“A study of hearing deterioration following treatment for head and neck cancer in a UK population”

THESIS

By Presanna Premachandra MSc, BSc (Hons)

A thesis submitted for the Doctorate of Clinical Practice

THESIS PART ONE

Faculty of Health and Medical Sciences

School of Health Sciences

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<table>
<thead>
<tr>
<th>Table of contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement of originality</td>
<td>3</td>
</tr>
<tr>
<td><strong>Section A Research project</strong></td>
<td>4</td>
</tr>
<tr>
<td>Abstract</td>
<td>4</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>7</td>
</tr>
<tr>
<td>Abbreviations</td>
<td>9</td>
</tr>
<tr>
<td>Glossary of terms</td>
<td>11</td>
</tr>
<tr>
<td>List of chapters</td>
<td>16</td>
</tr>
<tr>
<td>List of tables</td>
<td>24</td>
</tr>
<tr>
<td>List of figures</td>
<td>26</td>
</tr>
<tr>
<td>List of appendices</td>
<td>27</td>
</tr>
<tr>
<td>Chapters</td>
<td>28</td>
</tr>
<tr>
<td>Appendices</td>
<td>247</td>
</tr>
<tr>
<td><strong>Section B Research log</strong></td>
<td>293</td>
</tr>
<tr>
<td><strong>Section C Overview of the integration of knowledge, research and practice</strong></td>
<td>301</td>
</tr>
<tr>
<td>References</td>
<td>308</td>
</tr>
</tbody>
</table>
Statement of originality

This thesis and the work to which it refers are the results of my own efforts. Any ideas, data, images or text resulting from the work of others (whether published or unpublished) are fully identified as such within the work and attributed to their originator in the text, reference/bibliography or in footnotes. This thesis has not been submitted in whole or in part for any other academic degree or professional qualification. I agree that the University has the right to submit my work to the plagiarism detection service TurnitinUK for originality checks. Whether or not drafts have been so assessed, the University reserves the right to require an electronic version of the final document (as submitted) for assessment as above.
Section A Research project

Abstract

Background information

The premise of this study was that hearing deterioration, associated with treatment for head and neck cancer, has a negative impact on patients’ quality of life. However, there have been no studies to assess this phenomenon in people receiving current UK treatment, and there is little information on the impact of subsequent hearing deterioration.

Objective

This study, conducted in one UK hospital, aimed to investigate the incidence and severity of hearing deterioration, and patient experience of it, following treatment for head and neck cancer.

Design

A sequential mixed methods explanatory design was chosen as it was the most appropriate for addressing the research aims. A critical realist framework underpinned the study. A prospective observational repeated measures design was employed to obtain quantitative data in Phase 1 of the study to assess changes in hearing at the end of treatment, and at 3-month follow-up post-treatment, using pre-treatment test level comparison. The Common Terminology Criteria for Adverse Events (version 4.03) were used to determine the incidence and severity of hearing deterioration. Results from Phase 1 were used to inform selection of participants for Phase 2 of the study. An approach informed by phenomenology
using interview methodology, was used to explore patient experience of hearing deterioration.

Study sample

Fifty adults who had been diagnosed with head and neck cancer were recruited to Phase 1 of the study using a consecutive sampling approach. These participants were due to receive standard UK curative radiotherapy (intensity modulated radiotherapy) or chemoradiotherapy (including the use of cisplatin or carboplatin). From the 50 participants recruited, 13 who had hearing deterioration were selected using purposive sampling for one-to-one interviews to obtain in-depth information on their experience of hearing loss.

Results

The incidence of hearing deterioration was 57% in the 42 participants who completed testing at the end of treatment, and 50% percent in those who completed 3-month follow-up testing. At 3-month follow-up, 26% of participants had major (Grade 3) hearing deterioration in at least one ear. Patients who had chemoradiotherapy were more likely to experience hearing deterioration compared with those who had had radiotherapy only (p=0.01). Older patients were more at risk of hearing deterioration than younger participants (p=0.03), but if hearing deterioration occurred it appeared that younger patients suffered more severe deterioration than older patients (p=0.02).

Aural change (including hyperacusis) experienced by some participants during treatment required a change in treatment regimen for them. Participants reporting either minor (Grade 1) or major hearing deterioration were adversely affected by their aural symptoms that manifested with treatment, and the impact of tinnitus (the incidence of which is not covered by existing studies), was extensive in head and neck cancer survivors. Another emerging finding in this study was that middle ear dysfunction, in the early post treatment phase, had a
negative impact on patient experience. A further novel finding was that participants with bilateral mild-moderate or moderate severity, mid-high frequency sudden-onset hearing loss required lip-reading to assist their communication.

There was evidence that some participants played down their aural symptoms, yet hearing deterioration had a negative impact on their overall quality of life, including generating a sense of loss (principally in older patients) and isolation (associated with younger patients). Finally, there was varied experience among participants receiving information on their hearing test results and on the process of receiving support for their hearing and tinnitus concerns.

Conclusions and recommendations

This current study provides evidence that could be used to increase awareness of the potential scale and impact of hearing deterioration following head and neck cancer treatment, in the early post treatment period. A larger multi-centre UK study would test the issues identified in the study to inform national policy, clinical practice and education.

The study suggests a number of changes for consideration in improving current clinical practice when designing care provision of patients preparing for and recovering from radiotherapy or chemoradiotherapy for head and neck cancer. One key recommendation is for the adoption of a multidisciplinary approach in developing appropriate protocols to inform and support patients about hearing and tinnitus concerns that may occur with their treatment. (Word count 678).
Acknowledgements

I am grateful for the support and guidance provided by all my supervisors throughout the course of this study: Dr Wendy Knibb, Professor Karen Bryan, the late Dr Jude Redfern, and Professor Nora Kearney during the early stages of the study; Professor Roma Maguire, Professor Emma Ream and Dr Margaret Lau-Walker in the last three years. I would like also to acknowledge Dr Alison Yeung Yam Wah for her advice in improving the writing style of the thesis.

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I dedicate this thesis in memory of Raymond Turner, who for many years was my mentor, friend, and inspiration. His cheerful outlook on life, his calm and steadfast presence, and his belief all helped to give me confidence that all will be well.
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D</td>
<td>2-dimensional</td>
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<tr>
<td>3D</td>
<td>3-dimensional</td>
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<tr>
<td>ABR</td>
<td>Auditory brainstem response <em>(see also glossary)</em></td>
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<tr>
<td>ACS</td>
<td>American Cancer Society</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
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<td>ASHA</td>
<td>American Speech Language Hearing Association</td>
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<tr>
<td>BS EN ISO</td>
<td>British, European and International Standard</td>
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<td>BSA</td>
<td>British Society of Audiology</td>
</tr>
<tr>
<td>CASP</td>
<td>Critical Appraisal Skills Programme</td>
</tr>
<tr>
<td>CINAHL</td>
<td>Cumulative Index to Nursing and Allied Health Literature</td>
</tr>
<tr>
<td>CRT</td>
<td>Chemoradiotherapy</td>
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<tr>
<td>CTCAE</td>
<td>Common Terminology Criteria for Adverse Events</td>
</tr>
<tr>
<td>dB</td>
<td>Decibel(s)</td>
</tr>
<tr>
<td>dBHL</td>
<td>Decibel hearing level</td>
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<tr>
<td>DH</td>
<td>Department of Health</td>
</tr>
<tr>
<td>DClinPrac</td>
<td>Doctorate of Clinical Practice</td>
</tr>
<tr>
<td>EBSCO</td>
<td>Elton B Stephens Company</td>
</tr>
<tr>
<td>EMBASE</td>
<td>Excerpta Medica database</td>
</tr>
<tr>
<td>ENT</td>
<td>Ear, nose and throat</td>
</tr>
<tr>
<td>EORTC</td>
<td>European Organisation for Research and Treatment of Cancer</td>
</tr>
<tr>
<td>HNC</td>
<td>Head and neck cancer</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papillomavirus</td>
</tr>
<tr>
<td>HQIP</td>
<td>Healthcare Quality Improvement Partnership</td>
</tr>
<tr>
<td>IMRT</td>
<td>Intensity modulated radiation therapy</td>
</tr>
<tr>
<td>kHz</td>
<td>Kilo Hertz</td>
</tr>
</tbody>
</table>

*(see also glossary)*
<table>
<thead>
<tr>
<th>M</th>
<th>MDT</th>
<th>Multidisciplinary team</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEDLINE (see also glossary)</td>
<td>Medical literature analysis and retrieval system online</td>
</tr>
<tr>
<td></td>
<td>MRC</td>
<td>Medical Research Council</td>
</tr>
<tr>
<td>N</td>
<td>NCI</td>
<td>National Cancer Institute</td>
</tr>
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<td></td>
<td>NICE</td>
<td>National Institute of Clinical Excellence</td>
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<tr>
<td></td>
<td>NHS</td>
<td>National Health Service</td>
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<td></td>
<td>NPC</td>
<td>Nasopharyngeal cancer</td>
</tr>
<tr>
<td>O</td>
<td>OAE</td>
<td>Otoacoustic emission(s) (see also glossary)</td>
</tr>
<tr>
<td></td>
<td>OCIU</td>
<td>The Oxford Cancer Intelligence Unit</td>
</tr>
<tr>
<td></td>
<td>OME (see also glossary)</td>
<td>Otitis media with effusion</td>
</tr>
<tr>
<td>P</td>
<td>PCI</td>
<td>Patients Concerns Inventory</td>
</tr>
<tr>
<td></td>
<td>PICO (see also glossary)</td>
<td>Population or Patient or Problem; Intervention; Comparison; Outcome</td>
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<tr>
<td></td>
<td>PROM</td>
<td>Patient reported outcome measure</td>
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<tr>
<td></td>
<td>PTA</td>
<td>Pure tone audiometry (see also glossary)</td>
</tr>
<tr>
<td></td>
<td>PRISMA (see also glossary)</td>
<td>Preferred Reporting Items for Systematic Reviews and Meta-Analyses</td>
</tr>
<tr>
<td></td>
<td>PubMed</td>
<td>see glossary</td>
</tr>
<tr>
<td>Q</td>
<td>QLQ</td>
<td>Quality of Life Questionnaire</td>
</tr>
<tr>
<td>R</td>
<td>RT</td>
<td>Radiotherapy</td>
</tr>
<tr>
<td>S</td>
<td>SCN</td>
<td>Supportive care needs</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>Standard deviation (see also glossary)</td>
</tr>
<tr>
<td></td>
<td>SNHL (see also glossary)</td>
<td>Sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td>SPSS (see also glossary)</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>T</td>
<td>TNM (see also glossary)</td>
<td>Tumour, Nodes and Metastasis</td>
</tr>
</tbody>
</table>
A
Acquired hearing loss Hearing loss developed after birth
Analysis of variance A statistical method used to compare the means of two groups that have even distribution of data
Auditory brainstem response test A hearing test that tells how the auditory nerve and the brain pathways for hearing are working
Auditory cortex Part of the brain that perceives sound
Auditory nerve The nerve that transmits sound from the ear towards the brain
Aural fullness Feeling of pressure within the ear

B
Bonferroni correction A test used to determine confirm statistical significance in multiple group analysis

C
Carcinoma A type of cancer
Categorical data Data arranged into groups for statistical analysis
Central auditory system Part of the hearing (auditory) system that includes the auditory cortex
CINAHL A health sciences database of nursing and allied health journals (see abbreviations)
Clarivate Analytics A company that owns a collection of services, including those for scientific and academic research
Cochlea The sense organ that translates sound into nerve impulses to be sent to the brain
COCHRANE A non-profit, non-governmental organisation that organises medical research to provide evidence-based information
Conductive hearing loss Hearing loss affecting the middle (and/or outer) ear component(s) of the peripheral auditory system
Consecutive convenience sampling A type of sampling that includes all accessible subjects
Constructivism A research paradigm which states that learning is an active, contextualised process of constructing knowledge rather than acquiring it
Critical realism A paradigm which states that phenomena exist and are understood uniquely within the environment in which they are explored

D
Department of Health A department within UK Government
| **Dialectical pluralism** | A research paradigm: a process theory for discussing and maintaining differences to enable integration of divergent views and methods to produce a more complex and meaningful whole |
| **Distortion product OAE** | A type of otoacoustic emission *(see abbreviations)* |
| **E** | Ear drum (tympanic membrane) The structure that separates the outer ear and middle ear |
| **EBSCO host** | A repository of research databases *(see abbreviations)* |
| **EMBASE** | A healthcare science database *(see abbreviations)* |
| **F** | Fisher’s exact test A statistical test used to assess categorical data of two small sized groups |
| **H** | Hearing deterioration A reduction in the ability to hear |
| **Hearing loss** | The inability to perceive and discriminate everyday sounds |
| **Hearing (auditory) system** | Part of the body used for sensing and processing sound, consisting of the peripheral and central auditory systems |
| **Hyperacusis** | Loudness discomfort to every day sounds |
| **Hypopharyngeal** | Pertaining to the hypopharynx |
| **Hypopharynx** | The lowest part of the pharynx which leads to the larynx |
| **I** | Inner ear Part of the peripheral auditory system that contains the hearing sense organ (cochlea) |
| **K** | kHz A unit for measuring the frequency of sound *(see abbreviations)* |
| **L** | Laryngeal Pertaining to the larynx |
| **Larynx** | Cavity in the throat containing vocal cords |
| **M** | Mann Witney U test A statistical test to compare the means of two groups that have uneven distribution of data |
| **Maximum purposive sampling** | A type of sampling in which subjects, who have diverse characteristics, are selected to obtain the widest understanding of a phenomenon |
| **MEDLINE** | An international literature database of life sciences and biomedical information *(See abbreviations)* |
| **Metaparadigm** | A framework in which more restricted structures of conceptual modules develop |
Middle ear
Part of the peripheral auditory system, usually air-filled, which contains the ossicles

Mixed hearing loss
Hearing loss affecting the middle (and/or outer) component(s) of the ear, together with damage to the inner ear (and/or the auditory nerve) of the peripheral auditory system

Mixed methods
A methodology for conducting research that involves collecting, analysis and integrating quantitative and qualitative data

Nasopharyngeal
Pertaining to the nasopharynx

Nasopharynx
The upper part of the pharynx that lies behind the nose

O
Otoacoustic emission(s)
Sounds generated from within the cochlea (see abbreviations)

OME
Fluid in the middle ear cavity (see abbreviations)

Oral cavity
The cavity of the mouth

Oropharyngeal
Relating to the oropharynx

Oropharynx
The part of the throat at the back of the mouth behind the oral cavity

Ossicles
Bones in the middle ear used to transmit sound

Otology
The study of the anatomy and diseases of the ear

Ototoxicity
Damage to the hearing function of the ear by drugs, chemicals or treatment

Outer ear
Part of the peripheral auditory system comprising the pinna and ear canal

P
Paranasal sinuses
Small hollow spaces in the bones around the nose

Peripheral auditory system
Part of the hearing system that consists of the ear and auditory (cochlear) nerve

Pharyngeal
Relating to the region of the pharynx

Pharynx
The passage that lead from the cavities of the nose and mouth to the larynx (throat)

Phenomenology
The philosophical study of the structures of experience and consciousness

PICO
An acronym for diagnostic questions based on these four areas of knowledge and action: Population, Patient or Problem; Intervention (or prognostic factor or exposure); Comparison (or intervention); and Outcome

Pinna
External part of the ear

Positivism
A philosophical system recognising only that which can be scientifically verified

Pragmatism
A research approach that evaluates theories or beliefs in terms of the success of their practical application

PRISMA
A method for searching databases reporting items for systematic review (see abbreviations)
<p>| <strong>ProQuest</strong> | A repository of databases that includes scholarly journals, newspaper articles and reports |
| <strong>Prospective observational repeated measures</strong> | A study design in which multiple recordings of a phenomenon are made over a period of time |
| <strong>PsycARTICLES</strong> | A healthcare science database of full-text articles from journals in behavioural sciences published by the American Psychological Association |
| <strong>PsychINFO</strong> | A healthcare science database devoted to peer-reviewed literature in behavioural science and mental health |
| <strong>Psychology and behavioural sciences collection</strong> | A database that includes journals which covers topics such as emotional and behavioural characteristics |
| <strong>PubMed</strong> | A full-text archive of biomedical and life sciences journal literature |
| <strong>Pure tone audiometry</strong> | A key hearing test used to identify an individual’s hearing threshold levels |
| <strong>Q</strong> | Qualitative research |
| <strong>Qualitative research</strong> | Research exploring human experience to convey why people have thoughts and feelings that might affect the way they behave |
| <strong>Quantitative research</strong> | A research method dealing with numbers and anything that is measurable in a systematic way of investigating phenomena and their relationships |
| <strong>R</strong> | Regression (analysis/test) |
| <strong>Regression (analysis/test)</strong> | A statistical test that assesses the strength of association between two or more groups |
| <strong>S</strong> | Salivary gland |
| <strong>Salivary gland</strong> | The tissue in the mouth that secretes saliva |
| <strong>Shapiro-Wilk test</strong> | A statistical test to verify how even is the distribution of data within a group |
| <strong>Sensorineural</strong> | Pertaining to the inner ear and/or the auditory nerve of the peripheral auditory system |
| <strong>SNHL</strong> | Hearing loss due to damage of the inner ear and/or the auditory nerve (see abbreviations) |
| <strong>Speech discrimination test</strong> | A type of hearing test to estimate ability to understand and repeat single-syllable words |
| <strong>Speech reception test</strong> | A type of hearing test to identify the lowest threshold level at which at least half the words spoken can be heard |
| <strong>SPSS</strong> | A statistics package of computer software (see abbreviations) |
| <strong>Squamous cell carcinoma</strong> | Most common cell type of cancer in the head and neck region |
| <strong>Standard deviation</strong> | A statistical term to quantify the amount of variation or dispersion of a set of values (see abbreviations) |</p>
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stapedial reflex test</td>
<td>A type of hearing test to monitor the muscle contraction that occurs in the middle ear in response to loud sounds</td>
</tr>
<tr>
<td>Survivorship</td>
<td>Quality of life after treatment</td>
</tr>
<tr>
<td><strong>T</strong></td>
<td></td>
</tr>
<tr>
<td>TNM</td>
<td>A system for classifying cancers (Tumour, Nodes and Metastasis)</td>
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<tr>
<td>Transient evoked OAE</td>
<td>A type of otoacoustic emission</td>
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<tr>
<td>Tympanic membrane (ear drum)</td>
<td>The structure that separates the outer and middle ear components</td>
</tr>
<tr>
<td>Tympanometry</td>
<td>A type of hearing test that measures middle ear function</td>
</tr>
<tr>
<td>Type of hearing loss</td>
<td>The identification of the location of damage within the hearing system</td>
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<tr>
<td><strong>W</strong></td>
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<tr>
<td>Web of science</td>
<td>An internet repository used to access multidisciplinary academic literature, including journals, books and conference proceedings</td>
</tr>
<tr>
<td>Wiley</td>
<td>A company that specialises in academic publishing</td>
</tr>
</tbody>
</table>
# List of chapters

<table>
<thead>
<tr>
<th>Chapter 1 Introduction</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 Background</td>
<td>28</td>
</tr>
<tr>
<td>1.1 Hearing</td>
<td>28</td>
</tr>
<tr>
<td>1.1.1 Types of hearing loss</td>
<td>30</td>
</tr>
<tr>
<td>1.1.2 Ototoxicity and grades of hearing deterioration</td>
<td>30</td>
</tr>
<tr>
<td>1.1.3 Descriptors of hearing level</td>
<td>31</td>
</tr>
<tr>
<td>1.1.4 Impact of hearing loss</td>
<td>31</td>
</tr>
<tr>
<td>1.2 Overview of head and neck cancer</td>
<td>32</td>
</tr>
<tr>
<td>1.2.1 Aetiology of head and neck cancer</td>
<td>33</td>
</tr>
<tr>
<td>1.2.2 Incidence trends</td>
<td>33</td>
</tr>
<tr>
<td>1.2.3 Survival rates</td>
<td>36</td>
</tr>
<tr>
<td>1.2.4 Treatment of head and neck cancer</td>
<td>38</td>
</tr>
<tr>
<td>1.2.5 Survivorship</td>
<td>38</td>
</tr>
<tr>
<td>1.3 Summary</td>
<td>41</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 2 Literature review</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Introduction</td>
<td>44</td>
</tr>
<tr>
<td>2.2 Search strategy</td>
<td>44</td>
</tr>
<tr>
<td>2.2.1 PICO</td>
<td>45</td>
</tr>
<tr>
<td>2.2.2 Databases and PRISMA</td>
<td>47</td>
</tr>
<tr>
<td>2.2.3 Inclusion and exclusion criteria</td>
<td>49</td>
</tr>
<tr>
<td>2.2.4 Data extraction</td>
<td>50</td>
</tr>
<tr>
<td>2.3 Quality assessment</td>
<td>53</td>
</tr>
</tbody>
</table>
2.3.1 Quantitative paper quality
2.3.1.1 Selection bias
2.3.1.2 Measurement bias
2.3.1.3 Reporting bias
2.3.2 Qualitative paper quality
2.3.3 Summary of quality assessment
2.4 Summary of findings
2.4.1 Overview of selected articles
2.5 Themes – Findings
2.5.1 Theme 1 - Incidence of hearing deterioration
2.5.1.1 Incidence of sensorineural hearing loss in general head and neck cancer
2.5.1.2 Incidence of sensorineural hearing loss in nasopharyngeal cancer
2.5.1.3 Incidence of conductive hearing loss
2.5.1.4 Incidence in hearing deterioration based on range of hearing
2.5.1.5 Tests used for assessing a change in hearing
2.5.2 Theme 2 - Risk factors associated with hearing deterioration
2.5.2.1 Patient characteristics
2.5.2.2 Treatment
2.5.2.3 Time after treatment
2.5.3 Theme 3 - Patient experience of hearing deterioration
2.5.3.1 Quality of life
2.5.3.2 Lived experience of hearing deterioration
2.6 Discussion of findings from the literature review
Chapter 2: Incidence of hearing deterioration

2.6.1 Incidence of hearing deterioration
2.6.1.1 Incidence in sensorineural hearing loss
2.6.1.2 Incidence in conductive hearing loss
2.6.1.3 Classifying hearing deterioration

2.6.2 Risk factors associated with hearing deterioration
2.6.2.1 Patient characteristics
2.6.2.2 Treatment
2.6.2.3 Time after treatment

2.6.3 Patient experience of hearing deterioration
2.6.3.1 Quality of life
2.6.3.2 Lived experience of hearing deterioration

Chapter 3: Methodology

3.1 Introduction
3.2 Context and theoretical framework
3.2.1 Critical realism
3.3 Methodology
3.4 Research design
3.4.1 Implementation – Determining sequencing of methods
3.4.2 Priority – Determining which phase was ascribed priority
3.4.3 Integration – Determining links between the phases
3.4.4 Theoretical perspective
3.4.5 Alternative theoretical frameworks
3.5 Quantitative methods
### Chapter 4 Methods

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.1 Introduction</strong></td>
<td>111</td>
</tr>
<tr>
<td><strong>4.1.1 Study timeline</strong></td>
<td>111</td>
</tr>
<tr>
<td><strong>4.2 Quantitative phase</strong></td>
<td>112</td>
</tr>
<tr>
<td><strong>4.2.1 Sample size</strong></td>
<td>112</td>
</tr>
<tr>
<td><strong>4.2.2 Recruitment</strong></td>
<td>114</td>
</tr>
<tr>
<td><strong>4.2.2.1 Inclusion criteria</strong></td>
<td>115</td>
</tr>
<tr>
<td><strong>4.2.2.2 Exclusion criteria</strong></td>
<td>115</td>
</tr>
<tr>
<td><strong>4.2.3 Instruments used to measure hearing deterioration</strong></td>
<td>116</td>
</tr>
<tr>
<td><strong>4.2.4 Data collection</strong></td>
<td>117</td>
</tr>
<tr>
<td><strong>4.2.5 Data coding</strong></td>
<td>118</td>
</tr>
<tr>
<td><strong>4.2.5.1 Defining and grading hearing deterioration</strong></td>
<td>118</td>
</tr>
<tr>
<td><strong>4.2.5.2 Defining descriptors of hearing level and types of hearing loss</strong></td>
<td>120</td>
</tr>
<tr>
<td><strong>4.2.6 Statistical analysis</strong></td>
<td>121</td>
</tr>
<tr>
<td><strong>4.2.6.1 Descriptive statistics</strong></td>
<td>122</td>
</tr>
<tr>
<td><strong>4.2.6.2 Inferential statistics</strong></td>
<td>122</td>
</tr>
<tr>
<td><strong>4.2.6.3 Missing data</strong></td>
<td>124</td>
</tr>
<tr>
<td><strong>4.2.7 Validity and reliability of quantitative findings</strong></td>
<td>124</td>
</tr>
<tr>
<td><strong>4.3 Qualitative phase</strong></td>
<td>125</td>
</tr>
<tr>
<td><strong>4.3.1 Sample size</strong></td>
<td>125</td>
</tr>
<tr>
<td><strong>4.3.2 Recruitment</strong></td>
<td>127</td>
</tr>
<tr>
<td><strong>4.3.3 Qualitative method</strong></td>
<td>128</td>
</tr>
</tbody>
</table>
4.3.4 Data collection 129
4.3.5 Data analysis 129
4.3.6 Validity and reliability of qualitative findings 132
4.4 Integration of quantitative and qualitative data 134
4.5 Ethical considerations 134
4.5.1 Data handling 135
4.5.2 Finance and indemnity 136
4.6 Summary 136

Chapter 5 Results – Quantitative data 137
5.1 Introduction 137
5.2 Recruitment 137
5.3 Test completion and attrition 139
5.4 Participant demographics 141
5.5 Incidence of hearing deterioration 143
5.6 Severity of hearing deterioration 144
5.7 Descriptors of hearing level 145
5.8 Types of hearing loss 145
5.9 Hearing deterioration and patient characteristics 147
5.10 Summary 150

Chapter 6 Results – Qualitative data 151
6.1 Introduction 151
6.2 Demographic information 151
6.3 Themes 153
6.3.1 Theme one – Sensation of impairment
  6.3.1.1 Hearing change
  6.3.1.2 Tinnitus
  6.3.1.3 Progression of aural change
6.3.2 Theme two – Functional changes
  6.3.2.1 Communication difficulties
  6.3.2.2 Problems with entertainment
  6.3.2.3 Problems with environmental sounds
6.3.3 Theme three – Coping mechanisms
  6.3.3.1 General coping strategies
  6.3.3.2 Use of assistive devices
6.3.4 Theme four – Emotional responses to aural change
  6.3.4.1 Attitude to hearing deterioration
  6.3.4.2 Downplaying of symptoms
  6.3.4.3 Sense of loss
  6.3.4.4 Social isolation
6.3.5 Theme five – Information and support
  6.3.5.1 Pre-treatment information
  6.3.5.2 Discussion of aural changes
  6.3.5.3 Further support
6.4 Summary

Chapter 7 Discussion
7.1 Introduction
7.2 Summary of research findings
7.3.7.2 Information during treatment 219
7.3.7.3 Support after treatment 221
7.4 The need for hearing monitoring 223
7.4.1 When to monitor 223
7.4.2 Who to be involved in monitoring 225
7.4.3 How to monitor 225
7.4.4 What tests to use 227
7.5 Strengths and limitations of the study 228
7.6 Summary 230

Chapter 8 Conclusion

8.1 Introduction 236
8.2 Recommendations for future research 236
8.2.1 Building on the incidence findings from this study 236
8.2.2 Verifying novel findings from this study 237
8.2.3 Assessing alternative treatments and tests 238
8.3 Recommendations for clinical policy and practice 239
8.3.1 Monitoring aural change 240
8.3.2 Information and support for patients 241
8.3.3 Targeted support for patients 243
8.4 Recommendations for education of survivors and practitioners 244
8.5 Conclusions 245
| Table 1.1 Subtypes of head and neck cancer (England and Wales) | 33 |
| Table 1.2 Proportion of head and neck cancer in overall new cancer cases | 34 |
| Table 1.3 Five-year survival rates for men in England compared to Europe | 36 |
| Table 1.4 Survival rates for head and neck cancer (England) | 37 |
| Table 1.5 Improved survival rates over time (England) | 38 |
| Table 1.6 First treatment received for head and neck cancer | 40 |
| Table 1.7 Side effects of treatment | 41 |
| Table 2.1 Papers excluded following full review | 50 |
| Table 2.2 Data extracted from included articles | 52 |
| Table 2.3 Summary table of data from articles for review | 62 |
| Table 2.4 Frequency range assessed | 71 |
| Table 2.5 Tests used in addition to pure tone audiometry | 72 |
| Table 2.6 Risk factors associated with hearing deterioration | 75 |
| Table 2.7 Incidence of hearing deterioration over time | 82 |
| Table 3.1 Characteristics of mixed methods studies | 104 |
| Table 4.1 Descriptors of hearing level | 120 |
| Table 4.2 Statistical analysis used | 121 |
| Table 4.3 Sampling framework for interview selection | 126 |
| Table 4.4 Coding matrix of initial categories | 131 |
| Table 4.5 Coding index | 131 |
| Table 5.1 Characteristics of participants who missed testing | 140 |
| Table 5.2 Patient, cancer and treatment characteristics | 142 |
Table 5.3 Incidence of hearing deterioration 143  
Table 5.4 Inter-test hearing change 144  
Table 5.5 Descriptors of hearing level 145  
Table 5.6 Hearing deterioration at 3-month follow-up after treatment 148  
Table 6.1 Characteristics of participants taking part in interview 152  
Table 6.2 Main themes and subthemes arising from the interview data 153
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 2.1</td>
<td>Outline of Chapter 2</td>
<td>45</td>
</tr>
<tr>
<td>Figure 2.2</td>
<td>Search strategy to identify articles on incidence and experience of hearing loss in people having had treatment for their head and neck cancer</td>
<td>48</td>
</tr>
<tr>
<td>Figure 3.1</td>
<td>Study design</td>
<td>103</td>
</tr>
<tr>
<td>Figure 4.1</td>
<td>Study timeline</td>
<td>112</td>
</tr>
<tr>
<td>Figure 4.2</td>
<td>Formation of themes</td>
<td>130</td>
</tr>
<tr>
<td>Figure 5.1</td>
<td>Recruitment and participation</td>
<td>138</td>
</tr>
<tr>
<td>Figure 5.2</td>
<td>Change in type of hearing loss</td>
<td>146</td>
</tr>
<tr>
<td>Figure 5.3</td>
<td>Comparison of age with hearing deterioration at 3-month follow-up</td>
<td>147</td>
</tr>
<tr>
<td>Figure 5.4</td>
<td>Hearing deterioration across subtypes of head and neck cancer</td>
<td>149</td>
</tr>
</tbody>
</table>
# List of appendices

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appendix 1.1</strong></td>
<td>Staging of head and neck cancers</td>
<td>247</td>
</tr>
<tr>
<td><strong>Appendix 2.1</strong></td>
<td>Data extraction form – quantitative study</td>
<td>248</td>
</tr>
<tr>
<td><strong>Appendix 2.2</strong></td>
<td>Data extraction form – qualitative study</td>
<td>254</td>
</tr>
<tr>
<td><strong>Appendix 2.3</strong></td>
<td>CASP quality rating form – quantitative studies</td>
<td>262</td>
</tr>
<tr>
<td><strong>Appendix 2.4</strong></td>
<td>CASP quality rating form – qualitative study</td>
<td>263</td>
</tr>
<tr>
<td><strong>Appendix 2.5</strong></td>
<td>UK papers excluded from review</td>
<td>264</td>
</tr>
<tr>
<td><strong>Appendix 4.1</strong></td>
<td>Pilot study</td>
<td>266</td>
</tr>
<tr>
<td><strong>Appendix 4.2</strong></td>
<td>Common Terminology Criteria for Adverse Events (CTCAE) V 4.03 (2010) – hearing</td>
<td>267</td>
</tr>
<tr>
<td><strong>Appendix 4.3</strong></td>
<td>Interview questions</td>
<td>268</td>
</tr>
<tr>
<td><strong>Appendix 4.4</strong></td>
<td>Study approval documents</td>
<td>269</td>
</tr>
<tr>
<td><strong>Appendix 5.1</strong></td>
<td>Participant characteristics – tested at 3-month follow-up after treatment</td>
<td>272</td>
</tr>
<tr>
<td><strong>Appendix 6.1</strong></td>
<td>Transcript from Interview 1</td>
<td>273</td>
</tr>
<tr>
<td><strong>Appendix 6.2</strong></td>
<td>Themes, subthemes and initial categories</td>
<td>286</td>
</tr>
</tbody>
</table>
Chapter 1 Introduction

1.0 Background

This thesis: “A study of hearing deterioration following treatment for head and neck cancer in a UK hospital”, arose from the researcher’s involvement in the assessment and management of adults with hearing loss at the audiological clinic of a major London hospital. Hearing is the perception of sound, and hearing loss is defined as the ‘inability to perceive and discriminate everyday sounds including warning signals, speech, and music’ (Luxon, 2014, p.533). In recent years, the clinic has received an increasing number of patients requesting support and advice on referral to audiology because of hearing loss following treatment for head and neck cancer (HNC). Sometimes these patients were referred up to two years after treatment, rather than at an earlier stage following it. Therefore, the researcher wanted to find out if patients have hearing difficulties soon after treatment, so that they might access support if required at an earlier time following treatment completion. He also wanted to determine the scale of the problem at his current hospital.

In a previous post at a children’s hospital, the researcher was involved in the systematic assessment and monitoring of children’s hearing following cancer treatment. Some children who developed hearing deterioration were offered alternative treatment that reduced damage to hearing. However, in the researcher’s current place of work in a general hospital, the systematic assessment and monitoring of hearing in adult patients receiving treatment for HNC has not been standard procedure in service provision. Thus, it was not clear if, and to what extent, hearing deterioration followed treatment of the cancer for this patient group.

To address this situation, the researcher, in consultation with oncologists specialising in the treatment of patients suffering from HNC, conducted a pilot study to measure patients’ hearing before and after treatment. This protocol involved testing hearing using pure tone
audiometry (PTA), the standard hearing test, at two time points: after a diagnosis of cancer but prior to treatment, and at a time point following the completion of treatment. The pilot study undertaken in 2013 at the researcher’s hospital compared the average threshold of hearing of two groups of patients: one prior to treatment (n=24), and the other at various time points after treatment (n=43). The average hearing threshold at different frequencies within the speech hearing range was poorer for each of the frequencies after treatment compared to pre-treatment equivalents.

This pilot study indicated that hearing deterioration occurred after treatment, but the conclusion was of limited value as different HNC patients were compared in each group. This finding further fuelled the desire to assess hearing deterioration following treatment of HNC in more depth. Therefore, the premise of this study was that hearing deterioration is both associated with treatment of patients with HNC, and that such a deterioration has a negative impact on these patients.

This introductory chapter provides a description of hearing, the impact of hearing loss, and an overview of HNC. Chapter 2 (Literature review) will present the findings of a review of current literature on ear-related side effects following treatment for HNC. Discussion of these findings indicate how the study aims were established to determine the incidence, severity and patient experience of hearing deterioration. Chapter 3 (Methodology) outlines the methodological approach adopted in the current study, and Chapter 4 (Methods) discusses the overall schema of the methods used in the study. Chapter 5 (Results – Quantitative data) presents statistics on the incidence and severity of hearing deterioration derived from testing the hearing of participants, and Chapter 6 (Results – Qualitative data) presents findings from interviews with patients on their experience of hearing change following their cancer treatment. The quantitative data and the findings on patient experience are considered and discussed collectively in Chapter 7 (Discussion), in the context of current knowledge and practice. Chapter 8 (Conclusion) offers conclusions from the study and
makes recommendations for clinical practice, and suggestions for education and future research.

1.1 Hearing

Hearing is the perception of sound, which begins with the collecting and processing of sounds by the ear (Pickles, 2012). The ear is structurally divided into three parts. The outer ear consists of the pinna, which is the visible and most external part of the ear, and the ear canal, which channels sound from the pinna inwards. The ear canal is separated from the middle ear by the ear drum – the tympanic membrane. The middle ear houses the three bones, or ossicles, that transmit sounds from the outer to the inner ear. The inner ear contains the cochlea, the hearing sense organ, which converts sound energy into an electrical form, for transmission along the auditory (cochlear) nerve. The ear and the auditory nerve consist of the peripheral auditory system. Electrical information emitted through the auditory nerve is delivered to the brain and is perceived as sound within the auditory cortex of the central auditory system (Luxon, 2014).

1.1.1 Types of hearing loss

Damage to any part of the hearing system from the ear to the auditory cortex within the brain may cause hearing loss (Luxon, 2014). Damage to different parts of the ear causes different types of hearing loss: conductive hearing loss when damage occurs to either outer or middle ear components; sensorineural hearing loss (SNHL) ensues following impairment to the inner ear and/or cochlear nerve; mixed hearing loss results from a combination of conductive or SNHL (Luxon, 2014). Different types of loss are detected using transducers that produce air conduction or bone conduction stimuli (Wood, 1995).
1.1.2 Ototoxicity and grades of hearing deterioration

Ototoxicity is damage to the ear (Collins English Dictionary, 2018) which is treatment induced, and usually associated with impairment of the inner ear (Chang, 2013), although other parts of the hearing system can be affected (Jereczek-Fossa et al., 2003; Landier, 2016). Ototoxicity can lead to hearing deterioration – a reduction in the ability to hear – by either developing an existing hearing loss, or creating a new loss. Changes in hearing are sometimes graded to indicate the quantity of change. There are different systems available to grade hearing deterioration that include clinician-rated assessments, such as the Late Radiation Morbidity Scoring Criteria, from the Radiation Therapy Oncology Group (Cox and Stetz, 1995), and psycho-acoustical measures, for example within the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 produced by the National Cancer Institute (NCI), (NCI, 2010). In these systems, Grade 0 usually indicates no change in hearing and Grade 1 reflects a slightly noticeable or minimally measured hearing change; the higher the grade number, the greater the increase in a change of hearing.

1.1.3 Descriptors of hearing level

Frequencies of sound important to human speech are most commonly measured in adults using the psycho-acoustic test of PTA (Wood, 1995). Decibels (dB) are units of sound pressure, and normal hearing is accepted as thresholds of hearing ≤20dB hearing level (dBHL) between 0.25 kilo Hertz (kHz - a unit to measure the frequency of sound) and 8kHz (Luxon, 2014). Severity of hearing loss ranges from mild to profound, depending on the average threshold over the speech frequencies. There are different classification systems for describing hearing levels including that from the World Health Organisation (World Health Organisation, 2018), although the system recommended for use in the UK derives from The British Society of Audiology (BSA), (BSA, 2011).
1.1.4 Impact of hearing loss

In an evaluation of the social and economic implications of hearing loss in Europe and the UK, Shield (2006) reported on the significance of acquired hearing loss in adults, and determined that it can lead to communication and other social difficulties. Other studies have described how hearing loss affects the well-being and quality of life of patients with age-related hearing impairment (Monzani et al., 2008; Wallhagen, 2010; Stark and Hickson, 2004; Preminger and Meeks, 2010; Preminger and Meeks, 2012) and those affected by sudden-onset hearing loss of unknown cause (Härkönen et al., 2017).

Experience of hearing loss is usually associated with negative connotations. Deaf people who use signing communication and have profound hearing loss (at birth, or before the acquisition of language) are prone to isolation and depression, as shown in an interview study by Sheppard and Badger (2010). A phenomenological investigation by Aquino-Russell (2006) conducted by email correspondence, showed that patients with acquired hearing loss (cause not provided) might also experience isolation and other problems with their hearing change. The study showed a developing awareness of mis-hearing, with feelings of frustration and inadequacy. Another interview study with participants who had acquired mild-moderate hearing loss also revealed that participants felt others perceived them as being ignorant, unfriendly and unapproachable (Heffernan et al., 2016). These negative experiences indicate that hearing loss can lead to feelings of frustration, inadequacy and isolation, negative self-image and negative perceptions that others may have of the person with hearing impairment – in short, a diminished quality of life. However, no studies have acknowledged the impact a deterioration in hearing of sudden-onset following HNC treatment has on a patient’s quality of life, and no study, until now, had undertaken to evaluate the impact of HNC treatment on patients’ hearing.
1.2 Overview of head and neck cancer

Cancers of the head and neck affect structures in the upper aero-digestive tract (Donovan and Glackin, 2012), and are classified by anatomical position. The major subtypes of the head and neck are: the oral cavity, nasal cavity and the paranasal sinuses, larynx, salivary glands and pharynx. The latter is further subdivided into the oropharynx, nasopharynx and hypopharynx areas (Palaniappan, Owadally and Evans, 2015). It can be seen in Table 1.1 below that cancers of the oral cavity, and those of the oropharynx, are the most frequently diagnosed in the UK, from information obtained by the Healthcare Quality Improvement Partnership (HQIP), from the 2014 National Head and Neck Cancer Audit (HQIP, 2014).

<table>
<thead>
<tr>
<th>Head and neck cancer subtype</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>2684</td>
<td>32.3</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>2439</td>
<td>29.4</td>
</tr>
<tr>
<td>Larynx</td>
<td>1763</td>
<td>21.2</td>
</tr>
<tr>
<td>Salivary Glands</td>
<td>504</td>
<td>6.1</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>423</td>
<td>5.1</td>
</tr>
<tr>
<td>Nasal cavity and paranasal sinuses</td>
<td>335</td>
<td>4.1</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>151</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Table 1.1 Subtypes of head and neck cancer (England and Wales) (Health Quality Improvement Partnership, 2014)

In addition to the 8299 patients, shown in Table 1.1, who were diagnosed with one of the seven subtypes of HNC in England and Wales, there were 130 with cancer of the mandible or maxilla (HQIP, 2014). These cancers were not included in the previous National Audit in 2012 (HQIP, 2012), and this demonstrates that definitions of HNCs differ. Consequently, it is difficult to obtain comparative information of the proportion of subtypes in other countries that have different definitions of HNC. For example, current information available from the US provides information on the number of new cases of laryngeal and pharyngeal cancer, but does not provide the numbers in each subtype of pharyngeal cancer, or give data on the number of either salivary gland or nasal cavity cancer (Siegel, Miller and Jemal, 2017). It is therefore difficult to obtain a consistent reporting of HNC statistics.
Head and neck cancers account for 5% of all cancers (Goon et al., 2009) and are the seventh most common cancer worldwide, with men typically affected more than women by a 2:1 ratio (Cancer Research UK, 2016). Ferlay et al. (2015) reported that there were approximately 529,000 new cases of HNC identified worldwide in 2012, when reporting on oral cavity, laryngeal and pharyngeal cancers. The HQIP reported in the 2012 National Head and Neck Cancer Audit that there were approximately 8,100 new cases of this disease in the UK in 2011 (HQIP, 2012).

Although cancer of the oral cavity provides the greatest number of all the HNCs (Ferlay et al., 2015), there is wide global variation regarding the proportion of HNCs that contribute to overall cancer diagnoses. Men in developed countries have a higher proportion of oral cancer (7%) than those in less developed countries (5%), whereas men in less developed countries have a higher incidence of nasopharyngeal cancer (NPC) (2%) than those in developed countries (0.6%; Ferlay et al., 2015).

In 2014, 3% of all new cancer cases in the UK (Cancer Research UK, 2016) originated in the head and neck region. Although information on the number of HNCs as a proportion of all cancers within many countries is not readily available, Table 1.2 provides information for comparing UK rates to those of The Netherlands and the United States:

<table>
<thead>
<tr>
<th>Country</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Netherlands</td>
<td>4.9</td>
</tr>
<tr>
<td>US</td>
<td>3.7</td>
</tr>
<tr>
<td>UK</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Table 1.2 Proportion of head and neck cancer of overall new cancer cases (Siegel, Miller and Jemal, 2017)

The percentage of HNC diagnosed in the UK is lower than that of all new cancer cases (4.9%) in the Netherlands (Ledeboer et al., 2005), and different to that in the US (Siegel, Miller and Jemal, 2017). Variation in these proportions is due to the underlying aetiology, including different smoking and alcohol consumption rates, which will be discussed in the next section.
1.2.1 Aetiology of head and neck cancer

Worldwide, tobacco smoking and alcohol consumption are the main causes of HNC (Donovan and Glackin, 2012). An article published by the American Cancer Society (ACS) for guidelines on Head and Neck Cancer Survivorship states that tobacco smoking and alcohol consumption account for 75% of cases of HNC (Cohen et al., 2016). Combined use of tobacco and alcohol increases the risk of developing HNC (Hashibe et al., 2009). In the UK, smoking and alcohol consumption (respectively) contribute up to 79% and 30% of HNC (Cancer Research UK, 2018a).

Another cause for HNC is the chewing of recreational substances (betel leaf and areca nut) native to South Asian countries. This is specifically associated with increased risk of oral cavity cancer (Ho et al., 2002). Ingestion of mate, a tea drink common in South America, affects the oral cavity and also causes cancer in the pharynx and larynx (Goldenberg, Golz and Joachims, 2003).

Occupational exposure to fine particles such as wood dust (Yu and Yuan, 2002) or chemicals including formaldehyde (Luce et al., 1993) can also cause HNC. Infection by the Epstein Barr virus causes nasopharyngeal (Chien et al., 2001) or salivary gland cancer (Chan et al., 1994), whereas the human papillomavirus (HPV) is another risk factor for oropharyngeal cancer (Adelstein et al., 2009; Cancer Research UK, 2017). Although alcohol consumption and smoking are still the main causes of HNC, trends in causation are changing due to efforts made to address substance use, and the rise in different sources of the disease.

1.2.2 Incidence trends

Health education programmes on smoking prevention in the US have been influential in decreasing US incidence of HNC due to tobacco use from 1985 to 2005 (Sturgis and Cinciripini, 2007). However, general lowering in incidence of HNC in the US due to tobacco
use has been countered by a rise in incidence due to HPV infection (Chaturvedi et al., 2011). This change in epidemiology of HNC in the US has been reflected in England. The 2010 document ‘Profile of Head and Neck Cancers in England’, produced by the Oxford Cancer Intelligence Unit (OCIU) provides trends for different types of HNC in England between 1990 and 2006, and noted that incidence of laryngeal cancer had fallen due to reduction in smoking. However, there had been an increase in oral cavity cancer incidence by 30% during that period, linked to an increase in migrants to the UK from South Asia who engage in betel leaf chewing. A doubling in the incidence of oropharyngeal cancer affecting younger people was detected, attributed to the rise in HPV infection (OCIU, 2010).

Overall, between the decade spanning 2003-2005 and 2013-2015, there has been an increase in incidence of HNC in the UK by 24% (Cancer research UK, 2018b), with the highest number of new cases diagnosed (between 2013-2015) in people aged between 65 and 69 years of age (Cancer research UK, 2018c). In addition to the rising incidence of HNC in the UK, there is an increase in survival rates from being diagnosed with HNC which is discussed below.

### 1.2.3 Survival rates

Survival rates for different types of HNC in England for men are given in Table 1.3 below alongside comparison with other European populations (Cancer research UK, 2017b).

<table>
<thead>
<tr>
<th>Location</th>
<th>England (%)</th>
<th>Europe (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>Tongue</td>
<td>47</td>
<td>39</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Larynx</td>
<td>63</td>
<td>59</td>
</tr>
</tbody>
</table>

*Table 1.3 Five-year survival rates for men in England compared to Europe* (Cancer research UK, 2017b)
Although there is some similarity between survival rates in England and Europe, there are notable differences with tongue and oropharyngeal cancer. Explanations for international differences include differences in the stage at which a diagnosis is made and access to high-quality care (De Angelis et al., 2013).

Cancer UK has compared overall 1-year and 5-year survival rates for each subtype of HNC, for patients diagnosed between 2009 and 2013 in England, summarised in Table 1.4:

<table>
<thead>
<tr>
<th>Head and neck cancer subtype</th>
<th>1 year (%)</th>
<th>5 years (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypopharynx</td>
<td>60.5</td>
<td>27.8</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>80</td>
<td>50</td>
</tr>
<tr>
<td>Nasal cavity and paranasal sinuses</td>
<td>74.8</td>
<td>51.4</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>78.4</td>
<td>56.1</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>83.7</td>
<td>65.6</td>
</tr>
<tr>
<td>Larynx</td>
<td>85.3</td>
<td>65.4</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>85.8</td>
<td>67.0</td>
</tr>
</tbody>
</table>

Table 1.4 Survival rates for head and neck cancer (England) (Cancer Research UK, 2017c)

In England, survival rates varied considerably, based on the location of the cancer within the head and neck region. It is interesting to note that patients who have cancers in the adjacent regions of the hypopharynx and larynx had widely different survivorship rates, due to the stage at which a diagnosis is made. Although laryngeal and hypopharyngeal cancers have similar aetiology (mainly tobacco use and alcohol consumption), laryngeal cancers are often diagnosed at an early stage (due to symptoms such as acquiring a hoarse voice), whereas the symptoms of difficulty in swallowing, that characterise hypopharyngeal cancers, are often detected at an advanced stage of disease (Palaniappan, Owadally and Evans, 2015).

