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Psychology | Lancaster University

HRA Protocol Compliance Declaration:

This protocol has regard for the HRA guidance and order of content.

Title: Chemotherapy-Induced Hearing Loss and Health Inequality

Short title: CANHEAR

Version 1.1 10/10/2025

RESEARCH REFERENCE NUMBERS

IRAS Number:	355684
FUNDERS Number:	**NWCRRCC2024.01**

CANHEAR
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KEY STUDY CONTACTS

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STUDY SUMMARY

This project aims to understand how platinum-based chemotherapy affects hearing function in cancer patients from different socioeconomic backgrounds in the North West of England. Platinum-based chemotherapy drugs, particularly cisplatin, are highly toxic, causing permanent damage to the hearing system. Patients from deprived backgrounds face additional risk factors, including limited healthcare access, greater occupational noise exposure, and poorer overall health, making them more vulnerable to hearing loss. This is especially concerning as hearing loss is linked to cognitive decline and, when combined with chemotherapy-related cognitive dysfunction (“chemo brain”), may further increase dementia risk. It is expected that patients from the most deprived backgrounds (e.g., quintile 1) would experience greater hearing loss than those from more affluent backgrounds (e.g., quintile 5). By identifying disparities in hearing loss, this research will help guide future hearing screening and intervention strategies for cancer patients.

Study Title	Chemotherapy-Induced Hearing Loss and Health Inequality

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Internal ref. no. (or short title)	CANHEAR
Study Design	Prospective cohort study
Study Participants	Cancer patients receiving platinum-based chemotherapy
Planned Size of Sample (if applicable)	Participants: n = 172 Cancer patients receiving platinum-based chemotherapy. An equal number of male (n = 86) and female (n = 86) patients will be used.
Follow up duration (if applicable)	Participants will complete an online hearing test and cognitive assessments before starting chemotherapy (baseline), at the end of chemotherapy (end), and 6-months after finishing chemotherapy (6-month follow-up).
Planned Study Period	2 years
Research Question/Aim(s)	Aim The project aims to further understanding of how platinum-based chemotherapy affects hearing function in cancer patients in the North West from a variety of backgrounds of deprivation. Hypothesis Platinum-based chemotherapy will lead to significant levels of hearing loss in cancer patients.

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
Rosemere Cancer Foundation – rosemere@lthtr.nhs.uk	Joint funding = £19,996 for Research Assistant (Grade 6, 0.5 FTE, 10 months), equipment (laptop & NIH Toolbox license),

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North West Cancer Research – research@nwcr.org	Patient public involvement, travel and subsistence (conference attendance)

ROLE OF STUDY SPONSOR AND FUNDER

Lancaster University will act as the sponsor for this study. The sponsor takes the responsibility for the initiation and management of the study. The sponsor and funders will not have any role in study design, conduct, data analysis and interpretation and manuscript writing, but the sponsor will maintain oversight through thorough review procedures, monitoring and auditing as required. The sponsor and funders will be involved in the dissemination of the results and of the study.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Groups

The study is overseen by several groups to ensure efficient coordination, ethical conduct, and successful implementation. Each group has distinct roles and responsibilities and varies in its degree of independence from the study Sponsor and Investigators.

Research Team

Roles and Responsibilities:

- Oversees the overall conduct of the study.
- Ensures adherence to the study protocol and ethical guidelines.
- Monitors study progress, addressing challenges related to recruitment, data collection, and analysis.
- Liaises with regulatory bodies and funding agencies.
- Ensures timely completion of study milestones.

Independence:

- Comprises key investigators, research staff, and external advisors.
- Works in collaboration with the Sponsor but maintains operational independence.

Patient & Public Involvement (PPI) Group

Roles and Responsibilities:

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- Contributes to study design and planning, ensuring that research is patient centred.
- Assists in refining study documentation to enhance clarity and accessibility.
- Provides insights to improve study acceptability and recruitment strategies.
- Identifies barriers to participation and offers solutions to enhance engagement.
- Shares firsthand experiences of cancer treatment and hearing loss.
- Offers feedback on study materials to enhance relatability and accessibility.

Independence:

- Independent from the Sponsor and Investigators but collaborates closely to ensure patient-centric research.

Collaborators and Charity Partners – North West Cancer Research and Rosemere Cancer Foundation

Roles and Responsibilities:

- Provides expertise in cancer research and socioeconomic disparities in cancer care.
- Supports recruitment through regional cancer networks.
- Assists in the dissemination of findings.
- Provides funding, advocacy, awareness and support for the study.
- Facilitates connections with relevant patient communities.
- Supports dissemination of study findings to a broader audience.

Independence:

- Collaborates with the study team but remains an independent research entity.
- Operates independently but works closely with the study team to ensure alignment with patient needs and advocacy goals.

Participant Identification Centres (PIC Sites)

Roles and Responsibilities:

- Assist in identifying and referring potential study participants.
- Provide clinical context and logistical support for participant recruitment.
- Ensure adherence to ethical and regulatory guidelines during recruitment.

Independence:

- Operates within NHS Trusts and other clinical settings, independent of direct study oversight but collaborates with the research team.

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By establishing these committees and groups, the study ensures rigorous oversight, inclusivity, and ethical integrity, ultimately enhancing the quality and impact of research findings.

PROTOCOL CONTRIBUTORS

The research team (Dr Helen Nuttall – Chief investigator; Dr Kate Slade – Co-Investigator; Mr Ewan Dean – Research Assistant) have designed all aspects of the study, including study design, recruitment, data collection and data analysis. The research team incorporated PPIE into the protocol design by consulting with chemotherapy patients and relevant stakeholders before designing the study to ensure its suitability. The PPIE feedback (discussed in detail later, section 8.4) guided decisions on the most appropriate timing for conducting hearing and cognitive tests post-chemotherapy.

