.Khoza-Shangase K, Masondo N. What are the current audiological practices for ototoxicity assessment and management in the South African healthcare context? *International Journal of Environmental Research and Public Health*. 2020 Apr;17(7):2613.
 - 24.De Andrade V, Khoza-Shangase K, Hajat F. Perceptions of oncologists at two state hospitals in Gauteng regarding the ototoxic effects of cancer chemotherapy: A pilot study.

- African Journal of Pharmacy and Pharmacology. 2009 Jun 1;3(6):307-18.
25. Gordon T, Booyesen F, Mbonigaba J. Socio-economic inequalities in the multiple dimensions of access to healthcare: the case of South Africa. BMC Public Health. 2020 Dec; 20:1-3.
26. Hess DR. Retrospective studies and chart reviews. Respiratory care. 2004 Oct 1;49(10):1171-4.
27. Etikan I, Bala K. Sampling and sampling methods. Biometrics & Biostatistics International Journal. 2017 May 4;5(6):00149.
28. Carlucci ME, Wright DB. Inferential statistics. Research methods in psychology. 2020 Oct 5:395.
29. Health Professions Council of South Africa (HPCSA) (2018). Audiologic management of patients on treatment that includes ototoxic medications Guidelines. Health Professions' Council of South Africa, Speech Language and Hearing Profess Board. <https://www.hpcs.co.za/Uploads/SLH/Guidelines%20for%20Audiological%20Management%20of%20Patients%20on%20Treatment%20that%20includes%20Ototoxic%20Medications.pdf>
30. Hendricks M, Cois A, Geel J, Van Heerden J, Dandara C, Mohamed K, Donald KA, Kruger M. Socioeconomic status significantly impacts childhood cancer survival in South Africa. Pediatric blood & cancer. 2023 Dec;70(12):e30669.
31. Brock PR, Maibach R, Childs M, Rajput K, Roebuck D, Sullivan MJ, Laithier V, Ronghe M, Dall'Igna P, Hiyama E, Brichard B. Sodium thiosulfate for protection from cisplatin-induced hearing loss. New England Journal of Medicine. 2018 Jun 21;378(25):2376-85.
32. Freyer DR, Brock PR, Chang KW, Dupuis LL, Epelman S, Knight K, Mills D, Phillips R, Potter E, Risby D, Simpkin P. Prevention of cisplatin-induced ototoxicity in children and adolescents with cancer: a clinical practice guideline. The lancet child & adolescent health. 2020 Feb 1;4(2):141-50.
33. Ma J, Foster JH, Rassekh SR, Malvar J, Chi YY, Sauer HE, Jeon J, Freyer DR, Rushing T, Orgel E. Real-World Experience Using Sodium Thiosulfate Pentahydrate Off-Label for Cisplatin Otoprotection in Children, Adolescents, and Young Adults. Pediatric Blood & Cancer. 2025 May;72(5):e31631.
34. Rybak LP. Pathophysiology of furosemide ototoxicity. The Journal of otolaryngology. 1982 Apr 1;11(2):127-33.
35. Bates DE, Beaumont SJ, Baylis BW. Ototoxicity induced by gentamicin and furosemide. Annals of Pharmacotherapy. 2002 Mar;36(3):446-51.