Cancer Research UK provides data to show that differences in survivorship may also occur within subtypes of HNC depending on the stage of disease at diagnosis. For example, survival rates for laryngeal cancer in England, at five years following diagnosis range from approximately 90% to 40% for early and advanced stage disease respectively (Cancer Research UK, 2018d).
Although there is an increasing number of HNC patients being diagnosed each year, the OCIU (2010) provides information showing that there has also been increased survivorship in England from the early 1990s to the 2000s, which is summarised in Table 1.5:

<table>
<thead>
<tr>
<th>Head and neck cancer subtype</th>
<th>1-year survival rate (%)</th>
<th>5-year survival rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypopharynx</td>
<td>49.0</td>
<td>58.9</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>65.9</td>
<td>78.5</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>72.5</td>
<td>78.7</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>65.6</td>
<td>79.2</td>
</tr>
<tr>
<td>Larynx</td>
<td>82.8</td>
<td>85.1</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>76.2</td>
<td>83.7</td>
</tr>
</tbody>
</table>

**Table 1.5 Improved survival rates over time (England)** (Oxford Cancer Intelligence Unit, 2010)

An increase in survival rates for all subtypes of HNC, at both one year and five years after diagnosis (Table 1.5), has been attributed to an improvement in diagnostic techniques and the development of new regimens incorporating a combination of treatments. The use of radiotherapy (RT) in addition to surgery has led to increased survivorship for salivary gland cancer, and the use of chemoradiotherapy (CRT) rather than RT alone has improved nasopharyngeal survival rates (OCIU, 2010). Increases in survival for people with HNC mean that more people are living with these cancers for longer and the quality of their survivorship needs to be addressed. Survivorship will be discussed after a more detailed update on current UK treatments.

### 1.2.4 Treatment of head and neck cancer

Cancer treatment is either curative or palliative in intent. Curative, or radical, treatment of HNC was the focus of the current study, as the purpose of this treatment regimen is to maximise cure and local control of the cancer. In addition, curative treatment aims to minimise functional damage to the region affected by the cancer, and reduce collateral damage to other organs, although current management guidelines do not refer to ear related side-effects from treatment (Palaniappan, Owadally and Evans, 2015). Palliative treatment, on the other hand, differs in intent, with the aim to control the disease rather than to provide
a cure (Palaniappan, Owadally and Evans, 2015). The principal curative treatments for HNC in the UK are surgery, RT and chemotherapy. Treatment regimens can involve the use of one (primary) treatment or a combination of modes of treatment – surgery is advocated for the removal of disease or to limit its spread.

Radiotherapy is used to target and kill local cancer cells using high-energy electromagnetic rays and is used in the treatment of 60-70% of patients with HNC (Palaniappan, Owadally and Evans, 2015). Radiotherapy can be used alone or following surgery. Another form of therapy is targeted molecular therapy that uses biological agents to block specific cellular pathways to hinder cancer growth (Rao, Fury and Pfister, 2012). Targeted molecular therapy can be administered in conjunction with chemotherapy (Russell and Colevas, 2012) or with RT (Palaniappan, Owadally and Evans, 2015). In the UK, standard RT treatment for HNC is typically a dose of 65 Gy delivered in 30 fractions over a six-week period, while the principal chemotherapy drugs used are the platinum-based compounds cisplatin and carboplatin. Typical chemotherapy regimens include administration of cisplatin 100 mg/m² twice (within a month) or weekly cisplatin at 40 mg/m² for six weeks (Palaniappan, Owadally and Evans, 2015). Cancers in the head and neck can be described by histology. The majority (90%) of cancers in this region arise from the squamous cell layer and are named head and neck squamous cell carcinoma (Bose, Brockton and Dort, 2013). Targeted molecular therapy includes the use of cetuximab, an inhibitor that specifically targets the epidermal growth factor receptor which commonly is over-expressed in squamous cell carcinoma (Bonner et al., 2006).

Planning treatment for patients with HNC requires careful consideration of the tumour characteristics, the cancer’s location, the patient’s overall health, and the morbidity associated with treatment (Palaniappan, Owadally and Evans, 2015). Cancers are classified as early (0-II) or late (III-IV) stage, based on the ‘TNM’ system of measuring: the size of the tumour (tumour – T); assessing whether the cancer has spread to local lymph nodes (N); and gauging if there has been metastasis of the cancer (M). Early stage cancers have not
spread to the lymph nodes, whereas late stage cancers may have done so. Appendix 1.1 shows detailed staging of HNCs (Cancer Treatment Centres of America, 2016).

<table>
<thead>
<tr>
<th>Location</th>
<th>Total cases</th>
<th>Curative treatment</th>
<th>Surgical</th>
<th>Non-surgical</th>
<th>% of curative treatment that is non-surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tongue</td>
<td>880</td>
<td>593</td>
<td>515</td>
<td>78</td>
<td>13.2</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>2035</td>
<td>1476</td>
<td>433</td>
<td>878</td>
<td>59.5</td>
</tr>
<tr>
<td>Larynx (early)</td>
<td>756</td>
<td>501</td>
<td>136</td>
<td>365</td>
<td>72.9</td>
</tr>
<tr>
<td>Larynx (late)</td>
<td>579</td>
<td>380</td>
<td>193</td>
<td>187</td>
<td>49.2</td>
</tr>
</tbody>
</table>

**Table 1.6 First treatment received for head and neck cancer** (Healthcare Quality Improvement Partnership, 2014)

Eighty-six percent of patients diagnosed with HNC in the UK (England and Wales) receive treatment (HQIP, 2014), although it is not clear what percentage receive curative or palliative treatment. Table 1.6 shows the first treatment received in curative treatment for some of the subtypes of HNC (HQIP, 2014). It can be seen that surgery is the main treatment used for cancer of the tongue, while the proportion of non-surgical treatment is greater in treating other cancers, such as oropharyngeal or laryngeal cancer. Palaniappan, Owadally and Evans (2015) note that the treatment type that is provided depends on the stage of cancer, with a greater proportion of early stage laryngeal cancers being treated using RT, compared with later stage cancers. Surgery is not advised for curative nasopharyngeal treatment, due to the location of the nasopharynx close to critical structures in the skull base; instead RT is used for early stage, and CRT for later stage treatment of NPC respectively.

The treatment regimen selected involves multidisciplinary team (MDT) discussion on the prospect of physical and functional organ preservation, and possible side effects of treatment (Simcock and Simo, 2016). While it is not clear what proportion of treatment regimens use singular or multimodal therapy, treatment for early stage HNC tends to be single modality, whereas advanced cancers of stage III and IV in any location within the head and neck are treated using a multimodal regimen (Palaniappan, Owadally and Evans, 2015). A patient’s age and overall health will affect the treatment selected for HNC. The Karnofsky performance scale is used as a measure of patient health and functional status.
prior to treatment and is used in HNC treatment services; higher scale scores indicate suitability of using radical, curative treatment (Bonner et al., 2006). Among older patients, the effects of alcohol and smoking related co-morbidities including cardiac and respiratory problems may lower performance scale scores and thereby reduce treatment options (Lalami et al., 2009).

1.2.5 Survivorship

Follow-up of patients with HNC has primarily focussed on ensuring that there is no recurrence of disease (Simo et al., 2014). More recently, concern has shifted to the overall well-being of cancer survivors post treatment, and an increasing emphasis has been placed on the need to cope with side effects of treatment (Simcock and Simo, 2016). Table 1.7 summarises some side effects resulting from treatment for HNC, following surgery, RT, chemotherapy, and combined CRT. It shows that hearing deterioration is clearly identified as a side effect for most treatments:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Side effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>Alteration of cosmetic appearance</td>
</tr>
<tr>
<td></td>
<td>Facial nerve paralysis</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Mucositis</td>
</tr>
<tr>
<td></td>
<td>Hearing deterioration</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td></td>
<td>Hearing deterioration</td>
</tr>
<tr>
<td>Combined chemoradiotherapy</td>
<td>Swallowing dysfunction</td>
</tr>
<tr>
<td></td>
<td>Hearing deterioration</td>
</tr>
</tbody>
</table>

**Table 1.7 Side effects of treatment**

Key: 1 – Simcock and Simo, 2016; 2 – Jerecz-Fossa et al., 2003; Bentzen and Trotti, 2007; 3 – Lalami et al., 2009; 4 – Frowen and Perry, 2006; Theunissen et al., 2015

Each of the side effects recorded in Table 1.7 may affect patient well-being. Patients are presently encouraged to provide feedback on any symptoms they experience following treatment. The London Cancer Alliance’s Holistic Needs Assessment (London Cancer Alliance, 2013) does not have hearing loss as a side effect of treatment, however, Aintree University Hospital has included hearing problems in their patients concerns inventories.
used for assessing well-being after diagnosis and following treatment (Aintree University Hospital, 2017 and 2018). While hearing-related problems are beginning to be recognised by some service providers, hearing problems following treatment have not been recognised at a national policy level.

The HQIP 2014 HNC audit recognises that patients require intensive multimodality treatments and prolonged rehabilitation/long-term support to achieve an adequate recovery. However, hearing loss is not included among the long list of side-effects suffered by HNC patients following treatment. Likewise, the Department of Health (DH) document on survivorship ‘Improving Outcomes: A strategy for Cancer’ (DH, 2011) recognises the need to reduce ill health associated with cancer treatment including unmet physical or psychological support needs, but does not mention the need to offer support to adult patients in the UK who have hearing loss as a result of their treatment, which is surprising as the use of RT, with or without chemotherapy, is associated with hearing deterioration following cancer treatment. It is important therefore to understand the extent and impact of hearing loss on HNC patients, which is what this study was designed to address.

1.3 Summary

Since the beginning of the early 2000s, there has been an increase in the incidence of HNC cases in the UK year on year. This increase is linked to changing aetiological factors, with the decrease in alcohol consumption and tobacco use (the principal causes of HNC), being countered by the increase of other factors that include HPV associated infection. In addition, there is evidence of enhanced survivorship attributed to improved diagnosis and treatment of the disease. Many more people are living five or more years following diagnosis when compared to the early 1990s. Consequently, there has been a shift in focus with cancer treatment, from solely reducing the risk of disease recurrence, to providing an effective cure with minimal side effects. However, a deterioration in hearing following treatment is not
thought to be a significant occurrence as it does not feature in current National Health Service (NHS) policy on cancer survivorship (DH, 2011), even though acquired hearing loss has considerable implications for patient quality of life because of its wide-ranging effects on communication and social effectiveness. The next chapter reviews the literature on ear-related side effects following HNC treatment.
Chapter 2 Literature review

2.1 Introduction

There already are reviews on hearing deterioration following HNC treatment (for example Mujica-Mota, Waissbluth and Daniel, 2013; and Theunissen et al., 2015), but these reviews are limited by including papers that: assessed hearing change using outdated treatment methods; focussed on one particular type of hearing loss – SNHL; included papers on children and adolescents; considered only the number of people affected rather than explored experience of hearing deterioration. These limitations helped to formulate the questions for the literature review presented in this chapter: how many adult patients who, following treatment for their HNC using current techniques, have hearing loss? What is their experience, and are there any factors that influence a change in hearing?

This chapter begins with an outline of the search strategy used to identify relevant literature, and then appraises the quality of the papers selected. It then continues with a narrative reporting on themes based on the review questions, and then continues with a synthesis of the findings to formulate the research aims. The outline for the chapter is provided by Figure 2.1 below:
2.2 Search strategy

A search undertaken systematically was adopted to identify literature and to answer the questions: how many adult patients who, following treatment for their HNC using current techniques, have hearing loss? What is their experience, and are there any factors that influence a change in hearing?

2.2.1 PICO

The PICO model was used for clarifying terms to be used in a literature search strategy (University of Illinois, 2017). For this search, the ‘P’ (Population) were patients who had HNC; the ‘I’ (Intervention, exposure, cause or prognosis) was treatment of HNC; ‘O’ (Outcome measured) was hearing deterioration following treatment. There was no ‘C’
(Comparison) in the search question. The search terms used for each of these three key phrases (head and neck cancer/ treatment/ hearing deterioration) were confirmed as appropriate by two academic librarians, with experience in searching literature from medical journals in general, and with one possessing particular experience in searching ear, nose and throat (ENT) journals.

The three key phrases were searched within the PubMed database using relevant terms or subject headings (in brackets) for each phrase:

1. Population – Head and neck cancer: {MH “Head and Neck Neoplasms”} OR {{cancer* OR carcinom* OR neoplasm* OR tumor* OR tumour*]} AND [head* OR neck* OR (MH “Head+”) OR (MH “Neck+”) OR ear* OR throat* OR laryng* OR (MH “Salivary Glands+”) OR salivary gland*];

2. Intervention – Treatment: [(MH “Drug Therapy+”) OR (MH “Radiotherapy+”) OR (MH “Otolaryngology+”) OR (MH “Surgical Oncology”) OR (MH “Medical Oncology+”) OR chemotherapy* OR radiotherapy* OR “surg* N3 cancer*” OR “surg* N3 carcinoma*” OR “surg* N3 neoplasm*” OR “surg* N3 tumor*” OR “surg* N3 tumour*” OR “treat* N2 cancer*” OR “therap* N2 cancer*” OR (MH “Molecular Targeted Therapy”) OR (MH “Antibodies, Monoclonal+”);

3. Outcome – Hearing deterioration: [(MH “Hearing Disorders+”) OR “hearing N3 disorder*” OR “hearing N3 loss” OR “hearing N3 problem” OR “hearing N3 difficult*” OR deaf* OR hypoacus* OR otot*].

The searches for key phrases 1, 2 and 3 were then combined using the AND command to identify relevant literature on: how many adult patients who, following treatment for their head and neck cancer using current techniques, have hearing loss? What is their experience, and are there any factors that influence a change in hearing? This search strategy was then translated for use across other databases that contained literature which used quantitative or qualitative methods to address research in the health sciences.
2.2.2 Databases and PRISMA

Searches of eight electronic databases were performed between 19 December 2017 and 17 January 2018; the following databases were used:

- MEDLINE, CINAHL, PsycARTICLES, PsychINFO, Psychology and behavioural sciences collection (assessed via the EBSCO host);
- EMBASE (via ProQUEST);
- COCHRANE (via Wiley) and
- Web of science (via Clarivate Analytics)

Although the researcher was aware that a systematic review would provide the most robust appraisal of the literature and synthesis of results (Mallett et al., 2012), it was decided to undertake a review conducted systematically from a pragmatic and time consideration perspective.

Articles were then selected using the PRISMA method (Figure 2.2) for identifying relevant literature (Moher et al., 2009). The PRISMA flow-chart has a clear format that was adapted in this study for selecting articles for a narrative review.
Figure 2.2 Search strategy to identify articles on incidence and experience of hearing loss in people having had treatment for their head and neck cancer
2.2.3 Inclusion and exclusion criteria

The researcher selected or excluded articles based on information contained in their title, abstract or full text, using the following inclusion and exclusion criteria:

**Inclusion criteria** – studies that were:

- Research using qualitative, quantitative or mixed-methods approaches to assess incidence of hearing loss, or patient experience of hearing loss, following treatment with curative intent for HNC at any point in time;
- Original articles in peer-reviewed journals;
- Conducted with human subjects;
- Conducted with adults – aged 18 years plus;
- Written in the English language.

**Exclusion criteria** – studies that were:

- Investigating benign tumours, skull-based cancer or cancer arising from outside the head, childhood cancer (including adolescents) or cancers of the auditory system;
- Assessing tinnitus [the perception of sound that is not generated from an external source (Baguley, Cope and McFerran, 2016)] only;
- Assessing balance problems only;
- Assessing the mechanics of hearing loss but not assessing perceptual change from baseline by psychoacoustic testing;
- Using novel or obsolete treatment methods;
- Case reports, review articles in peer-reviewed journals, presentations at conferences or editorials;
- Assessing recurrent or metastatic disease, solely measuring hearing loss caused by disease, multiple cancer studies (unless HNC was assessed independently), or
studies using palliative treatment. This approach resulted in 15 articles for in-depth
review, with 16 articles excluded following review of the full paper (Table 2.1):

<table>
<thead>
<tr>
<th>1st Author (year)</th>
<th>Focus</th>
<th>Why excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen (2006)</td>
<td>Sensorineural hearing loss following treatment of NPC</td>
<td>Included children</td>
</tr>
<tr>
<td>Hitchcock (2009)</td>
<td>Sensorineural hearing loss following treatment of HNC</td>
<td>Did not provide incidence rates of hearing loss or experience of it</td>
</tr>
<tr>
<td>Huang (2015)</td>
<td>Toxicity and quality of life in NPC following treatment</td>
<td>Included children</td>
</tr>
<tr>
<td>Hwang (2015)</td>
<td>Hearing assessment after treatment of NPC</td>
<td>Results from current treatment were not separated from obsolete treatment</td>
</tr>
<tr>
<td>Jereczek-Fossa (2011)</td>
<td>Hearing assessment after treatment of parotid cancer</td>
<td>Results from patients who had recurrent or metastatic disease were not separated from those who were newly diagnosed</td>
</tr>
<tr>
<td>Low (1996)</td>
<td>Hearing before and after radiotherapy of NPC</td>
<td>Did not measure a change in hearing</td>
</tr>
<tr>
<td>Low (2006)</td>
<td>Sensorineural hearing loss following treatment of NPC</td>
<td>Included children</td>
</tr>
<tr>
<td>Theunissen (2014a)</td>
<td>Cochlea function after treatment of HNC</td>
<td>Results from patients who had ear related disease, or from an unknown primary were not separated from those who had HNC</td>
</tr>
<tr>
<td>Tsang (2012)</td>
<td>Otologic function after treatment of NPC</td>
<td>Did not provide incidence rates of hearing loss or experience of it</td>
</tr>
<tr>
<td>Wang (2009)</td>
<td>Middle ear function following treatment of NPC</td>
<td>Results from patients who had recurrent disease were not separated from those who were newly diagnosed</td>
</tr>
<tr>
<td>Zuur (2007)</td>
<td>Ototoxicity after treatment of HNC</td>
<td>Results were duplicated within an included article</td>
</tr>
<tr>
<td>Zuur (2008)</td>
<td>Hearing assessment after treatment of HNC</td>
<td>Results from patients who had lung or oesophageal disease were not separated from those who had HNC</td>
</tr>
<tr>
<td>Zuur (2009)</td>
<td>Risk factors for hearing loss after treatment of HNC</td>
<td>Results from patients who had recurrent or metastatic disease were not separated from those who were newly diagnosed</td>
</tr>
</tbody>
</table>

Table 2.1 Papers excluded following full review
Key: HNC – head and neck cancer; NPC – nasopharyngeal cancer

2.2.4 Data extraction

The researcher extracted data systematically from the 15 selected articles using forms based on the COCHRANE data collection form (COCHRANE, 2017) for quantitative data. The forms were amended to include the COREQ checklist (Tong, Sainsbury and Craig, 2007), and Maxwell checklist (Maxwell, 1992), to obtain data from qualitative studies. Data that were extracted are shown in Table 2.2.
<table>
<thead>
<tr>
<th>General information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date the form was completed</td>
</tr>
<tr>
<td>Population and setting</td>
</tr>
<tr>
<td>Definition of head and neck cancer</td>
</tr>
<tr>
<td>Methods</td>
</tr>
<tr>
<td>Aims of Study</td>
</tr>
<tr>
<td>Participants</td>
</tr>
<tr>
<td>Total number</td>
</tr>
<tr>
<td>Quantitative method checklist</td>
</tr>
<tr>
<td>What Test was performed</td>
</tr>
<tr>
<td>Risk of bias and validity</td>
</tr>
<tr>
<td>Was patient assignment randomised?</td>
</tr>
<tr>
<td>Treatment group information</td>
</tr>
<tr>
<td>Type of treatment</td>
</tr>
<tr>
<td>Results: hearing deterioration incidence</td>
</tr>
<tr>
<td>Time point after treatment and hearing frequency (range) assessed</td>
</tr>
<tr>
<td>Quality assessment of results for randomised controlled trials and cohort studies</td>
</tr>
<tr>
<td>How precise are the results?</td>
</tr>
</tbody>
</table>
### Qualitative method checklist

<table>
<thead>
<tr>
<th>Question</th>
<th>Question</th>
<th>Question</th>
<th>Question</th>
<th>Question</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which author/s conducted the interview or focus group?</td>
<td>What were the researcher’s credentials?</td>
<td>What was the researcher’s occupation at the time of the study?</td>
<td>Was the researcher male/female?</td>
<td>What experience or training had the researcher?</td>
<td>Was a relationship established prior to starting the study?</td>
</tr>
<tr>
<td>What did the participants know about the researcher?</td>
<td>What characteristics were reported about the interviewer/facilitator?</td>
<td>What methodological orientation was stated to underpin the study?</td>
<td>How were participants selected?</td>
<td>Method of approach: How were participants approached?</td>
<td>Sample size: How many participants were in the study?</td>
</tr>
<tr>
<td>How many people refused to participate or dropped out?</td>
<td>Setting of data collection: Where was the data collected?</td>
<td>Was anyone else present besides the participants and researchers?</td>
<td>What are the important characteristics of the sample?</td>
<td>Were questions, prompts, guides provided by the authors? Was it pilot tested?</td>
<td>Were repeat interviews carried out? If yes, how many?</td>
</tr>
<tr>
<td>Did the research use audio or visual recording to collect the data?</td>
<td>Were field notes made during and/or after the interview or focus group?</td>
<td>What was the duration of the interviews or focus group?</td>
<td>Was data saturation discussed?</td>
<td>Were transcripts returned to participants for comment and/or correction?</td>
<td>How many data coders coded the data?</td>
</tr>
<tr>
<td>Did authors provide a description of the coding tree?</td>
<td>Were themes identified in advance or derived from the data?</td>
<td>What software, if applicable, was used to manage the data?</td>
<td>Did participants provide feedback on the findings</td>
<td>Were participant quotations presented to illustrate the themes / findings? Was each quotation identified?</td>
<td>Was there consistency between the data presented and the findings?</td>
</tr>
<tr>
<td>Were major themes clearly presented in the findings</td>
<td>Is there a description of diverse cases or discussion of minor themes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Results: Hearing deterioration – patient experience

#### Themes

#### Quality assessment of results for qualitative studies

<table>
<thead>
<tr>
<th>Question</th>
<th>Question</th>
<th>Question</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>How factually accurate is the account?</td>
<td>How well do findings represent meanings from the participants’ perspective?</td>
<td>How do the findings of the study support underlying theory?</td>
<td>How generalisable are the results</td>
</tr>
<tr>
<td>Have ethical issues been taken into consideration?</td>
<td></td>
<td></td>
<td>How reproducible are the results?</td>
</tr>
</tbody>
</table>

#### Other information

<table>
<thead>
<tr>
<th>Question</th>
<th>Question</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have important populations been excluded from the study?</td>
<td>Does the study directly address the review question?</td>
<td>Key conclusions of study authors</td>
</tr>
</tbody>
</table>

### Table 2.2 Data extracted from included articles
An example of a completed data extraction form that was used for obtaining data from a paper that used quantitative methods is in Appendix 2.1, and an example used for obtaining data from a paper that employed qualitative methods is in Appendix 2.2. Data from the extraction assessment forms included quality assessment derived from the Critical Appraisal Skills Programme (CASP) checklists for cohort and qualitative studies (CASP 2017a; CASP 2017b).

2.3 Quality assessment

The CASP checklists have a ‘yes’, ‘no’ or ‘cannot tell’ scoring system for nine (qualitative study) or 11 (quantitative study) aspects of quality assessed. However, CASP checklists do not provide an overall score of quality. Other research appraisal systems do provide an overall score, but these are focused solely on randomised controlled studies, e.g. the Jadad score (Moher et al., 1998) or systematic reviews, e.g. the Qualsyst evaluation tool (Kmet, Lee and Cook, 2004). The Mixed Methods Assessment Tool (Pluye et al., 2011) has the benefit of comparing studies of different methodologies within the same checklist. However, it too does not have an overall score for quality, and is limited to the quality of study methods without an assessment of results obtained. Therefore, to gain an overall assessment of quality, the researcher created a rating scale based on the number of ‘yes’ responses obtained using the CASP criteria. The CASP criteria and derived rating schemes are shown for quantitative studies (Appendix 2.3) and for qualitative studies (Appendix 2.4). The grading of low, medium or high quality for each study was entered into the final column of summary Table 2.3 (below), with low being poor quality, medium being moderate quality, and high being good quality.

The researcher made an assessment of quality for each of the 15 included articles. Nine of the papers were deemed to be of high quality, with four of moderate quality and two of low quality. One quantitative paper was chosen at random, and this, together with the qualitative
paper were independently assessed for quality by one of the student’s supervisors and a further independent researcher, using the developed criteria. There was complete agreement between all three researchers, implying that the results obtained by the researcher for all 15 papers would be representative of all three researchers. The different quality ratings that were obtained for the studies that employed quantitative methods will be discussed first, and will then be followed by a discussion on the quality of the one paper that utilised qualitative methodology.

2.3.1 Quantitative paper quality

For the 14 papers that used quantitative methodology, the CASP questions deemed most important on quality were:

- Question 2 – Was the cohort recruited in an acceptable way – was everybody included who should have been included? This question assessed selection bias;
- Question 4 – Was the outcome accurately measured to minimise bias – do the measures truly reflect what you want them to (have they been validated)? This question addressed measurement bias;
- Question 9 – Do you believe the results – can they be due to bias, chance or confounding? Are the design and methods of this study sufficiently flawed to make the results unreliable? Question 9 inquired about reporting bias.

Of these three questions, question 9 was scored ‘yes’ most often (eight out of 14 papers), with question 2 scored most poorly (only two out 14 papers marked ‘yes’). The main limitation of the quantitative papers therefore was in the selection of participants, and how many were included in analysis. None of the papers were scored ‘yes’ for each of these three questions, but those papers that were classified overall as being of high quality papers were characterised by being clear in how participants were recruited and in how audiological testing was performed, exemplified by Chan et al. (2009). Those that were of low quality
were characterised by not being clear how results were obtained for hearing deterioration, exemplified by Cho et al. (2016).

2.3.1.1 Selection bias

The third column of Table 2.3 shows a question mark before the sampling technique used for twelve of the papers that used a retrospective or prospective cohort study design. Although it was implicit that all suitable patients were available for recruitment, these papers were not explicit in the method in which subjects were selected, and it could not be assumed that all those diagnosed within the timeframes stated were indeed invited to participate. Only two papers (Chan et al., 2009 & Hsin et al., 2010) stated that the method of recruitment was consecutive sampling. However, this method of sampling has its limitations, as the sample may not be fully representative of the population (Bowers, House and Owens, 2011).

Attrition bias is a form of selection bias that is evident from the drop-out rate of participation. The drop-out rate varied between papers even when they were assessed at the same time period after treatment. Whereas some papers had participation rates within the 60-90% range a year after treatment (for example 86% in Li et al., 2010, and 76% in Loimu et al., 2015), one paper, Pan et al. (2005), had a much-reduced rate of 40%, but provided no detail as to why this rate was so low. It is possible that those participants who had not continued in the study by Pan et al. (2005) possessed different characteristics to those who remained in the study (for example they may have been exposed to a higher radiation dose), that may have influenced hearing deterioration rates. Therefore, the results from Pan et al. (2005) need to be treated with caution due to possible attrition bias.

2.3.1.2 Measurement bias

Measurement bias was potentially evident in all the 12 papers that measured hearing deterioration. Although PTA – used to determine the incidence in hearing deterioration – is
the basic and routine test conducted in audiology, it cannot be assumed that it is performed using standard techniques such as those recommended by the BSA (2011). It is important to specify what frequencies are tested in order to replicate findings. However, five articles (Cho et al., 2016; Cheraghi et al., 2015; Niemensivu et al. 2015, Pan et al., 2005; and Petsuksiri et al., 2011) were not clear in specifying what frequencies were tested for air and bone conduction levels, and consequently, it would not be easy to replicate the method used for PTA testing from each of these papers. In addition, none of the selected papers stated the technique used for performing PTA, and this could in part be explained by the majority of papers (62%) not being in audiology or otology journals, but being within oncology or radiology journals with less focus on testing technique compared to treatment regimes.

However, Chan et al. (2009) in their publication within the *International Journal of Radiation Oncology, Biology, and Physics*, stated that equipment was calibrated every six months, therefore ensuring that sound stimuli for testing were within prescribed limits. Papers written in otology journals would be expected to provide more detail on testing method. Niemensivu et al., 2015 mentioned that licenced audiologists performed the testing in their paper published in the *European Archives of Otorhinolaryngology*, whereas Li et al. (2010) in the *Journal of Laryngology and Otology*, made no mention of calibration details nor personnel involved in testing.

Although it was probable that testing was performed in routine and standard ways, there was greater potential for bias in how deterioration was classified because authors used different criteria for classifying hearing change (Table 2.3). Although there currently is no agreed level of clinical significance for hearing deterioration after treatment, the majority of papers in this review (seven out of 12) used a hearing deterioration of ≥15dB as significant.

Standard PTA records hearing thresholds, between 0.25 to 8kHz, in 5dB levels, and the accepted test-retest variability within a clinical test session (lasting between 15-30 minutes) is 5dB (BSA, 2011). Therefore, it would seem reasonable to assume that a change in 10dB
would be a clinically significant deterioration following treatment, and this was used by Niemensivu et al. (2015), Pan et al. (2005), Petsuksiri et al. (2011) and Shorter et al. (2017). However, there is minimal evidence to support the use of a 10dB change in standard practice. Konrad-Martin et al. (2010), referred to by Niemensivu et al. (2015), determined that ≥10dB threshold hearing change, at two adjacent frequencies, was reliable in detecting ototoxicity, and this provides a useful bench mark. However, Konrad-Martin et al. (2010) based their findings on patients tested up to 20kHz of hearing, whereas standard practice is to test up to 8kHz. Simpson, Schwan and Rintelmann (1992), referred to by Petsuksiri et al. (2011), did not recommend a threshold dB change but rather recommended that an assessment of multiple frequencies was more accurate for detecting the ototoxic effects of cisplatin. Simpson, Schwan and Rintelmann compared change in hearing tests from baseline to tests performed up to 6 months after treatment, of 31 subjects who received cisplatin treatment (for what disease was not provided) compared with 21 controls who received no medication. Therefore, there is limited evidence to support a change in ≥10dB threshold as clinically significant.

Most of the articles in this review (seven out of 12) used a ≥15dB change in threshold for determining a clinically significant change in hearing. In view of the difficulty in substantiating a clinically significant change, it is sensible to use a system employed by the majority of articles; five deemed to be of high quality. Two articles (Cheraghi et al., 2015, and Theunissen et al., 2014b) referred to guidelines produced by NCI. These guidelines are the CTCAE that are commonly used by oncologists to determine changes in function to different body systems following treatment. The CTCAE version used by Theunissen et al. (2014b) was v 3 (NCI, 2006), and that by Cheraghi et al. (2015) was v 4.03 (NCI, 2010). Each of the CTCAE versions 3 and 4.03 have the same criteria for changes in hearing, with the least change (Grade 1) being used by Theunissen et al. (2014b) and Cheraghi et al. (2015) to determine incidence in hearing deterioration. A Grade 1 change for hearing is an increase in hearing threshold of at least ≥15dB averaged at two contiguous test frequencies (1-8kHz) in
at least one ear (NCI, 2006 and NCI, 2010). Although the NCI do not provide references to support this criterion, Konrad-Martin et al. (2010) stated that the most reliable method for detecting hearing deterioration following ½-octave step frequency sizes was achieved for shifts ≥15dB at one or more adjacent frequencies. It has already been mentioned that Simpson, Schwan and Rintelmann (1992) recommended for an assessment across multiple frequencies in determining hearing deterioration. Therefore, combining the findings from Konrad-Martin et al. (2010) and Simpson, Schwan and Rintelmann (1992), it appears that a ≥15dB shift in threshold, across two or more adjacent frequencies is the most appropriate to use in determining a clinically significant change in hearing; this is used in the CTCAE criteria.

Measurement bias was also evident in one of the two papers that reported on quality of life rather than on incidence in hearing deterioration. The paper by Loimu et al. (2015) used the 15D questionnaire that had been validated and widely used in patients with cancers other than head and neck. In contrast, Lastrucci et al. (2017) used five questionnaires in their study but the authors did not state the reliability and validity of some of these instruments, and therefore caution is required regarding the generalisability of results obtained in their study.

2.3.1.3 Reporting bias

In contrast to the concerns raised above regarding participant sampling and measurement of outcomes, the majority of the quantitative papers in this review were good at reporting results and the rationale behind statistical analysis used. Two exceptions though were Cho et al. (2016) and Niemensivu et al. (2015).

Cho et al. (2016) were not clear in their methods how they arrived at a figure of <0.1% incidence in hearing deterioration in their study. In addition, Cho et al. (2016) investigated sudden deafness, which is defined as a rapid decline (less than three days) of more than (or
equal to) 30dB SNHL in at least three contiguous frequencies without an identifiable cause.

However, Cho et al. (2016) only performed monthly audiological assessment, and so it is not clear whether the hearing loss they reported was strictly defined as sudden deafness.

Reporting bias was also evident in the paper by Niemensivu et al. (2015). These authors addressed both hearing and tinnitus concerns in their paper. One table showed that two patients with a 0-score had slight tinnitus, yet others with a 0-score experienced no tinnitus – it was not made clear what was the distinction between ‘no tinnitus’ or ‘slight tinnitus’.

2.3.2 Qualitative paper quality

The one paper on patient experience, Nund et al. (2015), was of high quality. These authors described the use of maximum variation sampling to obtain a diverse sample to report on communication problems following HNC treatment. The authors also used open-ended interviews that were appropriate for the phenomenological stance adopted. The method for generation of themes was clearly stated using thematic analysis as outlined by Braun and Clarke (2006). Themes were explicated by incorporation of supportive participant quotes. However, there were some concerns with this paper regarding data density, as it was not clear how many interviewees were represented in each theme. There may also have been researcher bias, as the assumptions, reasons and interests in the research topic by the authors were not made clear.

2.3.3 Summary of quality assessment

There were some concerns regarding selection bias in the papers in this review that used quantitative methods, with the majority not being clear on how participants were recruited. It was noted that measurement bias was potentially evident in all of the quantitative papers reviewed, as none made clear the method for hearing testing. Only two papers referred to recommended guidelines that used evidence-based criteria for hearing change of ≥15dB averaged across several frequencies, although it was noted that there is no current standard
definition for clinically significant hearing deterioration. In contrast, the reporting of results overall in the quantitative papers was of good quality, and the one paper that used qualitative methods was also of good quality. Therefore, the overall method used for data collection and reporting in the 15 papers selected for this review was of good quality to draw valid conclusions from the following themes to be discussed.

2.4 Summary of findings

Data from the data extraction forms were used to create the literature review summary table, Table 2.3, depicting: the 1st author; the site of the cancer; the number of participants; what treatment was used; the classification used to identify a change in hearing; the study findings or results, and risk factors for hearing deterioration. The final column in Table 2.3 has a rating of study quality, which was derived from the CASP checklists.
<table>
<thead>
<tr>
<th>1st Author (year)</th>
<th>Site of Cancer No. of participants</th>
<th>Study Design Sampling Method</th>
<th>Treatment</th>
<th>Classification of psychoacoustic hearing change (Frequencies)</th>
<th>Study findings/ results</th>
<th>Risk factors discussed *significant (p&lt;0.05)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan (2009) Hong Kong</td>
<td>Nasopharynx N=87 Nasopharynx</td>
<td>Quantitative RC ? consecutive Pre-Post</td>
<td>RT or CRT</td>
<td>Increase in bone conduction thresholds ≥10dB (0.5-4kHz)</td>
<td>Incidence of hearing loss range: 9-55% (see sections on incidence based on range of hearing, and time after treatment)</td>
<td>Gender, *age, baseline hearing, *treatment dose and treatment regime, time of testing after treatment</td>
<td>High</td>
</tr>
<tr>
<td>Cheraghi (2015) Iran</td>
<td>General Head and Neck N=29</td>
<td>Quantitative PC ? consecutive Pre-Post</td>
<td>RT or CRT</td>
<td>Increase in hearing thresholds ≥15dB (0.25-12kHz)</td>
<td>Incidence of hearing loss = 51%</td>
<td>Age, treatment dose and treatment regime (no significance testing done)</td>
<td>Medium</td>
</tr>
<tr>
<td>Cho (2016) Taiwan</td>
<td>Nasopharynx N=1636</td>
<td>Quantitative RC Consecutive Pre-Post</td>
<td>RT or CRT</td>
<td>Increase in hearing thresholds ≥30dB (0.5-4kHz)</td>
<td>Incidence of hearing loss &lt;1%</td>
<td>*Treatment type, *treatment dosage, age, gender, time of test,</td>
<td>Low</td>
</tr>
<tr>
<td>Hsin (2010) Taiwan</td>
<td>Nasopharynx N=26</td>
<td>Quantitative RC Consecutive Pre-Post</td>
<td>RT or CRT</td>
<td>Increase in bone conduction thresholds ≥20dB (0.5-4kHz)</td>
<td>Incidence of hearing loss = 46%</td>
<td>*Tumour size *Treatment type</td>
<td>High</td>
</tr>
<tr>
<td>Lastrucci (2017) Italy</td>
<td>Nasopharynx N= 56</td>
<td>Quantitative RC ? consecutive Questionnaire</td>
<td>RT or CRT</td>
<td>Not measured</td>
<td>Clinician rated hearing loss not related to questionnaire scores on quality of life</td>
<td>Gender, age, tumour stage, time of assessment after treatment, * treatment type</td>
<td>High</td>
</tr>
<tr>
<td>Li (2010) China</td>
<td>Nasopharynx N=42</td>
<td>Quantitative PC ? consecutive Pre-Post</td>
<td>RT</td>
<td>Increase in bone conduction thresholds ≥15dB (0.5-4kHz)</td>
<td>Incidence of hearing loss range: 10-98% (see sections on incidence based on range of hearing, and time after treatment)</td>
<td>*Time of test after treatment</td>
<td>Medium</td>
</tr>
<tr>
<td>Loimu (2015) Finland</td>
<td>General Head and Neck N=64</td>
<td>Quantitative PC ? consecutive Questionnaire</td>
<td>RT or CRT</td>
<td>Not measured</td>
<td>Questionnaire hearing scores at 1-year post treatment did not differ from those at baseline</td>
<td>Time of test after treatment Type of cancer</td>
<td>Medium</td>
</tr>
<tr>
<td>Niemensivu (2015) Finland</td>
<td>General Head and Neck N=28</td>
<td>Quantitative RC+PC ? consecutive Pre-Post</td>
<td>CRT</td>
<td>Increase in bone conduction thresholds ≥10dB (0.5-8kHz)</td>
<td>Incidence of hearing loss range: 0-32% (see section on incidence in hearing deterioration based on range of hearing)</td>
<td>Treatment dose (no significance testing done for hearing)</td>
<td>Low</td>
</tr>
<tr>
<td>1st Author (year) country</td>
<td>Site of Cancer No. of participants</td>
<td>Study Design Sampling Method</td>
<td>Treatment</td>
<td>Classification of psychoacoustic hearing change (Frequencies)</td>
<td>Study findings/ results</td>
<td>Risk factors discussed *significant (p≤0.05)</td>
<td>Quality</td>
</tr>
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</tr>
<tr>
<td>Nund (2015) Australia</td>
<td>General Head and Neck Survivors: N=14; Carers: N=9</td>
<td>Qualitative Phenomenology Purposive Interview</td>
<td>Non-surgical therapy</td>
<td>N/A</td>
<td>Theme 1: Impairments in communication; 2: Challenges in everyday communicating; 3: Broad ranging effects of communication changes; 4: Adaptations made</td>
<td>Not discussed</td>
<td>High</td>
</tr>
<tr>
<td>Oh (2004) South Korea</td>
<td>Nasopharynx N=25</td>
<td>Quantitative PC ? consecutive Pre-Post</td>
<td>CRT</td>
<td>Increase in bone conduction thresholds ≥15dB (0.5-4kHz)</td>
<td>Incidence of hearing loss range: 4-27% (see sections on incidence based on range of hearing, and time after treatment)</td>
<td>Gender, age, *middle ear status, *treatment type, *treatment dose</td>
<td>High</td>
</tr>
<tr>
<td>Pan (2005) US</td>
<td>General Head and Neck N=35</td>
<td>Quantitative PC ? consecutive Pre-Post</td>
<td>RT or CRT</td>
<td>Increase in bone conduction thresholds ≥10dB (0.4-0.8kHz)</td>
<td>Incidence of hearing loss range: 22-100% (see sections on incidence based on range of hearing, and time after treatment)</td>
<td>Gender, *age, *Treatment dose</td>
<td>Medium</td>
</tr>
<tr>
<td>Petsuksiri (2011) Thailand</td>
<td>Nasopharynx N=27</td>
<td>Quantitative RC ? consecutive Pre-Post</td>
<td>CRT</td>
<td>Increase in bone conduction thresholds ≥15dB (0.5-4kHz)</td>
<td>Incidence of hearing loss range: 7-37% (see section on incidence in hearing deterioration based on range of hearing)</td>
<td>Age, co-morbidity, time after treatment, middle ear status, treatment type, *treatment dose</td>
<td>High</td>
</tr>
<tr>
<td>Shorter (2017) Australia</td>
<td>General Head and Neck N=38</td>
<td>Quantitative RC ? consecutive Pre-Post</td>
<td>CRT</td>
<td>Increase in bone conduction thresholds ≥10 or ≥15dB (0.5-8kHz)</td>
<td>Incidence of hearing loss range: 4-93% (see section on incidence in hearing deterioration based on range of hearing)</td>
<td>HPV status, *alcohol consumption and tobacco use, tumour stage/location, baseline hearing, treatment type, *treatment dose</td>
<td>High</td>
</tr>
<tr>
<td>Theunissen (2014b) The Netherlands</td>
<td>General Head and Neck N=36</td>
<td>Quantitative RC ? consecutive Pre-Post</td>
<td>CRT</td>
<td>Increase in hearing thresholds ≥15 (0.25-12kHz)</td>
<td>Incidence of hearing loss range: 78-81% (see section on time after treatment)</td>
<td>*Time of test after treatment</td>
<td>High</td>
</tr>
</tbody>
</table>

Table 2.3 Summary table of data from articles for review
Key: RC – retrospective cohort; PC – prospective cohort; RT – Radiotherapy; CRT – Chemoradiotherapy
2.4.1 Overview of selected articles

Across 15 papers, 2184 patients were assessed who received HNC treatment, and nine carers were assessed in the work of Nund et al. (2015) (Table 2.3). The range of patients assessed in each paper ranged from 14 (Nund et al., 2015) to 1636 (Cho et al., 2016). All 15 papers provided demographic information on the age of participants, with ages ranging from 18 years (Petsuksiri et al., 2011) to 83 years (Lastrucci et al., 2017). The median age range across the papers was 42 years (Cheraghi et al., 2015) to 60 years (Theunissen et al., 2014b). Thirteen papers provided the gender of participants; Petsuksiri et al. (2011) did not provide information on gender, whereas the gender of the participants in Chan et al. (2009) was not clearly provided. All thirteen articles that did provide the gender of HNC patients recruited a greater proportion of male participants, with almost equal numbers in Pan et al. (2005) (male to female ratio of 18:17) to the most extreme difference in numbers in Shorter et al. (2017) (male to female ratio of 33:5). As men are typically more affected with HNC than women by a 2:1 ratio (Cancer Research UK, 2016), it is not surprising that there were more males who received treatment in these studies compared with females. However, the ratio provided by Shorter et al. (2017) suggests that there was an over-representation of men in their study. This may have affected the results of incidence in hearing deterioration in the study by Shorter et al. (2017), if being male or female is considered a greater risk in developing hearing loss following treatment (see section 2.6.2 on risk factors associated with hearing deterioration).

Eight papers focussed on NPC, whereas seven were on cancers within the HNC region in general (Table 2.3). Seven of the articles selected for review originated from South East Asia, and all of these focussed on cancers of the nasopharynx. Nasopharyngeal cancer is the most common cause of HNC in Southern China, and the 5th most common of all cancers in Hong Kong (Tsang et al., 2012), whereas NPC accounts for only 2% of HNC in the UK (HQIP, 2012). Although the initial search identified some papers that were conducted in the UK, these were excluded for various reasons (Appendix 2.5), including hearing loss as a
presenting feature of NPC (Glynn et al., 2006), rather than following treatment for this disease.

Fourteen articles used quantitative methodology, whereas one used qualitative methodology; there were no mixed methods articles (Table 2.3). Twelve articles assessed incidence of hearing deterioration following treatment, whereas two measured quality of life. Only one of the papers used qualitative methodology to gain patient experience of hearing change (Nund et al., 2015). This was not unexpected given the relatively few articles using qualitative research in Audiology compared with quantitative studies (Vestergaard Knudsen et al., 2012), and within medicine in general (Gagliardi and Dobrow, 2011).

Seven papers assessed the use of RT or CRT; six papers assessed only CRT treatment, and one paper assessed the use of RT alone (Li et al., 2010). Nund et al. (2015) did not make it clear what treatment was used, apart from that it involved non-surgical techniques. There was no initial restriction imposed for date of publication when performing the literature search, but only papers from 2004 onwards were selected. This reflected change in treatment regimens for HNC that arose around this time: radiotherapy advanced from earlier conventional 2-dimensional (2D) delivery to 3-dimensional (3D) and intensity modulated radiotherapy (IMRT), and bleomycin ceased to be used with these patient groups. However, although RT or concurrent CRT were used within the 15 selected papers, there was much variation in the combination and dosages of RT and chemotherapy used. It is noted that none of the papers assessed the effect of surgical intervention alone on hearing.

A range of classification criteria was used for determining hearing deterioration, based on how much change in hearing was deemed to be clinically significant, and the hearing frequency range that was assessed (Table 2.3). The different criteria used contributed to the wide variation in reported incidence of hearing deterioration – from none (Niemensivu et al., 2015) to 100% (Pan et al., 2005). This wide variation has been identified and reported in similar reviews (Theunissen et al., 2015; Mujica-Mota, Waissbluth and Daniel, 2013).
was also large variation reported in the incidence of hearing deterioration within individual articles (including: Chan et al., 2009; Li et al., 2010; Shorter et al., 2017). These papers assessed hearing change across a different range of time-points after treatment: between one and three months after treatment (n=4 papers); at six months after treatment (n=5); one year after treatment, (n=5); two years after treatment (n=4); more than two but less than five years after treatment (n=4); and more than five years after treatment (n=3).

Different factors were discussed that could contribute to hearing deterioration after treatment, with the treatment regimen itself being the factor most assessed in eleven papers Table 2.3). Other factors assessed were: age (seven papers); gender (five); tumour stage (four); time after treatment (seven), and middle ear status (three) for the development of SNHL. In view of the heterogeneity of factors that could contribute to the incidence of hearing deterioration, including different treatment regimens and the variety of hearing deterioration classification systems, the results of this literature review are presented as a narrative synthesis of themes derived from Table 2.3.

2.5 Themes – Findings

Information from Table 2.3 will be discussed in more depth within the following themes that address different aspect of the review questions:

Theme 1 – Incidence of hearing deterioration -
Incidence of sensorineural hearing loss in general head and neck cancer;
Incidence of sensorineural hearing loss in nasopharyngeal cancer;
Incidence of conductive hearing loss;
Incidence in hearing deterioration based on range of hearing;
Tests used -
Tympanometry;
Other.
Theme 2 – Risk factors associated with hearing deterioration

Profile of patients;
Age;
Gender;
Co-morbid disease;
Recreational activity;
Tumour size;
Pre-treatment hearing level;
Middle ear status;
Type of treatment -
Radiotherapy technique;
Radiotherapy dosage;
Chemotherapy;
Time after treatment.

Theme 3 – Patient experience -
Quality of life;
Lived experience.

2.5.1 Theme 1 – Incidence of hearing deterioration

The first question of this review was: how many adult patients who, following treatment for their HNC using current techniques, have hearing loss? Within the 12 articles that measured hearing deterioration following HNC, there was the widest possible range of 0-100% incidence. Five of these articles reported on treatment of general HNC (Cheraghi et al., 2015; Niemensivu et al., 2015; Pan et al., 2005; Shorter et al., 2017; Theunissen et al., 2014b), whereas the remaining seven focussed only on cancer of the nasopharynx (Chan et al., 2009; Cho et al., 2016; Hsin et al., 2010; Li et al., 2010; Oh et al., 2004; Petsuksiri et al., 2014b).
2011; Wang et al., 2015). All 12 papers measured the incidence of SNHL, however, only five (Hsin et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Theunissen et al., 2014b; Wang et al., 2015) also measured mixed or conductive loss.