Neither the sponsor nor the funders have played any role in the study design and will not collect data, analyse data, or write the manuscript. The sponsor and funders may help with the dissemination of results through their social media and website platforms.

KEY WORDS: Chemotherapy, hearing loss, cancer.

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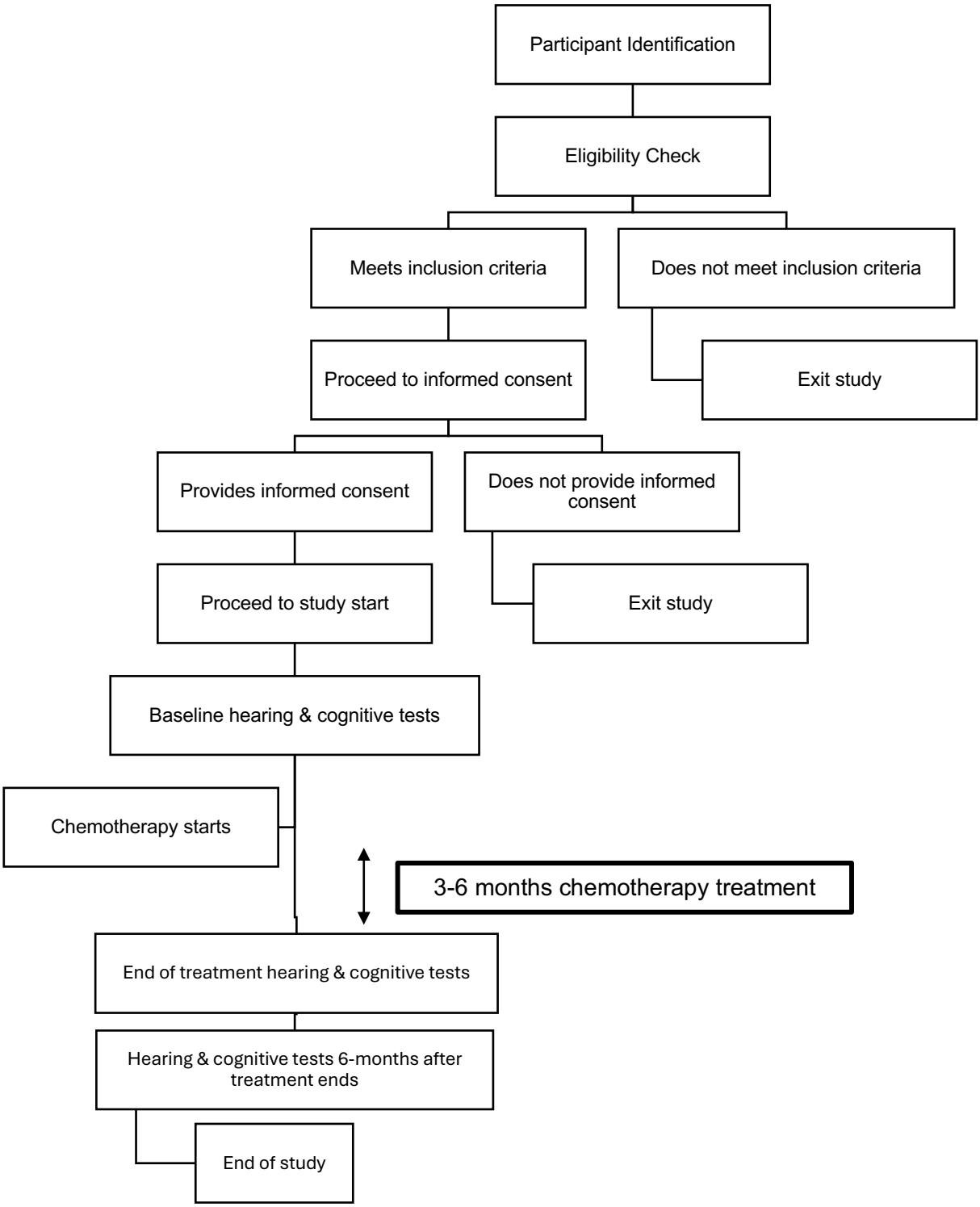

Flow chart of study design

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STUDY PROTOCOL

Chemotherapy-Induced Hearing Loss and Health Inequality

1 BACKGROUND

The project will inform and guide future care for cancer patients by investigating how cancer patients are affected by chemotherapy-induced hearing loss. Platinum-based chemotherapy drugs are known to cause damage to the ear [1]. The most toxic chemotherapy drug is cisplatin, which is used to treat testicular, ovarian, lung, bladder, head & neck, oesophageal, cervical, and stomach cancers. Platinum-based chemotherapy agents cause oxidative stress and cell death in cochlear cells in the ear, which leads to permanent damage to the hearing system [2].

This presents as hearing loss, and hearing loss is not routinely screened for or detected in cancer patients. Furthermore, individuals from deprived backgrounds (based on indices of multiple deprivation quintiles, e.g., Q1-Q5) are more likely to also experience hearing loss through barriers to accessing health services and education; variations in lifestyle, such as working in manual jobs where noise exposure is high; and experiencing poor cardiovascular health [3]. They are also likely to recover less well from the acute effects of chemotherapy due to reduced overall health and physiological resilience. Therefore, for example, patients from quintile 1 are particularly vulnerable to experiencing chemotherapy-induced hearing loss, and therefore a reduced quality of life, after receiving platinum-based chemotherapy. No research has ever explored if patients from more deprived quintiles may be disproportionately affected by chemotherapy-induced hearing loss. Furthering understanding of this area will help to guide future hearing screening and intervention following platinum-based chemotherapy.