This theme will report first on the findings of SNHL in people following treatment of general HNC, secondly on papers reporting SNHL in people following treatment of NPC only, and thirdly on conductive hearing loss following treatment. It will then conclude with the variation in incidence based on which frequency range was assessed, and the tests used in assessment.

2.5.1.1 Incidence of sensorineural hearing loss in general head and neck cancer

There were five papers that reported on sensorineural hearing deterioration following treatment for general HNC, ranging from 0-100% incidence (Cheraghi et al., 2015; Niemensivu et al., 2015; Pan et al., 2005; Shorter et al., 2017; Theunissen et al., 2014b).

There was only one paper reporting 0% incidence (Niemensivu et al., 2015), and also only one that reported 100% incidence (Pan et al., 2005). Both Niemensivu et al. (2015) and Pan et al. (2005) reported their findings on a small sample of general HNC patients. Although Niemensivu et al. (2015) assessed 28 patients in their study, only 22 underwent hearing testing before and after treatment. Pan et al. (2005) conducted serial hearing tests and reported 100% incidence of hearing loss in two patients tested at 2½ years after treatment. However, it is difficult to draw conclusions from Pan et al. (2005) and from Niemensivu et al. (2015) given the small sample sizes.

Three studies on general HNC reported incidence of sensorineural hearing deterioration between 4-93% (Cheraghi et al., 2015; Shorter et al., 2017; Theunissen et al., 2014b). These three papers were assessed as being of moderate to high quality (Table 2.3), and reported their incidence rates of hearing deterioration on larger, albeit still small, sample sizes of: n=29 (Cheraghi et al., 2015); n=38 (Shorter et al., 2017); n=36 (Theunissen et al.,
Therefore, there is a little more confidence in the validity of results from these three studies compared with the studies by Niemensivu et al. (2015) and Pan et al. (2005) regarding the range in incidence of hearing deterioration. However, there were limitations in each of these three studies in the range of subjects who were assessed.

The paper by Theunissen et al. (2014b) only assessed patients with oropharyngeal, oral cancer or hypopharyngeal cancer. In contrast, Cheraghi et al. (2015) included patients with a greater range of HNCs, including those who had NPC, parotid cancer, or cancer of the sinuses. These three subtypes of HNC accounted for 72% of the patients in the study by Cheraghi et al. (2015), but account for only 12% of patients who have HNC in the UK (HQIP, 2012). The study by Shorter et al. (2017) included patients with cancer of the oropharynx who received treatment, and these patients accounted for 70% of their study sample. However, only 28% of HNC patients have oropharyngeal cancer in the UK (HQIP, 2012). Therefore, although there is evidence to suggest that sensorineural hearing deterioration following treatment of general HNC has ranged between 4-93%, it is not clear if this range applies to a general cohort of UK HNC patients eligible for treatment.

2.5.1.2 Incidence of sensorineural hearing loss in nasopharyngeal cancer

The incidence of sensorineural hearing deterioration reported in the seven articles on treatment of NPC range from <1% (Cho et al., 2016), to 98% (Li et al., 2010). However, the paper by Cho et al. (2016) was deemed to be of overall low quality (Table 2.3), and incidence in hearing deterioration was based on a higher change (30dB) compared with the other papers that assessed changes in hearing following treatment of NPC. Therefore, the results from Cho et al. (2016) have limited generalisability, and a more accurate representation of incidence of hearing change in treating NPC was arguably derived from the other papers (Chan et al., 2009; Hsin et al., 2010; Li et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015).
After Cho et al. (2016), the next lowest incidences in hearing deterioration following treatment of NPC were 4% (Oh et al., 2004) and 7% (Petsuksiri et al., 2011). The authors of both these papers used the definition of hearing deterioration as an increase in bone conduction thresholds by ≥15dB. This definition is argued as being the most appropriate to use for determining a change in hearing (section 2.4.1.2 – measurement bias). These authors conducted their studies in other similar ways. They recorded a change of hearing in the same low frequency range (average of 0.5, 1 and 2kHz), and at the same time after treatment (one year). In addition, both Oh et al. (2004) and Petsuksiri et al. (2011) assessed larger numbers of participants from which to draw valid conclusion (27 and 48 respectively) and both papers were judged to be of high quality (Table 2.3). Consequently, there is much to commend the validity in the lower end of incidence in hearing deterioration as being 4% following NPC treatment.

At the other end of incidence in hearing deterioration were the studies by Li et al. (2010) and Wang et al. (2015), who provided the two highest rates of incidence in hearing deterioration following treatment of NPC (98% and 61% respectively). Li et al. (2010) assessed hearing deterioration in 48 ears from 29 patients, and Wang et al. (2015) assessed a similar number of cases (51 patients). Both authors assessed hearing change at the same time after treatment (5 years), employed the same classification (≥15dB change), and were judged to be of medium or high quality. However, there was a difference in the treatment used in the studies by Li et al. (2010) and by Wang et al. (2015). Li et al. (2010) reported on change following 3D-conformal RT, whereas Wang et al. (2015) reported on change following more recent RT in the form of IMRT. Consequently, although there is evidence to support the assertion of the upper end of sensorineural hearing deterioration as being 98% following treatment of NPC, consideration must be taken of the type of treatment used (please refer to section 2.5.2.2 – treatment).
2.5.1.3 Incidence of conductive hearing loss

The incidence of conductive loss in the papers reviewed ranged from 3-44% (Hsin et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Theunissen et al., 2014b; Wang et al., 2015). All five of these papers were assessed as being of high quality (Table 2.3), therefore the findings from them are viewed as being of high validity. Four of these papers assessed treatment for NPC (Hsin et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015), whereas only one was on treatment for general HNC (Theunissen et al., 2014b). It is noted that the radiation exposure to the cochlea differed greatly between these two patient groups, and that different incidence rates were recorded.

The incidence of conductive loss following NPC treatment ranged between 19-44%, with radiation exposure to the cochleae ranging between 34-66 Gy (Hsin et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015). In contrast, there was only 3-7% incidence in conductive loss in patients treated for cancers of the oropharynx, oral cavity or hypopharynx, with radiation dosage to the cochleae at 13 Gy (Theunissen et al., 2014b).

Although there is less evidence on findings of conductive loss compared with SNHL following treatment of HNC, that which is available has high validity and suggests a range of between 3-44%. It is noted that this range may be influenced by radiation dosage to the cochlea (please refer to section 2.5.2.2 – treatment).

2.5.1.4 Incidence in hearing deterioration based on range of hearing

Incidence in hearing deterioration varied greatly depending on which frequency range was assessed. Table 2.4 below expands on Table 2.3 to provide the speech frequencies that were assessed in each article, and incidence of hearing loss at each of these frequency ranges.
Table 2.4 Frequency range assessed

Table 2.4 shows that different frequency ranges were assessed to determine incidence of hearing deterioration following treatment for HNC. The incidence of hearing deterioration for low frequency speech hearing ranged from 0-60%, that for mid frequency speech from 14-98%, and that for high frequency speech from 32-100%.

The marked difference in incidence between the different hearing ranges is made clear in those eight articles that assessed more than one frequency range (Chan et al., 2009; Li et al., 2010; Niemensivu et al., 2015; Oh et al., 2004; Pan et al., 2005; Petsuksiri et al., 2011; Shorter et al., 2017; Wang et al., 2015). In each of these articles, there was higher incidence of hearing deterioration in the higher frequencies. As five of these articles were of high quality (Table 2.3), there is much evidence to support the finding that incidence in hearing deterioration depends on the range of frequencies assessed, with higher speech frequencies being more affected. There is therefore evidence to support the testing of higher frequencies as these are more sensitive to changes in hearing during treatment, however, there is also the need to detect lower frequency changes, as low and mid-frequency hearing (≤4kHz) contribute to 95% of speech intelligibility, whereas >4kHz frequencies contribute to only 5% of speech understanding (Pavlovic, 1987).
2.5.1.5 Tests used for assessing a change in hearing

All 12 articles included in this review that measured incidence in hearing deterioration assessed a perceptual change in hearing using PTA. Although the majority of articles used PTA only (Chan et al., 2009; Cho et al., 2016; Cheraghi et al., 2015; Oh et al., 2004; Petsuksiri et al., 2011; Shorter et al., 2017; Theunissen et al., 2014b; Wang et al., 2015), four studies employed other tests in their assessment of hearing change (Table 2.5):

<table>
<thead>
<tr>
<th>1st Author (year)</th>
<th>Other hearing tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsin (2010)</td>
<td>Tympanometry</td>
</tr>
<tr>
<td>Li (2010)</td>
<td>Tympanometry; stapedial reflexes; auditory brainstem responses</td>
</tr>
<tr>
<td>Niemensivu (2015)</td>
<td>Otoacoustic emissions</td>
</tr>
<tr>
<td>Pan (2005)</td>
<td>Tympanometry, stapedial reflexes; speech reception; speech discrimination</td>
</tr>
</tbody>
</table>

Table 2.5 Tests used in addition to pure tone audiometry

Tympanometry

Tympanometry is an objective test used to measure middle ear function (BSA, 2013) and is often performed to confirm the nature of middle ear dysfunction with conductive hearing loss found on PTA. Three papers in this review all used tympanometry in addition to PTA (Hsin et al, 2010; Li et al., 2010; Pan et al., 2005). However, neither Hsin et al. (2010) nor Pan et al. (2005) referred to the tympanometry results obtained in their studies. Li et al. (2010) mentioned that only 12 ears of 42 patients either produced a type B tympanogram (a lack in a change of compliance function of the middle ear to a pressure change), or a type C tympanogram (negative pressure within the middle ear cavity). Therefore, tympanometry was used minimally within the articles included in this review.

Other

The stapedial reflex test assesses the function of different structures, including the auditory nerve and muscles within the middle ear, in response to loud sounds. Stapedial reflex testing is sometimes used in addition to tympanometry, and the reflex test was used to
confirm middle ear dysfunction in one patient in the study by Li et al. (2010). Only Pan et al. (2005) also mentioned stapedial reflex testing as part of their testing battery. These authors also included speech reception and speech discrimination tests as part of the test battery in their article, yet only mentioned PTA results. It is most likely that speech tests were performed as usual practice but were not relevant to the study by Pan et al. (2005). Stapedial reflex testing and speech testing were used minimally within the articles of this review.

Li et al. (2010) used auditory brainstem response (ABR) testing to assess the nerve pathway from the auditory nerve to the brain, following RT for NPC, and determined that ABR were significantly delayed at one-year post treatment compared to pre-treatment hearing levels. ABR deterioration included an increase in wave I to wave V inter-peak latency, indicating that central processing of auditory stimuli may be adversely affected by 3D RT. As ABR testing was only reported in one article, it is apparent that most authors in this review focussed on changes in peripheral hearing ability, as measured by PTA.

It is of interest that only one of the 12 articles (Niemensivu et al., 2015) that measured incidence of hearing deterioration used otoacoustic emission (OAE) testing in addition to PTA. Otoacoustic emission testing objectively assesses inner ear function, and it is advocated by the American Speech-Language-Hearing Association (ASHA) (Konrad-Martin et al., 2005) as a sensitive measure of ototoxic damage. This is because changes of OAEs precede changes of PTA thresholds in patients receiving ototoxic drugs (Lonsbury-Martin and Martin, 2001). Niemensivu et al. (2015) reported that there was no change in OAEs for patients in their study, but mentioned using transient evoked OAE. This type of OAE detects frequencies up to 4kHz, whereas the use of distortion product OAE detects higher frequency change, and Niemensivu et al. (2015) mentioned that distortion product OAE may have been more suitable to use.
2.5.2. Theme 2 – Risk factors associated with hearing deterioration

The second question of this literature review was: ‘are there any factors that influence a change in hearing?’. Table 2.3 shows the summary of risk factors, which are expanded upon in Table 2.6 below. Incidence of hearing deterioration in each of the 12 papers of this literature review was determined using descriptive statistics. However, risk factors associated with hearing deterioration were assessed in the majority of the papers by using inferential statistics; only Cheraghi et al. (2015) did not use inferential statistics. Other papers used inferential statistics that were not directly related to the purposes of this review: Pan et al. (2005) confined their statistical assessment to comparison in hearing change between the irradiated and non-irradiated ears of patients, and therefore their results are not considered in this assessment of change of hearing from baseline assessment of the same ear; Cho et al. (2016) made comparison only of IMRT to the older obsolete use of 2D RT; Niemensivu et al. (2015) assessed difference in the experience of tinnitus. Therefore, Table 2.6 does not include the statistics from Cheraghi et al. (2015), Cho et al. (2016), Niemensivu et al. (2015), or from Pan et al. (2005). In addition to risk factors that may be associated with treatment, Table 2.6 also includes ‘time after treatment’ as some papers also assessed if hearing deterioration progressed with time.
<table>
<thead>
<tr>
<th>1st Author (year)</th>
<th>Age</th>
<th>Gender</th>
<th>Comorbidity</th>
<th>Recreational activity</th>
<th>Tumour size</th>
<th>Baseline hearing</th>
<th>Middle ear status</th>
<th>Treatment</th>
<th>Time after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan (2009)</td>
<td>S</td>
<td>NS</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>S p=0.013</td>
<td>Radiotherapy p=0.020</td>
</tr>
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<td></td>
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<td></td>
<td>– Chemotherapy</td>
</tr>
<tr>
<td>Hsin (2010)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>S p=0.007</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>NS</td>
</tr>
<tr>
<td>Li (2010)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>NS</td>
</tr>
<tr>
<td>Oh (2004)</td>
<td>NS</td>
<td>NS</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>S p&lt;0.050</td>
<td>NS</td>
<td>S p&lt;0.050</td>
<td>Radiotherapy p=0.047</td>
</tr>
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<td></td>
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<td></td>
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<td>– Chemotherapy</td>
</tr>
<tr>
<td>Petsuksiri (2011)</td>
<td>NS</td>
<td>X</td>
<td>NS</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>NS</td>
<td>S p=0.047</td>
<td>Radiotherapy p&lt;0.006</td>
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<td></td>
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<td></td>
<td>– Chemotherapy</td>
</tr>
<tr>
<td>Shorter (2017)</td>
<td>NS</td>
<td>NS</td>
<td>X</td>
<td>S p=0.006 – smoking</td>
<td>NS</td>
<td>NS</td>
<td>X</td>
<td>S p=0.006</td>
<td>Radiotherapy p&lt;0.006</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.008 – alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>– Chemotherapy</td>
</tr>
<tr>
<td>Theunissen (2014b)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>NS</td>
</tr>
<tr>
<td>Wang (2015)</td>
<td>S</td>
<td>NS</td>
<td>X</td>
<td>X</td>
<td>S p=0.011</td>
<td>X</td>
<td>X</td>
<td>S p=0.022</td>
<td>Radiotherapy p=0.035</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>– Chemotherapy</td>
</tr>
</tbody>
</table>

Table 2.6 Risk factors associated with hearing deterioration

Key: S – statistically significant; NS – not statistically significant; X – not tested (no results)
2.5.2.1 Patient characteristics

Table 2.6 shows that age, gender, co-morbid disease, recreational activity, tumour size, baseline hearing level, and middle ear status were assessed as potential factors for influencing the developing of, or being associated with, hearing loss.

Age

Five papers in this review considered a patient’s age as a potential risk factor in hearing deterioration (Chan et al., 2009; Oh et al., 2004; Petsuksiri et al., 2011; Shorter et al., 2017; Wang et al., 2015). Two papers reviewed found a statistically significant association of an increase in age with an increased incidence in hearing deterioration (Chan et al., 2009: p=0.026; Wang et al., 2015: p=0.034). Chan et al. (2009) used regression analysis, whereas Wang et al. (2015) used Fisher’s exact test, and used 40 years of age as the cut-off in their categorical analysis. However, no explanation was given as to why Wang et al. (2015) used 40 as the cut-off age; the median age of participants in their study was 42 years.

In contrast, the three other authors (Oh et al., 2004; Petsuksiri et al., 2011; and Shorter et al., 2017) all determined that there was no association in hearing loss with age, even though they also used Fisher’s test or regression statistics for their analysis. As similar statistics were employed across these five papers, there was no agreement in the effect of age on hearing deterioration.

Gender

Only four papers assessed gender and hearing deterioration after treatment (Chan et al., 2009; Oh et al., 2004; Shorter et al., 2017; Wang et al., 2015). The statistical assessments from all of these high-quality papers were in agreement that gender did not influence hearing deterioration; Chan et al. (2009) determined p=0.61, and Wang et al. (2015) reported p=0.33, whereas Oh et al. (2004) and Shorter et al. (2017) reported p>0.05.
Co-morbid disease

The co-morbid diseases assessed were diabetes mellitus and hypertension. The two articles in this literature review that assessed diabetes and hypertension as risk factors for developing hearing change, Pan et al. (2005) and Petsuksiri et al. (2011), determined that there was no association between these conditions and hearing deterioration.

Recreational activity

Only one paper (Shorter et al., 2017) assessed the effect of smoking and drinking as potential risk factors in the development of hearing loss after treatment for HNC. Shorter et al. (2017) used regression analysis and determined statistical significance in the development of high frequency (8kHz) hearing deterioration with increased smoking and alcohol consumption. The mean tobacco use was described as 28.7 ‘pack years’, and alcohol consumption was 18.6 ‘standard drinks’ per week for patients acquiring high frequency hearing deterioration. Although interesting findings, it is difficult to utilise these results as they derive from one paper only.

Tumour size

Three papers investigated tumour size and risk of hearing deterioration, with conflicting findings (Hsin et al., 2010; Shorter et al., 2017; Wang et al. 2015). Shorter et al. (2017) found no significant difference in hearing deterioration between different tumour sizes (p>0.05), whereas Hsin et al. (2010) and Wang et al. (2015) found a statistically significant association of tumour size with the amount of hearing deterioration (p=0.007 and p=0.012 respectively). However, information provided by each author on tumour staging was different that made it difficult to make meaningful comparison. Shorter et al. (2017) grouped together stage 1 and 2 tumours in their calculations on statistical significance, whereas Wang et al. 
(2015) grouped together stages 1-3 tumours in their calculations. Hsin et al. (2010) provided the number of cases for each tumour size from 1 to 4 in their analysis.

Hsin et al. (2010) investigated different tumour sizes, on the premise that the larger the primary tumour, the greater the radiation treatment volume over the skull base and temporal bone (which houses the ear). Hsin et al. (2010) found that the development of middle ear effusion (which causes a conductive hearing loss) was associated significantly with greater tumour size (p=0.007). In contrast, Wang et al. (2015) found significance in the development of SNHL with tumour size; the larger the tumour size, the higher the incidence of hearing loss (p=0.012). As both Hsin et al. (2010) and Wang et al. (2015) reported on treatment for NPC using IMRT, it is not clear why they found significance in deterioration to different parts of the ear.

**Pre-treatment hearing level**

As hearing deteriorates with age (Davis, Ostri and Parving, 1990; Shield, 2006), it was reasonable to expect that the pattern of hearing deterioration associated with pre-treatment hearing would be similar to that of age, discussed above. However, only Shorter et al. (2017) assessed the statistical significance of pre-treatment hearing level in determining hearing deterioration in their study, and determined that there was no significance. Chan et al. (2009) did not assess the effect of pre-treatment hearing, as they performed univariate analysis and found that pre-treatment hearing level was closely associated with age. They therefore used age instead of pre-treatment hearing level in their multivariate analysis on risk factors.

**Middle ear status**

Table 2.6 shows that only three papers studied the effect of middle ear dysfunction on further development of a hearing change, and all three assessed patients being treated for
NPC (Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015). These three papers assessed the development of SNHL in relation to middle ear dysfunction either before treatment or following treatment of NPC. Two of these papers (Oh et al., 2004, and Petsuksiri et al., 2011) determined that pre-existing otitis media with effusion (OME – fluid in the middle ear cavity) was not significant in the development of SNHL. The presence of OME after treatment was a significant factor in determining SNHL after treatment by Oh et al. (2004) and Wang et al. (2015), but these findings contrasted those of Petsuksiri et al. (2011) who also assessed OME after treatment and development of SNHL. As all three papers were deemed to be of high quality (Table 2.3) it is not clear whether or not post-treatment OME is significantly associated with the development of SNHL.

2.5.2.2 Treatment

The main factor that influenced deterioration in hearing was the treatment regime used. Table 2.6 shows that five papers in this review that used inferential statistics to determine changes from baseline hearing in the same ear found statistically significant differences depending on the type of treatment used, and the dosages administered.

Radiotherapy technique

Articles included in this review reported on incidence of hearing deterioration following the more modern techniques of RT, such as 3D conformal or IMRT. Consequently, comparison of these techniques with the older technique of 2D RT is not assessed in detail. However, it is important to note that statistical difference was reported in five papers of this review (Cho et al., 2016; Hsin et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011 and Theunissen et al., 2014b), with less hearing deterioration obtained with the newer techniques. This is because IMRT and 3D-conformal RT allow radiation to conform precisely to the 3D shape of the primary tumour, thereby reducing radiation of adjacent structures (Teo, Ma and Chan, 2004;
It is therefore important to review incidence rates using the most current treatment modalities, and the dosages used.

**Radiotherapy dosage**

Five papers specifically assessed the effect of radiation dosage on hearing deterioration using IMRT or 3D-conformal RT (Chan et al., 2009; Oh et al., 2004; Petsuksiri et al., 2011; Shorter et al., 2017; Wang et al., 2015), although others mentioned the radiation dosages used in their studies. Radiotherapy that is effective in treating primary cancer in the head and neck ranges from 50-70 Gy, regardless of whether this is for general HNC (Cheraghi et al., 2015; Shorter et al., 2017; Theunissen et al., 2014b) or for specifically NPC (Cho et al., 2016; Hsin et al., 2010; Li et al., 2010). With 3D and IMRT imaging techniques, it is possible to calculate radiation dosages to structures adjacent to the primary HNC. Radiation dosage to the cochlea varied depending on the type of primary cancer being treated.

The range of the median dose to the cochlea was between 45-49 Gy when treating NPC only (Chan et al., 2009; Petsuksiri et al., 2011; Wang et al., 2015). However, there was a wide difference in the median dose delivered to the cochlea when treating general HNC, with 11, 18 and 47 Gy reported by Shorter et al. (2017), Theunissen et al. (2014b), and Pan et al. (2005) respectively. This difference was due to each of these three papers containing different proportions of HNC subtypes, including that of NPC. The proportion of patients with NPC was: 3% in Shorter et al. (2017), 0% in Theunissen et al. (2014b), and 11% in Pan et al. (2005), reflecting the differences in the median radiation dose exposure to the cochlea. All three of these papers also showed a large variation in the incidence rate of hearing deterioration (Table 2.3). The variability in incidence rate with radiation dose was shown to be statistically significant in most of the papers that assessed radiation dose and hearing deterioration.
Four out of five papers reported that an increase in radiation dosage to the cochlea was associated with a statistically significant increase in hearing deterioration (Chan et al., 2009; Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015). Some papers reported a cut-off dosage at which hearing deterioration was either reduced or avoided if cochlea exposure was less than this amount. Wang et al. (2015) determined the lowest cut-off at 39Gy. Other authors determined similar cut-off dosages: 47Gy (Chan et al., 2009) and 50Gy (Petsuksiri et al., 2011). However, Oh et al. (2004) found that the much higher cut-off dosage of 64Gy was important in determining treatment induced hearing loss when using 3D-conformal RT. Other studies either used mean IMRT dosage treatment (Petsuksiri et al., 2011) or used a dose response relationship to determine their lower cut-off dosage (Chan et al., 2009). The only paper not to have found a relationship between radiation dosage and hearing deterioration was Shorter et al. (2017), but this was probably due to the median radiation dosage to the cochlea of patients in their study being low at 11Gy.

Chemotherapy

Five papers assessed the effect of cisplatin chemotherapy on hearing deterioration following HNC treatment (Wang et al., 2015; Chan et al., 2009; Oh et al., 2004; Petsuksiri et al., 2011; Shorter et al., 2017). Three of these papers reported that an increase in chemotherapy dosage was associated with an increase in hearing deterioration (Wang et al., 2015; Chan et al., 2009; Shorter et al., 2017) although there was a wide variation in what was deemed to be a significant cut-off dosage. Wang et al., 2015 found a cut-off of 200mg/m² of cisplatin dosage to be important in determining hearing deterioration, whereas Shorter et al. (2017) found a greater value of 588mg/m² as their cut-off. Both Wang et al. (2015) and Shorter et al. (2017) used Fisher’s test and categorical values to determine significance.

However, there were also two papers that did not find chemotherapy as a risk factor to hearing change. Oh et al. (2004) did not find any effect of cisplatin dose on hearing loss in their study; this may be due to the large RT dosages used (65 Gy exposure to the cochlea).
over-riding the effect of cisplatin. Petsuksiri et al., 2011 also reported that cisplatin dosage (cut-off 600mg/m²) was not a factor in determining hearing deterioration, and this contrasted the finding by Shorter et al. (2017) who also assessed hearing change with high dosage chemotherapy. It was not clear why Petsuksiri et al. (2011) and Shorter et al. (2017) gave contrasting findings, but it is noted that whereas all the patients in the study by Petsuksiri et al. (2011) received IMRT, a third of patients in the study by Shorter et al. (2017) were treated by 3D RT.

Interestingly, Wang et al. (2015) reported that carboplatin, when used instead of cisplatin, due to cisplatin intolerance or renal problems, did not increase the risk of hearing loss in the 11 patients in their study.

2.5.2.3 Time after treatment

Although there is much evidence to show that hearing deteriorates with HNC treatment (section 2.5.1 – incidence in hearing deterioration), it is not clear whether hearing further deteriorates over time following treatment. Table 2.6 shows that five papers assessed the incidence of hearing deterioration over time (Chan et al., 2009; Li et al., 2010; Oh et al., 2004; Petsuksiri et al., 2011; Theunissen et al., 2014b). Table 2.7 below shows more clearly the effect of time after treatment on hearing deterioration across different frequency ranges.

<table>
<thead>
<tr>
<th>1st Author</th>
<th>Incidence of HL % 1-3 months PT</th>
<th>Incidence of HL % 6 months PT</th>
<th>Incidence of HL % 1 year PT</th>
<th>Incidence of HL % 2 years PT</th>
<th>Incidence of HL % &gt;2 and &lt;5 years PT</th>
<th>Incidence of HL % ≥5 years PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan</td>
<td>9/49</td>
<td>14/55</td>
<td>12/43</td>
<td>22/50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Li</td>
<td>10/15</td>
<td>32/26</td>
<td>42/73</td>
<td>60/98</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>Oh</td>
<td>22/47</td>
<td>25/38</td>
<td>50/46</td>
<td>33/100</td>
<td></td>
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</tr>
<tr>
<td>Theunissen</td>
<td>78</td>
<td>81</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 2.7 Incidence of hearing deterioration over time

Key: L – low frequency average (0.5, 1 and 2kHz threshold); M-mid frequency average (1-2-4kHz); H-high frequency threshold at 4kHz; E-extended high frequency (>4kHz)
There was no agreement on the effect of treatment on the incidence of hearing deterioration over time (Table 2.7), with three papers showing an overall increase (Chan et al., 2009, Li et al., 2010, and Pan et al., 2005), and two papers showing no change (Oh et al., 2004, and Theunissen et al., 2014b).

However, only Theunissen et al. (2014b) accounted for the effects of ageing on hearing over time, and found no change in the incidence of hearing deterioration at 4½ years after treatment, compared with three months after treatment. However, when assessing changes in average threshold changes (rather than incidence of hearing change), Theunissen et al. (2014b) did find statistically different thresholds in hearing, of p=0.045 in low frequency bone conduction thresholds (0.5-2kHz), and of p=0.014 in mid frequency air conduction thresholds (1-4kHz) when comparing hearing 4½ years after treatment with hearing three months after treatment. Although these results were statistically significant, they were clinically limited to <5dB deterioration in thresholds from three months after treatment to 4½ years after treatment.

Although the focus of this current study is on hearing deterioration, changes in hearing within the early post treatment phase (up to one year) may also be of improvement, which was reported by Oh et al. (2004) due to resolution of middle ear dysfunction. Cheraghi et al. (2015) also reported transient deterioration in hearing following RT, but the authors were not clear whether the inner ear or middle ear was initially affected. It is therefore unclear whether hearing always deteriorates with time following HNC treatment, or if there may be some improvement during the early post treatment phase.

2.5.3 Theme 3 – Patient experience of hearing deterioration

The third question assessed in this literature review was to discover patient experience of hearing loss following treatment of HNC. Three papers were identified: Lastrucci et al. (2017) and Loimu et al. (2015) both used quantitative methodology with questionnaires and
focussed on quality of life, whereas Nund et al. (2015) used interviews and qualitative methodology to explore lived experience.

2.5.3.1 Quality of life

Lastrucci et al. (2017) and Loimu et al. (2015) assessed quality of life in general following treatment of HNC, rather than specifically focussing on hearing related change. Whereas Loimu et al. (2015) assessed quality of life in patients with different types of HNC, Lastrucci et al. (2017) examined quality of life only of patients with NPC.

Lastrucci et al. (2017) had two aspects to their study. The first aimed to identify any risk factors related to side effects after treatment, and the second aimed to assess if toxicity was related to questionnaire scores about quality of life and functional status. Fifty-six patients completed the toxicity assessment, whereas 25 of these went on to complete the questionnaires.

The first aspect, on risk factors related to side effects and toxicity, was assessed in Lastrucci et al. (2017) using the CTCAE v 4.03 (NCI, 2010), at a median time of seven years after treatment. The CTCAE has a hearing related scale that can be monitored using hearing tests (as discussed in section 2.5.1 of this study) or by a clinician rated score. The three grades that are rated by clinicians are: Grade 1 – A subjective change in hearing; Grade 2 – Hearing loss but hearing aid intervention not indicated; Grade 3 – Hearing loss with hearing aid or intervention indicated; (NCI, 2010). Hearing loss of Grade 1 and 2 was reported in 20 patients (32%), second only to xerostomia (lack of ability to produce saliva) as a side-effect following treatment; no Grade 3 hearing loss was reported. Lastrucci et al. (2017) determined that there were no risk factors (age, gender, stage of cancer, time elapsed from the end of treatment, RT technique, chemotherapy) identified with this subjective clinician-rated assessment of hearing loss.
The second aspect, on quality of life, was conducted at a median of four years after treatment, using five questionnaires, of which three were self-rated patients and related to general well-being in NPC patients. One of these questionnaires specifically assessed quality of life following treatment of NPC: The Functional Assessment of Cancer Therapy Nasopharyngeal Cancer Questionnaire (FACT-NP). This questionnaire includes a question on hearing: ‘I have trouble hearing’. Another questionnaire, Functional Assessment of Cancer Therapy (FACT-G) was used to rate quality of life following treatment for any type of cancer, and it has four subscales that are used to assess physical, social/family, emotional, and functional well-being. A third questionnaire used by Lastrucci et al. (2017), the EQ-5D-3L, is a generic instrument used to measure quality of life across the five domains of: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Toxicity scores (obtained from the first aspect of this study, including those for hearing loss) were analysed together with questionnaire scores using the chi-squared test, and there was no statistically significant association between any of these questionnaires and with hearing loss, indicating that hearing concerns did not appear to have an impact on quality of life.

In contrast to Lastrucci et al. (2017), Loimu et al. (2015) assessed quality of life with patients with a range of head and cancers, including those who had cancer in the oropharynx, larynx, hypopharynx, nasal cavity, as well as the nasopharynx. Also, Loimu et al. (2015) assessed quality of life in the early post-treatment phase, using questionnaire scores from baseline as a comparison with those obtained up to one year post-treatment. Loimu et al. (2015) used the validated quality of life 15D patient self-report that has a question on hearing. This question has a 1-5 Likert scale for answering:

- 1 – *I can hear normally*, i.e. normal speech (with or without a hearing aid);
- 2 – *I hear normal speech with a little difficulty*;
- 3 – *I hear normal speech with considerable difficulty; in conversation, I need voices to be louder than normal*;
- 4 – *I hear even loud voices poorly; I am almost deaf*;
• 5 – *I am completely deaf.*

The questionnaire scores obtained were compared with those in the general population and were weighted to reflect the age distribution of the patients. Mann-Whitney U testing was used to determine significant differences between the patients’ own scores, as well as those with the general population. Loimu *et al.* (2015) also used CTCAE for assessing treatment related toxicity (NCI, 2006).

Loimu *et al.* (2015) determined that the dimension of hearing within the 15D questionnaire did not differ significantly throughout the 12 months period, nor did it differ from the general population. Hearing did not differ between the subtypes of laryngeal and pharyngeal cancer, whereas there were differences in other dimensions between these subtypes including the dimensions of speech, breathing, sleeping and mental function. Clinician rated hearing loss was determined in only one patient (2%) with Grade 3 change.

### 2.5.3.2 Lived experience of hearing deterioration

Nund *et al.* (2015) conducted interviews to investigate the experience of communication changes following non-glottic HNC treatment, using a phenomenological approach. They interviewed 14 patients and nine carers to assess the impact of changes to voice, speech and hearing, and they used variation sampling to explore common and shared experiences (Patton, 2002) across different ages (greater or less than 65 years) and gender (male or female).

The four themes that emerged from the study by Nund *et al.* (2015) – listed in Table 2.3 – related to communication difficulties for both patients and carers following cancer treatment. This exploration of hearing related difficulties experienced by survivors and carers was a strength of the study by Nund *et al.*, (2015), and contrasted to quality of life studies by providing real life examples of how daily living was affected. The phenomenological approach adopted by Nund *et al.* (2015) therefore appeared to be successful in obtaining an
understanding of how communication difficulties produced a negative impact on patient experience. However, a weakness was that it excluded survivors who suffered from pre-existing hearing loss and it was not clear how many of those interviewed developed a deterioration in their hearing, nor the extent of deterioration if this occurred. Another observation was that maximum variation sampling was used for selecting patients, but no comment was made on differences in experience regarding age, gender, nor with difference in the severity of hearing loss.

2.6 Discussion on findings from the literature review

This section discusses the findings of this literature review within the wider context of other articles and policy in the field of HNC.

2.6.1 Incidence of hearing deterioration

From the literature examined in this chapter, the majority (12 out of 15) reported the incidence of hearing loss following HNC treatment, and specifically following sensorineural damage. It is noted that half of these papers were on cancers of the nasopharynx. This is not surprising as structures in the nasopharynx lie in close proximity to the ear, and RT for structures in the nasopharynx directly irradiates one or both ears such that the inner ear may receive 80-100% of the prescribed radiation dose (Raaijmakers and Engelen, 2002).

There was a wide variation in the incidence of hearing loss reported, from 4-93% in general HNC, and from 4-98% in treatment of NPC, even after disregarding incidence rates from papers with questionable results (Cho et al., 2016; Niemensivu et al., 2015; Pan et al., 2005). Therefore, further work is needed to establish incidence rates in the UK to gain an understanding of the problem of hearing deterioration in a UK population, using UK current treatment.
2.6.1.1 Incidence in sensorineural hearing loss

All the selected articles reviewed assessed sensorineural type of hearing loss following HNC treatment. The large variation in SNHL obtained in this study was similar to other studies that conducted systematic reviews on HNC treatment. Mujica-Mota, Waissbluth and Daniel (2013) assessed the impact of RT and determined a range in hearing deterioration from 0-85% in the speech frequencies. However, Mujica-Mota, Waissbluth and Daniel (2013) included the results of studies using the now obsolete 2D RT in their findings, as well as those that used non-irradiated ears as the comparator for assessing hearing change. Theunissen et al. (2015) included the assessment of chemotherapy in their review, and reported the range of hearing deterioration of 0-58% in the speech frequencies after RT, and of 5-79% in these frequencies after chemoradiation. As with Mujica-Mota, Waissbluth and Daniel (2013), Theunissen et al. (2015) included results from 2D RT. Therefore, even with the most current therapies used, as examined in the current review, there is a wide range reported in incidence of sensorineural hearing deterioration following HNC treatment.

What is apparent, though, is that it is not possible to apply the results examined in this review of incidence in hearing loss to a general cohort of patients undergoing treatment for HNC in the UK. Papers were restricted in the range of general HNC patients that were assessed (Theunissen et al., 2014b); were not clear if all eligible patients for treatment were recruited (Shorter et al., 2017); or had a different proportion of patients to that diagnosed with HNC in the UK (Cheraghi et al., 2015). There also were no articles pertaining to studies in the UK found in the literature reviewed, and it was difficult to apply those results that were obtained to a UK population because of variation in HNC subtypes that were studied, and variation in treatment used. Such findings highlight the need for an investigation of hearing deterioration following standard UK treatment on a UK cohort of patients with general HNC, to help with forming policy in support of cancer patients. This is important as the UK documentation on improving care in cancer survivorship (DH, 2011) does not include treatment related hearing loss.
2.6.1.2 Incidence in conductive hearing loss

Fewer papers reviewed assessed a conductive (or mixed) type of hearing loss following treatment, compared with those that investigated SNHL, therefore, a study on hearing deterioration in the UK needs also to capture middle ear dysfunction. None of the papers selected for this review focussed on conductive hearing loss, although five of them recorded the incidence of conductive loss change, ranging from 3-44%. The findings also showed that patients who received treatment for NPC were more prone to develop middle ear dysfunction, presumably due to higher radiation dose exposure compared to other subtypes of HNC. However, a reason for a lack of focus in conductive loss is that this type of loss is more associated with transient changes of hearing compared to SNHL (Jereczek-Fossa et al., 2003). When conductive hearing loss does occur, it can be as disabling and handicapping as SNHL (Lutman, Brown and Coles, 2009), and therefore should not be discounted.

In this review, it was seen that incidence of hearing deterioration was less in the low speech frequency range compared with the high frequency range (Chan et al., 2009; Li et al., 2010; Oh et al., 2004; Shorter et al., 2017). These findings are consistent with those reported in animal studies (Konishi, Gupta and Prazma, 1983; Schweitzer et al., 1984; Talmi, Finkelstein and Zohar, 1989). There is merit in assessing low and mid-frequency hearing, as these frequencies contribute to 95% of speech intelligibility, whereas >4kHz frequencies contribute to only 5% of speech understanding (Pavlovic, 1987). However, as shown above, higher frequencies are more susceptible to treatment-induced changes, and are also important in the perception of music and in sounds of nature (Theunissen et al., 2014b). Therefore, incidence of hearing deterioration depends on which frequency range is assessed: whether the focus of enquiry is mainly on speech perception, or on damage to cochlea function. As there is a lack of information in how much hearing deterioration occurs following treatment of a UK population, a study conducted in the UK should first assess SNHL damage of the speech frequencies, essential for communication, rather than the higher frequencies. In
addition, there is need to determine the incidence of conductive hearing loss following treatment of HNC in the UK.

2.6.1.3 Classifying hearing deterioration

There were also different classification systems employed for denoting significant hearing deterioration. The use of single frequency changes, and use of less than a 15dB change may be due to normal variation when performing serial audiometry for the detection of treatment related hearing deterioration (Simpson, Schwan and Rintelmann, 1992). In their study on ototoxicity, Waissbluth, Peleva and Daniel (2017) compared different classification systems currently in use, and reported that the same patient group had incidence in hearing deterioration of 29%, 38%, 54% or 61% depending on which system was used. It is therefore argued that ≥15dB change in hearing, averaged over several frequencies, is most appropriate to use (Konrad-Martin et al., 2010), which is used within the CTCAE classification schemes versions 3 and 4 (NCI 2006; NCI 2009). The CTCAE schema was used in three papers of this review (Cheraghi et al., 2015; Shorter et al., 2017; Theunissen et al., 2014b). This scale assesses changes in the 1-8kHz speech hearing range, so it not only assesses the mid-frequencies that are important for understanding speech, but also the higher frequencies that are more sensitive for detecting ototoxicity (Simpson, Schwan and Rintelmann, 1992).

As it is not clear what is the incidence of hearing deterioration in a cohort of general HNC patients, any future studies on incidence should use standard PTA, and assess standard speech frequencies up to 8kHz. However, such studies must state the conditions and method in which audiometry is performed, as it cannot be assumed that the test is conducted in a standard way. This lack of transparency was a common failing in the literature reviewed in this study. Although other tests, such as OAE tests, have merit in detecting pre-clinical changes in auditory function, in this review there was no evident change in cochlea function in the one paper that assessed these emissions (Niemensivu et
Therefore, it is best first of all to ascertain the scale of perceptual hearing loss using PTA and also use tympanometry as this is important in confirming dysfunction of the middle ear system.

Although it is advocated to establish incidence in hearing deterioration within the peripheral hearing system using PTA and tympanometry, dysfunction of higher auditory pathways needs to be considered. The findings by Li et al. (2010) in the delay of auditory brainstem responses one year following RT, support those of Lau et al. (1992) but contrast those of Low et al. (2005) who found no change in these responses in the longer term. Earlier in this chapter it was mentioned that Li et al. (2010) reported 98% incidence in hearing deterioration with 3D RT, whereas Wang et al. (2015) reported 61% incidence following IMRT. Therefore, it may be that newer radiation techniques reduce radiation exposure to the cochlea, but retrocochlear loss still needs to be considered as possible with newer treatment for HNC.

### 2.6.2 Risk factors associated with hearing deterioration

There were various risk factors assessed in this review, including age, gender, co-morbid disease, recreational activity, tumour size, baseline hearing level, and middle ear status, but there was little agreement in which of these were associated with hearing deterioration.

#### 2.6.2.1 Patient characteristics

**Age**

Hearing deterioration is known to develop with increasing age (Shields, 2006; Davis, Ostri and Parving, 1990), and it has been postulated that the ears in older patients might have pre-existing degenerative changes that make them more vulnerable to irradiation toxicity with HNC treatment (Ho et al., 1999). However, in the current review there were contrasting
findings: two out of five papers that assessed age with hearing deterioration showed a significant change in hearing with increasing age. Other studies on HNC also report contrasting findings on whether age affects hearing deterioration: Honore et al. (2002) found a significant association, whereas (Wang et al., 2015) found no association.

**Gender**

There is evidence to suggest that difference in gender is associated with difference in hearing in general, with men voicing more complaints with hearing compared to women (Shields, 2006; Davis et al., 2007). This may be due to differences in high frequency hearing ability. Men have poorer higher frequency thresholds than women (Gates et al., 1990), due in part to greater exposure to industrial noise (Shields, 2006). Also, higher frequency hearing may be afforded protection by ovarian hormones in women (Murphy and Gates, 1997). Conversely, men have better hearing at low to mid-speech frequencies (Pearson et al., 1995), for reasons not known. However, regarding hearing deterioration in this review, there was agreement in that there was no significant association in the four papers that assessed gender (Chan et al., 2009; Oh et al., 2004, Shorter et al., 2017; Wang et al., 2015). This is in agreement with other studies on HNC (Bhandare et al., 2007; Herrmann et al., 2006), although men have been shown to have significant deterioration in one study assessing long term changes in hearing after NPC treatment (Kwong et al., 1996).

**Co-morbidity**

There is little agreement in general as to whether being diagnosed with diabetes mellitus or hypertension (causing microvascular insufficiency or oxidative stress) makes an individual more susceptible to developing hearing loss (Agrawal, Platz and Niparko, 2009; Aladag et al., 2009; Amoni et al., 2010; Harner, 1981; Parving et al., 1990). However, in this review, both Pan et al. (2005) and Petsuksiri et al. (2011) failed to find an association with these diseases and hearing deterioration.
Recreational activity

Cigarette smoking is thought to contribute to hearing deterioration by adversely affecting antioxidative mechanisms or the blood supply to the ear (Cruickshanks et al., 1998), and high alcohol consumption also is associated with hearing deterioration (Dawes et al., 2014). Both smoking and alcohol consumption are associated with the majority of HNC cases (Donovan and Glackin, 2012; Cohen et al., 2016), however only one paper in this review (Shorter et al., 2017) assessed the association of these substances with hearing deterioration after HNC. Shorter et al. (2017) found a significant association in both high alcohol consumption and high smoking use with an increased incidence in hearing deterioration, although it was not clear what was meant by ‘standard drink’ in their study. In contrast, in one other paper that assessed the effects of alcohol, there was less hearing deterioration in those who consumed alcohol than in those who did not, with the authors speculating that this finding may be due to alcohol improving perfusion of the inner ear (Herrmann et al., 2006), so it is difficult to draw definitive conclusions.

Tumour size

There was a lack of agreement as to whether tumour size affected hearing deterioration in this literature review, with two (Hsin et al., 2010; Wang et al., 2015) out of three papers determining a significant association. It may be that with these two papers that assessed treatment of NPC, there was more radiation dosage affecting the cochlea with an increase in the nasopharynx tumour size. However, in the paper by Shorter et al. (2017) on general HNC, tumour size was not found to be significantly associated with hearing deterioration, probably as cancers in their study were more distal to the cochlea than those of the nasopharynx.
Pre-treatment hearing level

Only Shorter et al. (2017) in this review assessed baseline hearing level, and these authors found no significant association between this and hearing deterioration. This finding agreed with Grau et al. (1991). However, these findings contrasted with Zuur et al. (2007) who found that patients with better pre-treatment hearing levels suffered more severe hearing loss than those who possessed poorer hearing to start with.

Middle ear status

It has been suggested that middle-ear effusion after RT is evidence of radiation complication and a potential cause for damage in the inner ear and development of persistent SNHL (Wang et al., 2004). However, there was no agreement in three papers within this review as to whether middle ear dysfunction was a factor in determining further hearing loss: Oh et al. (2004) and Wang et al. (2015) found a significant association with development of SNHL with post treatment OME, whereas Petsuksiri et al. (2011) failed to do so.

2.6.2.2 Treatment

There was evidence to suggest that an increase in radiation dose was associated with hearing deterioration. Four out of five papers in this review reported that an increase in radiation dosage to the cochlea was associated with a statistically significant increase in hearing deterioration (Chan et al., 2009; Oh et al., 2004; Petsuksiri et al., 2011; Wang et al., 2015). This finding is consistent to that reported in other literature (Schot et al., 1992; Bhandare et al., 2007). Only Shorter et al. (2017) in the current review did not find a significant association with dose and hearing deterioration, but this was probably because of the low radiation dosages with IMRT used in their study.

However, there was less agreement in the effect of chemotherapy on hearing deterioration, with only three out of five studies finding a significant association between increased
cisplatin levels and increased hearing deterioration (Wang et al., 2015; Chan et al., 2009; Shorter et al., 2017). Those that did not find an association between chemotherapy and hearing deterioration either investigated patients exposed to large radiation dosages (Oh et al., 2004), or to 3D RT (Petsuksiri et al., 2011) that may have masked the effect of the chemotherapy. Other papers suggest that increased hearing loss does occur with increase in cisplatin dosages (Chen et al., 2006; Zuur et al., 2007). Interestingly, Wang et al. (2015) reported that carboplatin, when used instead of cisplatin, due to cisplatin intolerance or renal problems, did not increase the risk of hearing loss in the 11 patients in their study. This merits consideration of carboplatin as an alternative to cisplatin treatment for aural protection in treatment of HNC.

Although none of the 15 papers included in this literature review assessed hearing deterioration following surgery alone, Cancer Research UK report that conductive hearing loss can occur with surgery to treat paranasal cancer (Cancer Research UK, 2018e). Hyde and Bailey in 2000 reported conductive hearing loss amongst patients who received surgery for maxillary sinus cancer. However, UK guidelines now advocate that RT or CRT is always used following surgery for all stages of paranasal cancer (Palaniappan, Owadally and Evans, 2015), and a study by Won et al. (2009) reported no incidence of hearing loss in 44 patients treated for paranasal cancer by a combination of surgery with RT or CRT, which may indicate improvement in surgical techniques to minimise damage to the ear.

2.6.2.3 Time after treatment

Chan et al. (2009) and Li et al. (2010) reporting on NPC, and Pan et al. (2005) reporting on general HNC, recorded an increase in the incidence of hearing deterioration with time. However, hearing deterioration is known to increase with increasing age (Shields, 2006; Davis, Ostri and Parving, 1990). It is therefore important to correct for the effect of ageing with hearing change, which was not performed in any of these three studies. Only Theunissen et al. (2014b) accounted for the effect of ageing on hearing in their study, and
although they noted statistically significant deterioration in hearing at 4½ years after treatment, the change was less than 5dB which is of minor clinical significance. Of interest was the finding that hearing within the first year after treatment may not only deteriorate, but may also show improvement, and this is important to consider when informing patients of the possible outcomes of their hearing after treatment.

Therefore, there was no conclusive evidence from the studies reviewed regarding the influence that the following factors have with hearing deterioration after HNC treatment: a patient’s age or gender, their pre-existing hearing status, their tumour size or location, or when after treatment the assessment is made. However, there is strong evidence to suggest that more modern techniques of radiation treatment (e.g. IMRT) decrease incidence of hearing deterioration, and that an increase in RT dosage or in chemotherapy (cisplatin) dosage increases the rate in incidence of hearing change. Therefore, to help inform UK policy, it is important to study hearing deterioration on a general cohort of HNC patients using current UK treatment regimen.

### 2.6.3 Patient experience of hearing deterioration

#### 2.6.3.1 Quality of life

The two questionnaire studies included in this literature review appeared to indicate that hearing changes following HNC treatment do not have an impact on quality of life (Lastrucci et al., 2017; Loimu et al., 2015). However, part of these studies involved the use of clinician rated scoring. Clinician rated scoring is known to underestimate the effect of speech and voice problems encountered by patients (Lazarus et al., 2014; van der Molen et al., 2012). Therefore, it is not clear whether the toxicity assessment made by the clinicians regarding hearing change, according to CTCAE, could also be an underestimate. Also, a sizeable number of patients who had toxicity assessment did not complete the questionnaires. Five refused to take part and it is assumed that the remaining 18 had died. It is not certain how
many of these 23 patients were affected by hearing difficulties, and how they would have answered the questionnaires; their responses could have been significantly different regarding quality of life. However, the study by Loimu et al. (2015) did use a patient rating self-assessment questionnaire that also indicated that hearing change following HNC treatment did not have an impact on patients. However, in comparison to other dimensions assessed in the 15D questionnaire, hearing change may not be a priority to patients, so that when answering questions together, hearing may not be scored that highly. It might be better to have a study that only assesses hearing on its own, or in the context of communication, to tease out difficulties that are encountered, as in an interview study.

2.6.3.2 Lived experience of hearing deterioration

The one interview study in this current review on lived experience (Nund et al., 2015) clearly suggested, in contrast to Loimu et al. (2015) and Lastrucci et al. (2017), that communication change arising from hearing deterioration does adversely impact patient experience. Another article on the lived experience of patients with HNC found that patients felt isolation due to their difficulties with speech articulation in communication (Swore Fletcher et al., 2012). Patient experience of hearing loss is generally negative, with associated feelings of loss and isolation, and of stigma associated with the loss (Aquino-Russell, 2006). One strength of the study by Nund et al. (2015) was its exploration of hearing-related difficulties experienced by survivors and carers, but a weakness was that it excluded survivors with pre-existing hearing loss and it was not clear how many of those interviewed suffered from a hearing deterioration, nor the extent of deterioration if this occurred. In order to obtain an understanding of the contribution that hearing has on patient experience, it will be necessary to conduct a separate study that focusses on hearing alone, and includes those who may have pre-existing hearing loss. In view of the lack in sensitivity of quantitative methods in drawing out this experience, a qualitative study appears to be most suited to do this.

As this literature review has indicated, there is limited awareness of the impact of hearing
deterioration following HNC treatment. The NHS (2016) has focussed on the need to have patient-centred care, and has developed a holistic needs assessment of patients who have had cancer. Although some local centres have created patient concerns inventories that include patient rating of hearing concerns after treatment (Aintree University Hospital, 2017), others have inventories that do not yet include hearing (London Cancer Alliance, 2013). There is therefore a need to identify patient experience in hearing deterioration more widely to update policy as required to improve living well in cancer survivors.

2.7 Summary of literature review

This literature review has shown that hearing deterioration is an important side-effect to consider following HNC treatment. However, there is a wide variation in the rates in incidence of hearing loss following HNC treatment, mainly due to different classification systems used to define clinically significant hearing deterioration, and also due to different subtypes of HNC that were treated. In addition, there were no papers found on hearing deterioration following current treatment of a UK population. Also, there is little understanding of the impact that hearing loss has on patient experience for those who have hearing-related change with HNC treatment. Although there is a rising incidence of HNC cases in the UK, current UK policy and associated research indicates that there is a lack of awareness of hearing related problems resulting from cancer treatment (DH, 2011).

In view of these findings, this current study aimed first to assess the incidence of hearing deterioration in patients following current treatment of HNC in order to gauge the extent of this problem in a UK centre, and to explore patient experience following this deterioration. It is proposed that this study would create a clearer picture of the risk and incidence of hearing loss in UK HNC patients, and therefore this study could be of use to raise awareness of the issue with practitioners about the needs of patients, with updating policy as required, and improving quality of life for cancer survivors by better monitoring and early intervention.
Chapter 3 Methodology

3.1 Introduction

Chapter 2 reviewed literature on hearing deterioration in HNC patients following treatment, and it became apparent that there were no UK publications describing the incidence of hearing deterioration in this population. In addition, the review revealed that there was limited exploration on the impact of this deterioration on the patient experience of HNC in the UK or elsewhere. To address this lack of information, the aims of the current study were delineated as follows:

The primary research aims were, for patients who were due to receive current treatment in a UK hospital -

1. to assess the incidence and severity of hearing deterioration after treatment for head and neck cancer;

2. to explore the lived experience of participants with hearing deterioration after treatment for head and neck cancer.

The secondary aims were -

a. to describe overall hearing levels;

b. to determine types of hearing loss; and

c. to explore the incidence and severity of hearing deterioration in relation to patient demographics and types of treatment.

This chapter discusses the chosen methodology, and gives an overview of the methods, appropriate to investigate the research aims as set out above. It will provide the rationale behind the design used. The chapter begins with the context of the study and the theoretical perspective underpinning the research, as these elements were integral in formulating the research aims.
3.2 Context and theoretical framework

The premise of this study was that hearing deterioration, associated with treatment for HNC, has a negative impact on patients. At the study centre, some adult patients had completed treatment more than two years before seeking help with their hearing. It was not clear as to why patients were being seen two years after treatment: was hearing loss progressive and only caused a problem many years after treatment? Did patients suffer hearing loss soon after treatment but were not aware of support they could receive? Did patients experience hearing loss soon after treatment, but were not concerned as they had survived their cancer? These questions formed the basis of the primary research aims -

- First, to determine the extent of the phenomenon of hearing deterioration following head and neck cancer treatment by measuring hearing change. The focus here was to assess the incidence and severity of hearing deterioration, particularly in the early post treatment stage, for patients undergoing current UK treatment;
- Secondly, to explore patient experience of hearing deterioration for this patient group.

The literature review in Chapter 2 revealed that there have been many articles (all conducted outside the UK) that investigated measurable hearing deterioration following CRT or RT alone (Theunissen et al., 2015). This was the first UK study to explore incidence and severity of hearing deterioration in patients with general HNC undergoing current UK treatment, including single or multimodal treatment. Following this quantitative enquiry, participants with varying levels of hearing deterioration were selected for assessment of their experience of hearing change in the context of cancer treatment. Therefore, both quantitative and qualitative methods were required to investigate hearing deterioration after HNC treatment for this study.
3.2.1 Critical realism

All aspects of this study were consistent with the theoretical framework (paradigm) of critical realism; critical realists believe that phenomena exist, but that all aspects of phenomena cannot be fully known (Illing, 2010). The phenomenon of hearing deterioration was the focus of enquiry for this study, and deterioration can be identified and measured using different criteria (Theunissen et al., 2015). Arguably, experience of hearing deterioration will vary depending on the context in which the deterioration occurs, and this variation accords with the critical realist understanding of phenomena. Further, critical realists believe that phenomena are understood by employing both quantitative methods and qualitative methods (Bazeley and Kemp, 2012). The majority of research enquiries discussed in Chapter 2 focussed on measuring hearing deterioration following treatment of HNC. The hypothesis for those studies (Chan et al., 2009; Cheraghi et al., 2015; Cho et al., 2016; Hsin et al., 2010; Li et al., 2010; Niemensivu et al., 2015; Pan et al., 2005; Petsuksiri et al., 2011; Shorter et al., 2017; Theunissen et al., 2014b) was that there was an association between hearing deterioration and treatment. For example, Chan et al. (2009) stated that ‘sensorineural hearing loss is a common and important complication after RT in patients with nasopharyngeal carcinoma’; and Theunissen et al. (2014b) mentioned that ‘both RT and cisplatin are known for their ototoxic effects, leading to hearing loss’. These studies used deductive (quantitative) methods for determining incidence of hearing deterioration.

However, the researcher was aware that individuals experience similar hearing impairment levels differently (Meddis et al., 2010; Harrison, 2016). Consequently, it can be difficult to predict how an individual will be affected in every-day life following a deterioration in their hearing, as there will be variation in people’s attitude to hearing impairments, and also variation in people’s communication and other hearing difficulties (Thomas, 1988).

In addition to assessing the extent of hearing deterioration, the researcher wanted to explore patient experience of hearing deterioration, and thereby gain an understanding of the range of problems specific to this group of patients. Two papers that were reviewed in Chapter 2
used quantitative questionnaire studies which indicated that hearing deterioration following HNC treatment does not have an impact on quality of life (Lastrucci et al., 2017; Loimu et al., 2015). However, it is known that clinician rated measures (as used in these studies), may under-estimate problems encountered by patients (Lazarus et al., 2014; van der Molen et al., 2012). Subsequently, the findings from Lastrucci et al. (2017) and Loimu et al. (2015) contrasted those of Nund et al. (2015) who reported that hearing deterioration did impact on patient experience in their study on broad communication difficulties following HNC treatment. Nund et al. (2015) used the process of induction to gain knowledge of patient experience using qualitative methods; induction is the process of piecing together information from participants to see if there are common themes (Carlsson, Nilbert and Nilsson, 2006).

In addition to the belief that an understanding of phenomena can only be approximate, critical realists also believe that interpretation of this information is influenced by the experience and background of the researcher (Phillips and Burbules, 2002). Through his clinical work, the researcher came to this project with an awareness of the impact that hearing deterioration has on patients. He also brought to the project knowledge and expertise in interpreting the severity of hearing deterioration, and an awareness that patients are affected by their hearing deterioration in different ways. Consequently, his experience contributed to his interpretation of the results obtained in this study. The critical realist paradigm was deemed to be the most appropriate theoretical framework to use for underpinning this research.

3.3 Methodology

As stated above, most studies on hearing deterioration have focussed on measuring the incidence of hearing change (Theunissen et al., 2015; Mujica-Mota, Waissbluth and Daniel,
2013) using quantitative methods. To explore both incidence and patient experience of hearing deterioration, the methodology of mixed methods was used for this study. Mixed methods research draws on the results from quantitative and qualitative methods by incorporating both the importance of the physical world as well as that of human experience (Johnson and Onwuegbuzie, 2004). The mixed methods approach was required to explore both measurable psychoacoustic change (a change in the perception of sound) and the lived experience in suffering from hearing deterioration following HNC treatment. Mixed methods methodology has two distinct phases for each of the quantitative and qualitative methods used, and also requires a level of integration between the phases (Leech and Onwuegbuzie, 2009). There are various designs for these different phases (Terrell, 2012) that may require weighting of the relative importance of each (Creswell, 2003). The research design for this study will be discussed in the next section.

3.4 Research design

The current study employed a sequential model design (Terrell, 2012; Ivankova, Creswell and Stick, 2006) with the quantitative phase followed by the qualitative phase (Figure 3.1 above). It was necessary for the phases to be arranged this way because the quantitative phase data was used for selecting participants for the qualitative phase, as it was important
to recruit people with hearing deterioration for the qualitative interviews. There were two levels of integration between the phases: first, the selection of participants for the qualitative phase, using the data from the quantitative phase, and secondly in the interpretation of the results from each phase. The study design was constructed to address the four areas outlined by Creswell (2003):

**Implementation**: what sequence of (qualitative and quantitative) methods is used in the overall research design?

**Priority**: which methods are most important in data analysis, particularly in influencing decisions when findings from different methods do not agree?

**Integration**: at what stage of the research design are the data from the different methods put into relation with each other?

**Theoretical perspective**: is the theory informing the analysis explicit from the beginning or emergent during the research process?

Table 3.1 Characteristics of mixed methods studies (from Creswell, 2003)

### 3.4.1 Implementation – Determining sequencing of methods

The first aspect to consider when conducting mixed methods study is how the two phases are undertaken time wise in relation to each other (Table 3.1). Selection of participants for an exploration of their experience of hearing deterioration required first the identification of participants with a measured deterioration in their hearing. The study needed to start therefore, with the quantitative phase. The sequential design, with completion of the quantitative phase prior to starting the qualitative phase, was therefore chosen in preference to a concurrent or nested design, where there is overlap in the phases (Terrell, 2012).

Another mixed methods approach that could have been used was for the qualitative phase of the study to be conducted concurrently with the quantitative phase, so that the examination of the lived experience of each participant was conducted at the same interval.
in the early post treatment stage. This design would have provided a full exploration of the
experience of hearing deterioration, as all participants identified with hearing change would
have been selected for the qualitative phase. However, this design was not adopted for
theoretical and practical reasons. It was not known how many participants would have
hearing deterioration, and there was the possibility of repetition and duplication of responses
in conducting an exploration of experience on all the participants. Corbin and Strauss (2014)
discussed this idea of theoretical saturation when a researcher has explored in-depth
categories or themes identified in qualitative research. On the practical front, there were time
constraints in conducting the study, as it was necessary to plan the quantitative and
qualitative phases separately, to accommodate the researcher’s limited time available in
maintaining both study and work requirements.

An alternative method would have been to perform a quantitative assessment on one group
of participants and a qualitative study performed on another group, resulting in two separate
studies. Even if the same criteria of hearing deterioration were used for selection of
participants for the qualitative assessment, because the two groups would have different
demographic characteristics, the phenomenon of hearing deterioration would be assessed in
different contexts, making it difficult to integrate data from each group. If different criteria of
hearing deterioration were used in selection of participants for the qualitative phase, different
patient experience would be obtained, and again it would be difficult to integrate the data to
obtain the benefits of mixed methods study. Consequently, it was necessary to conduct the
two phases of study on the same patient group.

3.4.2 Priority – Determining which phase was ascribed priority

The second aspect to consider when conducting mixed methods study is which, if either, of
the two phases that are conducted, is given priority (Table 3.1). The data from the two
phases provided information on different aspects of hearing deterioration; Phase 1 provided
data on a measured amount of hearing change, whereas Phase 2 provided patients
experience of this change. Therefore, an assessment of convergence, divergence or correlation of the results from each phase was not applicable, and both the quantitative and qualitative phases were given equal importance. However, the phases were ascribed different priority based on novelty and policy perspectives:

- **Novelty** - In this study, the qualitative phase was given more priority and weight of significance than the quantitative phase from a novelty aspect, because up until the present study there was limited information on patient experience of hearing deterioration. There is only one other study (Nund et al., 2015) that includes some aspect of qualitative methodology to explore experience of hearing deterioration following HNC treatment. Consequently, it was anticipated that the current study would provide novel findings on the experience of hearing deterioration, as the qualitative phase focussed on the impact of the experience of hearing change, rather than on more broad communication change as in Nund et al. (2015). Conversely, although there have been no recent studies that have assessed the extent of hearing deterioration following HNC treatment in a UK hospital, there are already many other studies from other countries that have measured the extent of hearing deterioration (for example Chan et al., 2009; Cho et al., 2016; Pan et al., 2005). So, although the quantitative phase was expected to provide new data from a UK population to add to existing knowledge on incidence of hearing deterioration, the qualitative phase was expected to produce more novel findings.

- **Policy** - The quantitative phase of this study had more priority than the qualitative phase for informing policy, as arguably, health policy in both audiology and HNC is currently dominated by quantitative evidence. The quantitative phase of the study provided data on incidence of hearing deterioration, types of hearing loss, and risk of hearing deterioration following HNC treatment which would be used for planning services effectively. However, it was the contention of this study that findings from the qualitative phase of the study should have considerably more importance than has been the case in the shaping of policy, as patient experience of cancer survivorship is now being recognised (NHS, 2016).
3.4.3 Integration – Determining links between the phases

The third aspect to consider when conducting mixed methods study is how data from each of the phases mix, or integrate with each other (Table 3.1). There were two areas of integration in this study and these are shown in Figure 3.1. The first stage of integration was in the sampling for the qualitative phase of the study. Results of the quantitative phase were used to inform the sampling for qualitative data collection; participants identified with hearing deterioration were eligible for selection for the qualitative phase of study. The second stage, at which the data from each of the different phases were mixed was in interpretation (which took place in both Chapters 6 and 7), where the results were explored to understand experiences of patients who had different levels of hearing deterioration, and to establish if there were any patterns or risk factors that were related to patient experience.

It has been argued that a truly mixed methods study is one that integrates results from quantitative and qualitative data (Kroll and Neri, 2009), with the conversion of data into either quantitative or qualitative forms for comparison (Onwuegbuzie and Teddlie, 2003). A study that does not integrate results could possibly be regarded as two distinct studies viewing the same phenomenon from different angles, and studies that utilise mixed methods in this way often publish results in separate papers (O’Cathain et al., 2007). Although, data were not integrated by conversion, the results of the quantitative and qualitative phases were brought together to provide a more complete understanding of hearing deterioration, including whether this phenomenon was homogeneous or heterogeneous for study participants.

3.4.4 Theoretical perspective

The premise of this study was that hearing deterioration, associated with treatment of patients with HNC, has a negative impact on these patients. To help inform policy for cancer survivorship in the UK, it was necessary to quantify the incidence and severity of deterioration for a population receiving treatment of hearing deterioration using UK treatment
protocols, prior to exploring the lived experience through qualitative enquiry. The critical realist approach underpinning this study has been discussed as being appropriate to use earlier in this chapter. However, alternative frameworks could have been used.

3.4.5 Alternative theoretical frameworks

The use of both quantitative methods and qualitative methods (in mixed methods methodology), was required to address the research for this study. Research paradigms that focus only on the use of either quantitative methodology alone (positivism – Guba and Lincoln, 1994) or qualitative methodology alone [for example constructivism – Guba and Lincoln, 1994; or phenomenology – (Lopez and Willis, 2004)] were not appropriate for underpinning this research.

However, there are other paradigms that facilitate the use of both quantitative and qualitative methods that may have been suitable for underpinning this research. The pragmatist uses whatever methods are most suitable to answer the research question, rather than focussing on what the nature of reality is (Morgan, 2007; Creswell and Plano Clark, 2007; Feilzer, 2010). Dialectical pluralism is a metaparadigm that allows researchers and stakeholders from different paradigmatic positions to embrace these differences and create a holistic understanding of phenomena (Burke Johnson, 2015). However, it appears to the researcher that the dialectical pluralistic approach may be another form of pragmatism to answer research questions. As the researcher believes that different aspects of reality are discovered through different types of research, the critical realist stance appeared most suitable for formulating ideas of how to study the phenomenon of hearing deterioration. In this research project, hearing deterioration was the reality being investigated, with insight obtained specifically on incidence, severity and patient experience in the context of HNC treatment. A detailed description of which type of quantitative and qualitative methods that was used in this study will now be discussed.
3.5 Quantitative methods

To assess incidence and severity of hearing deterioration after HNC treatment (the first of the primary aims of this study) it was necessary to assess changes in psycho-acoustic hearing levels before and after treatment, using a non-experimental, observational prospective repeated measures method. The repeated measures method enables the measurement of hearing at different time points for a cohort (Mark and Reichardt, 2009). This method, used in other studies discussed in the literature review (Li et al., 2010; Oh et al., 2004), was the most appropriate to use for this study, as it did not seek to establish causality (required for experimental methods) – nor did it seek to establish the effectiveness of an intervention (used in quasi-experiment methods – Walliman, 2006). The repeated measures method, using psycho-acoustic hearing tests, was also used for addressing the secondary research aims of this study that were: (a) to describe overall hearing levels; (b) to assess types of hearing loss; and (c) to explore the incidence and severity of hearing deterioration in relation to patient demographics and types of treatment.

3.6 Qualitative methods

For this study, the second primary research aim was to assess the lived experience of participants with hearing deterioration after treatment for HNC. The significance that patients gave to their lived experience was of interest, rather than a description of the reality of their experience, so an approach informed by interpretive phenomenology (Lopez and Willis, 2004), appeared most appropriate to use.

The approach informed by interpretive phenomenology fits within the critical realist stance underpinning this study and provided the qualitative approach to the mixed methods design. The qualitative inquiry provided an understanding of how patients experienced, and were affected by, hearing deterioration in the context of HNC treatment. The specific context from which experiences are being drawn is considered important within interpretive
phenomenology, as is the specialist knowledge of the researcher. Both these aspects were relevant for this study. Because of his awareness of the impact of hearing deterioration, and desire to provide knowledge and inform policy, the researcher determined to explore the phenomenon of deterioration in the context of cancer treatment.

3.7 Summary

This chapter has demonstrated how the critical-realist paradigm adopted by the researcher underpinned both the research aims and the mixed methods approach used for investigation in this study. The critical-realist approach provided the philosophical framework for determining both the incidence and severity of hearing deterioration, and the assessment of patient experience of this deterioration, following HNC treatment. This study employed a sequential design, with the quantitative data collection phase followed by a qualitative data phase, in a mixed methods design. This design included integration between the two phases of study at two stages: first, with quantitative data used to inform appropriate sampling for the qualitative phase; and secondly, with integration of results by interpretation of data in Chapters 6 and 7 (Results – Qualitative data, and Discussion, respectively) of the study. A non-experimental, observational prospective repeated measures method was used for obtaining quantitative data, and a method informed by interpretive phenomenology was used to provide qualitative data to explore and assess the lived experience of hearing deterioration following HNC treatment.

The next chapter provides an account of the methods used for conducting the research study, and the instruments that were selected as most appropriate for data collection in both the quantitative and qualitative phases of this study, based on the methods of repeated measures, and an approach informed by interpretative phenomenology, respectively.
Chapter 4 Methods

4.1 Introduction

This chapter presents the chosen methods for determining hearing deterioration, and the chosen research instrument to explore patient experience. It first shows the timeline for the study, and then presents the overall schema of the quantitative and qualitative methods used. The chapter continues to discuss the methods used for conducting the study and presents each phase of the study in turn, starting with the quantitative phase. For each phase, criteria used for determining the study sample for data collection will be discussed, followed by an outline of the process for recruiting participants, and then an in-depth discussion of the instruments used for data collection. The method employed for data collection and analysis is then described. The chapter concludes with ethical and governance considerations for conducting the study.

To re-iterate, the primary research aims were, for patients who were due to receive current treatment in a UK hospital:

1. to assess the incidence and severity of hearing deterioration after treatment for head and neck cancer; and
2. to explore the lived experience of participants with hearing deterioration after treatment for head and neck cancer.

The secondary aims of this study were:

a. to describe overall hearing levels;
b. to determine types of hearing loss; and
c. to explore the incidence and severity of hearing deterioration in relation to patient demographics and types of treatment.
4.1.1 Study timeline

The timeline for conducting the study is shown in Figure 4.1:

![Figure 4.1 Study timeline](image)

4.2 Quantitative phase

This first phase of the study, outlined in Figure 4.1, comprised a series of hearing tests: within two weeks of cancer diagnosis (Test 1), at the end of treatment (Test 2), and three months after completion of treatment (Test 3). Data obtained within this phase were used to address the first of the primary aims of the research project, and all three of the secondary aims.

4.2.1 Sample size

The quantitative phase of the study was conducted to collect data to determine the incidence (by proportion) of patients who had hearing deterioration following treatment and to differentiate levels of severity. Participants for the project were invited from among patients who were consecutively diagnosed with HNC by oncologists at the researcher’s hospital.
This method of selection is called ‘convenience consecutive sampling’, where study participants are drawn from a population receiving treatment in one institution (Teddlie and Yu, 2007). Consecutive sampling is convenient for recruitment in studies, particularly if there is limited time for conducting the research, but the sample may not be fully representative of the population (Bowers, House and Owens, 2011). For this study, participants were recruited over a 6-month period. The one-year survival rate of HNC patients varies considerably, between 60-90%, depending on location and stage of the cancer with an aggregate of 80% survivorship (OCIU, 2010). Consequently, an attrition rate of approximately 20% was assumed in this study.

It was necessary to estimate how many participants should be recruited to increase the validity of the results obtained. The estimate was determined using data obtained from the pilot study performed prior to the current project (Appendix 4.1). The pilot compared the hearing of a group of patients (from a range of HNCs) prior to treatment, with those tested after treatment, and assessed the average difference in 6 or 8kHz (high speech frequencies), as RT and CRT affect mainly high frequencies of hearing (Zuur et al., 2007). A hearing difference of approximately 15dB was determined across these frequencies, and this criterion was deemed to be most appropriate for detecting hearing deterioration (see discussion in Chapter 2).

The focus of the current study was to identify the quantity of patients who had an average of 15dB deterioration in hearing following treatment, rather than to determine the average threshold shift. However, it was necessary to estimate how many patients would have at least a 15dB deterioration for recruitment. Siobhan Crichton, statistician from King’s College London, used raw data from the pilot data, and stated: ‘With 38 patients, there will be 80% power to detect a change of 15dB between pre and post treatment (averaged across frequencies of 6 or 8kHz) between time 1 and 2, or time 1 and 3 (of the three time points used in the study), using a paired T-test and assuming a standard deviation of 8.9 (taken from the pre-treatment hearing pilot data) and an overall 5% level of significance. Allowing
for 15% drop-out rate 44 patients will be recruited’. Adapting the attrition rate from 15% to 20% meant that 48 participants needed to be recruited for 38 to complete the study and enable 80% power for the study. The throughput of newly diagnosed HNC patients at the study centre is 200 per year, of which 60-70% would require RT or CRT (Palaniappan, Owadally and Evans, 2015); therefore, approximately 60 patients would be eligible within the 6-month recruitment period allowed for this study. Although it was not known how many of these patients would be eligible to participate, or who would decline participation, it was suggested that approximately 20% may not be recruited, as van den Berg et al. (1997) determined a refusal rate of 17% in their clinical trial. Therefore, it was anticipated that 48 patients would be recruited to the study over a period up to six months, to allow for those who would not consent or would not be eligible for involvement. Of these, 38 would complete the study (due to 20% attrition rate, OCIU, 2010), which would be sufficient to enable 80% power.

Although 50 participants would be sufficient to draw statistical significance from this study, more would need to be recruited for identifying the incidence of hearing deterioration in the UK. However, due to timeframe constraints for completing the study, it was not possible to increase the time for recruiting at the study centre. In addition, it would be necessary to conduct studies across different UK centres to allow for regional differences in diagnosis of HNC subtypes. Therefore, the results from this study would only reflect incidence of hearing deterioration at this local tertiary UK centre.

### 4.2.2 Recruitment

Patients were recruited from the study centre on a consecutive convenience sampling basis following a diagnosis of HNC from February 2015 to August 2015, over a period of six months. It is recognised that consecutive sampling has limitations as it may not account for seasonal variation and the sample population may not be fully representative of the population being assessed, however consecutive sampling is convenient particularly if there
is limited time for conducting research (Bowers, House and Owens, 2011). An oncologist who diagnosed the HNC of potential participants gave them an information sheet to explain the purpose and nature of the study. On the same day, the potential participant met the researcher to discuss any questions that the patient had regarding involvement in the study. Following a period of at least 24 hours, the researcher again met the potential participant to obtain written, informed consent to participate in the study. Patient demographics including age, date of birth, gender, type of cancer and the treatment method to be used, were recorded. Additional information on aetiology of HNC, and type and dosage of treatment was obtained from medical notes. Participant information was stored on an excel spreadsheet that was password secured (see section 4.5.1 on ethical considerations). Participants were recruited using the following inclusion and exclusion criteria:

4.2.2.1 Inclusion criteria

- newly diagnosed with HNC;
- aged 18 years and over;
- due to receive standard curative treatment using calibrated equipment and administered by trained clinicians [RT, administered as IMRT using calibrated equipment, and if administered chemotherapy (adjuvant to RT or concurrent with RT), using cisplatin, carboplatin or cetuximab];
- able to provide written informed consent.

4.2.2.2 Exclusion criteria

- patients requiring interpreter services (there was no funding arrangement to obtain interpreters for this study);
- patients with a pre-existing audiological condition e.g. Meniere’s disease;
- patients with ear wax not removed prior to testing.
4.2.3 Instruments used to measure hearing deterioration

Pure tone audiometry is the standard technique used to measure psycho-acoustic hearing thresholds (BSA, 2011). The PTA technique requires participants to respond each time they hear a sound. Sound stimuli are presented at different intensity levels within the speech frequency range, and the threshold of hearing for each frequency of sound is recorded. Test stimuli can be produced from either air or bone conduction transducers. Responses made from air conduction stimuli represent a subject’s ability to hear sounds throughout the whole hearing pathway; those made from bone conduction stimuli assess hearing from the cochlea to the auditory cortex. Difference in air and bone conduction thresholds may demonstrate a block in sound transmission, such as temporary build-up of fluid within the middle part of the ear (Hsin et al., 2013).

Pure tone audiometry hearing testing was performed by different audiologists within the study centre using a standard technique (BSA, 2011). Each audiologist has been trained and assessed as competent in performing PTA. Testing was performed in a standardised, soundproofed room, using audiometers calibrated to deliver standard audiometric sound pressures for speech frequencies at 0.25, 0.5, 1, 2, 3, 4, 6 and 8kHz for air conduction stimuli, and at 0.5, 1, 2, 3 and 4kHz for bone conduction stimuli. Air conduction and bone conduction thresholds at each of these frequencies were measured for each ear at the three hearing testing time points for this study. Testing used a standard, reliable and reproducible approach, and generated valid measurements. The use of audiologists in addition to the researcher minimised researcher bias for this study, and each audiologist used the same standard technique.

Tympanometry is an audiology test that assesses the function of the middle ear component of the peripheral auditory system. Tympanometry was performed in addition to PTA to identify if hearing loss comprised a component of middle ear dysfunction, and so assisted with determining type of hearing (being normal hearing or hearing loss of sensorineural, conductive
or mixed type). Tympanometry was performed using standard impedance meters within a standardised environment and using a recognised technique (BSA, 2013). Middle ear measurement parameters of peak pressure, maximum compliance, and ear canal volume were recorded for each ear at the three hearing testing time points, and the numerical values were recorded and stored on an excel spreadsheet.

Audiometers for performing PTA, and middle ear analysers for performing tympanometry, in this study were calibrated to deliver test stimuli and record responses in accordance with relevant BS EN ISO standards (BSA 2011; BSA 2013). The use of standard equipment and techniques for performing and interpreting hearing test results were required for obtaining valid and repeatable results. Ethical approval for the study is found in section 4.5 of this chapter.

4.2.4 Data collection

All of the participants who enrolled in the study were due to have hearing testing (PTA and tympanometry) at Test 1, Test 2 and Test 3:

- Test 1 – within two weeks of diagnosis and prior to their treatment, all participants had a baseline hearing test by a trained audiologist at the hospital where the study was conducted and where this procedure is standard practice. It was anticipated that this would be the participant’s scheduled routine hearing test prior to the commencement of their cancer treatment. The majority of participants had their pre-treatment hearing test immediately after consenting to take part in the study. Testing was on a day that participants also had a pre-treatment dental appointment to minimise inconvenience and maximise attendance compliance. Some participants required dewaxing of their ears and this was arranged with the specialist nurse service at the study hospital before undertaking hearing tests. Participants undertook cancer treatment lasting between six to 15 weeks;
• Test 2 – the second test assessment was set to coincide with the completion of oncology treatment, and this assessment was co-ordinated with the radiotherapy department at the study centre;
• Test 3 – the third test assessment was set to coincide with the date of the participants’ routine 13-week post treatment follow-up oncology appointment.

The hearing assessments took place in the audiology department of the study hospital and each assessment took up to 30 minutes to complete.

Hearing thresholds for each required frequency were recorded as numerical figures that were stored in an audiology patient management system and then transferred to an excel datasheet for data analysis. Standard tympanometry parameters of middle ear pressure, peak compliance and ear canal volumes were also recorded as numerical figures on an excel datasheet for data analysis.

4.2.5 Data coding

Results obtained from conducting hearing tests and tympanometry were brought together and coded in different ways (described below) to provide information on the incidence and severity of hearing deterioration, the overall description of hearing loss severity, and the type of hearing loss.

4.2.5.1 Defining and grading hearing deterioration

In Chapter 2 it was discussed that there are different methods for determining hearing deterioration, and that, combining findings from Konrad-Martin et al. (2010) and Simpson, Schwan and Rintelmann (1992), it appeared that ≥15dB shift in threshold, across two or more adjacent frequencies was the most appropriate for determining a clinically significant deterioration in hearing. This definition is used within the CTCAE criteria produced by NCI, with the latest version being version 4.03 (NCI, 2010) prior to starting the project. The
CTCAE criteria for hearing were used in some of the studies discussed in the literature review (Cheraghi et al., 2015; Theunissen et al., 2014b). The CTCAE criteria are familiar to the oncologists at the study centre, as the scale is used for assessing whole body systems and the impact of cancer treatment. Therefore, the CTCAE scale was used in this study to enable results to be readily understood by both oncology and audiology disciplines.

The CTCAE scale (in Appendix 4.2) has a grading system on hearing deterioration that may follow cancer treatment, with Grade 1 being the most minor deterioration, and Grade 4 the most major. A Grade 1 deterioration in hearing for adults enrolled in a hearing-monitoring programme (for a 1, 2, 3, 4, 6 and 8kHz audiogram of air conduction thresholds) is one where there is an average threshold shift of between 15 and 25dB across two contiguous frequencies in at least one ear. For this study, a clinically significant loss was defined as any grade of deterioration, when comparing pre-treatment hearing thresholds with those obtained at the end of treatment or at 3-month follow-up post treatment. Air conduction threshold values were used, rather than bone conduction, to demonstrate a change in functional hearing, although both air and bone conduction results were recorded. Air conduction thresholds provided the overall level of hearing, regardless of whether the hearing change was permanent or temporary, whereas bone conduction thresholds provided levels of more permanent loss. For this study, it was important to determine overall hearing and the impact of hearing loss, whether temporary or permanent, on patients. Any graded change in hearing was included in the statistic for determining the incidence of hearing deterioration, as any grade may be detrimental to patients, particularly if participants already possessed hearing loss prior to treatment. In addition, hearing loss had the potential to deteriorate further with time (Bentzen and Trotti, 2006).

Hearing deterioration was graded according to the four numerical grades for hearing in the CTCAE criteria (see Appendix 4.2). The criteria used a comparison of air conduction hearing thresholds measured at 1, 2, 3, 4, 6 and 8kHz obtained pre-treatment with those obtained at either the end of treatment or at 3-month follow-up post treatment. Graded data were
entered and analysed as categorical data in an excel spreadsheet. Using comparison of 3-month follow-up hearing levels with those obtained pre-treatment, participants who had any grade of hearing deterioration were eligible for recruitment for the second phase of the study. A full sampling framework for the qualitative phase is provided in section 4.3.1 of this chapter.

**4.2.5.2 Defining descriptors of hearing level and types of hearing loss**

There are different ways to describe levels of hearing, mainly based on which country data are derived from. This study used the UK system, summarised in Table 4.1:

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Average hearing threshold levels (dBHL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No loss (normal hearing)</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Mild hearing loss</td>
<td>20-40</td>
</tr>
<tr>
<td>Moderate hearing loss</td>
<td>41-70</td>
</tr>
<tr>
<td>Severe hearing loss</td>
<td>71-95</td>
</tr>
<tr>
<td>Profound hearing loss</td>
<td>In excess of 95</td>
</tr>
</tbody>
</table>

*Table 4.1 Descriptors of hearing level* (British Society of Audiology, 2011)

The BSA describes hearing levels based on the average of air conduction pure tone frequencies at 0.25, 0.5, 1, 2 and 4kHz. Using these criteria, the researcher was able to establish the proportion of participants in the study project within each severity level of hearing loss. However, there are no statistics using these BSA criteria for comparing the proportion of people in the UK who have hearing loss with those who have normal hearing.

In addition to air conduction thresholds, bone conduction thresholds were measured to determine hearing through direct stimulation of the cochlea, and both these thresholds were used to determine types of hearing loss. The type of hearing loss for each ear was
determined to assess potential temporary or permanent hearing change using BSA guidelines for tympanometry (BSA 2013), and PTA as follows:

- Normal hearing: air conduction hearing thresholds between 0.25 and 8kHz ≤ 20dBHL
- Conductive hearing loss: bone conduction thresholds between 0.5-4kHz ≤ 20dBHL, and air-bone gap in at least one of the frequencies between 0.5-2kHz ≥ 15dB.
- Sensorineural hearing loss: air conduction hearing thresholds between 0.25 and 8kHz > 20dBHL, and air-bone gap between 0.5-2kHz < 15dB.
- Mixed loss: bone conduction thresholds between 0.5-4kHz > 20dBHL, and air-bone gap in at least one of the frequencies between 0.5-2kHz ≥ 15dB.

Tympanometry was performed to confirm normal hearing or to assist with the classification of hearing loss type as being conductive, mixed, or sensorineural. Therefore, for this study, the BSA guidelines on PTA and tympanometry were used to describe hearing level, and classify type of hearing loss before treatment, at the end of treatment and at 3-month follow-up.

4.2.6 Statistical analysis

Data obtained following coding were analysed using either descriptive or inferential statistics (Table 4.2) depending upon different characteristics that were measured:

<table>
<thead>
<tr>
<th>Descriptive statistics</th>
<th>Patient demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence and severity of hearing deterioration</td>
</tr>
<tr>
<td></td>
<td>Descriptor of hearing loss severity</td>
</tr>
<tr>
<td></td>
<td>Type of hearing loss</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inferential statistics</th>
<th>Severity of hearing deterioration with participant demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Missing data</td>
</tr>
</tbody>
</table>

*Table 4.2 Statistical analysis used*
4.2.6.1 Descriptive statistics

In order to assess incidence and severity of hearing deterioration in context, it was necessary to obtain data on the characteristics of the participant population. Demographic data on age, gender, location of cancer, stage of cancer, aetiology, treatment regime and pre-treatment hearing loss status were kept on an excel spreadsheet. Text data were transformed as numerical category data, and then transferred to the Statistics Package for Social Sciences (SPSS) software v22 for analysis. Descriptive statistics were obtained for: the age and gender of participants; the location, stage and aetiology of the cancer; the treatment regimen used; and the descriptor of hearing loss severity prior to treatment.

Descriptive statistics were used to determine the incidence and severity of hearing deterioration (the first of the primary research aims) by comparing hearing levels at the end of treatment and at 3-month follow-up with pre-treatment levels. Incidence of hearing deterioration was based on the proportion of participants with any grade of deterioration (in one or both ears) according to the CTCAE for hearing (NCI, 2010). Severity of hearing deterioration was based on the proportion of participants with each grade of deterioration (in one or both ears) according to the same CTCAE scale, with the greater severity taking precedence.

The proportion of participants who had hearing described as normal, or as a mild/ moderate/ severe/ or profound loss, according to BSA criteria, was calculated for each hearing level status. The proportion of ears amongst the participants that had normal hearing, conductive loss/ mixed loss/ or SNHL was also calculated to identify each different type of hearing loss.

4.2.6.2 Inferential statistics

In Chapter 2, it was noted that pre-treatment hearing levels, a patient’s age, the type of treatment, and time of follow-up may be covariables to treatment in influencing the degree of hearing deterioration following treatment, and that multivariate analysis is required to assess
the impact of covariables. In this study, however, hearing deterioration was not measured as a continuous variable but as a categorical variable. Consequently, as hearing deterioration was the dependent variable, it was not applicable to use multivariate analysis of continuous data on hearing.

However, it was possible to use the effect of age on hearing deterioration, by making age the dependent continuous variable. The analysis of variance (ANOVA) test was used to assess for statistical significance in the mean values of the age of participants with different degrees of hearing deterioration. The ANOVA test is used in the analysis of continuous variables and suitable for within-participant repeated measures design, when more than two measurements over time are made on an individual participant. There are three assumptions required for performing ANOVA tests: first, that the distribution of data is normal (assessed using the Shapiro-Wilk test); secondly that scores from participants are independent of each other; thirdly, that group variance and covariance are homogenous (Martin and Bridgmon, 2012). If ANOVA was found to be significant, it was necessary to employ the Bonferroni test to assess for a true difference in multiple analysis. The Bonferroni test reduces type I error (identifying a significant result when, in fact the result could be because of chance) in multiple analyses on the same data (Statistics solutions, 2017).

The association of factors, other than age, with hearing deterioration were assessed using analysis of categorical data. The Fisher’s exact test of categorical variables was the inferential statistical analysis used to assess the relation between the potential covariables of pre-treatment hearing level, gender and treatment type, with different levels in severity of hearing deterioration. Stage of cancer was also tested as a covariable. Fisher’s test is used for comparisons of independent categorical data arranged within a two cell times two cell table, to assess significant differences within the table, either when the total data is less than 20, or when the total sample is less than 20, and one cell value is less than five (Zibran, 2017). The assumption for using the Fisher’s test is that the row and column values of the table are treated as fixed quantities, so that variation within these rows and tables is allowed,
if there is no variation in the totals for the rows or columns respectively (Mould, 1998). If Fisher’s test was found to be significant, the Bonferroni test was again employed to confirm any significance found in multiple analyses.

4.2.6.3 Missing data

Raw numerical data on hearing threshold levels were kept on an excel spreadsheet and transferred to a SPSS version 22 database. The one-year survival rate of HNC patients varies considerably, between 60-90%, depending on the location and stage of cancer, with an aggregate of 80% survivorship (HQIP, 2012). Consequently, attrition was expected in this longitudinal study, and the Fisher’s exact test was used to determine patterns of missing data to assess whether there was any difference in patient demographics between those who partially completed testing scheduling and those who completed all the tests. However, as no statistical comparison of absolute hearing level was made either for individual participants or for groups of participants, computation of missing values was not required.

4.2.7 Validity and reliability of quantitative findings

The CASP checklist for cohort studies (Appendix 2.3) was adapted to use as a quality assessment for the quantitative phase of data collection for this study -

- Does the study address a clearly focused issue? Yes – The aims of the study are given – Section 4.1;
- Was the cohort recruited in an acceptable way? Yes – A consecutive convenience sample of participants with general head and neck cancer was recruited – Section 4.2.2;
- Was the exposure accurately measured to minimise bias? Yes – An outline of what treatment patients received is provided – Section 4.2.2.1;
• Was the outcome accurately measured to minimise bias? Yes – The hearing test method is provided in detail – Section 4.2.3;
• Have the authors identified all-important confounding factors? Yes – Age, pre-treatment hearing level, type of treatment and time after treatment – Section 4.2.6.2;
• Have they taken account of the confounding factors in the design and/or analysis? Yes – Using modified methods – Section 4.2.6.2;
• Was the follow-up of participants long enough? Yes – To identify hearing change in the early post treatment phase – Section 4.2.4.

4.3 Qualitative phase

The second phase of the study, outlined in Figure 4.1, entailed conduct of 13 interviews with participants to generate qualitative data, and so to address the second main aim of the research project, namely: ‘to explore the lived experience of participants with hearing deterioration after treatment for HNC’. The reason for choosing interviews will be discussed in section 4.3.3 below.

4.3.1 Sample size

It was anticipated that from the sample of 50 participants from the quantitative phase (data collected from hearing tests) there would be 20% attrition, leaving 40 participants available for the qualitative phase. It was predicted that 38 participants would be required to complete testing for 80% power to obtain a 15dB difference in hearing following treatment using pilot data prior to this study.

Guest, Bunce and Johnson (2006) suggested that between six to 12 interviews are sufficient to obtain breadth of information on a phenomenon, particularly if an in-depth assessment is required as in interpretive phenomenological studies (Smith and Osborn, 2008). Such
studies are conducted on small sample sizes, to gain a detailed analysis of the perceptions of a group of individuals (Smith and Osborn, 2008).

Therefore, it was determined that a purposive sampling technique be employed, and in order to obtain as much breadth of information and maximum variation as possible, at least 12 interviews be conducted. More than 12 participants were invited to interview, to allow for any who were not able to attend at short notice and the difficulty in re-arranging appointments within the timeframe of conducting the study. Consequently, more than 12 participants were interviewed.

<table>
<thead>
<tr>
<th>Grade of deterioration</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Pre-treatment hearing status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Male</td>
<td>Young</td>
<td>Normal</td>
</tr>
<tr>
<td>3-4</td>
<td>Female</td>
<td>Old</td>
<td>Hearing loss</td>
</tr>
</tbody>
</table>

Table 4.3 Sampling framework for interview selection
Key: a- based on CTCAE (v4.03) for hearing deterioration; b- based on mean age of participants who had hearing deterioration at 3 months following treatment (mean age determined in Chapter 5); c- based on BSA criteria.

Purposive sampling techniques are used in qualitative studies that deliberately select individuals for the important information they can provide for answering a research study’s questions (Teddlie and Yu, 2007). It is noted that maximum purposive sampling has its limitations. Although participants are selected to provide a broad understanding of the phenomenon of hearing deterioration, it cannot be guaranteed that the full range of experiences of hearing deterioration are obtained, as some participants not selected for interview may have different experiences (Cook, 2015). However, to maximise the greatest range in information obtained (Scott et al., 2007), Table 4.3 above shows the sampling framework used for this study. Each of the eight characteristics in the sampling framework was used to guide sampling to provide maximum divergence in participant demographics, for a broad understanding on patient experience of hearing deterioration. The categories were chosen to represent different degrees of deterioration (minor, Grades 1-2; or major, Grades 3-4) to explore the impact on patient experience of participants who had a minor or
major hearing deterioration. As the researcher wanted to obtain maximum diversity in this study, different characteristics of gender, age and pre-treatment hearing status were selected, as each of these characteristics has been linked with different amounts of hearing deterioration (Theunissen et al., 2015). Multiple variation sampling enabled the researcher to assess if the phenomenon of hearing deterioration was homogenous or heterogeneous across different patient characteristics.

4.3.2 Recruitment

All participants identified with any Grade (1-4) of hearing deterioration, as specified in the CTCAE criteria version 4.03 (NCI, 2010), were eligible for interviewing. Purposive maximum variation sampling, based on the sampling framework shown in Table 4.3, was used to select participants for exploring patient experience of hearing deterioration as widely as possible.

The researcher approached participants by telephone after they had their 3-month follow-up hearing assessment (and within a year of this assessment) to inform them of Phase 2 of the study. Those participants who verbally agreed to participate in Phase 2, or those who were not contactable by telephone, were sent an information sheet by first class post, giving details of the purpose and nature of the second phase of the study. Following a period of at least 24 hours from posting the participant information sheet, the researcher phoned potential participants and arranged an interview for those wishing to continue with their participation in the study. Written, informed consent was obtained prior to their interview. Interviews were held after the 3-month follow-up hearing tests were completed and not before, as it was considered appropriate to allow participants time to recover from their treatment.
4.3.3 Qualitative method

The qualitative method of interviewing was chosen for Phase 2 data collection, as this is often used for exploring patient experience in many studies, and has been used successfully in the one study identified in the literature review (Chapter 2) on hearing problems in HNC patients using a phenomenological approach (Nund et al., 2015).

Of the different types of interview available, semi-structured interviewing was chosen to provide rich data on opinions, feelings and experiences, with pre-set questions and flexibility to enable the participants to develop ideas and speak more widely on issues (Denscombe, 2010). Semi-structured interviews were of benefit for this research because they enabled participants to give in-depth information of their experience of hearing deterioration, and allowed greater flexibility for the researcher to probe more deeply, when appropriate. This approach was also appropriate for use within a critical-realist framework. The interviews were held in the hospital premises in a private and quiet room used for clinical investigation in the Audiology department, and were conducted by the researcher. The interviews lasted up to one hour. The semi-structured format enabled the researcher to ask pre-determined questions, to have flexibility in the order of asking these questions, or to modify them according to what was most appropriate for the interviewee (Robson, 2002). The interviews had a few specific questions that were open-ended to allow patients to elaborate (Barbour, 2008) on their experience of hearing deterioration.

The main areas addressed at interview were:

1. The experience of hearing deterioration: hearing loss prior to treatment, and deterioration during and following treatment were explored, with the particular focus on the impact on daily living;

2. Information and support: questions were asked to determine what information and support the interviewees were aware of – and what they felt was available – that would help them understand and manage their condition;
3. Further support: interviewees were asked what further support would help them manage or cope with their hearing deterioration following cancer treatment.

The main questions that were asked in the interview schedule are provided in Appendix 4.3. By referring to the interview schedule, it was possible for the interviewer to maintain the focus of the interview on the main subject areas, however participants were allowed to digress if this enabled them to discuss other areas of concern, and allow the interview to be free flowing.