2 RATIONALE

Individuals with hearing loss are at greater risk of experiencing cognitive decline and dementia [4]. Previous research indicates that hearing loss is associated with brain atrophy in auditory brain areas [5], which in turn will reduce the signal received by other brain areas involved in listening [6]. Additionally, hearing loss depletes limited cognitive resources, which are redirected to support listening, meaning there are reduced cognitive resources available for other daily tasks [7]. This is highly significant in the context of cancer, as chemotherapy is already known to cause cognitive dysfunction, so-called ‘chemo brain’, which is also a risk

factor for cognitive decline [8]. This means that patients receiving platinum-based chemotherapy drugs relative to non-platinum chemotherapy drugs have double the risk for cognitive decline: 1) they have the risk from neural dysfunction, and 2) the risk from hearing loss. Not only that, but hearing loss also leads to social withdrawal due to difficulties listening in noisy environments, which in turn is associated with increased feelings of loneliness and reduced mental well-being, further increasing dementia risk [9].

Relevant to the North West, cancer outcomes, incidence of dementia, and hearing loss are all adversely affected by health inequalities. As such, the prevalence and severity of hearing loss following chemotherapy must be better understood to ensure appropriate management and intervention.

3 THEORETICAL FRAMEWORKS

This study is grounded in auditory neuroscience to explain disparities in chemotherapy-induced hearing loss.

Auditory Neuroscience and Cognitive Load

Platinum-based chemotherapy drugs cause oxidative stress and cell death in cochlear cells, leading to permanent hearing damage. The Effortfulness Hypothesis suggests that hearing loss increases listening effort, depleting cognitive resources needed for memory and attention [11]. This is particularly concerning for cancer patients, who already experience cognitive impairment from chemotherapy (“chemo brain”).

4 RESEARCH QUESTION/AIM(S)

The project aims to further understanding of how platinum-based chemotherapy affects hearing function in cancer patients in the North West from a variety of backgrounds of deprivation.

4.1 Objectives

To investigate the impact of platinum-based chemotherapy on hearing function in cancer patients across different socioeconomic backgrounds in the North West of England.

4.2 Outcome

1. **Primary Outcome:**
    - Change in hearing function (measured by the Digit Triplet Test) from baseline to end of chemotherapy and 6 months after completing chemotherapy.
2. **Secondary Outcomes:**
    - Change in global cognitive function (measured via the Flanker Test, Forwards and Backwards Digit Span tests) from baseline to the end of chemotherapy, and 6 months after chemotherapy to assess potential confounding effects on hearing outcomes.

5 STUDY DESIGN AND METHODS OF DATA COLLECTION AND DATA ANALYSIS

Procedure

Participants will complete an online hearing test (Digits Triplet Test) at baseline, at the end of chemotherapy treatment, and 6 months after treatment has finished. Participants will also complete a cognitive assessment (Flanker test, forwards digit span, backwards digit span) at baseline, at the end of chemotherapy treatment, and 6 months after treatment has finished, controlling for changes in cognition confounding hearing test data. At baseline, the tests will be completed within two days before chemotherapy is due to start. The tests will be conducted within seven days after chemotherapy ends.

Hearing Test

Participants will complete the Digit Triplet Test (DTT), which is an automated, smartphone-compatible speech-in-noise test created for screening a person's hearing ability. The test takes five minutes to complete, and patients will identify three digits in background noise, where the volume of the digits decreases with each correct answer. The test determines the signal-to-noise ratio (SNR) at which 50% of the speech can be understood. The test is a fast and efficient tool that approximates how a person hears in a typical environment. If

participants meet the recognised cutoff score for hearing loss (-6 decibels [dB]), they will be contacted and advised to seek further guidance from their GP or audiologist.

The Digit Triplet Test (DTT) is a validated speech-in-noise screening tool designed to identify potential hearing difficulties. It estimates the signal-to-noise ratio (SNR) at which 50% of speech can be correctly identified, and a cutoff of -6 dB is widely recognised as indicating possible hearing impairment. However, the DTT is not a diagnostic test and does not provide clinically actionable results on its own.

Given the limited scope of the DTT and its intended use for screening rather than diagnosis, we do not consider it appropriate to base clinical decision-making or adjustments to care solely on this result. Instead, participants whose results exceed the threshold for potential hearing loss will be informed in a timely and supportive manner and advised to contact their GP or an audiologist for further assessment, in line with best practice for population hearing screening.

If the participant has provided consent, we will also share this information with a named healthcare professional (e.g. their GP or oncology team) for information only. This approach respects participant autonomy, avoids over-medicalisation, and aligns with how screening tools like the NHS online hearing check are managed in public health settings. It also ensures that clinical teams are only informed when participants have explicitly agreed for this to occur.

However, we recognise that receiving an unexpected result may cause concern. To minimise this:

- Participants will be informed during consent that the DTT is a screening tool, not a diagnostic test.
- Results will be framed clearly and reassuringly, with emphasis that a score above the cutoff suggests follow-up may be helpful but does not confirm hearing loss.

Participants who score ≥ -6 dB SNR will receive a letter or email with:

- A simple explanation of the DTT and their result.
- Clarification that the result does not confirm hearing loss.

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- Advice to contact their GP or audiologist for further assessment.
- Links to trusted NHS and hearing support resources.

If the participant has provided consent and supplied the relevant contact details, a copy of this information will also be shared with their named GP or oncology team for information only. A sample letter is included for ethics review.

Cognitive tests

1. **Executive function**

Flanker test

Participants will complete the Flanker Test, which is a computerised cognitive task used to assess executive function. The test takes approximately five minutes to complete, during which participants will identify the direction of a central target arrow, flanked by distractor arrows on either side. The arrows may be congruent (pointing in the same direction) or incongruent (pointing in opposite directions). The test measures how well patients can focus on the target stimulus while ignoring irrelevant distractions. The Flanker Test provides insight into an individual's ability to manage interference and selective attention, offering a quick and efficient evaluation of executive function in a controlled environment.

2. **Memory tests**

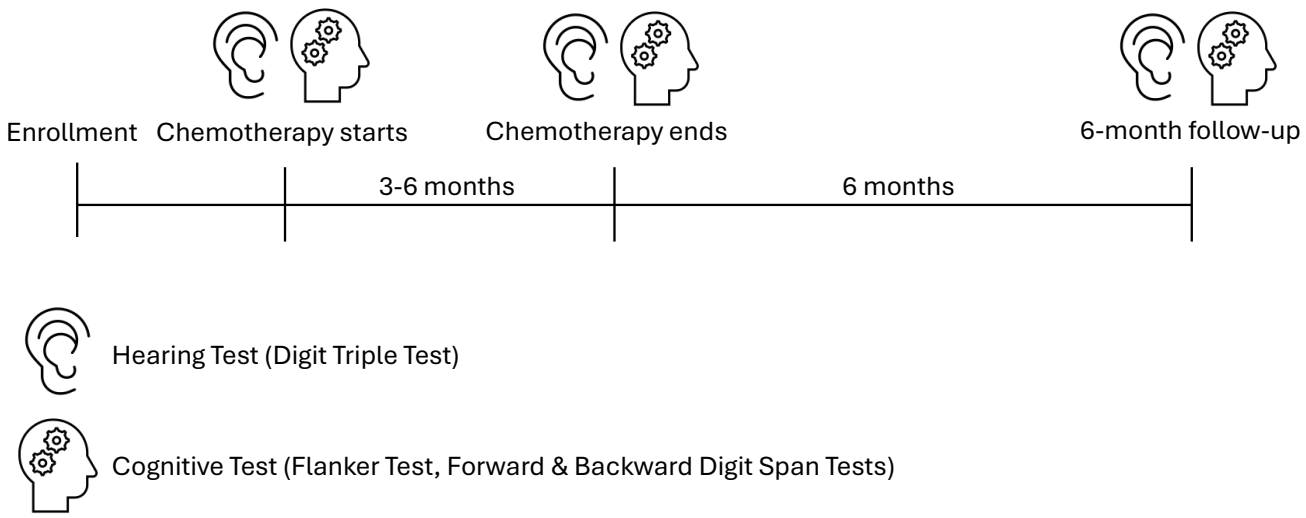
Forward Digit Span Test

Patients will complete the Forward Digit Span Test, a cognitive assessment used to evaluate short-term memory and attention. The test takes approximately five minutes to complete, during which patients will be shown a sequence of digits on a screen and required to recall them in the same order. The length of the digit sequence increases with each correct response. This test measures short-term memory, providing insight into an individual's ability to temporarily store and recall information in everyday settings.

Backward Digit Span Test

Patients will complete the Backward Digit Span Test, a cognitive assessment designed to

measure working memory. The test takes approximately five minutes to complete, during which patients will be shown a sequence of digits on a screen and must recall them in reverse order. The test becomes progressively more challenging as the digit sequences increase in length. This test evaluates an individual's working memory.



Study schematic and timeline

End of study

The end of study is defined as the last data collection point (i.e., 6-month follow-up) for the final participant.

Statistical Approach

Using linear multiple regression, we will model how socioeconomic quintile group, dosage, age, and cognition and hearing at baseline influence the degree of hearing loss at the end of chemotherapy treatment. All data will be analysed using R.

Confidentiality

The research team will preserve the confidentiality of participants taking part as stipulated under the Data Protection Act. All data collected will be accurately recorded and securely

stored by the team and no identifiable information will be available to members outside the study team.

Anonymity and Data Governance

The data will be collected via Qualtrics and via online platforms - Redcap and Pavlovia - used to administer online hearing and cognitive tests. There will be an initial questionnaire presented in Qualtrics, which participants will access anonymously. This questionnaire will record the research data related to medical data (chemotherapy drug, dosage, etc) and socioeconomic data (education, postcode, etc). After this is completed and participants provide us with the dates for their chemotherapy sessions, they will be sent a link to complete the anonymous hearing and cognitive tests on the specified dates. Their anonymous unique ID (generated by Qualtrics) will be embedded in the test links so that the data from the hearing and cognitive tests can be matched to responses on the initial Qualtrics questionnaire.

With regards to the DTT, data will be identifiable to the research team for a period of 2 weeks following completion. This will allow us to send a letter to participants who do not meet the -6 dB cut off advising them to seek medical advice from their clinical team, GP or audiologist.

The data from the online hearing and cognitive tests is stored on a secure, password-protected cloud server in the EU with two-factor authentication. It can only be accessed by the manager of the online hearing/cognitive test (Dr Helen Nuttall, CI) or other members of the research team (Dr Kate Slade, Co-I, Ewan Dean, RA). While postcode data will be recorded, it will be stored separately from test responses and will not be used to identify individuals. No other identifiable or personal information is stored on the online server. The data will be removed from the online server once data collection is complete.