4.3.4 Data collection

The responses from interviews were recorded using a dictaphone and transcribed verbatim by an external agency used by the researcher’s hospital for transcribing medical notes. A copy of the transcript was available on request to give participants an opportunity for review and comment. No comments were received, so there was no need to make any corrections to transcripts. The raw data from the dictaphone was erased at the end of the study. The transcribed accounts were then stored on encrypted computers at the study centre for data analysis. A study supervisor reviewed the transcript from the first interview and gave advice on enhancing the interview technique and stressed the need to avoid asking leading questions. The validity and reliability of the qualitative data from this study are discussed later in this chapter.

4.3.5 Data analysis

The researcher listened to the transcribed data to enhance his memory of the context in which the data was obtained, and to ensure accuracy and immersion in the data. The framework analysis method (Ritchie and Lewis, 2003) was systematically used to obtain themes from the transcribed interview data, as shown in Figure 4.2:
All interviews were read through to gain an overview of their content.

All quotes from each transcript were marked and identified as ‘in vivo’ codes. Each code was described to give an initial meaning.

The meaning of each code was made to create initial categories.

Initial categories from Transcript 1 that were on similar topics were identified and grouped together to form initial themes.

Initial categories from the other transcripts were grouped into the initial themes from Transcript 1 if possible, or used to create additional initial themes.

The initial themes were integrated to create the final themes.

Figure 4.2 Formation of themes

Each transcript was printed out into a hard copy. Each quote that was obtained from the interview transcripts was identified and marked using a highlighter pen. Each quote was an ‘in vivo code’ (Ritchie and Lewis, 2003). A preliminary thought or meaning was ascribed to each code. Each of these thoughts or meanings was then used to form ‘initial categories’.

All the transcripts were read to form a coding matrix (part of which is shown in Table 4.4) of initial categories:
Interview transcript 1

Description (In-vivo codes)

Preliminary thoughts or meanings

Initial categories

‘before the treatment that he [husband] never had to repeat himself and that but he is realising that's how it is or just does not talk to me’

‘before the treatment that he never had to repeat himself’

To make the patient understand, the husband needed to repeat what he said

Others needed to repeat themselves

‘It is like a very high-pitched whistle in my head constantly but it does not affect my sleeping and I have sort of learnt to sort of ignore it during the day’

‘high-pitched whistle in my head constantly’

Perception of tinnitus is constant

Withdrawal by partner from communication

‘I have sort of learnt to sort of ignore it’

Cope with tinnitus by ignoring it

Continuous tinnitus

To make the patient understand, the husband needed to repeat what he said

Husband ceased communication

Communication adaptation

Ignore tinnitus

Table 4.4 Coding matrix of initial categories

The initial categories from Transcript 1 were then grouped to create initial themes, using a coding index. Table 4.5 shows part of the coding index. These initial themes were used to group initial categories in other transcripts, with the coding index extended with the formation of additional initial themes.

Table 4.5 Coding index (example)

<table>
<thead>
<tr>
<th>Initial categories</th>
<th>Initial Theme</th>
</tr>
</thead>
<tbody>
<tr>
<td>White noise</td>
<td>Tinnitus sensation</td>
</tr>
<tr>
<td>Whistle sound</td>
<td></td>
</tr>
<tr>
<td>Buzzing sound</td>
<td></td>
</tr>
<tr>
<td>Asks speaker to repeat</td>
<td>Communication adaptation</td>
</tr>
<tr>
<td>Asks speaker to speak louder</td>
<td></td>
</tr>
<tr>
<td>Tells others there is a hearing problem</td>
<td></td>
</tr>
<tr>
<td>Not bothered by hearing change</td>
<td>Attitude to hearing deterioration</td>
</tr>
<tr>
<td>Not bothered with hearing aids</td>
<td></td>
</tr>
<tr>
<td>Hearing in context of cancer treatment</td>
<td></td>
</tr>
</tbody>
</table>

Final themes were generated from related initial themes ensuring that each final theme had responses from at least 50% of the participants so that the data represented a level of patterned response (Braun and Clarke, 2006). The final themes had categories that covered all aspects of data on patient experience of hearing deterioration following treatment for
HNC. These themes also contained similar responses made by patients to identify patterns of responses. Framework analysis provides a process where it is possible to link original source data to the generated themes, thereby increasing the validity of findings (Smith and Firth, 2011).

4.3.6 Validity and reliability of qualitative findings

The validity and reliability of the results obtained in the qualitative phase of study was assessed based on a checklist provided by Maxwell (1992) on threats to validity of qualitative research, and how these threats can be addressed:

- **Descriptive validity**: How factually accurate is the account? To ensure all aspects of each interview were captured, the interviews in this study were recorded and then transcribed verbatim;

- **Interpretive validity**: How well do the findings presented by the researcher represent meanings from the participants’ perspectives? The researcher employed an approach informed by phenomenology in this study, to draw out understanding of how research participants experienced their hearing deterioration following HNC treatment. The use of open-ended questions made it easier for participants to share their experiences, and where necessary enabled the researcher to probe more deeply. Interpretations by the researcher on what was said could be traced back to participants’ own quotes (using framework analysis) to determine conscious beliefs and feelings. Unstated or subconscious intentions were given greater validity by grouping similar quotes from different participants and from relevant sources in the wider literature. The researcher was mindful of this approach to minimise his interpretations on what was said by participants. The researcher was also aware that the participants might have responded differently if someone else had conducted the interview, as the participants were known to the researcher from the quantitative phase of the study.
• **Theoretical validity:** How do the findings of the study support underlying theory? Hearing deterioration in general is associated with poorer quality of life, and it was expected to be associated with negative patient experience following treatment of HNC. However, some participants acknowledged their hearing loss, and this appeared to minimise the impact on quality of life.

• **Generalisability:** How generalisable are the results to the patient group, or to other groups? Purposive sampling was used to enable participants to give as wide a variation as possible on patient experience. The findings are generalisable to other patients who have had similar treatment and have had hearing deterioration based on the CTCAE criteria (v4.03), and who have been interviewed around a year following the completion of their treatment.

• **Evaluative validity:** How reproducible are the results obtained? Using framework analysis, each theme that was generated included responses from at least 50% of interviewees, showing that they were representative of the experiences of the participants as a whole. It is possible to link the original data to the generated themes, thereby increasing the validity of the findings.

• **Researcher bias:** How has the researcher minimised his bias on the research? It was noted that participants might have responded differently to the researcher than to another interviewer, as the researcher knew the participants. However, as the interviewer had to be flexible and ask appropriate probing questions on the key subject area of hearing deterioration, it was necessary for the study researcher to perform the interviews. In interpretive phenomenology, the experience and expertise of the interviewer is a significant feature. If the interviewer has an understanding of the subject area, they are better able to clarify responses and ask relevant additional questions. The researcher asked questions that were not leading but open-ended to enable participants to express their views, and all responses were recorded and included in interpretation.
4.4 Integration of quantitative and qualitative data

In this mixed methods study, data from the quantitative phase (from testing) was used to inform selection of participants for interview in the qualitative phase. Data was not converted into either a textual or numerical format for comparison, but the results from each of the quantitative and qualitative phases were integrated in a narrative form to provide a broader understanding of the phenomenon of hearing deterioration after HNC treatment. Patterns of responses in Phase 2 were drawn from patients’ characteristics and severity of deterioration data, obtained from Phase 1 data, and these patterns were reported in Chapter 6 of this thesis. Further, data from the quantitative and qualitative phases were discussed together in Chapter 7, to assess if there were patterns in patient experience, based on data obtained from the quantitative phase, that were separate to patient characteristics and severity of deterioration data. The bringing together of data in this way provided a more complete understanding of the phenomenon of hearing deterioration, including whether it was homogeneous or heterogeneous for participants.

4.5 Ethical considerations

The ethical threats in conducting the study were mainly generic to research. The information sheet, on the nature and reason for the project, was given to patients eligible for inclusion, and signed consent was obtained. Participants were informed that the study would follow standard research ethical and legal practices, were free to withdraw at any point, and were informed that data collected would be kept strictly confidential. Participants were identified by a unique study number rather than by their name or address, so that they could not be recognized from any information obtained. The NHS code for confidentiality was adhered to with this anonymisation of data. Interview transcripts were also made anonymous.

With the introduction of additional hearing testing that was not part of usual procedure (at the end of treatment and at 3-month follow-up), specific ethical approval for this study was
required. Similar approval was required for the interviews, recognising that the time involved in attending these assessments could cause inconvenience for participants with the disruption of their daily routine. Furthermore, participants’ permission was required before any information that was of a sensitive nature could be shared with a clinical nurse specialist in head and neck oncology. An inventory of all the necessary requirements to proceed with this project is provided in Appendix 4.4 including:

- details of the organisations that provided approval for the study;
- the standard statement for compliance and non-compliance of research studies;
- the standard monitoring and audit framework for this study.

Initial acceptance from Ethics, and Research and Development Departments was sought and granted in January 2015, further approval granted in May 2016, and an amendment was required to address in full the stated aims of the study. Ethics approval was granted as the study showed the necessary beneficence, non-maleficence, respect for autonomy and justice required for a UK research study. In particular for this study, the participant information sheet provided details for patients on support they could receive if they became unduly upset in their interview. The information sheet also told patients of any inconvenience they may have due to the requirement to attend additional appointments for the study.

4.5.1 Data handling

The researcher had access to the participants’ identifiable personal data, but the study supervisors had access only to anonymised personal data. National Health Service computers used for the study were password secured for the safe keeping of electronic files, and participant information sheets, consent forms and transcriptions of interviews were kept in secure storage in a locked filing cabinet located on the study premises to which only the researcher had access. After the study ended, research data was kept for 12 months by the researcher and then given to the University of Surrey for archiving in accordance with their data storage policy for ten years.
4.5.2 Finance and indemnity

The study was insured by the NHS Indemnity scheme for providing cover for non-negligent and negligent harm. The University of Surrey provided indemnity for the overall study methodology and framework.

4.6 Summary

This chapter has provided the rationale for the instruments used to address the research aims of this study. The chapter has also shown the process by which participants were selected for the study, and the method for obtaining and analysing data that were reliable and valid. The chapter has concluded with the framework for conducting the study to ensure it adhered to standard research governance policy.

The following chapters, 5 and 6, present the results of the data collection for each of the two phases of the study: Chapter 5 with the results of Phase 1 data obtained using quantitative methods, and Chapter 6 with the results of Phase 2 data acquired using qualitative methods.
Chapter 5 Results – Quantitative data

5.1 Introduction

This chapter presents the results of the quantitative (first) phase of the research, addressing the first primary research aim: to assess the incidence and severity of hearing deterioration; and the secondary aims: (a) to describe overall hearing levels; (b) to assess types of hearing loss; and (c) to explore differences in severity of hearing deterioration in relation to patient demographics and types of treatment. Patients included those who were due to receive treatment for HNC at a UK hospital.

Data was collected from hearing tests on 50 patients over a period of one year (February 2015 to February 2016). The chapter provides a description of the demographics of participants, both those who completed the hearing tests and those who did not. The chapter then presents statistics addressing this primary research aim, and the three secondary aims [the other primary research aim (to explore the lived experience of participants involved in this study) will be covered in Chapter 6, which presents the results of qualitative data gathered from patient interviews].

5.2 Recruitment

Of the 62 patients invited to participate in the study, one declined participation, and 11 were excluded, so that 50 were recruited (80.6%). The reasons for exclusion from the study, and the number of participants at each stage of testing are shown in Figure 5.1 below:
Figure 5.1 Recruitment and participation

Invited 62

- Declined 1
- Excluded 11
  - No longer having treatment 2
  - Already started treatment 7
  - Audiological condition 2

Pre-treatment

Tested 50

End of treatment

- Tested 42
  - No longer having treatment 1
  - Died 1
  - Changed treatment 2
  - Declined testing 2
  - Missed 2

Follow-up

- Tested 42
  - Not tested 8
    - Missed 2
  - Not tested 2
    - Declined testing 1

44
It can be seen in Figure 5.1 that of 12 patients who were not included in the study, two had a pre-existing audiological condition: one had Meniere’s disease (a balance condition that is characterised by fluctuating hearing loss) and the other had profound hearing loss in one ear such that deterioration in hearing could not be measured.

### 5.3 Test completion and attrition

All 50 participants who consented to the study had pre-treatment hearing tests (Test 1) with the expectation that they would have treatment. However, one participant did not start treatment as a watchful-wait policy was subsequently adopted for their care. For the remaining 49 participants, the mean time between completion of Test 1 and the start of treatment was 2.3 weeks.

Of the 49 participants who started treatment, there were 42 who completed Test 2, and 42 who completed Test 3 (Figure 5.1). However, only 40 completed all three hearing tests for this study. The largest drop-out rate that was expected, based on a one-year survival rate for HNC patients, was 20% (HQIP, 2012). One participant died during Phase 1 data collection of the study; this participant did not have either Test 2 (end of treatment) or Test 3 (3-month follow-up). Other reasons for nine participants not completing either Test 2 or 3 were: a change in treatment to palliative care; a change to non-UK standard treatment (proton therapy); incomplete treatment by voluntary withdrawal; one participant was too ill to attend a test appointment; difficulty in scheduling the hearing test. The attrition rate for not attending the post-treatment test was 16%, and at 3-month follow-up was also 16%. These rates were less than the 20% anticipated based on survival rates (HQIP, 2012), but testing for this study for each participant was less than a year. The mean time between the end of treatment and Test 2 was 0.8 weeks, and that for the end of treatment and Test 3 was 14.0 weeks.
There were ten participants who did not complete either the end of the treatment test (Test 2) or the 3-month follow-up test (Test 3), and their characteristics are shown in Table 5.1 below:

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Test missed (Test)</th>
<th>Age</th>
<th>Gender</th>
<th>Location of cancer</th>
<th>Stage of cancer</th>
<th>Treatment plan</th>
<th>Pre-treatment hearing level descriptor*</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>2 + 3</td>
<td>70</td>
<td>M</td>
<td>Oropharynx</td>
<td>IV</td>
<td>CRT</td>
<td>Mild HL</td>
<td>V</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>81</td>
<td>F</td>
<td>Salivary gland</td>
<td>II</td>
<td>RT</td>
<td>Mild HL</td>
<td>S</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>72</td>
<td>M</td>
<td>Oral cavity</td>
<td>IV</td>
<td>RT</td>
<td>Moderate HL</td>
<td>A + S</td>
</tr>
<tr>
<td>24</td>
<td>2 + 3</td>
<td>62</td>
<td>M</td>
<td>Oropharynx</td>
<td>IV</td>
<td>CRT</td>
<td>Mild HL</td>
<td>S</td>
</tr>
<tr>
<td>26</td>
<td>2 + 3</td>
<td>69</td>
<td>M</td>
<td>Oropharynx</td>
<td>IV</td>
<td>CRT</td>
<td>Normal</td>
<td>A + S</td>
</tr>
<tr>
<td>31</td>
<td>3</td>
<td>54</td>
<td>M</td>
<td>Larynx</td>
<td>I</td>
<td>RT</td>
<td>Normal</td>
<td>S</td>
</tr>
<tr>
<td>32</td>
<td>2 + 3</td>
<td>62</td>
<td>M</td>
<td>Oropharynx</td>
<td>IV</td>
<td>CRT</td>
<td>Mild HL</td>
<td>A + S</td>
</tr>
<tr>
<td>33</td>
<td>2 + 3</td>
<td>67</td>
<td>M</td>
<td>Larynx</td>
<td>I</td>
<td>RT</td>
<td>Mild HL</td>
<td>None</td>
</tr>
<tr>
<td>38</td>
<td>3</td>
<td>72</td>
<td>M</td>
<td>Oropharynx</td>
<td>III</td>
<td>RT</td>
<td>Mild HL</td>
<td>A + S</td>
</tr>
<tr>
<td>39</td>
<td>2 + 3</td>
<td>37</td>
<td>F</td>
<td>Nasopharynx</td>
<td>III</td>
<td>CRT</td>
<td>Mild HL</td>
<td>None</td>
</tr>
</tbody>
</table>

Table 5.1 Characteristics of participants who missed testing
Key: Gender (M-Male; F-Female); Treatment plan (CRT-Chemoradiotherapy; RT-Radiotherapy only); HL – hearing loss; * descriptor of the worse ear; Aetiology (V-Virally confirmed; A-Alcohol use (>14 units/week); S-Having smoked)

Eight of the ten participants who did not complete either Test 2 or 3 were male, with equal numbers (n=5) receiving RT or CRT (Table 5.1). The difference in characteristics of the ten participants who missed either Test 2 or 3 was not significant statistically (p≥0.05, using Fisher’s exact test) compared with the 40 who completed both Test 2 and 3, with:

- the male to female ratio (p=0.09)
- the older patient to younger patient ratio (using the median age of 61 years to define the age split; p=0.47), and
- the ratio of participants receiving RT only to those who were treated with CRT (p=0.47).

As there appeared to be no pattern to, or prediction of, the participants who missed either Test 2 or 3, data that was missing were therefore viewed as 'missing at random'.
Consequently, statistical selection bias was minimised when interpreting results from either the full (Test 1) or partially completed (Test 2 or Test 3) data sets.

### 5.4 Participant demographics

The demographics of the participants recruited to the study are shown in Table 5.2. The mean age of the 50 participants recruited was 60.7 years [standard deviation (SD) 10.6 years]. The male to female ratio in the study population was two to one, which reflects the proportion of patients diagnosed with HNC in a UK population. The largest proportion of patients in this study had oropharyngeal cancer (52%); this cancer accounts for 28% of all patients diagnosed with HNC in the UK.

The majority of participants had hearing loss (n=43) that was mainly sensorineural in type (n= 74 ears). Among eight participants, eight ears manifested mixed hearing loss on PTA before treatment, six with abnormal tympanometry results: three with type B (flat – indicating middle ear effusion or a tympanic membrane perforation), two with type C (negative middle ear pressure) tympanograms, and one with a Type A₀ (high compliance) tympanogram, which indicated healing of the tympanic membrane following perforation. The proportion of participants with bilateral hearing loss, using BSA criteria, was 36%.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Study %</th>
<th>UK population %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>34</td>
<td>68</td>
<td>67 (^k)</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>6</td>
<td>12</td>
<td>31</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>3</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>26</td>
<td>52</td>
<td>28</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>3</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Salivary</td>
<td>3</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Larynx</td>
<td>8</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>45</td>
<td>90</td>
<td>85 (^j)</td>
</tr>
<tr>
<td>Non-squamous cell carcinoma</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td><strong>Stage of cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>12</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>29</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td><strong>Aetiology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subgroup</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use (^a)</td>
<td>18</td>
<td>36</td>
<td>75 (^m)</td>
</tr>
<tr>
<td>Smoking history (^b)</td>
<td>33</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Viral infection (^c)</td>
<td>12</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy only (^d)</td>
<td>22</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>28</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td><strong>Hearing type (patients)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (^e)</td>
<td>7</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Hearing loss (^f)</td>
<td>43</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td><strong>Hearing type (ears)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (^g)</td>
<td>18</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Mixed loss (^h)</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>SNHL (^i)</td>
<td>74</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td><strong>Hearing level descriptor (patients)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal bilaterally</td>
<td>22</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Unilateral loss</td>
<td>10</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Bi mild loss</td>
<td>15</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Bi mild/moderate loss</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bi moderate loss</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5.2 Patient, cancer and treatment characteristics**

Key: a- Heavy alcohol use > 14 units per week; b- current or ex-smokers; c- Epstein-Barr or human papillomavirus confirmed infection; d- including cetuximab; e- Normal: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz ≤ 20dBL, bilaterally; f- Hearing loss: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz > 20dBL, in at least 1 ear; g- Normal: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz ≤ 20dBL, bilaterally; h- Hearing loss: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz > 20dBL, in at least 1 ear; i- Normal: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz ≤ 20dBL, bilaterally; j- Hearing loss: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz > 20dBL, in at least 1 ear; k- Cancer research UK (2016); l- HQIP (2012); m- Hobbs (2010)
Twenty-eight of the participants received IMRT with chemotherapy. Twenty-one of these received the administration of cisplatin only (200-500mg/m$^2$). Five participants started with cisplatin, but then were changed onto carboplatin treatment due to adverse events during treatment (on review of their medical notes); three of these participants had developed tinnitus (the perception of sound when there is no external source). Two participants received carboplatin treatment only, as they had pre-treatment hearing loss. Three participants received cetuximab administration along with their IMRT. The remaining 19 participants had IMRT only treatment.

### 5.5 Incidence of hearing deterioration

One of the main aims of the study was to determine the incidence of hearing deterioration following treatment of HNC. The findings presented in Table 5.3 show results of hearing deterioration following end of treatment and at 3-month follow-up. Participants were classified as experiencing: ‘no hearing deterioration’ if neither ear had hearing deterioration; a ‘minor hearing deterioration’ if hearing deteriorated by only Grade 1 or 2 criteria in one or both of their ears; or a ‘major hearing deterioration’ if at least one ear had Grade 3 change:

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Proportions %</th>
<th>Incidence of hearing deterioration %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(a) End of treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No hearing deterioration</td>
<td>18</td>
<td>43</td>
<td>57</td>
</tr>
<tr>
<td>Minor hearing deterioration</td>
<td>13</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Major hearing deterioration</td>
<td>11</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Missing at random</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>(b) 3-month follow-up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No hearing deterioration</td>
<td>21</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Minor hearing deterioration</td>
<td>10</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Major hearing deterioration</td>
<td>11</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Missing at random</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5.3 Incidence of hearing deterioration (n=42)
Part (a) of Table 5.3 shows that 57% of the participants who completed testing at the end of treatment had hearing deterioration, with 26% experiencing a major deterioration. Part (b) of Table 5.3 shows that 50% of participants who completed testing at 3-month follow-up had hearing deterioration compared to pre-treatment hearing levels, with 26% developing major change.

There were 40 participants who completed all three hearing tests for this study. Although the majority of these participants had no change in hearing when comparing end of treatment to 3-month follow-up testing, Table 5.4 below shows that some participants had an improvement in hearing, whereas others had a deterioration:

<table>
<thead>
<tr>
<th></th>
<th>Test 3 to Test 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>No change</td>
<td>30 (75%)</td>
</tr>
<tr>
<td>Deterioration</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

**Table 5.4 Inter-test hearing change**

It can be seen that 15% of participants had improved hearing between the end of treatment and 3-month follow-up tests (Tests 2 and 3). An improvement in hearing may be due to resolution of OME that restores normal middle ear function. This finding supported the more detailed assessment of hearing deterioration at 3-month follow-up rather than at the end of treatment, to determine severity of persistent (or developed) hearing deterioration instead of a more transient state of hearing deterioration. The characteristics of the participants who completed Test 3 (n=42) of this study are shown in Appendix 5.1.

**5.6 Severity of hearing deterioration**

Determination of the severity of hearing deterioration was part of one of the main aims of this study. As none of the 42 participants who were tested at 3-month follow-up had Grade 2 or Grade 4 deterioration, results of minor deterioration and major deterioration corresponded to
Grade 1 and Grade 3 deterioration respectively. Of the 21 participants who had hearing deterioration, ten (24%) had minor deterioration, and 11 (26%) had major deterioration (Table 5.3).

5.7 Descriptors of hearing level

One of the secondary aims of the study was to describe the overall hearing levels of patients before and after treatment. The descriptors of hearing level for participants before treatment, and at 3-month follow-up is shown in table 5.5 below:

<table>
<thead>
<tr>
<th>Description</th>
<th>Pre-treatment hearing (%)</th>
<th>Post-treatment hearing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal bilaterally</td>
<td>19 (45.2)</td>
<td>12 (28.6)</td>
</tr>
<tr>
<td>Unilateral mild hearing loss</td>
<td>6 (14.3)</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td>Unilateral moderate hearing loss</td>
<td>1 (2.4)</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Bilateral mild hearing loss</td>
<td>13 (31.0)</td>
<td>18 (42.9)</td>
</tr>
<tr>
<td>Bilateral mild/moderate hearing loss</td>
<td>1 (2.4)</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Bilateral moderate hearing loss *</td>
<td>2 (4.8)</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>42</td>
</tr>
</tbody>
</table>

Table 5.5 Descriptors of hearing level (n=42 at pre-treatment and at 3-month follow-up)

Hearing levels shown in Table 5.5 are those described according to BSA guidelines (BSA, 2011) using the 5-frequency octave average of 0.25, 0.5, 1, 2 and 4kHz. The proportion of participants with bilateral hearing loss increased from 38.1% before treatment to 57.1% at 3-month follow-up, with a doubling in the proportion of those who had moderate severity hearing loss.

5.8 Types of hearing loss

Another of the secondary aims of this study was to determine types of hearing loss, and to assess if hearing loss prior to and after treatment was due to damage to the middle ear, inducing a conductive hearing loss, the inner ear and/or the auditory nerve, inducing a
SNHL, or a combination of these anatomical areas, causing a mixed hearing loss. Prior to treatment, the majority of the 42 participants (72%), who completed Tests 1 and 3 had SNHL (in at least one ear) due to high frequency loss between 6 and 8kHz, which is common in age-related hearing loss (Davis et al., 2007). The proportion of patients with each type of hearing loss found by PTA and tympanometry prior to treatment and at 3-month follow-up is shown in Figure 5.2. Participants who had at least one ear with a mixed loss was assigned to the ‘mixed hearing loss’ group; none of the participants had conductive hearing loss at baseline or at 3-month follow-up testing. Those participants who had at least one ear with SNHL and the other not with a mixed hearing loss were placed in the SNHL group.

![Figure 5.2 Change in type of hearing loss](image)

The majority of patients (approximately two-thirds) developed SNHL hearing loss, with approximately one-third developing mixed loss in at least one ear (Figure 5.2), and as a mixed loss is a combination of sensorineural and middle ear dysfunction, all 21 participants who suffered a hearing deterioration developed a sensorineural loss in at least one ear. One patient, who had borderline SNHL prior to treatment had improvement in their hearing to normal levels following treatment, and this improvement was within the usual test-retest variation for PTA. The eight ears from seven participants who had mixed hearing loss at 3-
month follow-up had abnormal tympanometry: six with type B (flat tympanograms), one with type C tympanograms (negative middle ear pressure), and one with a Type A tympanogram (high compliance tympanogram). The tympanometric tests therefore confirmed middle ear dysfunction within these nine ears.

5.9 Hearing deterioration and patient characteristics

Another secondary aim of this study was to explore the incidence and severity of hearing deterioration in relation to patient demographics and types of treatment. Because there were no significant associations between the presence and severity of hearing deterioration with gender, type of cancer or stage at diagnosis, this section concentrates on the severity of hearing deterioration by age. The mean age of the 42 participants completing the testing at 3-month follow up was 60.5 years (SD 10.5). Table 5.7 (below) provides the mean values of participants with no hearing deterioration, and with those who had either a minor or a major deterioration at 3-month follow-up. This information is provided graphically in Figure 5.3;

![Figure 5.3 Comparison of age with hearing deterioration at 3-month follow-up](image)

Figure 5.3 Comparison of age with hearing deterioration at 3-month follow-up
The age of participants in each of the three groups shown in Figure 5.3 was normally distributed (using Shapiro-Wilk test) such that a comparison of the means was possible using ANOVA. The Bonferroni test, that reduces type 1 error in multiple analyses, showed a statistically significant difference between the mean age of those participants who had a minor hearing deterioration when compared with those participants who had no deterioration (p=0.03). There too was a statistical difference between the mean age of those participants who had a minor deterioration when compared with those who had a major hearing deterioration (p=0.02), implying that if deterioration took place, younger patients suffered a major deterioration in their hearing. Comparison of all participant characteristics with hearing deterioration is shown in Table 5.7 below:

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No deterioration (%)</th>
<th>Minor deterioration (%)</th>
<th>Major deterioration (%)</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>b. Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (52)</td>
<td>7 (26)</td>
<td>6 (22)</td>
<td>27</td>
<td>*1.00</td>
</tr>
<tr>
<td>Female</td>
<td>7 (46)</td>
<td>3 (20)</td>
<td>5 (33)</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>c. Stage of tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>6 (75)</td>
<td>2 (25)</td>
<td>0</td>
<td>8</td>
<td>*0.23</td>
</tr>
<tr>
<td>Late</td>
<td>15 (44)</td>
<td>8 (24)</td>
<td>11 (32)</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>d. Hearing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>4 (57)</td>
<td>0</td>
<td>3 (43)</td>
<td>7</td>
<td>*1.00</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>17 (49)</td>
<td>10 (29)</td>
<td>8 (23)</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>e. Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>14 (74)</td>
<td>4 (21)</td>
<td>1 (5)</td>
<td>19</td>
<td>*=0.01</td>
</tr>
<tr>
<td>Chemoradiotherapy</td>
<td>7 (30)</td>
<td>6 (26)</td>
<td>10 (44)</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio = 6.4, relative risk = 2.4, of developing hearing deterioration with chemoradiotherapy verses radiotherapy

<table>
<thead>
<tr>
<th>Age - Mean (years)</th>
<th>58.8</th>
<th>68.7</th>
<th>56.3</th>
<th>.03</th>
<th>.02</th>
</tr>
</thead>
<tbody>
<tr>
<td>All 42 participants</td>
<td>60.4 years (CI 57.4 – 63.7)</td>
<td>58.8</td>
<td>68.7</td>
<td>56.3</td>
<td>.03</td>
</tr>
</tbody>
</table>

**Table 5.7 Hearing deterioration at 3-month follow-up after treatment**

Key: (%) percentage per category. *Fisher’s exact test (p <0.05 significant – comparison of no deterioration with hearing deterioration). ** Bonferroni test (p <0.05 significant – minor deterioration to no deterioration). *** Bonferroni test (p <0.05 significant – minor deterioration to major deterioration; a: Normal: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz ≤ 20dBHL, bilaterally; b: Hearing loss: Pure tone audiometry: - air conduction hearing thresholds between 0.25 and 8kHz >20dBHL, in at least one ear
There was an odds ratio of 6.4 and a relative risk of 2.4 of participants developing hearing deterioration with CRT when compared with RT (Fisher’s exact test; p=0.01). There were 21 participants with hearing deterioration. All of the 16 participants with chemotherapy-induced hearing loss had cisplatin as part of their treatment regime; neither of the participants who had carboplatin only treatment developed further hearing loss. Of the five participants who had radiotherapy-induced hearing loss, three had cetuximab administration along with their IMRT; the remaining two had IMRT only treatment.

![Diagram showing hearing deterioration across subtypes of head and neck cancer](image)

**Figure 5.4 Hearing deterioration across subtypes of head and neck cancer**

The bar graph above (Figure 5.4) shows that hearing deterioration occurred across all seven subtypes of HNC; there appeared to be no pattern to the hearing deterioration in each subtype.
5.10 Summary

Fifty participants were recruited for hearing testing in Phase 1 of this study, and all completed pre-treatment tests. Forty-two participants completed end of treatment testing and 3-month follow-up testing.

The incidence of hearing deterioration found in this study of patients receiving standard curative UK treatment for HNC was 57% for those completing testing at the end of treatment, and 50% at 3-month follow-up. These percentages were obtained using CTCAE v4.03 criteria for hearing deterioration. Major hearing deterioration was evident in 26% of participants at the end of treatment and at 3-month follow-up; however minor hearing deterioration was evident in 31% of participants at the end of the treatment, and this reduced to 24% at 3-month follow-up. Hearing deterioration was found in all seven subtypes of HNC.

The majority of participants at 3-month follow-up had sustained hearing deterioration, although some (15%) had improvement compared to end of treatment tests. All participants developed SNHL at 3-month follow-up, however mixed hearing loss was evident for a third of these. The proportion of patients with bilateral hearing loss rose from 38.1% before treatment to 57.1% after treatment (using BSA, 2011) criteria.

In relation to types of treatment, participants had a statistically significant (p=0.01) greater risk (2.4) of developing hearing deterioration if they had CRT rather than if they had RT alone. Although older participants (mean age 68.7 years) had a greater risk of developing hearing deterioration compared with participants who suffered no deterioration (mean age 58.8 years; p=0.02), if deterioration occurred, major hearing deterioration was more evident in younger participants (mean age 56.3 years; p=0.03).

The next chapter presents the results of interviews with a sample of participants who were selected to provide a qualitative perspective on the experience of hearing deterioration after treatment on quality of life.
Chapter 6 Results – Qualitative data

6.1 Introduction

This chapter presents findings from patient interviews undertaken to address the second of the two primary research aims: to explore the lived experience of participants with hearing deterioration after treatment for head and neck cancer. The key objective of this qualitative element of the investigation was to explore patients’ experience of hearing loss within a year of treatment completion, by ascribing meaning to statements made by participants at interview.

The demographics of participants interviewed are presented first and are followed by a summary table of the themes that emerged from analysis of the interview data. Each theme, representing different aspects of patient experience, will then be presented with reference to characteristics that were identified for selecting participants for interview to assess patterns in responses that were provided (see Chapter 4, section 4.3.1). The findings on the perception of tinnitus are also included, as this symptom accompanied that of hearing deterioration for the majority of participants. The chapter concludes with a summary of the qualitative findings.

6.2 Demographic information

Thirteen participants out of 21 with measured hearing deterioration (determined from the quantitative data – Chapter 5) were interviewed. The demographic details of these participants are shown in Table 6.1 below. Participants were interviewed on average (mean) 11½ months post treatment (range eight to 13½ months).
<table>
<thead>
<tr>
<th>Participant number</th>
<th>Hearing deterioration Grade</th>
<th>Gender</th>
<th>Age</th>
<th>Location</th>
<th>Stage</th>
<th>Aetiology</th>
<th>Treatment type</th>
<th>Pre-treatment hearing level descriptor **</th>
<th>**</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 3</td>
<td>2</td>
<td>F</td>
<td>52</td>
<td>Hypopharynx</td>
<td>IVA</td>
<td>None</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>5 1</td>
<td>2</td>
<td>M</td>
<td>59</td>
<td>Tongue</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>6 3</td>
<td>2</td>
<td>F</td>
<td>56</td>
<td>Nasopharynx</td>
<td>III</td>
<td>V</td>
<td>CRT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
<tr>
<td>7 3</td>
<td>2</td>
<td>M</td>
<td>46</td>
<td>Tongue</td>
<td>IVA</td>
<td>None</td>
<td>CRT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
<tr>
<td>9 1</td>
<td>2</td>
<td>M</td>
<td>61</td>
<td>Tongue</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>11 3</td>
<td>2</td>
<td>M</td>
<td>51</td>
<td>Tonsil</td>
<td>IVA</td>
<td>None</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>12 1</td>
<td>2</td>
<td>M</td>
<td>72</td>
<td>Tongue</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
<tr>
<td>17 3</td>
<td>2</td>
<td>M</td>
<td>59</td>
<td>Tongue</td>
<td>IV</td>
<td>S A</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>29 3</td>
<td>2</td>
<td>F</td>
<td>67</td>
<td>Gingiva</td>
<td>III</td>
<td>None</td>
<td>RT</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>30 1</td>
<td>2</td>
<td>M</td>
<td>64</td>
<td>Tongue</td>
<td>IVA</td>
<td>A</td>
<td>CRT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
<tr>
<td>42 1</td>
<td>2</td>
<td>F</td>
<td>75</td>
<td>Nasal cavity</td>
<td>II</td>
<td>S</td>
<td>RT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
<tr>
<td>51 3</td>
<td>2</td>
<td>F</td>
<td>44</td>
<td>Oropharynx</td>
<td>IVB</td>
<td>S</td>
<td>CRT</td>
<td>Normal</td>
<td></td>
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<tr>
<td>53 3</td>
<td>2</td>
<td>M</td>
<td>65</td>
<td>Glottis</td>
<td>III</td>
<td>S</td>
<td>CRT</td>
<td>Hearing Loss (Mild)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6.1 Characteristics of participants taking part in interview**

Key: *Greatest grade for a participant; Aetiology (S: smoker or ex-smoker; A: alcohol intake > 14 units per week; V: viral infection either Epstein-Barr or human Papilloma virus positive). Treatment type (CRT: chemoradiotherapy; RT: radiotherapy); Pre-treatment hearing level descriptor (BSA, 2011) ** of ear with poorer hearing*

The demographic information contained in Table 6.1 shows that the mean age of participants was 60 years (range 44 to 75), and that the majority of those who were interviewed were male (62%). Over half the participants had smoking-related cancer, and high alcohol consumption was associated with 38% of participants. One participant had virally confirmed cancer, but four participants had no known aetiological factor. Participants with cancer in each of the head and neck subtypes (apart from the salivary glands) were interviewed, with the majority of participants presenting with late (III or IV) stage cancer (92%); most participants had CRT (77%) to treat it.

Approximately equal numbers of participants had either normal hearing or mild hearing loss prior to treatment. The proportion of participants who developed bilateral hearing deterioration was 69%, with 62% acquiring Grade 3 (major) deterioration in at least one ear at 3-month follow-up. To obtain as wide a range of experiences as possible (and to determine if hearing deterioration was experienced differently) participants included men and
women, those who were younger or older (and equal) than the mean age (60 years) of those who were interviewed, those who had normal hearing or mild hearing loss pre-treatment, and those who had either mild or major hearing deterioration at 3-month follow-up.

6.3 Themes

The coding framework that was used for generating categories in the first interview is shown in Appendix 6.1, and the categories that were assigned to create themes according to framework analysis (described in Chapter 4, section 4.3.5), is shown in Appendix 6.2. Five themes with subthemes were identified from the interview data (Table 6.2 below):

<table>
<thead>
<tr>
<th>Themes</th>
<th>Subthemes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Sensation of impairment</td>
<td>Hearing change</td>
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<tr>
<td></td>
<td>Tinnitus</td>
</tr>
<tr>
<td></td>
<td>Progression of aural change</td>
</tr>
<tr>
<td>2 Functional changes</td>
<td>Communication difficulties</td>
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<td></td>
<td>Problems with entertainment</td>
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<td></td>
<td>Problems with environmental sounds</td>
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<td>3 Coping mechanisms</td>
<td>General coping strategies</td>
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<td></td>
<td>Use of assistive devices</td>
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<tr>
<td>4 Emotional responses to aural change</td>
<td>Attitude to hearing deterioration</td>
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<td></td>
<td>Downplaying of symptoms</td>
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<td></td>
<td>Sense of loss</td>
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<td></td>
<td>Social isolation</td>
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<td>5 Information and support</td>
<td>Pre-treatment information</td>
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<td></td>
<td>Discussion of aural changes</td>
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<td></td>
<td>Further support</td>
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</tbody>
</table>

Table 6.2 Main themes and subthemes arising from the interview data

Each theme is discussed below, with reference made to participant quotes (presented in italics). Demographic information regarding the following characteristics are presented alongside the quotes to assist with identifying patterns in responses made by participants: their study number, gender (male=M or female=F), age in relation to the mean age (60 years) of participants interviewed [younger than mean age=Y; older (or equal) than mean age=O], the severity of their hearing deterioration (Grade 1=G1 or Grade 3=G3), and pre-treatment hearing status (N=normal or HL= hearing loss). As the majority of participants who had hearing deterioration had combined chemotherapy rather than RT alone, it was difficult to compare directly the impact these therapies had on patient experience.
6.3.1 Theme one – Sensation of impairment

This section begins with a general consideration of participants’ experience of hearing change, and then gives specific attention to the sensation of tinnitus among those who had this additional symptom.

6.3.1.1 Hearing change

The majority of participants who had a measurable deterioration in hearing noticed a difference in their hearing after treatment, whether it was a sudden change: “It was immediately…after I had day 1 and 29 of Cisplatin” (P51, F, Y, G3, N), or a less dramatic change: “Just a decline in the hearing; just that I couldn’t hear” (P17, M, Y, G3, N). Whereas some participants felt a non-specific decline in hearing, others were more specific: “I lost all the high-pitched hearing” (P11, M, Y, G3, N), indicating that these participants were acutely aware of which part of their hearing range had been affected by treatment. However, there appeared to be no difference in the perception of hearing change between men and women, those who were young or old, or those who had a hearing loss or had normal hearing before treatment. Whereas all participants who had Grade 3 hearing deterioration were aware of a change in their hearing, not all those with Grade 1 change felt much difference: “Bearing in mind I’m old, I’m 76, I don’t feel it is much worse than it was before” (P42, F, O, G1, HL), or had a change that suggested a minor difference: “I did feel that there were things that I was able to hear before, that I do not hear now. I cannot be specific about what that is” (P12, M, O, G1, HL). Therefore, it seemed that participants who had a major measured deterioration in hearing following treatment either had a sudden or less dramatic change in hearing, whereas those who had a minor measured deterioration either had a vague perception of hearing change, or noticed no change at all.
Sudden changes in hearing appeared to occur during treatment, whereas more gradual change was experienced after the completion of treatment: “I think it was when the radiotherapy had finished, probably a few days after” (P11, M, Y, G3, N). These findings showed that hearing change manifested at different times for participants in relation to when they received their treatment. Thus, it was not possible to predict when hearing deterioration was to be experienced; also, there was no pattern in relation to different participant characteristics. However, those who were aware of a hearing change or tinnitus during treatment may have been offered an alternative treatment to complete their therapy.

In addition to experiencing general deafness and/ or reduced pitched hearing, some participants felt a sensation in the ear such as fluid, pressure, a popping or a blocked sensation: “My left ear filled with fluid or it felt like that, and it felt pressurized…” [my ear] just blocked itself… it is almost like something is stuck, there is something in my ear to stop hearing at all, so the high pitch goes at the same time as the pressure is there as well” (P11, M, Y, G3, N), or “I noticed my ear was like being on a plane, so I could feel it popping” (P7, M, Y, G3, N). This sensation of pressure change, or of fluid, is most probably due to middle ear effusion that sometimes follows RT treatment for HNC. It was interesting to note that participants felt that this pressure made them ‘stop hearing at all’, which suggests that this experience had a significant negative impact. Participants with only Grade 3 deterioration in hearing mentioned fluid sensation, possibly indicating that those who had minor deterioration may have had a resolution of fluid by the time of their interview.

6.3.1.2 Tinnitus

Although this study was primarily focused on hearing change, the majority of participants who experienced hearing deterioration had also acquired tinnitus. Some participants experienced tinnitus at the same time as their hearing deterioration yet, as will be reported below, in this study tinnitus was often the more distressing symptom.
A common finding was that participants experienced tinnitus in different ways, and one participant at the beginning of his treatment experienced hyperacusis (the intolerance to everyday sounds) with his tinnitus. Each participant experienced a different type of sound, for example: “It is literally just like a mmmmmm, but very very faint and very high pitched” (P11, M, Y, G3, N). They also experienced tinnitus in different locations: in the head, in the ear or over the ears, for example “It sort of hovers [participant gesticulating with his hand moving over his head]” (P12, M, O, G1, HL). These findings suggested that the sensation of tinnitus following hearing deterioration manifested itself in various different ways. Also, there appeared to be no pattern as to whether participants experienced hearing deterioration and tinnitus concurrently, or at different times. However, the distress with tinnitus was evident in some participants: “In the left ear I’ve got terrible ringing for quite some time” (P53, M, O, G3, HL), and was particularly evident in the one participant who had hyperacusis: “The noise…combined with external stimulus, I guess that caused the ears to hurt” (P7, M, Y, G3, N). This distress led to a change in treatment for this participant. It was noted that more severe tinnitus was experienced by those participants with Grade 3 deterioration in hearing.

6.3.1.3 Progression of aural change

Participants experienced different progression in their symptoms of hearing deterioration during and after treatment. Some participants experienced temporary hearing loss during their treatment that indicated first, the presence, and then secondly, the resolution, of middle ear effusion: “When I had the first [dose of cisplatin], day two I woke up and it was like I was under water. My hearing was very like I had got water in my ears, and I sort of was not shouting at people, but could not hear myself talk. Well after about a week that improved, it went, and my hearing went back to normal” (P51, F, Y, G3, N). After the completion of treatment up to the time of interview, some participants felt that their hearing deterioration fluctuated in intensity: “[my] hearing could be a bit all over the place at times” (P7, M, Y, G3, N). Others mentioned that their hearing difficulty was maintained in severity: ‘It feels like I am
underwater with my left ear so everything is really muffled and then it just stayed like that” (P11, M, Y, G3, N), whereas others, following the initial deterioration, subsequently perceived an improvement: “I mean [the hearing] is improving slowly” (P53, M, O, G3, HL). An improvement in hearing indicated that participants could have had confirmed psycho-acoustical (measurable) change if hearing testing was performed at the time of interview. Although maintained severity, or decreased severity, in hearing loss following treatment was apparent, further deterioration in hearing was not clearly stated by participants. However, some participants were uncertain when asked if there had been a change in their hearing: “I really could not say. I mean after a while you just get on with things so you do not really pay too much attention [to your hearing]” (P12, M, O, G1, HL). These findings indicated that the sensation of hearing deterioration was most prominent during or within a few months following treatment, as it was in this period that the majority of participants experienced their hearing problems most acutely, although others had maintained difficulty with hearing by the time of their interview one year after receiving either RT or CRT for their cancer.

There was also variation in the progression of tinnitus. Some participants experienced continuous tinnitus: “It is like a very high-pitched whistle in my head, constantly [present]” (P51, Y, F, G3, N), fluctuating tinnitus: “[The tinnitus] seems to come and go I think, because sometimes I’m not aware of it, and then I think oh I’ve got that noise in my ear” (P29, F, O, G3, N), or a lessening in the severity in tinnitus from when first experienced with treatment “With the treatment there was the tinnitus…it is very mild now” (P12, M, O, G1, HL). Some participants experienced a change in how they perceived their tinnitus: “The high-pitched whistling that I had went…and was replaced by… a white noise…it is just kind of a shhhhh noise these days” (P7, M, Y, G3, HL). It was clear that participants not only experienced hearing deterioration and tinnitus at different times and in different ways during or after treatment, but also experienced the progression of their symptoms differently. Arguably, this may make it difficult to advise patients when or how they would experience these symptoms after treatment, and how their symptoms would progress.
Therefore, all participants with a major measured hearing deterioration were aware of a change in hearing, whereas only some of those with a minor deterioration experienced a loss. Some participants noticed their hearing change first during treatment, whereas others perceived their change following the completion of their RT or CRT, with some participants with Grade 3 deterioration experiencing the sensation of fluid build-up, as well as hearing loss, with their treatment. In addition, most participants who suffered a loss in hearing also experienced tinnitus, and that those with major deterioration expressed more distress with their tinnitus than those with Grade 1 change. There was no pattern to the progression of either hearing loss or tinnitus, so that it was not possible to predict symptom progression.

Apart from the observations made above on the different sensations perceived by participants who had Grade 1 or Grade 3 deterioration, there were no patterns apparent based on other patient characteristics. This first theme described how participants perceived their aural symptoms. The next theme presents how these symptoms affected daily living of participants interviewed.

6.3.2 Theme two – Functional changes

For the eight participants with Grade 3 hearing deterioration there were more circumstances where they encountered hearing difficulty compared with the two who perceived a change in hearing with their Grade 1 deterioration. This difference may be due in part to the different lifestyles of participants as well as different severity in their hearing deterioration levels; however the majority of the quotations included in this section are from participants with Grade 3 deterioration.

6.3.2.1 Communication difficulties

All but one of the participants who perceived a change in hearing experienced difficulty in communication; participant 30 (M, O, G3, HL) may not have noticed this difficulty as he
mentioned leading a mainly solitary life. The other participants were either specific in the type of speech they had difficulty with: “If they had a voice which was sort of a pitched voice or a high-pitched voice, like a lady’s type of voice, I could hear them, but I couldn’t tell you what they were saying” (P53, M, O, G3, HL), or were less clear: “[I have] general deafness” (P17, M, Y, G3, N). Hearing in background noise was a particular concern: “But it’s really if there’s noise, background noise, that’s when I have a problem” (P29, F, O, G3, N). Some participants spoke of the difference they had noticed with listening in certain situations following treatment: “I find it very difficult, and you know, I have my phone turned up loud, say that again, can you say that again?…the telephone’s been more difficult” (P17, M, Y, G3, N), or “I was pretty good at distinguishing [and understanding speech in] noise. I could focus on what was being said and I could hear what people were saying” (P12, M, O, G1, HL). Therefore, hearing deterioration had an impact on everyday communication, particularly for participants used to socialising when there was background conversational noise, when before treatment there was less or no difficulty.