The data stored online on the Qualtrics server and the online platform Redcap and Pavlovia used to administer online hearing and cognitive tests will be stored until the required sample size for the study is met. Then, the data will be saved on Lancaster University's secure OneDrive server. The data will then be stored on OneDrive for a maximum of 10 years from the date of the completion of the study, that is when all planned data collection has been concluded, and all data has been analysed. This will be managed by the CI, who will be

responsible for the deletion once the 10-year institutional retention period is complete. The anonymous research data will however also be made publicly available online indefinitely on the Open Science Framework repository. This data will be unidentifiable.

6 STUDY SETTING

Study Setting

Data collection will be conducted within the participant's place of choosing, such as their home, as the tests require a laptop or tablet and an internet connection. The study recruitment will be conducted across multiple cancer treatment centres in the North West region (East Lancashire Hospitals NHS Trust, Lancashire Teaching Hospitals NHS Foundation Trust, and University Hospitals of Morecambe Bay NHS Foundation Trust). These centres have been selected due to their diverse patient populations, which will allow for the inclusion of participants from various socioeconomic backgrounds.

Site Selection and Justification

Cancer treatment centres within hospitals in the North West have been chosen as the primary study sites due to their high patient numbers and their representation of individuals from different socioeconomic backgrounds. These sites have all been identified as using platinum-based chemotherapy drugs. The selection of these sites is further justified by their accessibility to patients and their established protocols for chemotherapy administration and patient follow-up. These sites will act as participant identification centres (PIC) only.

Participant Recruitment and Access

Participants will be accessed through oncology clinics within the selected PIC sites. Eligible participants set to receive platinum-based chemotherapy will be identified by their oncologists, invited to participate in the study and directed to sign up online. Recruitment will be facilitated through clinic visits and posters in waiting rooms, where patients will be directed to an online link or scan a QR code, informed about the study and provided with online participant information sheets and consent forms.

Appropriateness of the Research Setting

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The selected research setting aligns with the study's objectives as it provides direct access to cancer patients receiving platinum-based chemotherapy.

Multicentre
This is a multicentre study, allowing for a broader and more representative sample of cancer patients from different socioeconomic backgrounds. Conducting the study across multiple centres enhances the generalisability of the findings and ensures a diverse participant pool.

Site-Specific Requirements
Participant Identification Centres (PIC Sites): Each site included in the study will act solely as a PIC site, meaning that they will only be responsible for identifying and referring eligible participants to the central research team via an online sign-up link. This structured multicentre approach ensures a robust investigation into the impact of platinum-based chemotherapy on hearing function, in cancer patients from a range of socioeconomic status, while streamlining recruitment through PIC sites.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

- 18 years +
- Patients receiving platinum-based chemotherapy drugs
- Living and treated within North West England
- Able to complete an online hearing and cognitive test
- Fluent in English

7.1.2 Exclusion criteria

- Following cancer types: brain tumour/metastasis, head + neck, skin cancers around the ear, and adenoid cystic carcinoma of the auditory cortex
- World Health Organisation performance status score of 3 or more
- Stage 4 cancer
- History of childhood deafness

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- Current or recent ear infections
- Cochlear implant user
- Known neurological impairment (e.g., stroke, traumatic brain injury, dementia)
- Patients who look capacity to consent or complete study tasks

7.2 Sampling

7.2.1 Size of sample

The minimum required sample size for this study was determined using a linear multiple regression model. The sample size calculation was based on a small effect size (f^2) of 0.085, an alpha level of 0.025, and a statistical power of 80%. The analysis included four tested predictors, with a total of four predictors in the model. Based on these parameters, the minimum sample size required to achieve sufficient power for detecting the expected effect was calculated to be 172 participants. An equal number of male (86) and female (86) patients will be used.

7.2.2 Sampling technique

The study will employ convenience sampling, a non-probability method where participants are selected based on availability and accessibility. This approach is practical for identifying eligible patients already set to receive platinum-based chemotherapy within the selected PIC sites.

Sample Source:

Participants will be identified through oncology clinics within hospitals in the North West of England, where PIC sites are located. Oncologists will assess eligibility and invite patients to sign up via an online link, ensuring minimal disruption to their ongoing treatment.

Rationale for Sampling Strategy:

- **Accessibility & Feasibility:** Convenience sampling ensures efficient recruitment within a clinical setting where patients are already present, reducing additional burdens on healthcare staff.

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- **Diverse Representation:** Multiple cancer treatment centres enable recruitment from various socioeconomic backgrounds, improving the generalisability of findings.
- **Alignment with Study Objectives:** Since the study focuses on the impact of platinum-based chemotherapy on hearing function, selecting patients actively receiving this treatment ensures relevance and applicability.

This approach ensures streamlined recruitment while maintaining methodological rigour and feasibility within a real-world clinical setting.

7.3 Recruitment

Participants will be identified through oncology clinics within the selected PIC sites. Eligible patients set to receive platinum-based chemotherapy will be identified by their oncologists, invited to participate in the study and directed to sign up online via a link or QR code. If interested, potential participants will be presented with a participant information sheet and consent form, which they must sign and date before being eligible for enrolment in the study.

To identify the socioeconomic status of participants, we will use the Index of Multiple Deprivation (IMD) from the postcode data of the participants. Participants will also be required to provide relevant demographic information such as:

- Sex
- Age
- Postcode
- Ethnicity
- Education level

Participants will also be required to disclose the following medical information:

- Cancer type
- Cancer location
- Type of platinum-based chemotherapy drug
- Drug dosage
- Other health conditions
- Current or previous hearing loss
- Neurodevelopmental disorders (e.g., dyslexia)

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- Languages spoken

We will also require participants to inform us of the dates they will be receiving chemotherapy, due to the hearing and cognitive tests being completed before the start of chemotherapy, after chemotherapy ends, and 6 months after the end of chemotherapy.

7.3.1 Sample identification

Participant Identification and Recruitment Methods

Participants undergoing platinum-based chemotherapy at the PIC sites will be identified through their oncology clinics. Oncologists within these clinics, as members of the patient's existing care teams, will determine eligibility and direct interested patients to an online sign-up link or QR code, which will provide study information and instructions for enrolment.

Recruitment Methods and Resources

- **Oncology Clinics:** Oncologists will identify eligible participants and introduce the study during routine clinical consultations.
- **Posters and Publicity Materials:** Study posters will be placed in oncology and cancer clinic waiting rooms to raise awareness and encourage participation.
- **Online Access:** Patients will receive a QR code or web link to access study details, consent forms, and enrolment instructions online.

Recruitment Through PIC Sites

All participants will be recruited through PIC sites, where clinics will act solely as referral centers. No direct research activities will occur at these sites.

Use of Identifiable Personal Information

Only members of the patient's existing clinical care team (i.e., oncologists) will identify potential participants. **No patient records will be accessed by external researchers** without explicit consent. The initial approach will be made by oncologists to ensure confidentiality and compliance with ethical guidelines.

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Referral and Consent Process

Once identified, interested participants will self-refer by accessing the online portal via the provided QR code or link. They will review study details, complete consent forms, and proceed with enrolment independently.

Confidentiality and Data Protection

Since no external research team will access identifiable patient data directly, there is no breach of confidentiality. All recruitment efforts comply with data protection regulations.

Payments and Reimbursements

Participants will receive a £10 voucher for taking part in the study.

7.3.2 Consent

All participants participating in the study will be provided with online participant information sheets describing the nature and goals of the research and a study consent form. This will also contain the contact details of members of the research team who will be available to clarify and answer any questions. Consent forms must be completed online after the participant has received detailed information about the study and made their decision. As the study involves repeated assessments of hearing function and cognition, participants must understand their role, the timeframe of data collection, and the use of the hearing and cognitive assessments. Any concerns regarding potential impacts on their well-being can be discussed with a member of the research team via email.

The consent process:

- Cancer patients who show an interest in taking part in this study will be directed to an online link which will provide them with information about the study.

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- All potential participants will be provided with approved written materials, such as a participant information sheet and consent forms, clearly detailing the study's purpose and what participation entails.
- All participants will have the opportunity to ask questions and receive clear, comprehensive answers. A discussion with a member of the research team via email regarding the study's objectives, procedures, potential risks, and benefits will be made available.
- It will be made explicitly clear to all participants that their participation is entirely voluntary and that participant interests are protected throughout.
- If participants wish to take part in the study, they will complete and sign the online consent form.

8 ETHICAL AND REGULATORY CONSIDERATIONS

Ethical Framework and Justification

This study aims to assess the impact of chemotherapy on hearing function in cancer patients, utilising an online hearing test and cognitive assessments. The research design ensures ethical integrity by minimising risks, maximising benefits, and upholding participant dignity throughout the study.

Risk and Benefit Assessment

Risks: The study poses minimal risk to participants. Potential risks include mild discomfort or frustration while completing the hearing and cognitive assessments. To mitigate these, participants will receive clear instructions and the option to take breaks as needed, and it will be made explicitly clear that their participation is entirely voluntary, and they can withdraw from the study at any point during their participation in the study. Confidentiality risks related to data collection will be addressed through secure data storage and anonymisation techniques.

Benefits: The study may contribute to a better understanding of chemotherapy-induced hearing loss, potentially informing clinical practice and improving patient care. Participants

may benefit from increased awareness of their hearing function, which could facilitate early intervention if needed.

Considerations for the Sample Population

Cancer patients undergoing chemotherapy may have varying physical and cognitive abilities. To accommodate this, the study is designed to be accessible online, allowing patients to complete assessments at their convenience. Assistance will be available via email for those who require help navigating the online tools.

Upholding Participant Dignity

The study ensures participant dignity through voluntary participation, informed consent, and clear communication of study procedures. Participants will be provided with an easy-to-understand consent form and participant information sheet outlining the purpose, risks, and benefits of the study. They retain the right to withdraw at any stage during their participation in the study without consequences.

The assessments themselves are designed to be non-invasive and user-friendly. The hearing test (Digit Triplet Test) is brief and widely validated, reducing participant burden. The cognitive assessments (Flanker Test, Forward Digit Span, Backward Digit Span) have also been carefully chosen to minimise fatigue and distress.

Compliance with Ethical and Regulatory Requirements

All members of the research team will preserve the confidentiality of participants taking part in the study and will abide by the Data Protection Act 2018, the UK GDPR, and the Declaration of Helsinki as amended from time to time and any successor legislation in the UK, and any other directly applicable regulation relating to data protection and privacy. Ethical approval will be sought from the appropriate research ethics committee before commencing the study.

Data Protection and Confidentiality

Data will be stored securely, and personally identifiable information will be separated from research data to maintain confidentiality. In accordance with Lancaster University standards, all participants are anonymised. Therefore, any personal information or any of the data generated or secured will not be disclosed to any third party. The research team will preserve

the confidentiality of participants taking part. All data collected, consent forms and recruitment logs will be accurately recorded and securely stored by the team and can only be accessed via password on a Lancaster University owned PC, and no identifiable information will be available to members outside the study team.