All participants with minor hearing deterioration, or unilateral (affecting one side only) major hearing deterioration (P29, F, O, G3, N; and P11, M, Y, G3, N), said they had no difficulty when hearing in quiet situations. This was not unexpected, as people with mild hearing loss usually do not have difficulty in these situations as normal conversational speech levels are loud enough for them to understand speech, and those with unilateral loss are able to hear well via their unaffected ear. However, responses provided by some of those participants with major bilateral (affecting both sides) hearing deterioration revealed that some were required to lip-read, even in quiet, due to their sudden-onset hearing deterioration. Some participants were aware that they needed others to face them: “I force [my daughter] to look at me…so I can focus on what she is saying…I find that if people are talking to me I am very, very good at picking up the visual cues” (P7, M, Y, G3, N), whereas others made comments that indicated they were not aware that they were lip-reading: “Sometimes my husband has a habit of sitting with his laptop on his lap and obviously the screen is right in
front of him so sometimes I cannot hear him. I know it sounds silly, it is as though it has been blocked by the screen” (P51, F, Y, G3, N). Participant 51 did not recognise that the difficulty with communication stemmed from her hearing deterioration, and that the computer screen blocked her from seeing her husband’s face and from lip-reading, although she felt that sounds were being physically blocked by the screen. Therefore, when some patients experienced sudden hearing deterioration following treatment, and discovered that they were required to lip-read, this change came as a surprise as they were not aware of this possible requirement prior to treatment. The fact that some participants did not recognise the value of lip-reading revealed a lack in service provision in preparing patients adequately to cope with possible hearing deterioration with treatment.

The effect of tiredness and hearing deterioration that followed cancer treatment combined to increase the negative impact of these symptoms: “A big contributory factor [to having hearing problems] is when I’m tired. A year on, I spoke to the oncologist today, and there are still some evenings when I get absolutely shattered…I notice things far more when I’m tired. So, I think that’s a contributory factor” (P7, M, Y, G3, N). Participant 7 also had difficulty in processing speech: “My … daughter is 13 and like all children, now she thinks she should talk at the speed of light… I was having difficulty un-jumbling the constant stream of information coming at me” (P7, M, Y, G3, N). In addition, tiredness exacerbated his tinnitus: “I find when I’m quite tired the white noise is more prevalent” (P7, M, Y, G3, N). Other participants did not clarify if they experienced tiredness, but the responses made by Participant 7 suggest that if patients suffer fatigue following their cancer treatment, they may have greater difficulty in understanding speech and an increased perception of tinnitus.

6.3.2.2 Problems with entertainment

All ten of the participants who perceived a change in their hearing were affected in their leisure activity and socialising. Difficulty with television listening was encountered by most participants: “if I am watching telly for example I used to be able to hear it at a very low
volume” (P12, M, O, G1, HL), although some did not experience this problem (for example, participant 29 who had a unilateral hearing deterioration). Understanding speech was particularly difficult when there was background noise in the programmes: “[With] a lot of programmes I’ve found these days, the background noise is so loud compared to the dialogue noise” (P7, M, Y, G3, N). For some participants with major hearing deterioration, their appreciation of music was also affected: “I like dance music, and I was not listening to dance music because they use high frequencies… and that was a definite no, no, [but] it’s reignited my love of guitar-based music, because obviously, a lot [of] lower tones and drum sounds [are] going on” (P7, M, Y, G3, N). A struggle to hear music was most problematic for participant 11 (M, Y, G3, N) who acquired a unilateral deterioration in hearing: “I am a musician… so that I have found really difficult obviously because I cannot hear in stereo anymore”. Other participants did not mention how their hearing loss affected their listening to music. However, not all participants experienced difficulty when participating in other forms of entertainment: “I go to the cinema a lot and when I’m at the cinema it causes no problems. There are no subtitles at the cinema obviously, but I don’t find I’m missing dialogue or I don’t get the film out after I’ve seen it at the cinema and go “I didn’t understand what they were talking about”” (P7, M, Y, G3, N). Cinema going as a hobby, though, was spoiled for another participant: “You cannot hear some things that happen at the cinema” (P51, F, Y, G3, N).

In summary, all participants experienced some difficulty when engaging in entertainment on their own, although it was noted that participants were affected in different ways depending on their type of hearing deterioration, and the form of entertainment. Comments made by some participants, with Grade 3 hearing change, indicated that their deterioration also had an impact on the quality of their social life in gatherings with background music: “If we have people round and we have a bit of music on and we’re talking, I have to say “do you mind, we’ve got to turn the music down if we’re going to have a conversation”, because I can’t really listen to both, you know, listen to the music and talk to you at the same time”. It’s all a
bit much” (P17, M, Y, G3, N), or “it is loud noisy social events… You know, what is the lesser of two evils? You are either really loud with the music and that, or you cannot hear people. They are the big ones, big social gathering events” (P51, F, Y, G3, N). Other participants did not comment on how they were affected in similar situations, either because they encountered these less frequently, or such situations were not problematic. It appeared, therefore, that for those participants who mentioned lifestyles that involved gatherings with background music, there was the dilemma of which activity to be involved in: listening to the music or engaging in conversation, whereas before their treatment they were able to enjoy both activities at the same time.

6.3.2.3 Problems with environmental sounds

Changes in hearing following HNC treatment also affected the hearing of non-speech sounds (other than music) that were mentioned by a few of the participants at interview. Computer use is part of everyday modern life, and sounds from the keyboard and mouse had now become silent “I do not hear anything now when I do the computer. I may have before, I do not know, I cannot really remember” (P12, M, O, G1, HL). It is noted that this participant experienced only minor unilateral deterioration, yet this small change in hearing, was sufficient to create this functional difficulty. Potentially, this patient’s baseline hearing level (of mild hearing loss) was a factor, however, there were no patients with Grade 1 deterioration and normal pre-treatment hearing to compare with. Another more concerning aspect of high-frequency hearing loss is the inability to hear doorbells (of high pitch): “the doorbell sometimes has been a problem yes. At times I may not have noticed it, but since I did not notice it I am not aware that I have not noticed it!” (P12, M, O, G1, HL). The lack of awareness of hearing the doorbell was discussed with this participant at interview, and it was suggested that a bell with a lower frequency pitch be obtained. Difficulty with hearing the doorbell was also mentioned by participant 7: “since the treatment finished, I have realised that some of the high tones…now [I] have difficulty hearing, …[including from] the
“doorbell” (P7, M, Y, G3, N), although others stated they were able to hear the doorbell, for example, participants 17 (M, Y, G3, N) and 30 (M, O, G1, HL). Reassuringly, when the majority of participants were asked, none had difficulty in hearing (high-pitched) fire or smoke alarms, as these alarms are usually much louder than doorbells.

In this theme it is reported that participants had functional changes in hearing that affected communication, entertainment and socialising, as well as hearing environmental sounds. There were more widely reported changes for participants with Grade 3 deterioration compared with Grade 1 deterioration, particularly in quiet situations where the requirement to lip-read following (sudden-onset) treatment associated hearing loss was evident for those who had Grade 3 change only. There were no differences in functional change based on other patient characteristics of age or gender, although it is noted that a subtle change in hearing was enough for a participant with pre-treatment loss to notice he could not hear sounds from the computer, and participants with unilateral hearing deterioration (both minor or major) were also adversely affected by their change in hearing.

6.3.3 Theme three – Coping mechanisms

This theme is closely related to the next theme on emotional response to hearing deterioration, as the attitude of participants towards the impact of their hearing deterioration had a bearing on what strategies they used to overcome their hearing difficulties. All ten of the participants who perceived a change in hearing found strategies to cope with their change. Those who had severe hearing deterioration (Grade 3) gave more examples of how they coped compared with those who had less severe (Grade 1) deterioration, but it was evident that younger participants discovered more strategies than older ones amongst those with Grade 3 deterioration. There are two parts to this theme: general strategies used to deal with difficulties in communication and entertainment, and the use of assistive devices to help deal with aural changes that occur with treatment for HNC.
6.3.3.1 General coping strategies

All the younger participants who perceived a change in hearing found ways, with their friends and family, to enhance communication. The most common was for the participant to ask for words to be repeated or made louder: “I’m really sorry I can’t hear you… can you speak up” (P6, F, Y, G3, HL) or “people had to keep repeating what they were saying or speak up louder” (P2, F, Y, G3, N). Other common tactics adopted were: to reduce background noise or move to a quieter place: “if there is a cacophony of sound and somebody is trying to talk to me you almost have to … go to somewhere quieter to hear” (P11, Y, M, G3, N); to lip-read: “I had to be more alert of what people were saying to me, you know, and watch their mouth to see if they was talking to me” (P17, M, Y, G3, N); to gain attention: “If I ignore them they do not take offence by it; they just nudge me and go “I was talking to you”” (P51, F, Y, G3, N – when talking with friends), to ask others to speak more slowly: “I have to say, look, slow down” (P7, M, Y, G3, N – when talking to his daughter). For one older participant, his wife made the adaption to the change in her husband’s hearing: “[There is] more communication from [my wife], having to repeat things” (P12, M, O, G1, HL); two older participants acquired hearing aids as part of this study (P53, M, O, G3, HL; P29, F, O, G3, N). Older participants generally gave no examples of initiating by themselves means to improve their communication.

A reason for the difference in the efforts made between older and younger participants to improve their communication could be that older participants were not aware of the need to do so, as those they spoke with may have had hearing problems themselves. When asked if others had commented on his hearing deterioration, one participant said “They wouldn’t notice” (P30, M, O, G1, HL). This participant mentioned that he led a fairly solitary life; however, other older participants who led more active lives chose not to clarify in their conversations what was being said: “Certainly in crowded rooms, I mean if there are several people around and there is a lot of chat going on it is difficult to distinguish what is being
said, so sometimes you just nod your head in anticipation that you have got the right notion!” (P12, M, O, G1, HL), or “I just make out I’m thick” (P53, M, O, G3, HL). Therefore, participants who perceived a deterioration in their hearing coped with changes in communication in different ways. It appeared that younger participants made efforts to enhance communication, whereas older participants tended to be less inclined to deal with the effects of their hearing loss. The differences found could be linked to different lifestyles of each individual, or to different attitudes towards hearing loss by different age groups, and this aspect will be developed further in the next theme.

Most participants found that they were able to listen to the television by simply increasing the volume: “The television, I normally have it on setting 1; I have had to put it up to 14 or 15” (P30, M, O, G1, HL). Another tactic was to use subtitles: “I put subtitles on the TV these days” (P7, M, Y, G3, N), or to concentrate more with television viewing: “I might have to strain a little bit harder” (P6, F, Y, G3, HL), or to use earphones: “I need a bit more volume and I use earphones. I find it easier to hear with earphones than with just the open speaker” (P12, M, O, G1, HL). Increasing the volume was also used for radio listening: “I have the radio up a little bit louder” (P6, F, Y, G3, HL), and the musician with unilateral hearing loss found the means for adapting to his loss when listening to music: “If I am working on a track I have to put my headphones on and listen to one side for the stereo and turn the headphones around and listen” (P11, M, Y, G3, N).

Most of the seven participants who had tinnitus dealt with it by ignoring it: “I try my hardest to ignore it, because otherwise I would just go mad. I mean, to have a continuous noise in your head all the time, you’d just go mad” (P6, F, Y, G3, HL). For some others who had persistent tinnitus following treatment, or had intermittent tinnitus, it was not clear how they managed their tinnitus, although hearing aids were of use for one participant (see the section on assistive devices, below). Therefore, it appeared that participants at interview had fewer strategies in coping with their tinnitus problems than they did with their hearing deterioration, yet tinnitus appeared to have a greater negative impact.
6.3.3.2 Use of assistive devices

Three of the 13 participants had acquired hearing aids by the time of their interview. These three had worn their aids for two months, and provided feedback on how hearing aids had made a difference. Two participants had noted benefit in some situations more than others. Hearing the television, or conversation in quiet was improved with hearing aiding: “I can hear the telly and if we’re there on our own, I can hear my husband talking to me, you know, I can hear all that” (P29, F, O, G3, N), or in company: “Once I have got my hearing aids in, in general conversation I am fine in a room of people, absolutely fine…If there’s company and there’s sounds [the hearing aids] make it easier for me to listen to somebody. I can hear somebody’s voice, you know. Otherwise if there’s sounds there and I haven’t got it in, I don’t hear the voice very well” (P51, F, Y, G3, N). However, hearing speech in background noise was still problematic: “I struggle in a crowded bar or a pub or anything like that, that has also got music…because then I cannot wear my hearing aids because everything is just way too loud” (P51, F, Y, G3, N). Participant 51 also found the hearing aids helped her deal with tinnitus: “If I put my hearing aids in, [the tinnitus] goes. So it is nice to have some peace and quiet”. However, the third participant, although stating that hearing aids were of general help, still struggled to obtain clarity in hearing speech: “I’ve got some hearing aids which did help, but as I always said, it’s not the volume which I think hearing aids are more designed for, it’s discerning the level of the person’s talking” (P53, M, O, G3, HL). Although there was only a limited time following fitting to gauge the benefit of hearing aids, these devices did improve listening for some participants, particularly where there was a reduced level of background noise; hearing aids also provided some relief from tinnitus.

Participant 7 (M, Y, G3, N) suffered from hyperacusis in a short period during treatment and resorted to his own method to cope: ”I changed my doorbell at home, because it was such a high-pitched noise it annoyed me so much when it came on that I had to change it for a lower tone noise”, and “I would just clap my hands over my ears. I bought some noise
cancelling headphones, anything to just try to shut everything out in the hope that [the tinnitus] would internally subside. In addition [I started] having the TV turned down”. The hyperacusis for participant 7 subsided so that he is now able to continue with everyday living, including watching the television without encountering pain. However, when experiencing hyperacusis, it appears that this participant found relief from his hyperacusis by the use of noise cancelling headphones, or changing the pitch of a doorbell to a lower tone following damage to high frequency hearing with his treatment. This younger participant sourced information himself, rather than obtaining advice from a health professional, possibly highlighting a gap in service provision for delivering necessary advice.

Although two participants mentioned being aware of fluid, or pressure in their ears following treatment for HNC, only one described management of his OME. Participant 7 (P7, M, Y, G3, N) referred to advice given by a clinical nurse specialist on how to alleviate his middle ear dysfunction: “…[obtain] a little blue tube, put a balloon on it, pinch nose, blow down it and it does the same thing as trying to pop your ears on a plane, but equalizes the pressure between the balloon and your ears, therefore not damaging it. I was also prescribed medication to try and get rid of the fluid in the ears as well, and that worked marvellously well over a period of about eight weeks. The popped feeling in my ear went away”. The other participant with OME (P11, M, Y, G3, N) still struggled with his middle ear dysfunction at the time of his interview, and, although he was offered a hearing aid for his affected ear, he declined its use: “I was offered a hearing aid if I wanted one, but I find I can cope without one and I am still hoping for the day that the hearing comes back better than it is now, so I can cope with that, but I was offered a hearing aid if I wanted one”. However, he was still affected by the pressure in his ear: “you just think I wish it would clear, but I know it has not and I cannot do anything about it to make it clear so you just kind of put up with it”. It was not clarified with this participant if he was offered the same advice given to participant 7; it is possible that he was not, and this would indicate variation in service provision.
All the participants found different ways to adapt to their hearing deterioration and deal with changes in communication and non-speech sounds. Those participants who had Grade 3 deterioration used more widespread solutions compared with those who had Grade 1 change. Lifestyle had a bearing on initiatives made to enhance the understanding of speech, although it was evident that younger participants made more effort than older participants for improving speech communication; it appears that older participants were less inclined to deal with their hearing problems. Assistive devices were generally of use for dealing with aural concerns, however, there were fewer tactics used, and devices available, for dealing with tinnitus compared with hearing deterioration. It appeared that information and management advice supplied by health care professionals to deal with aural concerns was in some instances variable or inadequate, given that patients searched for their own solutions.

6.3.4 Theme four – Emotional responses to aural change

This theme has four aspects to it: attitude to hearing deterioration; the downplaying of hearing deterioration or tinnitus; the sense of loss; and the experience of isolation through the tendency for patients and those they associated with to withdraw from interaction.

6.3.4.1 Attitude to hearing deterioration

In dealing with younger and older participants, there appeared to be a difference in their reactions to their hearing deterioration. Some younger participants were not afraid to let others know of their difficulty: “I’m not shy about saying ‘I can’t hear properly with that [noise], can we turn it down?’ So it hasn’t bothered me, you know” (P17, M, Y, G3, N). Many did not feel that hearing deterioration had affected their lifestyle: “[the hearing loss] is not causing a problem” (P2, F, Y, G2, N); or feel that the hearing loss affected how she felt: “[my hearing loss] has not made me self-conscious or I am not embarrassed by it or anything like that. You know how many people have hearing problems in this day and age? You know it...”
does not upset me, it does not embarrass me, it does not worry me, no, I am fine with it” (P51, F, Y, G3, N). Some also had an attitude of wanting to overcome the difficulties they encountered, be it their hearing problem: “I might have to strain a little bit harder [to listen following treatment], rather than just completely relaxing… but I try and fight it; I’m a fighter” (P6, F, Y, G3, HL), or hyperacusis: “I’m kind of a very very stubborn person who refuses to let things kind of get in the way” (P7, M, Y, G3, N). One participant showed indifference to both his blocked ear sensation: “you just kind of put up with it”, and his tinnitus: “[the tinnitus] …is one of those things I can put up with and it does not keep me awake, it does not affect me during the day or anything. You know you notice it more in quiet times, but you can tune out of it quite easily” (P11, M, Y, G3, N). The younger participant fitted with hearing aids even accepted the use of these devices: “I do not mind the fact that I have to wear hearing aids. I am fine with it…it has not made me self-conscious or anything like that, and I mean I have got long hair but I wear my hair up and when I have got my hearing aids in and I really do not mind if people see them or not” (P51, F, Y, G3, N). Participant 17 accommodated his hearing loss, experienced in the context of surviving cancer and treatment for it: “When you’re having your treatment and then the long recovery period, your hearing is sort of one of the lesser points you’re worried about. You’re more worried about your general health. Your biggest issue is your eating and everything like that, so your hearing comes sort of way down the line a little bit, you know, but it is important, but it’s not important at the time, you know, not quite as important, you know” (M, Y, G3, N). Each of the six younger participants who were interviewed mentioned that they were not bothered by their aural change or their use of hearing aids, and felt that their hearing deterioration had not made a negative impact on their day-to-day life.

Although some older participants also suggested that the hearing deterioration was not a problem to them: “I’ve got used to it now, don’t bother really” (P53, M, O, G3, HL), others were not sure, when asked how the change had affected them: “I do not know” (P12, M, O, G1, HL). There were comments made that indicated older participants seemed less ready to
come to terms with their hearing loss: “[My wife] has commented on [my hearing loss], only because there are things that I need to hear and I am constantly saying “what”, but she does tend to talk to me when she is miles away as far as I am concerned!” (P12; M, O, G1, HL), or the need for a hearing aid: “Well I had a hearing test. I didn’t really take much notice of it because my right ear was still perfect…it was recommended that I have a hearing aid” (P29, F, O, G3, N). Therefore, unlike younger participants, older patients appeared less ready to acknowledge their hearing deterioration, and seemed to put the onus on others to make up for and adapt to their (the patients’) hearing difficulties.

6.3.4.2 Downplaying of symptoms

Although most participants said that their hearing change did not bother them, some revealed emotions and attitudes which suggested that aural change had a negative effect on their well-being. Downplaying of symptoms was conveyed when participants stated that they were not adversely affected by their hearing loss or tinnitus, but they disclosed negative feelings of anxiety, disappointment, frustration, annoyance or guilt that showed the impact of hearing deterioration and tinnitus on their quality of life.

During treatment, some participants had an awareness of their hearing deterioration or tinnitus and voiced disappointment in their symptoms returning during treatment, or anxiety in the severity of their symptoms being maintained. For example, participant 51, who experienced hearing deterioration suddenly during treatment indicated disappointment when she said, “I thought it was going to get better like it did on day one when I had the first lot of chemotherapy” (F, Y, G3, N). Participant 7 shared his anxiety that the severity of his tinnitus that was experienced with treatment would not improve “the worry [was] whether or not it was going to subside with time as well, or if it was going to be a permanent fixture” (P7, M, Y, G3, N). These participants showed disappointment or anxiety at the prospect of their symptoms being maintained, or in the return of symptoms if there was temporary respite, perhaps because there was now another problem to deal with as a result of their cancer
treatment. Both participants 7 and 51 were younger participants, had Grade 3 deterioration, and had normal pre-treatment hearing. However, other participants with some similar characteristics who also first experienced their aural change during treatment (including P6, F, Y, G3, HL; P29, F, O, G3, N), as well as participant 30 (M, O, G1, HL) did not express similar feelings. It is possible that participants 7 and 51 experienced more severe symptoms during treatment than other participants because they hinted at feelings of anxiety or disappointment, and that these feelings were more related to this severity, rather than due to their younger age or normal hearing before treatment.

After treatment, some participants felt frustrated, annoyed or guilty because of their aural change. Frustration occurred when not being able to perform an everyday task of listening and understanding conversation, which was possible to do prior to hearing deterioration following treatment: “I mean it gets a bit frustrating, and I’d say it gets frustrating if I’m having a conversation or I can’t hear…” (P6, F, Y, G3, HL). Irritation in others was sensed by participants: “Things like the television, I might have it up higher than say normal, which annoys my mum” (P6, F, Y, G3, HL). The irritation of experiencing tinnitus was keenly felt at some times more than others and expressed as annoyance: “It is never overwhelming but sometimes it is really annoying” (P11, M, Y, G3, N), or as a nuisance: “Annoying, sometimes more annoying than others … Every once in a while, it comes to the fore of the brain and it is just a nuisance” (P12, M, O, G1, HL). The feeling of irritation or annoyance stemmed from the intermittency of tinnitus, and possibly a lack in control to overcome this symptom. It was not made clear in what circumstances the feeling of annoyance with tinnitus was exacerbated. The feeling of guilt was apparent on changes made to accommodate hearing deterioration: “It's not fair on, you know I live with my mum, and it's not fair on her if the television is up really loud, so I try and manage with it not quite so loud”; "It's just embarrassing to say, 'look I'm really sorry'; if I'm on the telephone and having a conversation with someone, other than a friend, it's a bit embarrassing, having to keep saying “I'm really sorry, but I can't hear you, can you speak up?”; it must be annoying for them and it's
embarrassing for me” (P6, F, Y, G3, HL). However, such feelings were not communicated by other participants (for example P2, F, Y, G3, N). Feelings of annoyance and guilt with tinnitus or hearing deterioration, therefore, impacted some participants and those whom they were with, although other participants were not affected in this way, indicating that hearing deterioration and tinnitus affected individuals differently.

6.3.4.3 Sense of loss

The sense of loss in experiencing a deterioration in hearing was sometimes revealed by some of the older participants. One shared her feelings of disappointment because of a change in her hearing: “I felt disappointed… because my hearing was perfect before the radiotherapy” (P29, F, O, G3, N). However, disappointment appeared to go deeper than being associated with a change in physical functioning; it, together with embarrassment, was also associated other types of loss: that of self-worth, identity, and self-confidence. Loss in each of these three attributes is commonly associated with hearing loss. There was stigma in being identified with a hearing problem after treatment that indicated deafness was associated with reduced self-worth: “I haven't allowed [my partner] to tell anybody” (P53, M, O, G3, HL). This finding would suggest that participant 53 was reluctant to use hearing aids that were provided. The wearing of a hearing aid affected the self-confidence of another participant: “I felt disappointed that I needed a hearing aid … It is vanity. I didn't want to wear a hearing aid. It just takes the confidence away” (P29, F, O, G3, N). The stigma of deafness also affected the self-identity of participant 29, by the feeling of suddenly ageing: ‘[I feel]…as if I'm about 90” (F, O, G3, N – aged 67), however, participant 12 (M, O, G1, HL) appeared not to be adversely affected by his hearing change. These findings indicate that hearing deterioration following treatment had a significant impact for some of the older participants in this study on their self-image, self confidence and identity with the stigma of hearing loss, or in receiving a hearing aid, whereas younger participants provided no evidence of being affected by the association of acquiring hearing loss, or by wearing hearing aids.
Some younger participants conveyed feelings of isolation by withdrawing from usual social activity. Isolation was indicated by reduced telephone use: “So I generally don't speak that much on the phone [to my children]... because I find it difficult to hear a lot of the conversation” (P17, M, Y, G3), withdrawal from social activity: “It is silly things, like I used to go to the pictures, I do not go to the pictures anymore because... [of] the noise” (P51, F, Y, G3, N), or reduced interaction with their partner: “I think ... because my hearing was so good before the treatment that [my husband] never had to repeat himself and that, but he is realising that’s how it is; or [he] just does not talk to me” (P51, F, Y, G3, N). Although participants declared some readiness to come to terms with their hearing deterioration, there was evidence to suggest that this symptom affected quality of life through reduced social activity and conversation with family. Withdrawal from social activity was not evident in the other participants. Although both participants 17 and 51 experienced Grade 3 deterioration, having had normal hearing prior to treatment, they appeared to have lifestyles that revolved around social activity. Therefore, the isolation sensed by these younger participants may be linked more to their lifestyle rather than because of their age.

There were patterns identified with emotional responses to hearing deterioration following HNC treatment. Whereas younger participants generally were ready to admit to their hearing deterioration, older participants tended to be more reluctant to acknowledge their loss. Younger participants experienced withdrawal from social interaction with friends and family, although isolation may be more related to patient lifestyle rather than age. The sense of loss was associated with older participants. Downplaying of symptoms was evident with some participants who expressed feelings including those of annoyance and guilt. There appeared to be no pattern to the responses made based on pre-treatment hearing level, or on patient gender.
6.3.5 Theme five – Information and support

Information participants received on hearing deterioration and on further support appeared in some instances to be insufficient and inadequate.

6.3.5.1 Pre-treatment information

Prior to treatment, participants were provided with information that hearing deterioration may take place with treatment: “I knew it was a possible side-effect of the treatment so I was half prepared for it” (P7, M, Y, G3, N), but the provision of so much other information at the same time reduced awareness of this possibility for other participants. The diagnosis of cancer became so significant that it caused a distraction from other issues such as hearing loss: “It is a lot to take on board, when you are first told that you have got cancer, and this is what is going to happen. They do briefly explain that this is possible what could happen from having chemoradiotherapy, so they talk about your loss of taste buds, saliva, the mouth ulcers, loss of hearing. They talk about it, but to be perfectly honest with you, you do not take it in. All you hear is the word cancer and then that is it. You really did not get much to start with, because they were more concerned with giving you how you were physically going to feel and cope with it for six weeks” (P51, F, Y, G3, N). Therefore, although information that hearing deterioration may occur with treatment was given to study participants prior to starting RT or CRT, the shock of being diagnosed with cancer may have reduced the realisation that hearing deterioration may follow treatment. Also, the focus of information prior to treatment may be prioritised to getting patients through treatment and the restoration of vital body functions, rather than alerting patients to the possibility of suffering a hearing change and details of what that change may involve.
6.3.5.2 Discussion of aural changes

During treatment, participants had regular meetings with staff (oncologists or radiographers) involved in monitoring the side-effects of treatment, although it was left to participants to report any aural concerns: “At no point throughout [the treatment] do they ask you how your hearing is. They just say to you “Any other things?“ and I just happened to mention about the hearing. But they never actually say “Have you noticed any hearing problems, difficulty, noises, tinnitus?” anything like that. Never do they mention that” (P51, F, Y, G3, N). Some participants were prepared to share changes that they experienced with treatment, as they were aware before treatment that hearing deterioration may occur: “We were able to, normally every week, get a comprehensive list of things we would talk to the doctor about, and normally the most pressing things, and at that time the hearing had suddenly gone… from everything was alright, to something’s a bit different now, so we immediately brought that up. Because I was kind of expecting it, they were on [my] list” (P7, M, Y, G3, N).

Therefore, although participants had regular meetings with clinicians (radiographers and oncologists) during treatment to discuss side-effects, the clinicians’ checklist did not contain hearing problems. Consequently, patients needed to mention aural changes (hearing deterioration or tinnitus), and these changes may not be apparent if patients are focused on other side-effects of treatment.

However, mentioning aural changes during treatment led to a change in treatment for some participants who were interviewed. This change occurred for a participant who had aural pain: “Initially the first two rounds were cisplatin with also 5FU, which I kept with me at home. Following some whistling in my ears, after the first two rounds of that… I went back for the consultation and said, “Look it’s quite painful” … They made a decision that they would try me on the carboplatin to see if that alleviated some of the symptoms” (P7, M, Y, G3, N).

It was found that other participants (P53, M, O, G3, HL; P51, F, Y, G3, N), following a review of their treatment plan, also had a change in treatment from cisplatin to carboplatin. Therefore, in some cases, a change in treatment took place following side-effects that
included aural change. This highlighted the need to have aural change as part of a checklist of side-effects used by clinicians during treatment.

The confusion and inadequacy within service provision was highlighted by the lack of clarity in who would discuss and manage hearing difficulties once they occurred. One participant gave a clear indication that the oncologists were expecting audiologists to do this: “When I actually spoke to the oncology team and explained that I had the hearing problem, they were very much, “Oh that is standard, that is going to happen, but do not worry, you are under audiology”. So, they did not go into it at all then” (P51, F, Y, G3, N). There appeared to be an assumption made by oncologists that the audiology team would provide information and support on hearing deterioration. However, this assumption did not seem to be communicated adequately between audiology and oncology, as there were varying levels of information shared by audiologists about participants’ hearing. Some participants felt the information provided by the audiologist was appropriate: “Everything was explained along the way and I understood it all so that was all fine” (P11, M, Y, G3, N). However, others had less comprehensive support: “I must admit some of the people I’ve had the hearing tests with haven’t really said too much about the results, and if there’s any real outcome of it, you know” (P17, M, Y, G3, N). This lack in consistency was apparent at interview, as although some participants had discussions about their aural concerns with audiologists or oncology staff soon after they experienced their hearing deterioration or tinnitus, others only got to discuss these concerns when they came to interview one year after treatment. One participant was not sure if what he was hearing was in fact tinnitus: “I am assuming it is tinnitus only because people have described sort of a high-pitched ringing, not quite like a mosquito, but it is sort of a similar thing. Maybe that isn't tinnitus, maybe it is something else, I do not know” (P12, M, O, G1, HL). Another stated at their interview: “I’ve had no real conversation…if there’s anything that could be done with my hearing” (P17, M, G3, Y, N).

These findings suggest that there was inconsistency in how information on hearing and tinnitus problems with study participants was provided, as some patients did not have the
opportunity to discuss their aural concerns until interview a year after treatment, even though they experienced these concerns during or soon after receiving CRT or RT. From these comments it was not clear which service, audiology or oncology, was to provide information and support to patients when they experienced hearing loss or tinnitus, and when such information was to be given.

6.3.5.3 Further support

Participants suggested that further support could be given in three areas: more indication pre-treatment of possible severity and progression of aural change with treatment; the implementation of more hearing tests with monitoring; and a fuller explanation of hearing loss and tinnitus management.

One participant expressed his surprise at the severity of their hearing deterioration: “Well, I mean [I was told] a lot of things like you would lose your taste and you would lose weight, but you know, nobody said your hearing’s [going to be so bad]” (P53, M, O, G3, HL). Others were uncertain about progression of their aural symptoms, and one suggested the use of a colour coded chart to help provide suitable information on aural changes: “Maybe having a graded list of potential side-effects and symptoms, and say these are really, really common, and… breaking it down into, you know, [a] green, yellow and red kind of scenario, saying “The green stuff - you're going to get that, it's going to die down, don't worry about it, and we normally expect these things to start here and finished around here If it's outside that, come and talk to us. These ones are more unusual, and these ones are potentials, we would not expect you to get that. If you do, you need to call us” And just ensure during the check-ups that those are…. pick[ed] up” (P7, M, Y, G3, N). It could be that pre-treatment information displayed in a colour-coded format may help patients be better aware of and prepared for the severity and progression of potential side-effects of treatment, including hearing deterioration and tinnitus.
All the participants were in favour of monitoring by hearing testing. Most found it convenient to have the three tests in the study at time points prior to treatment, at the end of treatment and three months after treatment, as these were arranged to coincide with other hospital appointments: “They were fine, because luckily they fitted in with appointments I already had, so it didn't put me out in any way, it was just like visiting this part of the hospital from another part, so it fitted in completely” (P42, F, O, G1, HL). However, one participant expressed his reservation at the timing of a test at the end of treatment: “I think [with] the middle one [the end of treatment test] I didn't really know much about, because I was so, with so many different drugs and everything, I wasn't quite on this planet, so I don't really remember much about the middle one, but yes the other two were fine, yes, OK” (P17, M, Y, G3, N). These responses suggested that, in addition to the baseline test, there is a need to arrange at least two tests after treatment to assess hearing deterioration, so that if patients are not well enough to attend the end of treatment test, they can still be investigated at the 3-month follow-up.

Some participants suggested that an additional test to monitor hearing be included during treatment: “Maybe if there had been one mid-way they could have seen if there had been a slight deterioration” (P30, M, O, G1, HL), and “I did wonder, because the business I'm in where I make people test software for example, the way they do it, maybe having one before, one during, one just at the end and then one x-months later, so just having an extra one so you have four different viewpoints over the timeline” (P7, M, Y, G3, N). There was additional merit in performing testing mid-treatment to help identify those who had a deterioration during treatment as, already mentioned, experiencing aural symptoms led to a change in treatment for some of the participants in this study. Therefore, there was evidence to support monitoring of hearing deterioration at four time points: pre-treatment, mid-treatment, at the end of treatment, and at three months follow-up.

For some participants, the study interview, a year after treatment, was the first time that they had an opportunity to discuss their aural concerns in depth. At interview, these participants
shared different ways in which there could be improvement in support, particularly in regard to tinnitus: "I think just whether or not hearing aids are advisable or appropriate in the circumstances…can they restore hearing or indeed get rid of tinnitus?" (P12, M, O, G1, HL).

This participant (subsequently fitted with hearing aids soon after the study interview) may have had further delay in receiving hearing aid support, if discussion of his hearing difficulties had not taken place at the study interview: "I do not know whether I would have initiated [hearing aid fitting], or others would have initiated it for me!" (P12, M, O, G1, HL).

Another participant was unclear what help could be given to overcome her tinnitus: "I would be grateful if there were any exercises that I could do, or if I could do anything to help myself to help [reduce] the tinnitus" (P6, F, Y, G3, HL). In addition to those who only discussed their aural concerns at interview, there was one participant who only became aware of their (unilateral) hearing deterioration as a consequence of being in the study: "I had a hearing test the day I finished radiotherapy and it had gone down a bit, but I had a hearing test then, about six weeks later, and that was when you noticed that it was down" (P29, F, O, G3, HL).

When it was suggested to participant 29 that she might need a hearing aid, she said: "I didn't realize I needed one", but aiding has been of benefit for her.

Therefore, hearing monitoring conducted for this study enabled participants to benefit from hearing aids within the early post-treatment period; likewise, participants were able to avail themselves of appropriate advice when they were interviewed one year after treatment. However, these interventions and advice could have been offered as soon as tinnitus and hearing loss were identified had protocols been in place to give clear guidance that such information was available from audiology services. There appeared to be no difference in the pattern of support or information given based on different characteristics used in selecting participants for interview.
6.4 Summary

Information on patient experience about hearing deterioration following HNC treatment revealed that there appeared to be little difference in experience between male and female participants, or those who had normal hearing prior to treatment compared with those who had a hearing loss before they started their treatment. There was no pattern on how hearing or tinnitus problems progressed, however participants with major hearing deterioration had more widespread problems with their change in hearing compared with those who had minor deterioration, and in some instances, younger participants experienced hearing deterioration differently to older ones.

The majority of participants interviewed experienced a hearing change together with tinnitus, although these two symptoms did not necessarily occur concurrently. Of particular interest was the incidence of tinnitus in the majority of participants, and in some instances it was more bothersome than hearing deterioration. In addition, one participant experienced hyperacusis. All participants with major hearing deterioration found that their hearing change impacted negatively on their communication and their enjoyment of leisure pastimes. For one participant, the ability to listen was particularly affected by tiredness following the effects of cancer treatment. Participants had fewer strategies available in coping with tinnitus in contrast to the way that they had dealt with their hearing deterioration, however hearing aids were useful in dealing with both symptoms. Additional devices used in this study were an auto-inflation balloon to deal with middle ear dysfunction, and a doorbell with a lower pitch to manage hyperacusis aggravated by high-pitched sounds. More strategies were used by younger participants in overcoming hearing difficulties, which reflected their overall acknowledgment of hearing deterioration.

The downplaying of symptoms was evident in some participants who showed a range of emotions that expressed their anxiety, annoyance, guilt and distress at experiencing tinnitus or hearing deterioration. Older participants indicated that they were less ready to admit to
their hearing deterioration, as this change highlighted loss of identity, self-worth, and self-confidence by the association of hearing loss with the ageing process. Social isolation was noted in some of the younger participants.

It appeared that the shock of receiving a cancer diagnosis distracted some participants from taking on board the information, where given, on the possibility of hearing deterioration as a result of treatment. Participants had to volunteer information of their aural concerns, as clinician checklists did not have hearing deterioration or tinnitus down as possible side-effects. It was evident that communication between oncology and audiology services required improvement, as it was not clear which of these services was to share hearing test results with patients. It was also determined that there was no consistency when support for hearing loss or tinnitus was provided, as some patients waited up to a year before discussing their aural changes, whereas others received advice and management soon after completion of their treatment. In general, participants found that hearing monitoring was helpful, but, they suggested that better pre-treatment information would help alleviate anxiety and shock.

The next chapter discusses the findings from quantitative data and qualitative data from this study together with the wider literature.
Chapter 7 Discussion

7.1 Introduction

This chapter will begin with a reminder of the research aims in this study, and by summarising the quantitative and qualitative results that were obtained. It will then discuss these findings with reference to wider literature, policy and practice on related topics. The chapter will continue by summarising what new knowledge was found and will then conclude by drawing out the significance of these findings for the clinical practice of caring for and supporting HNC patients.

7.2 Summary of research findings

7.2.1 Primary aims

In addressing the first primary aim: to assess the incidence and severity of hearing deterioration after treatment for HNC, it was found, drawing on the quantitative data, that the incidence of hearing deterioration in patients undergoing treatment for HNC was 57% at the end of treatment, and 50% at 3-month follow-up after treatment. This result is based on CTCAE criteria for hearing deterioration and indicates the potential scale of the problem of hearing deterioration of HNC patients following treatment from one tertiary UK hospital. Albeit with a small sample size, this study showed that there was a 24% rate of Grade 1-2 (minor) severity change in hearing, and a 26% rate in Grade $\geq 3$ (major) severity change at 3-month follow-up.

In addressing the second primary aim: to explore the lived experience of participants with hearing deterioration after treatment for HNC, information was obtained from both qualitative and quantitative data. Drawing on the responses made in the qualitative interview data, the study found that participants had variable hearing-related treatment experiences prior to,
during, and after their treatment. In these responses, patterns of patient characteristics (age and severity of deterioration) became apparent. Such characteristics were used for selecting participants from the quantitative data for the qualitative interviews; other patient characteristics (gender and pre-treatment hearing) appeared not to be relevant in patient experience. All those who suffered major measured deterioration experienced a reduction in their ability to hear, whereas only some of those with minor deterioration perceived an aural change. The impact of hearing deterioration had more wide-reaching consequences for participants with major deterioration compared to those with minor deterioration, and there were instances when difference in age had a bearing on patient experience.

In summary:

- **Experience of hearing change** – some participants were not aware of any change, but the majority did perceive either a sudden or gradual change. Those who had either minor or major grades of hearing deterioration experienced negative impact. There appeared to be no pattern in the progression of symptoms;
- **Tinnitus** – this was experienced and problematic for the majority of participants, particularly for those with more severe hearing deterioration;
- **Middle ear dysfunction** – this caused irritation for some participants who had Grade 3 deterioration;
- **Functional changes** – all participants who sensed a loss in hearing, including those who acquired unilateral hearing loss, had altered ability in performing every-day tasks. Those with Grade 3 deterioration had many more difficulties with general communication, and also with leisure or environmental noise, compared with those who had Grade 1 change;
- **Coping mechanisms** – General strategies, including the need to lip-read, were used, although younger participants made more effort to improve communication than older patients, who appeared to cope by putting less emphasis on their hearing loss. Those with Grade 3 deterioration found more solutions compared with those who had...
Grade 1 change. Participants acquired hearing aids through audiology service provision, whereas others adapted to their loss using their own means to enhance both communication and enjoyment of pastimes;

- Emotional responses – Younger participants overall were ready to recognise the change to their hearing, and felt that they were not adversely affected by their hearing loss, whereas older participants appeared less ready to acknowledge their hearing deterioration. Some younger participants with Grade 3 deterioration experienced isolation, although this may be linked more to lifestyle changes rather than to their age. It was evident that older participants felt a more general sense of loss. Downplaying of symptoms was displayed in some participants who asserted that their aural change did not have a negative impact on them or their lives, yet at the same time these people expressed feelings of anxiety, frustration or guilt.

- Information and support – there was inconsistency in when test results were shared with patients, and in how patients received support if they had a hearing deterioration.

These findings demonstrated that the experience of hearing deterioration was heterogeneous amongst the participants who were interviewed. Participants not only differed in how they sensed their deterioration, but also differed in how their daily living was affected, and in how they responded to change, both practically and emotionally. Patient experience was also varied in how and when participants received explanation of test results and were given advice to manage their aural change.

### 7.2.2 Secondary aims

These drew on the quantitative data.

In addressing the first secondary aim: to describe overall hearing levels, the study found that there was an increase in the proportion of participants who had bilateral mild or moderate
hearing loss, from pre-treatment to 3-month follow-up hearing, with one participant developing severe hearing loss in one of her ears. However, hearing deterioration for some participants was transient as six participants tested at 3-month follow-up had improved overall hearing compared with levels obtained at the end of treatment.

In addressing the second secondary aim: to determine types of hearing loss, it was found that there was a reduction in the number of participants with normal hearing at 3-month follow-up compared to pre-treatment hearing (from seven to two), and all of the 21 participants developed sensorineural damage to one or both ears. Of these 21 participants, six also developed a mixed hearing loss (both sensorineural and conductive loss) in at least one ear, whereas the remaining 15 developed permanent SNHL only in one or both ears. Amongst seven of the 42 participants, there were eight ears that had a conductive component to the hearing loss, with middle ear dysfunction confirmed by abnormal tympanometry results.

In addressing the third secondary aim: to examine the incidence and severity of hearing deterioration in relation to patient demographics and types of treatment, this study highlighted that older age (mean=68.7 years) was associated with a statistically significant (p=0.03) risk of developing hearing deterioration compared with participants who suffered no deterioration in hearing (mean=58.8 years). If hearing deterioration took place, younger age (mean=56.3 years) was associated with a greater severity of change compared with older age (p=0.02). The study also found that the use of chemotherapy in addition to RT administration was associated with a greater risk of developing hearing deterioration, than the use of RT alone (p=0.01).
7.3 Discussion of findings

Findings from the quantitative data and qualitative data are brought together where relevant in this chapter and are discussed with reference to articles and policy statements principally related to HNC care.

7.3.1 Incidence of hearing deterioration

This study provided information on incidence rates of hearing deterioration from patients following curative RT or CRT treatment at a UK hospital. The potential influencing factors of aspects of recruitment, type of HNC studied, and study location, will be discussed in the following section.

The method for recruitment used in this study was consecutive convenience sampling. All patients newly diagnosed with HNC who were eligible for RT or CRT treatment were invited to participate. It had been arranged with the oncology department in the study hospital for all newly diagnosed patients with HNC, due to have curative RT or CRT, to contact the audiology department and discuss participation in the study. Consequently, there was a high probability that all patients who were eligible for selection were invited to take part in the study. This methodology may have contrasted with other studies that also assessed a range of subtypes of HNC; in these latter studies, the method of recruitment was not clearly stated (Cheraghi et al., 2015; Niemensivu et al., 2015; Pan et al., 2005; Shorter et al., 2017; Theunissen et al., 2014b), and so the effect of selection bias is not known. As the methodology employed for recruitment in the current study was clearly stated, it is easier to understand and take account of the shortcomings of the recruitment process. Consecutive sampling imposed a limitation as there may have been seasonal variation in hearing deterioration within the 6-month period of recruitment. Hearing testing results, during the winter months, may have been affected by upper respiratory tract infection that is known to cause otological change (Doyle et al., 1999), and impair concentration (Smith, 2013); both
damage to the ear and poor concentration can affect behavioural hearing thresholds (Pichora-Fuller et al., 2016). Therefore, it is necessary that further studies are conducted with consecutive recruitment over at least a year period in order to mitigate any seasonal variation in hearing due to the common cold.

This study contributes to the field of HNC literature by determining incidence rates of hearing deterioration across a broad range of HNC within the one study. The incidence rates of this study (reported above in section 7.2) in the early post treatment phase (within the first few weeks of treatment – Bentzen and Trotti, 2007) were within the wide range reported in the literature for people receiving HNC treatment, that varies from 0% (Niemensivu et al., 2015) to 100% (Pan et al., 2005). However, it is difficult to make direct comparison with these previous studies because of different subtypes of HNC studied. The seven subtypes of HNC are cancers of the oral cavity, oropharynx, nasopharynx, hypopharynx, paranasal sinuses and nasal cavity, larynx, or salivary glands (Palaniappan, Owadally and Evans, 2015). This study incorporated similar proportions of patients with the three most common subtypes of HNC diagnosed in the UK: oral cavity, oropharyngeal and laryngeal cancer (accounting for 82% of all HNCs in the UK), having treatment (accounting for 80% of study participants). As reported in the chapter on quantitative results (Chapter 5), hearing deterioration occurred across all seven subtypes of HNC. The inclusion of all seven subtypes in this study differed from other studies, examined in the literature review (Chapter 2), on adult patients that reported hearing deterioration from a limited range of subtypes of HNC (Theunissen et al., 2014b; Pan et al., 2005; Niemensivu et al., 2015; Cheraghi et al., 2015). Theunissen et al. (2014b) reported 78% incidence of hearing deterioration, but only in patients (n=36) who had oral cavity, oropharyngeal, or hypopharyngeal cancer. Pan et al. (2005) found 100% incidence of deterioration, but their study did not include assessment of patients (n=35) who had laryngeal or hypopharyngeal cancer. Niemensivu et al. (2015) reported an 0% incidence rate of deterioration, but none of the patients they studied (n=22) had salivary gland cancer. Cheraghi et al. (2015) determined a hearing deterioration incidence rate of 51% from 29
patients in their study; however, the authors did not clarify the subtype of cancer in seven of these patients. Incidence rates reported in these other studies may have varied in part due to the different types of subtypes of HNC included, so this study helped to clarify that hearing deterioration may occur across all the different subtypes. However, a limitation to the current study, and in all these other studies (Theunissen et al., 2014b; Pan et al., 2005; Niemensivu et al., 2015; Cheraghi et al., 2015), was that subtype analysis was not performed. It was not possible to perform subtype analysis in this study due to the small sample size, and therefore, it was not ascertained if there was greater risk of hearing deterioration associated with particular subtypes than others, and treatment for each of these. Chapter 2 provided much evidence to show that hearing deterioration follows treatment for NPC, in the eight articles that focussed on this HNC subtype. However, there is less evidence of hearing deterioration in other HNC subtypes using current treatment techniques. Gudelj et al. (2014), investigating treatment of laryngeal and hypopharyngeal cancer, reported 26% incidence of hearing deterioration of sensorineural type at 6 months following the completion of radiotherapy (n= 23), but these authors commented only on laryngeal cancer in their findings, and the treatment used is now dated (2D RT). Other studies on parotid cancer (van der Putten et al., 2006; Chen et al., 1999; Schot et al., 1992) reported incidence of hearing deterioration between 20 and 57% following radiotherapy treatment, however all 3 of these studies used the ear contralateral to radiotherapy as the comparator rather than using baseline hearing tests, so it was not clear if hearing deterioration occurred in the ear exposed to RT. Further research is required to determine hearing deterioration either specifically in a particular subtype, or on a larger sample of general HNC with subtype analysis, to better inform patients of the risk of hearing deterioration based on their type of cancer and current treatment regimens. It is also important for these studies to use baseline hearing tests to ensure an accurate assessment and interpretation of hearing deterioration.

From evidence currently available, this study appears to be the first to assess incidence rates of hearing deterioration following treatment of HNC in a UK hospital using current
techniques (of chemotherapy – cisplatin or carboplatin; and of IMRT). The incidence rates obtained in this study could be useful to inform the planning of clinical services as 50% of patients who receive HNC cancer treatment may require audiological support as a result of hearing deterioration at 3-month follow-up. However, it is noted that much caution is needed not to overstate the findings from this study, as it had a limited time for recruitment of a small number of patients (already discussed above), and it was based at one tertiary audiology department in the UK. McCarthy et al. (2015) reported regional difference not only in overall incidence of HNC cancer in the UK, but also in incidence rates for different subtypes of cancer: for example, they found a greater decrease in incidence rate of laryngeal cancer in the north-east of England compared with the south of England between 2002 and 2011, due to a change in the industrial landscape in this period. Therefore, there is need to build on the results from this study by performing further studies at different UK centres to account for regional differences in HNC cancer subtypes, to obtain an overall picture of hearing deterioration following HNC cancer treatment in the UK.

Although this study focussed on hearing deterioration, it is important to note that transient hearing loss was also detected in the early post-treatment period. Some participants who had an initial deterioration in hearing, evident when comparing end of treatment test results to baseline test results, had improved hearing at the 3-month follow-up test. For these patients, the improvement in hearing was due to resolution of OME, with the restoration of normal middle ear function, as reported by Chan et al. (2009). In view of the possible improvement in hearing, some authors chose not to test hearing in the early post treatment phase (Schultz et al., 2010; Bhandare et al., 2007). Improvement in hearing is known to occur in the early stages after HNC treatment, not only due to resolution of OME, but also due to reversal of change to the inner ear (Zuur et al., 2006), although the mechanism for this reversal is unclear. Further research is required to confirm whether or not transient hearing loss occurs following initial damage to the inner ear with treatment for HNC.
7.3.2 Severity of hearing deterioration

This section will first discuss patient experience in relation to varying severity of hearing deterioration, including functional difficulties and the effect of fatigue on hearing.

This study provided information on severity of hearing deterioration for a consecutively diagnosed cohort of adult patients who received treatment for HNC. There were similar incidence rates of hearing deterioration of minor severity (Grade 1-2: 24%) and major severity (Grade ≥3: 26%) at 3-month follow-up. Two other studies (Cheraghi et al., 2015 and Theunissen et al., 2014b), also used the CTCAE criteria for assessing incidence rates for different degrees of severity that were employed in this study. However, Cheraghi et al. (2015) did not state clearly what these different degrees of severity were, and similarly, it is difficult to derive incidence rates of severity from the figures and tables included in their study. In contrast to Cheraghi et al. (2015), Theunissen et al. (2014b), in keeping with the current study, did provide clear information on incidence rates of hearing deterioration with different degrees of severity, and reported Grade 1 incidence of hearing deterioration at 25%, Grade 2 incidence at 44%, and Grade 3 incidence at only 8%, across the 36 patients who had treatment for HNC in their study. It is clear that these rates differed in proportion to those obtained in the current study. This difference may be due to the different subtypes of cancer assessed between the studies, as Theunissen et al. (2014b) assessed only patients who had cancer of the oral cavity, oropharynx or hypopharynx, whereas this study included treatment of patients from all seven subtypes of HNC. Whereas the finding from Theunissen et al. (2014b) on severity of hearing deterioration is limited to a small subtype of HNC, the findings from the current study applied to all seven subtypes. Therefore, it appeared that if patients who are newly diagnosed with HNC have hearing deterioration following treatment at this UK centre, they had an almost equal chance of acquiring a minor or major degree of severity in deterioration that was determined by hearing testing at 3-month follow-up after
treatment. Further studies would be necessary to inform national policy as this study’s results represented only one centre in England and may not reflect findings in other regions.

7.3.2.1 Major and minor hearing deterioration

Whereas Chapter 5 of this thesis provided data on the proportion of patients who had deterioration of hearing following HNC treatment, Chapter 6 presented the findings from interview of 13 patients (selected from 21) who had a measured deterioration. Participants who had a major (Grade ≥3) deterioration in at least one ear perceived hearing deterioration, had more widespread problems in communication, socialising, and in their leisure pursuits, compared with those who had minor deterioration. This finding is intuitive – the greater the impairment, the greater the range of problems, and these contrasting findings between different grades of deterioration will be discussed throughout this chapter.

The main contrast between participants with different grades of deterioration was that whereas all eight participants with major deterioration experienced aural change, only two out of five of those who had a minor Grade (1-2) deterioration perceived a deterioration. This lack in awareness of hearing deterioration for some participants with a minor deterioration is common with people who have age related change to their hearing; as there are small changes in hearing over a period of time, people with age-related hearing change naturally adapt without discerning a difference, and it is typically about ten years before people seek help with their hearing problems (Davis et al., 2007). However, both patients with minor hearing deterioration who perceived a change in hearing shared their difficulty in hearing the television at the usual volume prior to treatment, and one had problems that included understanding speech in restaurants, and difficulty in hearing alerting sounds such as the doorbell. This participant ultimately required hearing aids; two other participants with Grade 1 deterioration (not interviewed) were provided with hearing aids within six months of completing their treatment. Correlating the findings of both quantitative and qualitative data
from this study therefore demonstrated that even a minor (but none-the-less significant for the patient) deterioration in hearing had an adverse effect on well-being.

Hearing ability was measured using PTA, and a deterioration in hearing was determined using CTCAE criteria. Although Cheraghi et al. (2015) and Theunissen et al. (2014b) employed the same criteria, neither of these studies clearly indicated the effect of different severity grades of deterioration on patient experience. Most other studies do not use a measured deterioration in hearing, but rather a subjective deterioration that is rated by clinicians, and these studies reported only on higher grades of hearing deterioration (for example, Al-Mamgani et al., 2012; Wu et al., 2013; Huang et al., 2015; Bentzen and Trotti, 2007; Du et al., 2015). As this was the first study to explore lived experience of hearing deterioration after cancer treatment, let alone HNC treatment specifically, it is difficult to find literature to make comparison with the study findings on perception of hearing loss with different grades of deterioration. The study by Nund et al. (2015) on patient experience selected participants who had communication difficulties after treatment, but it was not clear in their study how many of the participants had hearing difficulties following treatment, and the study did not assess the effect of severity in hearing deterioration. Therefore, in contrast to other studies, the current study provides clear evidence of the value in measuring even minor grades of hearing deterioration as this can identify patients in need of audiological support, and it is suggested that audiological support should be offered to all patients who suffer a deterioration in their hearing following HNC treatment.

7.3.2.2 Lower speech frequency hearing deterioration

The method used in this study for detecting hearing deterioration focussed on change in the higher speech frequencies, however, it is also important to consider the impact made on those with only lower speech frequency hearing deterioration with treatment. A limitation of the measured CTCAE criteria is that it covers hearing deterioration from 1kHz and above,
and does not account for lower speech frequency hearing deterioration, which was detected in one participant in the current study. This participant only had deterioration at 0.25kHz and 0.5kHz, but required hearing aiding as she experienced difficulty in understanding conversation even in quiet conditions following her treatment. Her hearing difficulty was identified at her 3-month follow-up hearing test as part of the study, through conversation with the researcher. It is therefore important to ask patients if they have noticed a change in their hearing, even if hearing monitoring may not indicate that a deterioration has taken place. It was noted that this patient was recorded as having no problems with her hearing during the routine 3-month follow-up by an oncology specialist. It is known that clinician-rated scoring underestimates the effect of communication difficulties encountered by patients (Lazarus et al., 2014; van der Molen et al., 2012). There is also an under-reporting of less severe subjective hearing deterioration in the cancer literature (Bentzen and Trotti, 2007). These findings suggest that hearing deterioration may not be a priority consideration at routine oncology follow-up as there are so many other topics to cover on patient well-being following treatment. It is therefore suggested that both an assessment of subjective and measured hearing is performed within the context of a hearing test appointment by audiology clinicians who focus on hearing. However, to avoid variability with subjective assessment even by audiologists, it is preferable to measure lower frequency hearing deterioration either by extending the CTCAE criteria to apply also to lower frequencies, or by assessing lower frequency hearing within the overall descriptor of hearing levels following treatment, which will be discussed later in this chapter.

7.3.2.3 Functional changes

Although participants with Grade 3 deterioration had more wide-reaching problems with communication and their leisure pursuits compared with those with Grade 1 deterioration, each participant identified different difficulties in communicating. Although some participants were clear in describing what parts of speech they could not hear, such as high frequency
sounds which corresponded to damage in the speech-hearing range that commonly occurs with treatment (Chan et al., 2009; Shorter et al., 2017), others had non-specific deafness. This finding was consistent with those in a review by Vestergaard Knudsen et al. (2010) on help-seeking behaviour in hearing impaired adults, which also concluded that self-reported auditory difficulty was possibly a more important factor in aural rehabilitation than objective hearing sensitivity. It is therefore important to have individual assessment to identify which particular aspects of speech are most difficult to comprehend, and what environments cause most difficulty, as each participant was affected by their hearing deterioration differently, a common feature of having hearing loss (Thomas, 1988; Meddis et al., 2010; Harrison, 2016). Patients can then be given different advice and rehabilitation options (for example, the provision of an additional program if hearing aids are suitable) depending on their particular hearing difficulty.

7.3.2.4 Fatigue and hearing

The effect of fatigue was noted by one of the participants (with a major deterioration in hearing), who expressed that he was “absolutely shattered still” some evenings a year after treatment, and the effect of the tiredness meant that he had to ask his daughter to slow down speaking for him to understand her speech. Depletion of energy levels following cancer treatment cannot be underestimated, and fatigue remains highly prevalent in this patient population at least up to a year after treatment (Schaller et al., 2015; Molassiotis and Rogers, 2012). As listening effort causes tiredness due to hearing loss (Alhanbali et al., 2017), and poor concentration is known to adversely affect listening ability (Chermak and Somers, 1988; Pichora-Fuller et al., 2016), the combination of hearing deterioration and tiredness may make listening more difficult for this patient population. As fatigue following cancer treatment is a common and prolonged problem, it is important that patients are made aware that fatigue may exacerbate communication difficulties due to aural change following treatment. Fatigue also exacerbated the perception of tinnitus for this participant.
7.3.2.5 Tinnitus

An emerging finding in this study was the impact of tinnitus on HNC patients following treatment, particularly as this is absent from other studies. Seven out of the eight patients who had major hearing deterioration perceived both a change in hearing and experienced tinnitus, whereas one out of the two patients with minor hearing deterioration experienced both these symptoms. An exploration of tinnitus was not a direct aim of this study, but tinnitus was discussed during the participant interviews as part of patient experience of hearing deterioration, with eight out of the 13 participants suffering from the sensation of tinnitus following treatment. Four of these participants found that their tinnitus was annoying or distressing.

It is significant that tinnitus was experienced by the majority of participants at interview one year after treatment, whether they had either minor or major hearing deterioration. In addition, some of these participants were adversely affected by their tinnitus when interviewed. Some required advice regarding tinnitus only, while others required hearing aiding to help deal with their tinnitus, and reported benefit. Although tinnitus is a separate entity to hearing deterioration and can be experienced in the absence of hearing loss (Baguley, Cope and McFerran, 2016), in this study tinnitus was experienced with hearing deterioration, and the tinnitus was often more distressing to patients compared with their hearing loss. Although the majority of patients interviewed in this study experienced tinnitus, tinnitus is mentioned less often than hearing problems in the wider literature.

There are approximately ten times more articles in PubMed on ‘hearing’ compared with ‘tinnitus’, yet arguably in this study, tinnitus had more of a negative impact on patient experience than hearing change, and it has been reported that tinnitus severely affects the quality of life of people in 15-20% of chronic tinnitus sufferers (Durai, O’Keefe and Searchfield, 2017). Other studies on HNC treatment have measured the impact of tinnitus from a quantitative aspect only. Niemensivu et al. (2015) used the Tinnitus Handicap
Inventory (Newman, Jacobson and Spitzer, 1996) and reported that seven out of 31 patients had moderate to severe tinnitus, but they did not indicate how the tinnitus affected them, nor did the authors mention how patients were supported if they experienced these symptoms. Zuur et al. (2006) reported that 28 out of 146 patients experienced tinnitus during treatment, but they did not clarify how data was collected. In both of these studies it was not made clear how to manage tinnitus symptoms, nor what the impact of tinnitus was on patients. One participant interviewed in the current study experienced hyperacusis (causing pain and distress) with his tinnitus. Although there is not much known about hyperacusis, there is growing awareness of the negative impact that it has on quality of life (Baguley and Hoare, 2018), and it seems that the finding of hyperacusis accompanying tinnitus following cancer treatment is also a novel finding from this study. It therefore appears that this study is the first to report the impact of tinnitus (and hyperacusis) by qualitative analysis in HNC treatment literature, and it would be useful for further research to be conducted in this area to verify the findings of this study.

The lack of focus on tinnitus may be due in part to the knowledge that there is currently no cure for tinnitus (Hilton, Zimmermann and Hunt, 2013; Miroddi et al., 2015). However, there are strategies to help deal with tinnitus, including tinnitus retraining therapy, cognitive behavioural therapy (Baguley, Cope and McFerran, 2016), or use of hearing aids (NHS, 2017a). There is research into newer techniques such as the use of internet guided cognitive behavioural therapy (Beukes et al., 2017). Help for dealing with tinnitus is available from hearing therapists, audiologists and medical practitioners, so it is important to encourage patients to seek help from professionals when they experience tinnitus (British Tinnitus Association, 2017). A tinnitus specialist is usually associated with adult audiology services, as in the study hospital, although it is not clear who these specialists are in NHS guidance on tinnitus (NHS, 2017a). It is necessary to undertake more research specifically on the incidence of tinnitus in post-treatment HNC patients to understand accurately the scale of the problem, and how best to address it. In view of the current lack of adequate referral
systems, if findings from further research are consistent with this study, referral systems for tinnitus support should be set up at local and national levels, with such support being integrated into hearing services for a sustainable model provision.

**7.3.3 Hearing status**

There was no association found between risk of hearing deterioration and participant hearing level prior to treatment (Chapter 5). This finding concurred with that of Shorter et al. (2017) and Grau et al. (1991) in their assessments of hearing deterioration following HNC treatment. Although Zuur et al. (2007) reported that patients with better pre-treatment hearing levels suffered more severe hearing loss than those who had poorer hearing to start with, this finding was not upheld in the current study. There was also no difference found, in Chapter 6, of patient experience based on pre-treatment hearing level, as patients who had either normal pre-treatment hearing, or (mild) hearing loss (according to BSA descriptors – BSA, 2011) prior to treatment experienced similar hearing difficulty following treatment. Therefore, it appears that there is no need to alter treatment regimen to patients who have mild hearing loss or normal hearing prior to treatment based on the finding that there is a similar risk of hearing deterioration following treatment. In addition, similar support should be given to patients to deal with a deterioration in hearing regardless of their pre-treatment hearing status.

Although there was no difference found in the incidence of hearing deterioration based on pre-treatment hearing status (i.e. whether a participant had normal hearing or a hearing loss), quality of life was affected for some study participants following treatment with a change in their overall hearing level. The importance of measuring overall hearing was observed with one participant during their 3-month follow-up test appointment and was recognised with other participants following their interview one year after treatment. The significance of measuring different types of hearing loss became evident, not only because
each type impacted patients in different ways, but also because each type of loss required
different specialist intervention.

7.3.3.1 Descriptors of hearing level

Using the 5-frequency octave average of 0.25, 0.5, 1, 2 and 4kHz of the BSA criteria (2011),
it was found in this study that there was an increased severity in the level of hearing loss for
participants in the speech frequencies, when comparing hearing at 3-month follow-up after
treatment with baseline levels. The study found that there was an increase in bilateral mild
hearing loss from 31.0% to 42.9%, an increase in bilateral moderate hearing loss from 4.8%
to 9.5%, and an increase in the proportion of patients with bilateral hearing loss from 38.2%
before treatment to 57.2% after treatment (Chapter 5, Table 5.5). These findings suggest
that there was a significant rise in the proportion of patients who may benefit from aural
rehabilitation because of the deterioration in their overall hearing within the speech hearing
range.

It was important to measure overall hearing levels within the speech frequency range of
0.25-4kHz using the BSA criteria, as hearing deterioration used by CTCAE criteria may have
captured deterioration in the higher 6-8kHz region only. One participant, who had coped with
bilateral moderate hearing loss prior to treatment, developed severe loss in one ear, and at
her 3-month follow-up hearing test decided to acquire a hearing aid. Interestingly, Zuur et al.
(2007) mentioned that in the Netherlands, patients who had overall hearing greater than
35dBHL between 1-4kHz were entitled to a reimbursement for hearing aids. Normal hearing
occurs when air conduction hearing thresholds are ≤ 20dBHL (Luxon, 2014). Thresholds
greater than 35dBHL indicate moderate hearing loss, and if the criteria used by Zuur et al.
(2007) were applied to the current study, the number of ears amongst the participants that
were suitable for aiding would double from 9.6% (before treatment) to 19.1% (at 3-month
follow-up). Although 1-4kHz covers most of the speech hearing range, important information
on speech is also conveyed in the 0.25-1kHz range (Pavlovic, 1987), which is assessed in
the BSA criteria on overall hearing (BSA, 2011). Consequently, it is suggested that the BSA criteria are suitable for reporting the description of overall hearing level, as these criteria assess an extensive part of the speech range, and help to identify which patients may benefit from hearing aiding due to a development in the severity of hearing loss following treatment.

7.3.3.2 Lip-reading and sudden-onset hearing loss

Although the need to lip-read was adopted by some of the interview participants as a general strategy to improve their communication, it was noted that three participants, who had normal hearing [according to BSA (2011) guidelines] prior to treatment, gave comments that showed the importance for them to lip-read after their treatment. Each participant was aged less than the average age for participants interviewed in this study (<60 years old), and after treatment, they had normal low frequency (<2kHz) hearing but bilateral mild-moderate, or moderate severity, mid-high frequency hearing loss, and Grade 3 hearing deterioration. Nund et al. (2015) mentioned that some participants in their study had learned to lip-read, but the authors did not make clear what was the severity of hearing loss of participants following treatment. Therefore, the need for lip-reading with sudden onset hearing loss to address mild-moderate or moderate severity hearing loss due to HNC treatment appears as a novel finding in the literature.

Lip-reading is a common strategy used by people to assist with their communication, particularly with the gradual development of mild-moderate high frequency hearing loss that is associated with ageing, where lip-reading helps to ‘to fill in the gaps’ of speech (Action on Hearing loss, 2017). Some study participants with bilateral major hearing deterioration did not focus on the need to lip-read, possibly because they had mild hearing loss prior to treatment, and had already started the process of relying more on lip-reading. However, the three participants who needed to lip-read had normal hearing before treatment, and the
acute change in their overall hearing status from normal to impaired appeared to make them need to lip-read, whereas before they did not have to rely on this.

Each of the three study participants who needed to lip-read had a >30dB loss in hearing for each ear, constituting a sudden-onset hearing loss (Ira, Teh and Friedland, 2014). Although it was not clear exactly when the hearing loss took place, it was classed as sudden, as, according to criteria provided by The British Academy of Audiology (2009), it was detected within a week of completing CRT treatment. Sudden-onset hearing loss was the focus of the study by Cho et al. (2016) in their investigation of HNC patients. However, direct comparison with the current study is difficult, as Cho et al. (2016) assessed sudden loss at a much later time after treatment (median time of ten years), and the authors did not mention what, if any, aural rehabilitation of patients (including lip-reading) was offered. Other studies in the wider literature on sudden-onset loss provide little evidence of lip-reading support following the loss, and those that do, report on profound hearing loss (Galicia-Lopez et al., 2016). Other articles on sudden hearing loss focus more on quality of life measures rather than measuring hearing loss, and do not include lip-reading as a rehabilitation tool (Chen et al., 2013; Härkönen et al., 2017). So, although there are articles on sudden hearing loss, few provide advice on the benefits of lip-reading support. Therefore, it is important to acknowledge that mild-moderate sudden-onset hearing loss, occurring in the early post-treatment phase after HNC treatment, may have a negative impact on patients such that they require lip-reading to assist with their communication. Again, the findings of this study need to be verified by conducting further studies on larger sample sizes to establish the scale of the problem, which may then suggest amendments in policy to support patients who suffer hearing deterioration with treatment. Such policy should include information being provided to patients prior to treatment to inform them that they may require lip-reading after treatment, and to have protocols to direct patients on where to receive advice and training on
lip-reading, which is usually provided within audiology or hearing therapy services. It will also be necessary to conduct further study to ascertain the benefit provided by lip-reading support.

7.3.3.3 Types of hearing loss

Sensorineural loss

All the 21 participants who suffered hearing deterioration had sensorineural damage to one or both ears following treatment, with the majority of participants developing only SNHL as determined by PTA at 3-month follow-up hearing testing. In defining types of loss, normal hearing occurs when PTA testing produces air conduction hearing thresholds between 0.25 and 8kHz are ≤ 20dBHL, so that all sounds of human speech can be heard at normal conversational level (Pavlovic, 1987). Using this definition, unsurprisingly, the majority of patients prior to testing had mild high frequency SNHL, as the average age of patients in the study was 60 years, and high frequency hearing deteriorates with ageing (Davis et al., 2007). The increase in proportion of SNHL following treatment may be linked to ototoxicity by chemotherapy and by RT (Theunissen et al., 2015). All of the thirteen participants who were interviewed had a sensorineural element to their hearing loss at their 3-month follow-up. Ten of these had solely SNHL, and the majority (seven) experienced adverse effects on their quality of life, based on findings in each theme reported in Chapter 6. As SNHL is usually permanent, there is already much evidence on incidence of this loss following HNC treatment (see Chapter 2, sections 2.5.5.1 and 2.5.5.2), however, it appears that the current study is the first to clarify that SNHL has an impact on patient experience.

Mixed hearing loss

Using PTA and tympanometry tests, it was found that there was an increase in the number of participants with mixed hearing loss following treatment at their 3-month follow-up,
probably due to radiation treatment affecting structures in the middle ear (Bhandare et al., 2007; Jereckzek-Fossa et al., 2003). Participants in the current study at their interview expressed annoyance in obtaining the sensation of aural fullness (a feeling of fullness in the ear, or of fluid in the ear) that is associated with OME following RT (Jereczek-Fossa et al., 2003), during this early post treatment phase. Therefore, the findings from this study suggest that it is important to test hearing soon after treatment to detect middle ear dysfunction, and to let patients know before treatment that they may experience aural fullness as a result of their treatment.

Three of the thirteen participants interviewed had mixed hearing loss at 3-month follow-up hearing testing, although others gave responses that indicated they had experienced OME at some stage during or after treatment. For some participants, the sensation of aural fullness went away soon after RT treatment was completed, indicating that middle ear dysfunction due to OME had resolved itself. However, for others, the sensation of fullness either returned or persisted up to the time of their interview, one year after treatment completion, indicating permanence in middle ear dysfunction that required intervention.

Mills and Hathorn (2016) advocated treatment of OME by tympanoplasty and insertion of grommets (ventilation tubes that straddle the eardrum to deal with middle ear effusion). However, it is not advised to insert grommets following RT as this treatment may cause permanent tympanic membrane perforation or ear-infection (Liang et al., 2011; Chen et al., 2001). Therefore, an alternative method of treatment is required. One study participant acquired an auto-inflation balloon to ventilate his ears (following advice from a specialist nurse in aural care) and used a nasal decongestant (prescribed by an oncologist) to alleviate the discomfort he experienced. Two months after using this combined treatment, the ear discomfort subsided. However, there is little evidence of wider use of the auto-inflation balloon device in the care of HNC patients, although the device has been effective in adults who did not have malignancy in proximity to the middle ear (Wanscher and Svane-Knudsen, 2014). More research into the effectiveness of using of the auto-inflation balloon would be
helpful for patients who have permanent middle ear dysfunction due to OME after head and neck treatment.

The current study provided evidence on both the proportion of patients developing mixed hearing loss, and the negative impact of middle ear dysfunction on patient experience, but there is little recognition of this impact in the wider literature, which raises concern that patients may not receive appropriate support for dealing with middle ear dysfunction in an efficient manner. In Chapter 5 of this thesis, Figure 5.2 shows that of 21 patients who had a hearing deterioration, approximately two-thirds developed SNHL and one-third developed mixed hearing loss at 3-month follow-up (or 14% of n=42 participants who completed 3-month follow-up testing). This information may be useful for planning services, as each type of hearing loss after treatment completion can be managed differently: hearing deterioration of SNHL type can be managed by audiology, but deterioration that causes a conductive or mixed hearing loss needs first to be managed by ENT services.

Current UK HNC patient management guidelines do not mention hearing loss, let alone middle ear dysfunction (Palaniappan, Owadally and Evans, 2015). Although the most recent US guidelines do mention that hearing loss can be a side effect of treatment, these guidelines refer patients directly to audiology services rather than to otology specialists (Cohen et al., 2016), which means that middle ear problems may not be managed by ENT doctors to provide the necessary intervention. This lack of recognition in policy in general is also reflected in web-based sources that do not state that clinicians involved in HNC treatment can be specialists in ear-related problems (Macmillan Cancer Support, 2017). Although some primary articles use the involvement of otologists in confirming middle ear dysfunction (Wang et al., 2004), others do not (Wang et al., 2015; Kwong et al., 1996), which indicates a lack of consistency with the involvement of otologists in managing middle ear problems. Therefore, there is a clear need to develop policy for efficient communication
between oncology, audiology, and otology services, to ensure that otology support is readily available for those patients found to have middle ear dysfunction following HNC treatment.

Mixed loss due to middle ear dysfunction can become permanent (Bhandare et al., 2010; Oh et al., 2004; Wang et al., 2015), or may transform into SNHL with time, due to the effect of toxic materials from chronic inflammation affecting the auditory nervous system (Wang et al., 2003). The researcher advises that hearing testing (using PTA and tympanometry) is performed systematically to identify both mixed hearing loss and SNHL following treatment of HNC, as both types of loss may follow CRT or RT, and may have a negative impact on quality of life.

The previous sections in this chapter have discussed the incidence and experience of hearing deterioration based on severity of deterioration, and different aspects of hearing status. The following sections discuss the significance of gender, age, and treatment modalities on hearing deterioration after HNC treatment.

7.3.4 Gender

The results from Chapter 5 showed that there was no statistical association of hearing deterioration by gender. These results were similar to those found in other studies on hearing deterioration following HNC treatment (Chan et al., 2009; Oh et al., 2004; Shorter et al., 2017; Wang et al., 2015). In Chapter 6, it was also noted that there was no evident difference in patient experience of hearing deterioration between men and women, but this finding may have been due to the small sample size for this study. Saunders et al. (2005), in a survey study of attitudes to hearing loss among 325 participants with hearing loss, found that although there was no difference in negative associations with hearing loss between the sexes, men had poorer coping strategies than women for dealing with their hearing loss. Such poor strategies were withdrawal and pretending to hear. A suggestion from Saunders et al. (2005) to offer all patients coping strategies for dealing with hearing loss regardless of
gender is recommended by the researcher, and although no patterns in coping with hearing loss based on gender were found in the current study, there were patterns based on age, and these are discussed within the next section.

7.3.5 Age

In the current study, it was discovered that there were patterns of hearing deterioration associated with age, in both the quantitative and qualitative data. There was a statistically significant difference in the age of patients who suffered hearing deterioration compared with those who did not, with older patients more at risk of deterioration. However, younger patients were more at risk of developing more severe deterioration if this took place. There is no consensus in the literature regarding whether increasing age is associated with incidence of hearing deterioration. The study findings were consistent with those of Chan et al. (2009) and Wang et al. (2015) in that older patients were more at risk of hearing deterioration following treatment for HNC, but these findings contrasted with those of other studies on age and hearing deterioration (Oh et al., 2004, Petsuksiri et al., 2011, and Shorter et al., 2017). It is not clear why there is a lack of consistency in these findings, therefore more research is necessary to determine if age is a factor in predicting hearing deterioration, which could lead to either targeting support for patients, or potentially to offer alternative treatment to minimise hearing deterioration which is sometimes considered for paediatric oncology patients (Brock et al., 2012).

There is also little information available whether a patient’s age determines the severity of hearing deterioration, if deterioration takes place. The current study found that major deterioration (Grade 3 or 4 change according to the CTCAE criteria for hearing) was associated with patients who had a mean age of 56.3 years, whereas minor deterioration (CTCAE Grades 1 or 2) was associated with older patients with a mean age of 68.7 years. This difference in age was statistically significant (see section 7.2). This finding was in agreement with Zuur et al. (2007) in their study of patients treated for either oropharyngeal,
oral cavity or hypopharyngeal cancer, but the finding from Zuur et al. (2007) was limited to a small range of HNC patients in contrast to the finding from this study. However, other studies that assessed severity of hearing deterioration using baseline hearing comparison have not focussed on the association with age (Chan et al., 2009; Li et al., 2010). Therefore, from the findings of the current study, it is suggested that HNC patients aged 56 years or younger who are due to receive treatment should be warned that if they do get hearing deterioration from treatment, it could be severe. It will be necessary to conduct further studies to verify these findings concerning the risk of age on the severity of hearing deterioration, and to consider what age is a significant cut-off.

At interview, there were differences in the experiences of younger and older participants following treatment for HNC, including social isolation, a sense of loss and coping mechanisms. These experiences, as well as the downplaying of symptoms and the use of assistive devices, are discussed in the following section.

### 7.3.5.1 Social isolation

Social isolation was experienced, particularly by two of the younger participants in this study (aged 41 and 59). The husband of one participant withdrew from one to one conversation because of frustration at not being heard properly and the need to repeat words. Another participant reduced conversation with his family members as he could no longer hear them clearly in telephone conversations. The finding of isolation has been reported in other studies within acquired deafness literature, but not in studies on cancer and hearing loss. Aquino-Russell (2006) used descriptive phenomenology to explore the experience of acquired deafness and similarly found that seven participants sensed isolation due to their hearing loss. However, studies that have reported hearing deterioration in other cancers have not explored patient experience (Brydøy et al., 2009; Needles et al., 1982; Rademaker-Lakhai et al., 2006). Even the study by Nund et al. (2015) on the experience of communication difficulties following HNC treatment did not mention feelings of isolation.
Although increased isolation due to difficulty in speech articulation has been reported in HNC survivors (Swore Fletcher et al., 2012), it appears that the current study is first to identify the sense of isolation due to hearing deterioration following HNC. Isolation was evident among these two younger participants, but the isolation may be more due to changes within their busy social lifestyle rather than due to their age.

7.3.5.2 Sense of loss

The sense of loss with hearing deterioration seemed to be associated with older participants in this study. There was embarrassment with having loss, or disappointment in being provided with a hearing aid, as this highlighted for one participant that she once had perfect hearing and wearing a hearing aid made her feel old. This feeling of an increase in ageing has been reported in a questionnaire study on hearing aid use, in which 18% of respondents (n=97) indicated that they felt older when wearing hearing aids (Brooks, 1994). The study by Brooks (1994) also reported that one third of 95 respondents felt that others associated the use of hearing aids with senility. A recent qualitative study on age-related hearing loss reported that older adults associated shame with hearing loss, and that having a hearing loss made them feel older and stupid (David, Zoizner and Werner, 2018). The sense of loss due to disfigurement has been documented in HNC literature, most recently in a systematic review (Lang et al., 2013), but hearing loss is not mentioned. There is little other information on hearing loss and dismay, or even grief, in the wider literature. Kurtzer-White and Luterman (2003) explored parental grief among those who had children with hearing loss, and concluded that more support is required for those who have chronic grief. Therefore, hearing deterioration (or even aiding to address hearing loss) may cause feelings of a loss in mental capacity, as well as feeling older, and may compound other feelings of grief associated with HNC.

Patients could benefit in talking through feelings of isolation or loss if these are affecting well-being; older patients, in particular, could also be helped by discussing their attitude to
hearing loss. Advice and support could be provided by clinical nurse specialists in HNC who deal closely with patients, and have been identified as the preferred clinical profession to discuss feelings of anxiety or depression in cancer patients (Baker-Glenn et al., 2011). Further studies need to be conducted to verify the range of feelings reported from this study, and feasibility studies would be needed to see if intervention from clinical nurse specialists concerning negative feelings related to hearing loss is appropriate and provides benefit for patients.

7.3.5.3 Downplaying of symptoms

In general, participants in this study attested that their hearing difficulties did not affect them. At interview, the majority of participants who were aware of their hearing or tinnitus problems did not feel that these symptoms were major factors for them, but elements of discomfort and frustration at their situation were evident. Some expressed guilt in asking for things to be repeated, and were embarrassed at the inconvenience that this caused others. Some required hearing aids, and although they stated that they did not feel their hearing deterioration or tinnitus was a problem, responses they made and help they required indicated that they downplayed the significance of their symptoms.

This downplaying of the symptoms of hearing deterioration and tinnitus following HNC treatment appears to be an emerging finding from this study, although the downplaying of other problems following HNC has also been reported. Ganzer et al. (2015) investigated difficulties in eating of ten long-term survivors of HNC using a quality of life tool that assessed patients’ perception of problems, as well as the severity of their symptoms. The tool was used together with semi-structured interview, and findings were synthesised by content analysis. Downplaying of symptoms was evident because, although at interview patients gave a favourable response about being able to eat, the severity scale and the other interview findings suggested that patients had difficulty in eating due to problems encountered with swallowing and in salivary production. Therefore, practitioners need to be
aware of the potential support that patients may require if they display signs of the downplaying of symptoms following HNC treatment. It is important to help patients realise the actual impact of their hearing deterioration, and advise them that support can be given to improve their well-being. A method for helping patients gauge the effect of their change in aural symptoms is by using a patient related outcome measure (PROM), and this will be discussed further in the section below on information and support.

### 7.3.5.4 General coping mechanisms

There were differences with how older and younger participants coped with their aural change. This study found that in most cases younger participants and their families and friends found ways of adjusting to hearing change. They adapted in many instances by their own efforts and initiative rather than by receiving advice provided by health professionals. Some of these strategies were for the patient with hearing deterioration to inform others of their hearing problem, and for friends and family to gain the attention of the patient with the hearing deterioration before beginning a conversation with them. Some of the strategies reported in the study are commonly used for improving communication with people who have hearing difficulties (Dillon, 2001), and were mentioned in Nund et al. (2015) but within the context of communication difficulties as a whole in that study. The survey commissioned by Macmillan Cancer Support (2015) on attitudes and behaviours of older patients to cancer suggested that older patients are not necessarily aware of services to support them, and are likely to be passive by allowing health clinicians to be responsible for decisions about care. Therefore, it is important that patients who have hearing deterioration following treatment have an appointment with audiology services to discuss strategies for coping with their loss, particularly older patients who may place more responsibility on clinicians to inform patients of these strategies.
Although both younger and older participants interviewed suffered similar functional difficulties with their hearing change, and even though all the younger participants had greater severity deterioration, they readily acknowledged their loss and actively found ways to overcome their difficulty, even adopting a ‘fighting’ spirit. In contrast, older participants were less inclined to make changes to improve their hearing ability, whether they experienced minor or major deterioration. In a survey comparing the attitudes of older and younger patients with a range of different cancers (Macmillan Cancer Support, 2015), the majority of older patients surveyed felt they had achieved as much as they wanted in life compared with less than a quarter of those of working age, suggesting that younger patients had more to gain with a return to healthy living. This suggestion supported the finding in the current study that younger participants were active in dealing with their hearing loss. However, Hughes, Closs and Clark (2009) performed a qualitative systematic review on the experiences of older patients (age range 51 to 99 years) and reported that these patients adapted constructively to side effects of cancer treatment. As the majority of the patients in their review did not have HNC, it is probable that hearing deterioration was not considered as a side effect requiring adaptation. Furthermore, Armero (2001) discussed that denial of a hearing loss can often create conflict between older patients and their significant others. Although conflict was not reported in the current study, older participants were aware of the impact that their hearing deterioration had on others. Therefore, it is important for audiologists to meet with both younger and older patients who have measured hearing deterioration following HNC treatment, not only to address difficulties that are perceived by patients, but also to discuss with them the impact that hearing deterioration has on others, whether the patient recognises this or not.
7.3.5.5 Assistive devices

Although there was no apparent difference in this study between different age groups in the use of devices to help deal with hearing loss following treatment, there may be different access to technological support, according to age.

In this study, hearing aids were the most common device used to help overcome hearing difficulty. Three out of the 13 patients at the time of their interview had hearing aiding following treatment, and two more went on to be fitted with these aids. Of the 42 participants who completed the 3-month follow-up hearing test, nine (21%) went onto be fitted with hearing aids within 18 months of treatment completion. Participants who required the use of hearing aids had oropharyngeal, oral cavity or laryngeal cancer. For these participants, aiding has proved to be of use with various situations including: one to one conversations; group situations; and tinnitus management. Hearing aiding has also been mentioned in Zuur et al. (2007) who stated that 25% of participants in their study of patients with oral cancer, hypopharyngeal cancer or oropharyngeal cancer, received hearing aiding, although the authors did not state when patients received these. The results from this study indicate that patients with oropharyngeal, oral cavity or laryngeal cancer, within a cohort who receive treatment for their HNC, also may require the use of hearing aids. However, it is apparent that the lack of literature on hearing aiding following HNC treatment indicates that most literature is focussed on treatment delivery and survival, rather than on the side effect of hearing loss. Further studies specifically analysing HNC subtypes will help to determine whether certain subtypes are more at risk of hearing deterioration, and thereafter reinforce targeted support to be given to these groups.

The attitude to possessing a hearing aid was not always positive. Some study participants said it was vanity that made them not want to wear their aid. In their review, Hosford-Dunn and Huch (2000) suggested that violation of acceptable cosmetic appearance often leads to the rejection of hearing aid use. In this study, there appeared to be no pattern in attitude to
hearing aiding with age or gender. These findings were similar to those reported in the literature (Brooks and Hallam, 1998). However, there may be a difference in the overall attitude toward the acceptance of hearing aids of those who have a sudden-onset hearing deterioration (such as participants in this study), compared with those with age related hearing loss, though further research is needed to assess the acceptability of hearing aid use in patients who have hearing deterioration following HNC treatment.

In addition to helping overcome hearing difficulty, the use of hearing aids was useful in dealing with tinnitus for participants in this study. Although not offered in this study, sound generators could be used, but a COCHRANE review found no evidence of additional benefit in using sound generators over that of hearing aids for dealing with tinnitus in a randomised trial (Hoare et al., 2014). Although it is known that hearing aids can help to deal with tinnitus in general (Cabral et al., 2016; Hodgson et al., 2017), it appears that the use of hearing aids specifically for tinnitus management following HNC treatment is an emerging finding from this study. Further studies would be needed to assess the benefit of hearing aiding in dealing with tinnitus as a result of treatment for HNC.

There were other assistive devices used by study participants to improve their hearing, including amplifiers or earphones for use with the television (also reported by Nund et al., 2015), or their listening comfort such as using a doorbell that had a lower pitch sound to reduce hyperacusis, or to hear the doorbell, as patients had high frequency hearing loss after treatment. Study participants and their carers showed resourcefulness in adapting to hearing deterioration and tinnitus by finding these assistive devices themselves, but they may have obtained the devices more quickly, and received additional support for their hearing needs, if referral to audiology services had been systematically in place. A recent study showed that HNC patients used internet access the least out of all those patients attending otology clinics, and older patients were less likely to obtain help information than younger patients (Pagedar et al., 2018). Therefore, it is suggested that for patients with tinnitus and hearing disorder, a policy be developed that includes clear referral pathways to
audiology services. Such a policy should also include appropriate advice on assistive devices and technology for improvement in listening to speech, and how to deal with environmental sounds more effectively. In addition, policy needs to ensure that older patients in particular receive this audiological support regarding technology as they may not have as ready access to internet sources as younger patients in order to investigate healthcare options. Furthermore, older people are less likely to seek advice as readily as younger patients.

7.3.6 Treatment regimen

Incidence of hearing deterioration with the administration of chemotherapy in conjunction with RT was in this study statistically significant (section 7.2); it was greater than with the administration of RT alone. It was not possible to perform a detailed assessment of the differences in patient experience of those who received RT or CRT, as RT treatment only was used in one participant interviewed who perceived a change in hearing. The following discussion focusses on comparing the incidence rates reported in this study with other studies based on treatment regimen. It will also discuss the impact of unilateral hearing deterioration, assumed to be related to RT treatment of patients in this study.

Twenty-six percent of participants who had curative RT alone developed a deterioration in their hearing, compared with 70% or those who had curative treatment by concomitant CRT. These findings were similar to the majority of those reported in other studies on HNC. Some authors have also reported in their studies that CRT induced a greater hearing deterioration than RT which was statistically significant (Chan et al., 2009; Shorter et al., 2017; and Wang et al., 2015). This finding was reported by Du et al. (2015) in their systematic review on clinician-rated toxicity following treatment for NPC. However, other studies did not find a statistically significant association between treatment type and hearing deterioration [Oh et al. (2004) and Pitsuksiri et al. (2011)], but these studies had evident factors that could account for their results. The findings from Oh et al. (2004) may relate to patients in their
study who were prescribed large doses of RT over-riding the effect of cisplatin chemotherapy. The conclusions from Petsuksiri et al. (2011) may pertain to hearing deterioration assessed by change in one frequency only, whereas it is known that measurement of changes in hearing is most reliable when determined by assessment of multiple frequencies (Simpson, Schwan and Rintelmann, 1992; Konrad-Martin et al., 2010). Therefore, the current study provides information on a cohort of patients who have a range of HNCs receiving UK standard treatment, and the findings add more evidence to support the majority finding in the literature that patients who receive CRT are more likely to suffer hearing deterioration following HNC treatment than those who have RT. It is therefore suggested that risk stratification should be used to target the monitoring of hearing in those patients who are due to receive CRT because of their greater risk of hearing deterioration with treatment.

The one patient interviewed who had RT alone and perceived a change in her hearing suffered Grade 3 hearing deterioration in one ear only, and was only made aware of the deterioration during discussion of test results with an audiologist during the study. This participant was subsequently provided with a hearing aid, and found benefit not only with hearing in group situations, but also in quiet when talking with her husband. It was noted that two other participants interviewed also developed Grade 3 toxicity in only one ear although they received CRT (for hypopharyngeal and tonsillar cancer respectively); one of these participants also acquired a hearing aid to overcome his hearing difficulties. Each of these three participants had hearing loss of moderate severity in the high frequencies following treatment. A questionnaire study on unilateral, profound severity, sudden onset hearing loss reported that patients with this loss had hearing handicap similar to those who had bilateral, age-related, acquired hearing loss of moderate severity (Iwasak et al., 2013). Although there are approximately ten times fewer articles on unilateral hearing loss compared with bilateral hearing loss, recent National Clinical Institute of Clinical Excellence (NICE) guidelines have indicated that unilateral deafness in adults is important to address by including single-sided
deafness in the assessment and management of hearing loss (NICE, 2018). Unilateral deafness impacts on the ability to locate sounds (Kitterick, Lucas and Smith, 2015), and this impact may compromise patient safety. These findings suggest that patients who have unilateral hearing deterioration (change in one ear only) following treatment also require audiological advice and support, to make them aware of difficulties they may encounter by acquiring one-sided deafness following RT or CRT for HNC treatment, and of the possible benefit of hearing aid provision.

7.3.6.1 Treatment toxicity

In this study, Chapter 5 recorded that all 16 participants with chemotherapy-induced hearing loss had cisplatin as part of their treatment. Carboplatin was used at the start of treatment for two patients who had moderate hearing loss prior to treatment, and cetuximab for three others due to other factors. These five patients did not have hearing deterioration during their treatment, or in the early post treatment period to 3-month follow-up. These findings indicate that a change of treatment from cisplatin to carboplatin or cetuximab can minimise hearing loss, and the wider literature provides some evidence to support this.

Carboplatin has been shown to induce either transient (Steinbach et al., 2012; Williamson et al., 2005) or permanent ototoxicity (Ozguroglu et al., 2006; Salvinelli et al., 2003), in ovarian or lung cancers, but has been shown to be less ototoxic than cisplatin in a COCHRANE systematic review of paediatric oncology patients (van As et al., 2016), and in a general review article (Landier, 2016). In addition, when the targeted molecular agent cetuximab is used with RT for HNC, there has been no reported loss in hearing (Ye et al., 2013; Pryor et al., 2009). Landier (2016) further reported that the efficacy of carboplatin in treating cancer was equivalent to that of cisplatin, suggesting that carboplatin could be a viable alternative to cisplatin. However, as there is little other literature available at present to support the more widespread use of alternative agents, cisplatin is the main drug used in treatment of head neck cancer in the UK, with carboplatin only used as a substitute if there is compromised
renal function, or impaired hearing, and cetuximab (a monoclonal antibody) used when there is over-expression of the epidermal-growth factor receptor (Palaniappan, Owadally and Evans, 2015). Therefore, more research is required to determine the value of greater use of these alternative agents, and also, although not explored in this study, the possible use of potential otoprotective agents such as sodium thiosulphate (Zuur et al., 2007), or aspirin (Crabb et al., 2017).

7.3.7 Information and support

There was no evident difference in the way participants received information or support, based on characteristics of age, pre-treatment hearing level, gender, or severity of hearing deterioration. This following section discusses how patients received information and support and their experience of unexpected symptoms; it then goes on to address the adequacy of service provision and to suggest improvements to clinical practice.

7.3.7.1 Pre-treatment information

Prior to treatment, study participants were given either verbal or written information that their hearing may deteriorate with treatment, which would suggest that patients were adequately prepared for any hearing deterioration that took place. However, it appeared that participants were not sufficiently prepared, as some expressed surprise at the severity of the change in hearing that took place, others had uncertainty in the progression of their hearing change, and others were not sure that the noise that they were hearing was tinnitus. The lack in sufficient preparedness of participants acquiring a loss in hearing was possibly due to the shock of being diagnosed with cancer, or because the focus at diagnosis was on the recovery of basic life functions. Shock at diagnosis is a common feature following diagnosis, as will be discussed below.
At the time of her diagnosis, one study participant said, “All you hear is the word cancer, and then that is it”, meaning that the shock of being diagnosed made it difficult for her to process other information. Humphris and Ozakinci (2006) reported that patients with HNC are prone to psychological distress immediately following diagnosis and during treatment. These authors stated that patients felt well informed about the treatment they received, but felt less prepared for lifestyle changes in the early post treatment period, presumably due to the effect of shock. In another study, shock at being diagnosed with cancer was expressed by 12 patients who were due to receive surgery for their HNC, with the shock causing them to remember only half of what they were told (Parker et al., 2014). The experience of shock is common in other cancer patients, and Baker et al. (2013) reported that patients who had received a diagnosis of breast cancer were too emotionally distressed to engage with professionals prior to receiving treatment. The DH document ‘Improving Outcomes: A strategy for cancer’ (DH, 2011, p. 9), states that ‘patients and their carers are likely to want to have access to reliable and balanced information about their condition, possible treatments and side effects’. However, shock may affect how much information patients can absorb when receiving a diagnosis of cancer, including that their hearing may deteriorate with treatment.

Although participants in the study received information before treatment about hearing problems being a possible side-effect of treatment, many appeared not to process this information, not only it seemed from the shock of diagnosis, but also because other information appeared to take priority. One finding in this study was that participants felt that clinicians were concerned to get patients through treatment, and that the clinicians’ attention was understandably focused on necessary functions, such as swallowing and speech (Fritz, 2001). Another finding was that participants were more worried about eating rather than hearing problems. As patients are required to start treatment within 31 days of diagnosis (NHS, 2017b), there is not much time to absorb the combined news of receiving the diagnosis, starting treatment, and developing side effects of treatment. It is not surprising,
therefore that the focus at diagnosis is on preparing patients for treatment and on dealing with the immediate side-effects on basic functioning.

It is important that patients receive adequate written information prior to treatment for them to refer to about the possibility of experiencing hearing deterioration, and the progression of aural change if perceived, particularly if this happens during treatment. One participant mentioned that he was aware at diagnosis that hearing difficulties may occur with treatment, but indicated that he was not prepared for his hearing to be so bad. Another experienced temporary hearing deterioration during treatment, and expressed anxiety at the prospect of the hearing deterioration returning. A third, who suffered hyperacusis, expressed distress at the prospect of his symptoms persisting. It is known that patients who receive RT for HNC experience uncertainly because of the unpredictability of side effects (Wells, 1998), and patients with other cancers, such as lung cancer, have high levels of distress when experiencing unexpected symptoms (Lowe and Molassiotis, 2011). Conversely, adequate information received by HNC patients at the point of diagnosis contributes to positive recovery two to six years after the completion of treatment (de Boer et al., 1999). It is therefore important that written, pre-treatment documentation contains information on all aural symptoms that may occur during treatment.

It is also important that pre-treatment documentation contains information on the different ways that aural changes occur, not only during, but after treatment. Study participants experienced aural change in different ways: for some, hearing deterioration was noticed first; for others, tinnitus was the initial problem; for the remainder, they experienced both tinnitus and hearing deterioration simultaneously. Some experienced their symptoms suddenly, whereas others noticed their symptoms more gradually. Some who experienced deterioration at the end of treatment had a restoration of their hearing during the early post-treatment phase. Others who experienced hearing loss during or after treatment, had a maintained loss when they were interviewed a year later. Some participants had a reduction in the severity of treatment-induced tinnitus a year after treatment. From discussion with
patients, it became clear that anxiety, uncertainty and distress could be significantly reduced if written information was developed to highlight aural problems that may be experienced during or after treatment. One participant suggested that it would be helpful if patients received information in a chart format as a colour-coded grid, not only for indicating possible hearing changes but also other potential side-effects. In such a chart, the side effects following treatment could be listed in rows, and that the columns of the chart would include information on how severe the symptoms might be and how often they occur, and whether they come early or late after treatment. Although lists of side-effects are available for HNC (ACS, 2017), these lists do not include hearing loss, and it is not clear if there are charts that graphically or visually show the side-effects of HNC treatment. Such a chart could be adapted from one in use for breast cancer which does show the side effects of treatment (Breastcancer.org, 2013), although there is no indication of severity or frequency of side-effects in that chart. Not only could such a chart be readily available to patients prior to treatment, but it could be available during and following treatment. In addition, it is suggested that consent forms include information on side-effects such as hearing deterioration, to ensure that clinicians discuss at this early stage the possibility of a change in hearing.