Institutional and Site-Specific Approvals

Prior to initiating the study, appropriate approvals will be obtained from the sponsor, and any relevant hospital or research site committees. The study protocol aligns with site-specific regulatory requirements, ensuring compliance with local and international research guidelines.

8.1 Assessment and management of risk

There are minimal risks associated with this study due to it being conducted solely online. Participants will be required to complete a short online hearing test (5-10 minutes) and online cognitive tests (10-20 minutes) at three separate time points throughout chemotherapy treatment. As the study is observational, there will be no changes to participants' medical care.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the study, a favourable opinion will be sought from NHS REC and approval from the Health Research Authority will be obtained. The University of Lancaster will be the sponsor for the study. We will ensure that appropriate approvals from participating sites are in place through close liaison with participating Research and Development departments.

8.3 Peer review

This study has undergone independent peer review by an expert panel of researchers and medical professionals at the Surgery in Lancashire and South Cumbria Conference 2024. The review process was independent of the study investigators' host institution and included at least two experts with relevant clinical and methodological expertise.

Additionally, the study was reviewed by representatives of the funders, Rosemere Cancer Foundation and North West Cancer Research, ensuring that the research aligns with funding

priorities and quality standards. This review process was proportionate to the scope of the study, taking into account both its clinical relevance and methodological rigour.

This was an independent peer review process, meeting the standards outlined by the National Institute for Health Research (NIHR) Clinical Research Network (CRN) for high-quality peer review.

8.4 Patient & Public Involvement

A Patient and Public Involvement (PPI) group was established to provide insights into the acceptability, design, management, undertaking, analysis, and dissemination of this research on the impact of cancer treatment on hearing and brain function.

Acceptability of the Research

The PPI findings indicate varying levels of awareness regarding the impact of cancer treatment on hearing and brain function. While one participant had prior knowledge through independent research, the majority were unaware. This suggests that research in this area is valuable and necessary to increase awareness and provide clearer information to patients. Participants also emphasised the importance of studying the long-term effects of cancer treatment, such as chemo-brain or brain fog, which was described as a frightening experience.

To address this, we will ensure participants are signposted to appropriate sources of help and support regarding hearing and cognitive changes related to cancer treatment. This may include directing them to relevant patient support groups, healthcare professionals, or existing online resources that provide further information on these topics.

Design of the Research

The PPI group provided input on the feasibility of an online task designed to measure hearing and brain function after cancer treatment. Responses suggested that while some participants might be able to complete the task immediately after chemotherapy treatment, others indicated they would struggle even up to 24 hours post-chemotherapy due to fatigue or other side effects. This feedback highlights the need for appropriate testing conditions, such as asking participants to complete the hearing and cognitive tests within two days pre-

chemotherapy and within seven days post-chemotherapy. Careful consideration of participant burden has been incorporated when designing the study protocol.

To meet these recommendations, we have ensured that the study design utilises appropriate timeframes to ensure that participants are not too fatigued to complete the online tests. Additionally, the online format ensures minimal disruption to participants' daily lives.

Management of the Research

Insights from the PPI group emphasise the importance of ensuring that research participation is accessible and not overly demanding, particularly for individuals undergoing cancer treatment. Participants expressed concerns about fatigue following chemotherapy, which should be considered when scheduling assessments and developing participant instructions.

To address this, we will provide clear, step-by-step instructions and an option for participants to pause and resume the task if needed. The PPI group indicated that online hearing and cognitive tests were appropriate for chemotherapy patients to complete due to their low burden and limited impact on participants' time. We will also ensure that technical support is available for those who require assistance in accessing or completing the online tests.

Undertaking the Research

Findings from the PPI group highlight the need for clear communication about the research objectives, procedures, and potential impacts. Ensuring that participants fully understand the relevance of the study and how their involvement contributes to improved cancer treatment outcomes is essential.

To meet this need, we will develop patient-friendly study materials, including a lay summary to explain the purpose and methods of the research in an accessible manner.

Analysis of Results

The PPI group's perspectives underscore the importance of interpreting results within the context of patients lived experiences. For example, participants who attributed hearing loss to occupational noise exposure provide insight into potential confounding factors that must be

considered in the analysis. Additionally, experiences of cognitive changes post-treatment emphasise the necessity of examining long-term effects.

In response to this feedback, we will ensure that demographic and medical history data are carefully considered in the analysis to account for potential confounding variables.

Dissemination of Findings

The PPI group's input supports the need for broad dissemination of findings to healthcare providers, patients, and the general public. As some participants were unaware of the effects of cancer treatment on hearing and brain function, sharing results through accessible formats such as patient information leaflets, online resources, and public engagement events will be crucial.

To achieve this, we will collaborate with patient advocacy groups and healthcare professionals to ensure findings are distributed through appropriate channels. We will also consider hosting online webinars or discussion panels to engage with patients and the wider public, providing an opportunity for direct feedback and discussion.

8.5 Protocol compliance

To ensure effective management of protocol compliance, all protocol deviations, non-compliances, or breaches must be clearly documented and addressed promptly. Accidental protocol deviations may occur at any point during the study and must be reported immediately to the Chief Investigator and Sponsor, with full documentation on the relevant forms. These deviations should be reviewed to assess their impact and ensure appropriate corrective actions are taken. If deviations are found to recur frequently, they will be considered unacceptable and will require immediate remedial action. Persistent deviations may be classified as serious breaches, necessitating further review and potential regulatory action to safeguard the study's integrity.

8.6 Data protection and patient confidentiality

CANHEAR

The study will fully comply with the requirements of the Data Protection Act 2018, the UK GDPR, and the Declaration of Helsinki, along with any other applicable regulations concerning data protection and privacy. The Chief Investigator will ensure that patient confidentiality is maintained throughout the study and that all investigators and site staff adhere to these legal and ethical standards. Ethical approval will be sought from the appropriate research ethics committee before the study begins.

To safeguard participant confidentiality, any personal information will be collected, stored, processed, and disclosed in a secure and controlled manner. Personal data will be depersonalised and replaced with coded identifiers, where the participant's identifying information is substituted with an unrelated sequence of characters. The coded data and linking code will be stored separately in encrypted digital files within password-protected folders and secure storage media. Access to the data will be restricted to a minimal number of authorised personnel, strictly limited to those involved in quality control, audit, or analysis, in accordance with the principle of data minimisation.

Data confidentiality will be preserved when transmitting data to sponsors and co-investigators through secure methods that prevent unauthorised access. Data will be retained for the period specified by the study's requirements, after which it will be securely destroyed per institutional data retention policies. The designated data custodian will be the chief investigator and will be responsible for overseeing the secure handling and storage of all research data.

8.7 Indemnity

As the study involves online tests and no interventions, there is minimal risk of harm to any participant. The University of Lancaster will be the sponsor for the study and will fulfil the insurance/indemnity arrangements should harm to participants occur as a result of the negligent management or design of the project. Should harm to participants occur as a result of the negligent conduct at NHS sites, the NHS indemnity may apply.

8.8 Access to the final study dataset

CANHEAR

The final dataset from this study will be accessible to specific individuals involved in the research, including the Chief Investigator, selected study team members, and other authorised personnel. Access to the full dataset will be restricted to maintain the confidentiality and integrity of the study until the final analysis and publication are complete. In multicentre studies, access to the full dataset may be limited to the steering group to prevent individual study sites from disclosing results before the main publication. Site investigators may request access to the full dataset if a formal request, outlining their plans, is approved by the steering group. This process ensures that all requests are appropriately vetted and aligned with the study's objectives and timelines. If the dataset is to be used for secondary analysis, this will only occur with explicit consent from the participants. Any patient documentation, including consent forms, will clearly outline the potential future use of their data in additional research, ensuring that participants are fully informed of how their data may be utilised beyond the scope of the current study.

In line with open and transparent science, the findings of the study will be uploaded to the Open Science Framework indefinitely. This data will be unidentifiable.

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The data arising from this study will be owned by the Chief Investigator and the sponsoring institution, with appropriate permissions granted to collaborating investigators as outlined in the study agreement. Upon completion of the study, the data will be thoroughly analysed, and a Final Study Report will be prepared. The full study report will be made accessible via the sponsor's institutional repository or through publication in a peer-reviewed academic journal, depending on the study's findings and agreements with the research team. Participants will be informed about the outcome of the study, either through the publication of the findings or via a specifically designed communication such as a newsletter or presentation. Participants may request the results of the study from their Chief Investigator (CI), and this information will be provided after the Final Study Report is compiled or after the results have been published, depending on the nature of the request and the study's timeline The study protocol, full study report, anonymised participant-level dataset, and statistical code used for generating the results will be made publicly available in accordance with institutional policies. These

materials will be uploaded to the Open Science Framework (OSF) or a similar open-access platform, ensuring broad access and transparency. The data will be accessible after the publication process is completed, with a specified timeframe for access. Any conditions for accessing the data, such as ethical considerations or institutional requirements, will be clearly outlined.

9.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship on submitted manuscripts will be based on criteria set out by the International Committee of Medical Journal Editors.

10 REFERENCES

1. Dillard, L. K. et al. Cancer Epidemiol 79, (2022). 2. Chattaraj, et al. JCO Oncol Pract 19, 278–283 (2023). 3. Tsimpida, D. et al. BMJ Open 9, e031030 (2019). 4. Livingston, G. et al. The Lancet 396, 413–446 (2020). 5. Slade, K. et al. Front Neurol 13, (2022). 6. Griffiths, T. D. et al. Neuron 108, 401–412 (2020). 7. Slade K. et al. Trends Neurosci 43, 810–821 (2020). 8. Cascella, M. et al. RecenF Prog Med 109, 523–530 (2018). 9. Shukla, A. et al. Oto-Head and Neck Surgery (2020), 622–633. 10. World Health Organisation (2025). Available at: https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1. Accessed 07/03/2025. 11. McCoy, S.L., et al. Q. J. Exp. Psychol. A, 58(1), 22-33. (2005).

11. APPENDICIES

11.1 Appendix 1- Required documentation

List here all the local documentation you require prior to initiating a participating site (e.g. CVs of the research team, Patient Information Sheet (PIS) on headed paper etc.).

11.2 Appendix 2 – Schedule of Procedures

Procedures	Tasks for participants to complete

CANHEAR

	Screening	Baseline	Chemotherapy starts	Chemotherapy ends	6 Month follow up
Informed consent	x				
Demographics		x			
Medical history		x			
Hearing Test			x	x	x
Cognitive tests			x	x	x

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	1.1	10/10/2025	Ewan Dean	We have provided a clear study end date under the sub-heading "End of study" – "The end of study is defined as the last data collection point (i.e., 6-month follow-up) for the final participant."

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.