7.3.7.2 Information during treatment

It is important that hearing deterioration is detected in a methodical way during treatment, as currently there appears to be a lack in structure of reporting such a change. At the researcher’s hospital, during treatment patients meet with a radiographer or an oncologist to discuss a list of possible side effects that may occur during treatment. Although the list is comprehensive and includes questions on basic functioning such as eating and swallowing, aural changes are not currently listed; therefore, it was necessary for study participants to alert their clinician that they were experiencing aural symptoms. To ensure that the emphasis of reporting does not fall on patients volunteering information of hearing loss
during treatment, it is suggested that an item on hearing issues be included in the clinician’s list of side-effects during treatment.

An alternative to updating or amending a clinician checklist to capture hearing deterioration during treatment could be the adapting of an existing clinician-rated patient outcome measures scale. The Vanderbilt head and neck symptom survey v 2.0 (Murphy et al., 2010) is one such scale, and does have an item on hearing. However, in its existing form, the Vanderbilt scale is limited as it is difficult to correlate hearing difficulty with each point on the 0-10 scale. In addition, there is caution in using clinician-rated tools, as these may not fully reflect patient experience (Maguire et al., 2013; Falchook et al., 2016; Basch, 2010).

Following a systematic review of the literature, Maguire et al. (2013) concluded that existing supportive care need (SCN) tools in breast cancer did not address patients’ symptoms adequately, and that collaborative work between patients with lung cancer, health professionals, and tool developers was required for a SCN tool to address adequately the needs of patients. Falchook et al. (2016) compared practitioner and patient-reported toxic effects on voice and speech production following CRT for HNC treatment, and found that there was an under-reporting of patients’ concerns by practitioners; as a consequence, the advice and support for patients was inadequate. Therefore, there is evidence to favour the addition of an item on hearing deterioration in a clinician’s checklist of side-effects during a mid-treatment appointment, rather than relying on a clinician-rated outcomes measure.

In addition to a clinician’s checklist, it is suggested that patients should provide information on what side-effects they experience during treatment in a structured way. In this study, some patients were proactive in relating their hearing problems during treatment, although they had no questionnaire to prompt them to do so. Therefore, it is recommended that PROMs be used. A PROM is developed with the involvement of patients to reflect more fully their experiences and help to identify their needs, as devised for patients with gastrointestinal problems (Whiteing and Cox, 2010). One that has been developed for cancer care was sent by the DH in 2012 as a survey to approximately 5000 cancer sufferers
in England to assess quality of life (DH, 2012). However, this PROM does not include hearing problems and it was not made clear in the DH document what involvement patients had in creating the questions being asked. The lack of a PROM regarding hearing loss following cancer treatment is a concern, and, in view of the findings in the literature and from this study of the effects of hearing deterioration, there is a great need to develop an appropriate tool. The use of an appropriate PROM with hearing-related questions may help to identify patients earlier so that they can receive suitable audiological support. It is noted, however, that there is a recent ‘patients concerns inventory’ (PCI) that has been developed by Aintree University Hospital (2017) for HNC that includes hearing problems on the checklist. It is welcomed that a local service has recognised the need to include hearing difficulties as an item of concern in its PCI and it is suggested that there is more widespread use of such forms to enable patients to communicate their need for audiological support in a more structured way, than merely vocalising their concerns.

7.3.7.3 Support after treatment

Study participants had different experiences of when they had the opportunity to discuss their hearing deterioration. At the time of testing, some participants were informed that their hearing had deteriorated by the audiologist, whereas others did not have such a discussion, possibly because the audiologists who tested them thought the oncologist with overall clinical care would do so. However, it transpired that for some participants, the study interview one year after treatment was the first time that they had had a discussion in depth about their hearing problems. It is noted that poor communication has been a problem in the NHS, including liaison between services (Pincock, 2004) and even within MDTs. Fleissig et al. (2006, p. 951) stated that, ‘multidisciplinary teams [involved with cancer care] should improve coordination, communication, and decision making between health-care team members and patients, and hopefully produce more positive outcomes. The recommendation by Fleissig et al. (2006) is applicable to communication between services
and within MDTs for cancer care (if audiology, in the future, is considered part of MDTs) for supporting patients with aural concerns following HNC treatment. It is therefore important to establish between the disciplines of audiology and oncology which clinical service provides information on hearing deterioration, and when to provide this information, so that patients receive information (including what speech they may be missing as a result of developing a deterioration in their hearing) in a timely and systematic way.

Setting up of protocols between oncology, audiology, otology (to manage middle ear dysfunction) and hearing therapy services (to manage tinnitus) is important for cancer survivors to receive timely support to address their hearing deterioration and tinnitus concerns, and to live well in survivorship. It is now recognised that patients need to live well following cancer treatment, and Simcock and Simo (2016) recommended that HNC patients be referred to different services, including audiology for hearing support. This approach embraces NHS England’s vision mentioned in the 2016 document ‘Commissioning Person Centred Care for People Affected by Cancer’, that aims to support people ‘not only to live following cancer, but to live well’ (NHS, 2016, p 3). However, this document, which is an advance on the NHS cancer document of 2011 (DH, 2011) still does not mention hearing deterioration as one of the possible side effects of cancer treatment, indicating that there has been no advanced thinking in UK cancer policy over five years regarding the effects of hearing deterioration on cancer survivors. Whilst the ACS has guidelines recommending that patients be referred to audiological or other appropriate services for assessment and treatment of hearing loss (Cohen et al., 2016), it is disappointing that these guidelines do not mention tinnitus problems, which shows the lack of awareness of the negative impact of tinnitus. The guidelines also do not suggest involvement of otologists, which again shows that patient experience of middle ear dysfunction, which caused irritation and annoyance for patients interviewed in the current study, is not fully recognised as a feature of HNC treatment. Therefore, there is need to develop policy documents that involve
multidisciplinary input to ensure that patients receive the necessary support and management of their aural concerns.

### 7.4 The need for hearing monitoring

This study has shown the extent to which hearing deterioration occurs after treatment of a UK HNC patient group in the early post-treatment phase, and the impact this deterioration has on the well-being of cancer survivors. In view of these findings, it is recommended that hearing monitoring is implemented as part of care management for this patient group, as currently there are no national UK guidelines published or advocated by UK audiology professional bodies. Hearing monitoring schemes have been advocated over many years (Campbell, 2006), and recently the US have provided a framework (Cohen et al., 2016) that could be adapted for implementation in the UK. Although this framework provides good advice on monitoring, it needs to be adapted for use in the UK, based on findings from this study. This section will continue with a discussion on when and how to monitor, who should be involved and what tests should be used with the monitoring process.

#### 7.4.1 When to monitor

The ACS provides advice on HNC survivorship by advocating baseline hearing testing and monitoring of hearing for early recognition and on-treatment management of hearing deterioration (Cohen et al., 2016). This implies that hearing testing during treatment is recommended, but the Society does not state how patients are managed if a hearing change is found, nor does it recommend when to perform hearing testing after treatment has been completed.

In this study it was found that, in addition to baseline hearing testing, it was appropriate to perform end of treatment testing and 3-month follow-up testing. Testing at these time points enabled clinicians to identify patients who had a sustained hearing loss after treatment, and
such patients could then be referred to audiology for advice regarding hearing aiding and/or tinnitus support. In addition, patients who had sustained middle ear dysfunction could be referred to otology services to monitor this condition and provide appropriate management and support. It was convenient for patients to arrange tests at these time-points, as the patients were already in hospital for the end of treatment test, and it was possible to arrange the 3-month follow-up test to fit in with the patient’s scheduled review with the oncologists. Two study participants commented on the convenience in attending these test appointments, as the participants did not have to arrange another day out at hospital to attend them.

In addition to performing hearing testing before treatment, at the end of treatment, and at 3-month follow-up after treatment, it is suggested that testing mid-treatment may be beneficial for patients. Some participants mentioned that hearing testing mid-treatment might help to capture hearing deterioration within this period. If this were possible, it might lead to a change in treatment which occurred with some study participants, although participants in the study by Zuur et al. (2007) appeared to continue with the same regime even though hearing deterioration was documented during treatment. The ACS also recommended on-treatment monitoring of hearing deterioration (Cohen et al., 2016), for early recognition and management of hearing deterioration. Therefore, there is merit in performing a mid-treatment test, not only for considering a change in treatment if this were possible, but also for identifying patients who may require audiological support following it, even if treatment is prematurely stopped due to ototoxicity (Shorter et al., 2017). Again, further study is required, to assess the feasibility and usefulness of testing mid-treatment.

It is also suggested by the researcher that a hearing test be performed after the early post treatment period. During interview, one year after treatment completion, some participants mentioned that they felt ready to discuss their hearing concerns at that time, whereas they did not feel ready to do so earlier while still recovering from the effects of treatment. Hearing loss can also develop and progress after treatment (Yilmaz et al., 2008; Li et al., 2010) and
loss can be maintained as a long-term side effect of treatment (Kwong et al., 1996) reported in studies assessing hearing deterioration up to five years post treatment. Cho et al. (2016), in their study of sudden-onset post treatment deafness identified much later manifestation of hearing loss up to ten years after treatment, although caution is required in attributing the cause of hearing loss so long after treatment. Some other studies (Wang et al., 2004; Ho et al., 1999) have advocated follow-up of hearing up to at least five years following HNC treatment, but it is not clear whether resources of finance, manpower and capacity should be allocated to this as it is not clear if clinically significant deterioration takes place in the longer term (Theunissen et al., 2014b). Therefore, it is suggested that an audiology appointment is made one year after treatment completion to enable those identified earlier with hearing deterioration to have the opportunity to discuss their hearing concerns, if they have not felt ready beforehand. It is also an opportunity to repeat hearing testing to assess if there has been any deterioration in hearing after the early post treatment phase.

### 7.4.2 Who to be involved in monitoring

From the findings in this study, it is suggested that audiologists need to be involved in monitoring hearing deterioration by performing regular hearing tests. In addition, oncologists and radiographers need to be aware of any hearing or tinnitus concerns when consulting patients in clinic appointments during or after treatment. These clinicians will be assisted to ask about aural symptoms by possessing a clinical check list of side-effects of treatment that includes hearing loss and tinnitus, and for patients to have a PROM that includes both these symptoms.

### 7.4.3 How to monitor

This section discusses which classification system is best to detect hearing deterioration, and what tests are best used based on current knowledge of hearing deterioration following HNC treatment. It is suggested that the CTCAE criteria (NCI, 2010) are suitable for detecting
hearing deterioration in the higher speech frequencies, and in addition it is suggested that the BSA criteria (BSA, 2011) for describing overall hearing status is used to assess the impact of hearing deterioration in the lower speech frequency range.

There is an on-going debate as to what criteria are best for determining significant deterioration in hearing following treatment. In the literature review of this thesis (Chapter 2), it was mentioned that some studies used their own classification system to monitor changes in individual frequencies (for example Hsin et al., 2010, and Oh et al., 2004), but these lack evidence to substantiate their use. Waissbluth, Peleva and Daniel (2016) compared the strengths and limitations of 13 established classification systems, including those of Brock et al. (1991) and ASHA (1994) and concluded that each of these classifications had strengths, but the main weaknesses were that all were poor in detecting small adverse changes, and in indicating what changes would be clinically significant for communication and quality of life. Crundwell, Gomersall and Baguley (2016), further advocated that research is needed to establish the links between self-reported hearing function impairment and ototoxic classification systems. Whilst the current study did not use PROMs, it did provide information on patient experience in relation to the CTCAE classification system (NCI, 2010), by a measured hearing deterioration using PTA. Those who suffered a Grade 1 or greater severity hearing deterioration, suffered adverse hearing in the mid-high speech frequency range to the extent that eight participants obtained hearing aids (within 18 months of the completion of their treatment), indicating that the CTCAE criteria were useful in detecting clinically significant hearing deterioration that affected patient quality of life. Furthermore, the criteria are used by oncologists to assess damage to other body systems following CRT or RT, so that changes in hearing are readily understood by those who are overseeing cancer care.

In addition to monitoring high frequency hearing deterioration, it is also important to monitor overall hearing levels following HNC treatment. One patient in this study did not suffer hearing deterioration as per CTCAE criteria but they required hearing aiding. Following RT,
their overall hearing loss developed from a bilateral moderate loss to a severe loss in one ear after treatment according to the BSA guidelines (BSA, 2011) on describing hearing levels. This patient had a change in their low frequency hearing (less than 1kHz), which was not measured in CTCAE change, but the change was detected in the BSA (2011) descriptor guidelines. It is known that patients with low-frequency hearing loss benefit from aural support in addressing hearing difficulties (Halpin and Thornton, 1994). It is therefore suggested that overall hearing be recorded, using the BSA (2011) descriptors of hearing levels, that enable low-frequency hearing status to be monitored with HNC treatment.

7.4.4 What tests to use

This section will suggest that PTA and tympanometry be used in monitoring hearing deterioration in HNC treatment. Hearing monitoring requires the use of PTA prior to treatment, and at some time after treatment, to determine a measurable change in hearing. Testing needs to adhere to known protocols, such as the recommendation of the BSA (BSA, 2011). This recommendation advises on how to perform hearing testing, and advocates testing of the standard octave speech frequencies between 0.25 to 8kHz for air conduction, and 0.5 to 4kHz for bone conduction. In view of the need to test higher frequencies to detect ototoxicity, it is suggested by the researcher that testing of 3 and 6kHz takes place routinely in monitoring protocols, in addition to the usual octave frequencies tested in PTA (Konrad-Martin et al., 2010). The use of tympanometry in this study helped to confirm middle ear dysfunction, and this test is advocated by other authors (Waissbluth, Peleva and Daniel, 2016; Hsin et al., 2010; Li et al., 2010; Pan et al., 2005). Therefore, there is evidence to suggest that tympanometry should be used together with standard PTA (0.25-8kHz) for monitoring hearing in HNC treatment.

This study has provided evidence to support the implementation of hearing monitoring with HNC treatment to identify those with a hearing deterioration. However, as there is little evidence currently available that recommends a change in treatment for this patient
population if a hearing deterioration is detected, it is suggested that hearing monitoring should focus on the speech frequency range (up to 8kHz). Therefore, high frequency audiometry, although used to demonstrate hearing deterioration in frequencies >8kHz following head and neck treatment (Sakamoto et al., 2000; Zuur et al., 2008; Zuur et al., 2009), may not yet be of much clinical use for HNC patients if it does not affect treatment or management. In addition, there are no standard protocols for assessing high frequency hearing (Rieke et al., 2017), so these will need to be set-up before establishing its use. A similar argument is made for not yet using OAE testing (an objective test that is more sensitive to ototoxic change than PTA – Konrad-Martin et al., 2005) in this patient group. However more research is required to assess the impact of higher frequency loss (>8kHz) more fully, as this has not been explored in the literature. In addition, future research into the use of higher frequency audiometry and OAE testing is merited if alternative (less ototoxic) treatments become more readily available in HNC treatment.

7.5 Strengths and limitations of the study

The main strengths of this study were that:

- this was the first study to utilise a mixed-methods design to obtain information on hearing deterioration following HNC treatment, and to provide a unique understanding of this phenomenon by bringing together data from the qualitative and quantitative phases;
- the methodology was appropriate to answer the research aims, with new findings being obtained separately through qualitative and quantitative data, and by integrating the data, where appropriate, in this discussion;
- it was of good methodological quality: the study met all requirements to minimise potential threats to the validity of the findings self-assessed against the CASP cohort checklist (CASP, 2017b) for the quantitative phase of the study (section 4.2.7); and Maxell’s 1992 criteria for the qualitative phase (see section 4.3.6);
it provided findings that can be used as the basis for further research, and that has implications for improving service delivery for the local population.

The limitations in this study were that:

- it assessed a short phase following treatment completion: the side-effects of hearing deterioration only in the early phase were measured, and it could have been useful to assess hearing at later time-points. However, it was important to establish hearing deterioration in the early phase for general HNC, to capture both SNHL and mixed hearing loss, as most articles have focussed on later stage changes (Schultz et al., 2010; Tsang et al., 2012), or on SNHL (Li et al., 2010; Hitchcock et al., 2009). Assessment of longer term hearing deterioration after treatment could be the focus of another study;
- there was no HNC subtype analysis made, due to the small sample size, so it was not possible to identify if subtypes of this cancer were more at risk to hearing deterioration than others;
- there was no use of complementary findings: it could have been possible to ask participants to complete patient reported outcome measures on quality of life to complement the findings from qualitative interviewing. However, existing head and neck quality of life scales either omit hearing problems [for example, the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire QLQ-H&N35 (Bjordal et al., 2000)], or do not adequately address hearing difficulties. For example, the Vanderbilt head and neck symptom survey v 2.0 (Murphy et al., 2010), has been shown to indicate an increase in hearing problems from the early recovery (≤6 month) period to a year following treatment (Cooperstein et al., 2012), but it is difficult to correlate hearing difficulty with each point on the 0-10 scale. However, the development of quality of life tools could be another aspect for future research.
• it recruited over a 6-month period, and data was gathered at only one tertiary centre.

It will be necessary to verify the findings from this study by conducting future research at other UK centres to provide a national profile on hearing deterioration after HNC treatment, and to recruit over a year period to allow for any season variations in diagnosing the disease.

7.6 Summary

In conclusion, this study set out to determine the incidence and severity of hearing deterioration in a cohort of patients in a UK hospital with HNC following treatment. It also explored patient experience of hearing deterioration for this patient group. The results from this study were discussed with reference to the wider literature, and the synthesised findings are summarised below.

The study found that a substantial number of participants were affected by hearing loss following treatment of different subtypes of HNC. It was the first study in the UK to report incidence and severity figures for hearing deterioration, using current treatment regimen. The study determined that hearing deterioration after treatment occurred in patients across a broad range of HNC, with 57% deterioration at the end of treatment, and 50% deterioration at 3-month follow-up after treatment. It is difficult to make a direct comparison of the study findings of incidence of hearing deterioration with the wider literature due to different demographics of participants and treatments used, and to different classification systems employed to determine deterioration in hearing. However, the current study's findings of hearing deterioration after treatment supported the majority findings of studies conducted previously and discussed in the literature reviewed.

As a result of this study, it is suggested that monitoring of hearing across all the subtypes of HNC be conducted, as hearing deterioration occurred in all the seven subtypes of HNC, and as a substantial number of participants had hearing deterioration following treatment. Further
research in other UK cancer centres over a longer period would build a broader national picture of the impact of treatment on HNC patients.

In addition, this study provided information on what factors may influence hearing deterioration. In common with the majority findings in other HNC literature, participants in this study who had CRT had greater risk of hearing deterioration than with RT alone, and that gender did not affect hearing deterioration. This study supported other findings which showed that younger age was associated with greater severity of hearing deterioration and that older age with greater risk of experiencing hearing deterioration, although there is no firm evidence to support that age influences hearing deterioration with HNC treatment. Pre-treatment hearing level did not appear to affect the incidence of hearing deterioration, but there were not many other studies to compare this finding with. It was noted that participants who had carboplatin in this study had no further deterioration in their hearing, and carboplatin has been found to be less ototoxic than cisplatin in the wider literature.

This study also provided novel insights into the experience of hearing deterioration in patients with HNC following treatment, and appears to be the first to use a mixed methods study design. These insights emerged as this study specifically assessed patient experience of hearing deterioration using qualitative methods in this patient group, with patterns of different experience discerned drawing on characteristics obtained from quantitative data that determined that hearing deterioration following HNC is a heterogeneous experience. Further fresh insights were gained by bringing together qualitative and quantitative data within this chapter. This chapter discussed the following points -

- Some participants in this study were aware of aural changes during and after treatment. It appears that this study is the first to document this awareness in HNC literature;
- Study participants were shown to have different experiences in the progression of their aural symptoms when interviewed at one year follow-up; some participants had
improvement, yet others had further deterioration in their hearing. These mixed findings concur with that in the wider literature on HNC treatment with variability in progression determined by quantitative methods;

- Participants with major (Grade ≥3) hearing deterioration (as per CTCAE classification) had more wide-reaching problems with communication and their pastimes compared with those who had minor deterioration. However, some of those with minor deterioration in their hearing required hearing aiding as their change in hearing had a negative impact on their communication, providing new evidence in the importance to offer support to patients with any measured amount of hearing deterioration;

- Fatigue experienced by study participants, is common in cancer literature, and is known to affect hearing ability; patients with hearing loss following treatment may have greater difficulty with their hearing due to fatigue;

- A novel feature of this study was to report on tinnitus sensation from a qualitative aspect in HNC literature. It was noted that there was a large proportion of participants who experienced troublesome tinnitus alongside their hearing deterioration, with one participant suffering hyperacusis. However, there is less reporting of tinnitus in the wider literature than hearing deterioration, and a lack of recognition of tinnitus being a side effect in national guidelines. Referral protocols to health services are vague for tinnitus provision, and there appears to be no standard procedure for patients to access help for tinnitus following HNC care;

- This study clarified that patients with SNHL following treatment had a poorer quality of life, as other studies appear not to have identified patient experience with SNHL. In addition, middle ear dysfunction suffered within the early post treatment phase created negative patient experience, another novel finding from this study. However, it was not clear in the literature if there are standard procedures to monitor middle
ear problems in the early post treatment phase or those that may continue into the longer term;

- Although there was no greater risk in hearing deterioration based on pre-treatment hearing status, it was noted that patients who had normal hearing pre-treatment put emphasis on the need to lip-read after treatment. These participants acquired bilateral mild-moderate or moderate mid-high frequency sudden-onset hearing loss, and as current literature has focussed on congenital severe or profound or unilateral loss, the study results appear a novel finding. There are no national guidelines for accessing lip-reading services; consequently, patients are not made aware that they may need to lip-read in the early post treatment phase, and there are no clear pathways on how patients can receive support to improve lip-reading skills;

- There was no pattern to hearing deterioration, either due to measured change or in patient experience, based on gender;

- Although younger participants suffered greater measured severity in hearing deterioration, they appeared to acknowledge their loss more readily and found solutions to deal with it. However, older participants, more at risk of developing a measured deterioration, appeared less ready to acknowledge their loss. The wider literature shows that this reluctance can have a negative impact on the ‘significant other’.

- Some participants in this study had a sense of loss and isolation. Such emotions are common in the experience of people who have hearing loss, or who have HNC. Feelings of isolation appeared to be associated with younger participants, however this may be an incidental finding, whereas feelings of loss were more common among older participants, and this is supported by findings in the wider literature;

- Some patients received hearing aids from audiology services, but others sourced other assistive devices themselves rather than from health professionals. Concern
was raised to ensure all patients, especially older ones, access advice and support from audiological services;

- Participants who had unilateral hearing deterioration following RT or chemotherapy also had hearing difficulties that required addressing, a finding supported by recent NICE guidelines;
- There was evidence that participants played down their aural symptoms, yet these symptoms had a negative impact on their quality of life. It was noted that there is not an adequate PROM available regarding hearing deterioration for cancer in general, let alone for HNC, although there is a local PCI available that does include hearing problems;
- Study participants had varied experience in being prepared for the possibility of suffering a change in their hearing. It was recognised that the shock in receiving a diagnosis, reported in other cancer literature, meant that some patients were not able to absorb all information at diagnosis, so that written information on hearing deterioration should be in a format that is readily understood;
- There was varied experience among participants receiving information on their hearing test results, and on the process of receiving support for their hearing and tinnitus concerns. It was noted that poor communication within the NHS can occur between services in relaying information for continuing care, so there is need for improved communication between professionals on how hearing deterioration results are shared, and how help for patients can be obtained;
- During treatment, it was realised that both hearing and tinnitus concerns were not part of checklists that clinicians use for identifying side effects; this meant that it fell to patients to let clinicians know that they were experiencing either (or both) of these side-effects.

In view of the scale and impact of hearing deterioration encountered in this study, it is suggested that hearing monitoring for HNC patients is required, and for a baseline
assessment to be performed and be measured against testing performed at the end of treatment and at 3-month follow-up after treatment. Some patients were ready to receive hearing aid support at their 3-month follow-up, and testing appointments at these three time points coincided with other hospital appointments to reduce the burden on patients making multiple visits to attend hospital. In addition, it is suggested that a mid-treatment hearing test should take place, to alert clinicians to change treatment if possible and identify those patients who may need aural support after treatment. Also, it is advised that a 1-year post treatment hearing test takes place for those patients requiring more time to recover from the effects of treatment, and to identify those who may have further deterioration in their hearing.

There are many different classification systems used to measure and grade hearing deterioration in people with HNC, which made meaningful comparison of incidence and severity rates difficult. It is suggested that the CTCAE criteria be used for identifying hearing deterioration, for both research and clinical practice, based on the number of studies (including the current study) using these specific criteria, and others that support ≥15dB change in hearing across multiple frequencies as clinically significant, together with BSA descriptors to assess overall hearing levels, based on these criteria providing complementary clinically useful information presented in this study.

This chapter discussed the findings of this study in relation to the wider literature, and highlighted that tinnitus and hearing deterioration are neglected in the survivorship agenda, although both symptoms had a negative impact on patient experience, and were experienced amongst a substantial number of patients following HNC treatment. The following chapter will take forward these findings to suggest recommendations for research, for education, and for policy and for practice, in order to provide improved support and service for this patient group.
Chapter 8 Conclusion

8.1 Introduction

This thesis: “A study of hearing deterioration following treatment for head and neck cancer in a UK hospital”, employed a mixed method approach to explore hearing deterioration following treatment of HNC in the UK. There were two main aims: first to assess the incidence and severity of hearing deterioration, and secondly to explore patient experience of hearing deterioration. Following recommendations for future research to create a robust examination of the findings in this limited study, this chapter, with reference to the wider literature, will show the contribution made by this study to clinical practice and potential policy changes to create better patient care for HNC survivors in the UK.

8.2 Recommendations for future research

8.2.1 Building on the incidence findings from this study

The incidence rates of hearing deterioration after treatment of HNC found in this study were based on a small sample size in one UK hospital, and focussed on hearing testing up to three months in the early post treatment period. As it is not possible to make generalisations from the study findings, from a sample of this size, and make alterations in service provision in the longer term, it will be necessary to conduct further studies with a larger patient group to consider how best to manage hearing deterioration by gaining greater understanding in the following areas:

- **The scale of hearing deterioration in the UK**: To better understand the full scale nationally, research needs to be carried out with a larger sample size, in other UK centres, and with consecutive recruitment for at least a year, to account for any
regional variations in the proportions of the subtypes of HNC, and for any seasonal variation in hearing loss due to upper respiratory tract infections;

- **Performing subtype analysis**: Future studies should either provide subtype analysis, or focus on particular types of HNC to determine if patients with particular subtypes of HNC are more at risk of hearing deterioration than others;

- **The progression of hearing deterioration in the longer term**: From previous studies in published literature, it is not clear whether hearing deterioration following treatment further deteriorates over time to a clinically significant amount. More longitudinal studies should be conducted to measure the long-term effects of hearing deterioration on people with HNC (one and two years after treatment);

- **Identification of risk factors**: The study found that older patients and those who received combined chemotherapy and RT, were more at risk of hearing deterioration than younger patients and those who had RT only treatment respectively. However, where hearing deterioration did occur, younger patients were more severely affected. To better at facilitate the delivery of targeted supportive care, future research should focus on confirming the risk factors identified in this study.

### 8.2.2 Verifying novel findings from this study

Novel findings emerging from this study were the impact of tinnitus (including hyperacusis) on patients, and the impact of hearing deterioration on patients who found themselves suddenly depending on lip-reading even though they only had mild-moderate, mid-high speech frequency hearing loss. It was also found that isolation and loss were associated with hearing deterioration following cancer treatment. There is need to verify and expand upon these findings (on larger sample sizes) in the following ways:

- **Determining the impact of tinnitus**: More research should be conducted to determine the incidence of tinnitus and hyperacusis following HNC treatment, and
explore patient experience to understand more fully the extent and impact of tinnitus and hyperacusis on this population;

- **Determining the need to lip-read**: Further study is needed to determine what proportion of patients require lip-reading soon after they have received treatment. In addition, an investigation into the acceptability and use of lip-reading training for patients might also be valuable;

- **Further exploration of patient experience**: Drawing on the experience of the participants in the study, feelings of loss and isolation were identified. These findings need to be verified with a larger sample size, to find out if the patterns of isolation and loss associated with younger and older patients respectively are replicated. Where this occurs, it may be possible to provide targeted advice and support to patients, before and after treatment. In addition, it is recommended that a feasibility study is performed on the effectiveness of clinical nurse specialists in providing advice and support to patients who experience isolation or loss.

### 8.2.3 Assessing alternative treatments and tests

In Chapter 5 it was reported that all 16 participants with chemotherapy-induced hearing loss had cisplatin as part of their treatment regime, but that none who had carboplatin only chemotherapy incurred hearing deterioration. In Chapter 7 it was suggested that hearing deterioration could be minimised if alternative treatment was used, and that patients could be identified earlier with hearing problems if they were given self-report forms or were tested by instruments more sensitive in detecting hearing deterioration than standard pure-tone audiometry. There is the potential to improve patient well-being in minimising hearing deterioration, or if deterioration takes place, for it to be detected earlier, in the following ways:

- **Using alternative treatment**: In Chapter 7, it was proposed that carboplatin was a viable substitute for cisplatin due to it being less ototoxic than cisplatin. However,
there is need for more research into both the effectiveness of carboplatin in treating cancer, and the ototoxic effect of carboplatin, before advocating the regular use of carboplatin over cisplatin;

- **Using a standard PROM:** PROMS are instruments used by patients to document different aspects of side-effects from treatment. As there currently is no PROM available that assesses hearing related problems following treatment, it is recommended that future research should focus on developing a PROM that includes hearing deterioration and tinnitus following HNC treatment;

- **Using an auto-inflation balloon device:** The use of this device provided relief for a participant who had middle ear dysfunction following treatment. It is recommended that further studies are conducted to assess the effectiveness of this device on a larger number of participants;

- **Using additional tests:** Once the need to monitor hearing deterioration following HNC treatment has been recognised (using standard PTA and tympanometry), it is recommended that research is conducted on the usefulness of additional tests, such as distortion product OAE and higher-frequency audiometry testing, for earlier detection of hearing deterioration;

- **Using hearing aids:** Hearing aids provided relief for patients who suffered hearing deterioration and tinnitus following treatment. Further study on whether hearing aids are of benefit to or acceptable to patients would identify if there is greater uptake on these devices from those who have sudden-onset loss due to treatment related deterioration, compared with those who have age-related hearing loss.

### 8.3 Recommendations for clinical policy and practice

This study identified two main areas that required improvement in policy, practice and education to offer better support for patients who experience hearing deterioration (and/ or tinnitus) following their HNC treatment: monitoring of aural change, and information about
aural changes. In addition, it is recommended that targeted management should be offered to patients more at risk of hearing deterioration, or for those who display downplaying of symptoms. These areas of concern should be discussed in MDT meetings to obtain consensus in how to implement change, and how to create or adapt policy and protocols. The team should involve oncologists, ENT doctors, clinical nurse specialists in HNC, radiologists, and audiologists. Each speciality should understand their role in information sharing, monitoring and support, and offering targeted care to HNC patients who are due to receive treatment, and as a consequence may suffer aural change.

8.3.1 Monitoring aural change

- **When to monitor:** It is recommended that hearing monitoring become a standard procedure for assessing hearing deterioration of patients who have HNC treatment (Crundwell, Gomersall and Baguley, 2016; Waissbluth, Peleva and Daniel, 2017). It is also suggested that there should be at least five time points for monitoring hearing: pre-treatment; during treatment; at the end of treatment; at three months following the completion of treatment, and one year after treatment completion;

- **What to monitor:** This study reported that all the patients who had a hearing deterioration either suffered sensorineural damage, which caused difficulty in hearing and communication. In addition, some patients who also suffered middle ear dysfunction (Chapter 5, Figure 5.2) were adversely affected by owning feelings of irritation at not being able to hear, even if this dysfunction resolved in the longer term. As previously discussed in this chapter, tinnitus was bothersome for the majority of patients who suffered hearing deterioration following their HNC treatment. Therefore, it is recommended that SNHL, middle ear dysfunction and tinnitus are included in an aural change monitoring program;

- **How to monitor:** Hearing tests performed should include PTA to test speech hearing in the octave frequencies between 0.25 and 8kHz (for air conduction – including half
octave frequencies at 3 and 6kHz) and between 0.5 and 4kHz (for bone conduction) to identify SNHL and mixed hearing loss, and tympanometry to help identify the nature of middle ear disorder. In this study, it was difficult to compare incidence of hearing deterioration with other studies as different criteria were used for determining a clinically significant change. Based on the findings of this study, it is recommended that the CTCAE criteria are used for determining hearing deterioration, as these criteria involve the assessment of several frequencies (Simpson, Schwan and Rintelmann, 1992), and deterioration of at least 15dB was used in the majority of high quality articles reviewed in Chapter 2. In addition, it is recommended that overall hearing be recorded, using BSA (2011) descriptors of hearing levels with the calculation of PTA averages (including 250Hz), to enable low-frequency hearing to be measured and to gauge the overall level of hearing difficulty of a patient. Although low-frequency change may be temporary due to middle ear dysfunction, it is still important to be aware of this change, as patients with low-frequency hearing loss also benefit from aural support in addressing hearing difficulties (Halpin and Thornton, 1994). Tinnitus could be assessed using a self-report measure such as the Tinnitus Handicap Inventory;

- **Who to perform the monitoring:** During treatment, oncologists and radiographers should ask patients if they have experienced hearing loss or tinnitus using checklists updated to inform of aural change, and to review PROMs provided by patients for confirmation. In addition, during and after treatment, audiologists can verify a change in hearing using hearing tests, and assess the development and impact of tinnitus, if experienced, by discussing the Tinnitus Handicap Inventory completed by patients.

### 8.3.2 Information and support for patients

- **Pre-treatment information:** From a participant interview, it was found that information given to patients prior to treatment could be considerably improved. It is
recommended that patients be alerted to the possibility of aural change, including the manifestation and severity of hearing loss and tinnitus, to minimise anxiety if these symptoms occur. For strong visual effect, this information could be presented within a colour-coded grid alongside other side-effects of treatment. Pre-treatment consent forms should also include information on possible hearing deterioration;

- **Information sharing during and after treatment:** Participants during their study interview mentioned that they needed to proactively volunteer information of their hearing deterioration (or tinnitus) experienced during treatment. Therefore, it is recommended that the clinicians’ checklist of side effects that occur with treatment should be updated to include hearing deterioration and tinnitus. In addition, while patient self-reporting measures are available, they do not adequately cover aural changes with treatment. Therefore, it is recommended that a patient self-reporting measure is developed to include hearing deterioration and tinnitus;

- **Discussing test results:** It was found that some patients received information on their hearing status at the time of testing with the audiologist who tested them, whereas others discussed their hearing concerns for the first time at interview a year after the completion of their treatment. Therefore, protocols need to be created or adapted to ensure that there is clarity and consistency on which clinical specialty shares test results with patients. It is recommended that audiologists should discuss test results with patients, and refer patients on to appropriate specialities to manage aural change;

- **Managing aural change:** In Chapter 5 of this study, Figure 5.2 showed that participants experienced SNHL or middle ear dysfunction with their hearing deterioration; patients were also adversely affected by either minor or major hearing deterioration, including those who experienced deterioration in one ear only (see discussion in Chapter 7). Clear sign-posting is required as soon as possible to direct patients to receive the appropriate advice or support they require if they have a measured aural change on testing, or if they are found to be adversely affected by
their change in hearing by either clinician-rated or self-report questionnaires. It is recommended that those who have purely SNHL deterioration should be seen by an audiologist to discuss and manage the hearing loss. Audiologists can share strategies to improve communication, and make patients aware of the impact of hearing loss on patients' families and friends, even if a measured change in hearing is not perceived by the patient. Audiologists can make patients aware of assistive devices including hearing aids and alarm systems, and also discuss with them how best to address their functional difficulties, as each individual patient experiences hearing deterioration differently (Thomas, 1988). It is therefore suggested that patients who have middle ear dysfunction be first seen by ENT to manage the dysfunction, and then by audiology to manage hearing loss caused by persistent dysfunction. Those patients who have tinnitus should be seen first by audiologists, if the tinnitus occurs with hearing deterioration that could be helped by fitting of a hearing aid, or if hearing aids are not suitable, patients should be referred to hearing therapy services for general advice on tinnitus. Patients who are struggling in their communication following sudden-onset hearing deterioration, with or without hearing aiding, may benefit from lip-reading. Therefore, patients should receive more information about the possible need to lip-read following treatment of their HNC. Appropriate support in helping patients to develop lip-reading skills should also be provided, by hearing therapy or an alternative service.

8.3.3 Targeted support for patients

- **Using risk stratification:** This study identified certain factors that were associated with hearing deterioration: older patients with a mean age of 68.7 years were most at risk of developing a hearing deterioration, although younger patients with a mean age of 56.3 years were at greater risk of experiencing more severe deterioration if they experienced a hearing change. Patients who were treated with CRT were more at
risk of developing hearing deterioration compared with those who had RT alone. Therefore, risk stratification could be used to target more frequent measurements and interventions to those at risk of developing severe deterioration. However, as discussed earlier, further research to verify at-risk groups should be conducted before any modifications to current practice are made;

- **For those who express symptoms of loss and isolation:** Some patients experienced a sense of loss and social isolation following hearing deterioration after cancer treatment. If such feelings affect their well-being, patients could benefit by talking through these emotions with clinical nurse specialists in HNC.

### 8.4 Recommendations for education of survivors and practitioners

As a result of conducting this study, the researcher and colleagues in his audiology department have been invited to talk at local Well-being events for HNC survivors. At these events, audiologists have given presentations on how the ear works, and survivors or carers have asked questions related to hearing and tinnitus problems. Feedback from these talks has been positive and has shown the benefit of sharing information on the problems that hearing deterioration and tinnitus create. It is therefore recommended that aural symptoms should be part of HNC survivorship events. There is also a need to educate those involved in caring for HNC patients of aural changes with treatment:

- **At a multidisciplinary event:** From the findings of this study, it is recommended that health care practitioners in the MDT, involved in the care of HNC patients, are educated about the incidence of hearing deterioration and tinnitus as side effects in the early post treatment phase of current UK treatment. All members of the team should also be alerted to the fact that each of these symptoms adversely affects patient experience. In addition, these clinicians should be made aware that different services (audiology, ENT and hearing therapy) ought to be involved in providing
patient advice and support. This education could be achieved during teaching within a HNC MDT research or audit meeting;

- **Through formal training:** Given that cancer incidence and survivorship from treatment are on the increase, although ototoxicity is taught in audiology degree courses, it is surprising that the extent of treatment-induced hearing deterioration or tinnitus, and the impact of these symptoms, is not more adequately covered. Audiology courses should therefore give emphasis to treatment-related hearing deterioration and tinnitus, and to training on how best to manage these symptoms;

- **Emphasising the effect of tiredness:** It is well known that patients recovering from cancer suffer fatigue, and that people who have hearing loss need to concentrate to hear effectively. Oncologists and audiologists need to be aware that tiredness following recovery from treatment can affect patients' concentration, which can make it more difficult for patients who have hearing deterioration to hear well. Awareness training of oncologists and audiologists can be accomplished at scheduled team audit meetings. Patients who are struggling with their hearing, particularly due to tiredness, may benefit from sleep management support.

### 8.5 Conclusions

This study has provided new insights into the incidence and experience of hearing deterioration (and tinnitus) in a UK hospital, demonstrating the significance of this side-effect following treatment of HNC. Patients in this study reported that at the time of their cancer diagnosis, they had so much information to absorb, they were not fully aware that hearing change may occur with their treatment. They were also surprised at the severity of their hearing deterioration. Therefore, oncologists need to be aware that at diagnosis patients may not be fully alert to the possibility that they may develop hearing deterioration or tinnitus with treatment, and consequently oncologists should be ready at any point during the post-treatment phase to sign-post patients to audiology services.
Although the NICE 2004 document ‘Improving Outcomes in head and neck cancer’ mentions, in the ‘After Care and Rehabilitation’ section, that hearing problems can occur after treatment, no detail is provided within the document of involvement with audiology services for addressing aural problems. The more recent NHS document on survivorship ‘Improving Outcomes: A strategy for Cancer’ (DOH, 2011), does not even include hearing deterioration as a consequence of cancer treatment. This study shows that there is a significant gap in professional awareness of post-treatment experiences of patients which needs to be addressed if cancer survivorship policy is to effectively address the impact of hearing deterioration and tinnitus on quality of life; and the consequent need to involve audiology services for managing these side-effects from HNC treatment. Cancer clinicians should be made aware of the high incidence of hearing deterioration and tinnitus in this patient group. Oncologists should also actively involve audiology and otology specialists in creating care pathways to provide timely specialist assessment, management and support of patients who experience hearing deterioration or tinnitus in the early post-treatment phase.

Importantly, this study has highlighted the fact that hearing deterioration and tinnitus are neglected side-effects following HNC treatment. Arguably, they have been overlooked for too long in relation to patient well-being if the absence of hearing deterioration from the NHS document ‘Improving Outcomes; A strategy for cancer’ can be taken as an indicator.

While survivorship from head and neck cancer is improving, it is important to provide fuller and more effective post-treatment support to improve patients’ quality of life. This could be achieved by simple, cost-effective and timely interventions by audiological services in providing advice and support to address hearing deterioration and tinnitus. It is the contention of this study that all these measures would make a significant impact in improving these patients’ quality of life by extending and adjusting our current provisions and protocols to create a more holistic and patient-centred care programme that recognises and responds to the incidence of hearing deterioration in recovering head and neck cancer patients.
**Appendix 1.1 Staging of head and neck cancers**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Example</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis, N0, M0</td>
<td>The cancer is only growing in the part of the head and neck where it started. No cancer cells are present in deeper layers of tissue, nearby structures, lymph nodes, or distant sites.</td>
</tr>
<tr>
<td>I</td>
<td>T1, N0, M0</td>
<td>The primary cancer is 2 cm across or smaller, and no cancer cells are present in nearby structures, lymph nodes, or distant sites.</td>
</tr>
<tr>
<td>II</td>
<td>T2, N0, M0</td>
<td>The cancer measures 2–4 cm across, and no cancer cells are present in nearby structures, lymph nodes, or distant sites.</td>
</tr>
<tr>
<td>III</td>
<td>T3, N0, M0</td>
<td>The cancer is larger than 4 cm across, and no cancer cells are present in nearby structures, lymph nodes, or distant sites. Or The cancer is any size but has not grown into nearby structures or distant sites. However, cancer cells are present in one lymph node, which is located on the same side of the head or neck as the primary cancer and is smaller than 3 cm across.</td>
</tr>
<tr>
<td></td>
<td>T1–3, N1, M0</td>
<td>The cancer is any size but has not grown into nearby structures or distant sites. However, cancer cells are present in one lymph node, which is located on the same side of the head or neck as the primary cancer and is smaller than 3 cm across.</td>
</tr>
<tr>
<td>IVA</td>
<td>T4a, N0/N1, M0</td>
<td>The cancer is any size and is growing into nearby structures. Cancer cells may not be present in the lymph nodes, or they may have spread to one lymph node, which is located on the same side of the head or neck as the primary cancer and is smaller than 3 cm across. Cancer has not spread to distant sites. Or The cancer is any size and may or may not have invaded nearby structures, it has not spread to distant sites, and one of the following is true: cancer cells are present in one lymph node, located on the same side of the head or neck as the primary cancer and measuring 3–6 cm across (N2a); cancer cells are present in one lymph node on the opposite side of the head or neck and measuring less than 6 cm across (N2b); cancer cells are present in 2 or more lymph nodes, all smaller than 6 cm across and located on either side of the head or neck (N2c).</td>
</tr>
<tr>
<td></td>
<td>T1–4a, N2, M0</td>
<td>The cancer is any size and is growing into nearby structures. Cancer cells may not be present in the lymph nodes, or they may have spread to one lymph node, which is located on the same side of the head or neck as the primary cancer and is smaller than 3 cm across. Cancer has not spread to distant sites. Or The cancer is any size and may or may not have invaded nearby structures, it has not spread to distant sites, and one of the following is true: cancer cells are present in one lymph node, located on the same side of the head or neck as the primary cancer and measuring 3–6 cm across (N2a); cancer cells are present in one lymph node on the opposite side of the head or neck and measuring less than 6 cm across (N2b); cancer cells are present in 2 or more lymph nodes, all smaller than 6 cm across and located on either side of the head or neck (N2c).</td>
</tr>
<tr>
<td>IVB</td>
<td>T4b, any N, M0</td>
<td>The cancer has invaded deeper areas and/or tissues. It may or may not have spread to lymph nodes and has not spread to distant sites or The cancer is any size and may or may not have grown into other structures. It has spread to one or more lymph nodes larger than 6 cm across, but has not spread to distant sites.</td>
</tr>
<tr>
<td></td>
<td>Any T, N3, M0</td>
<td>The cancer has invaded deeper areas and/or tissues. It may or may not have spread to lymph nodes and has not spread to distant sites or The cancer is any size and may or may not have grown into other structures. It has spread to one or more lymph nodes larger than 6 cm across, but has not spread to distant sites.</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T, Any N, M1</td>
<td>The head and neck cancer is any size and may or may not have spread to lymph nodes. Cancer cells have spread to distant sites.</td>
</tr>
</tbody>
</table>
Appendix 2.1 Data extraction form – quantitative study

Review aim: “How many adult patients who have treatment for their head and neck cancer have hearing loss and what is their experience?”


General information

| Date form completed: Feb 8 2018 |
| Name of person extracting data: Presanna Premachandra |
| Title: Sensorineural hearing loss after treatment of nasopharyngeal carcinoma: a longitudinal analysis |
| Date of publication: 2009 |
| Country of Study: Hong Kong |

Population and setting

| Definition of Head and Neck cancer: N/A |
| Sub Type of cancer: NPC |
| Histology: Not given |
| Stage of cancer: I-IV |
| Aetiology: Not given |
| Inclusion criteria: newly diagnosed, non-metastatic NPC |
| Exclusion criteria: baseline threshold >55 dB was excluded, because accurate detection of bone conductive hearing loss at >70 dB was not feasible. |
| Method/s of recruitment: Consecutive |
| Was recruitment done in an acceptable way? Recruitment period greater than a year. Accounting for seasonal variation. In a single hospital. |
| Notes: May not reflect any regional differences/ susceptibility due to different aetiology/ histology |

Methods

| Aims of Study: A longitudinal study was conducted to quantitatively analyse the effect of RT with or without chemotherapy in relation to the probability of SNHL development and to derive a cochlea tolerance dose in the setting of concurrent chemoradiotherapy. |
| Are aims clear? Yes. Identify how many are affected with SNHL following radiotherapy treatment, risk factors, and maximum radiation dose to the cochlea allowed before hearing loss occurs |
| Design: Pre and post treatment design to assess the effect of the intervention on hearing |
Methodology: Quantitative
Start date: September 2004
End date: December 2005
Duration of participation: Up to 2 ½ years
Was research design appropriate to answer research question? Yes

Notes:

**Participants**

| Total number of participants: 97 invited to participate. 87 recruited | 1335 |
| (Or if no. of ears, can no. of participants be calculated? If so, what?): 170 ears | 1337 |
| People per cluster: 15 Stage I and II (RT only); 72 Stage III and IV CRT | 1336 |
| Were there baseline imbalances between groups? Yes – patients with different stages of cancer were given different treatments |  |
| Withdrawals and exclusions: 10 patients excluded due to pre-treatment hearing threshold. 18 ears (equivalent 9 patients) completed testing at 2 ½ years | 1335 |
| Age: 23–78; Median 50 | 1137 |
| Sex: M- 112; F - 58 | 1137 |
| Co-morbidities: Not given |  |
| Subgroups reported: N/A |  |
| Notes: At least 4 patients had only one ear included in assessment. Difference in the effect of chemo could be related to the cancer stage, if a difference is noted between RT and CRT |  |

**Quantitative method**

| What Test was performed: PTA | (p) |
| Definition of hearing change: Hearing loss was divided into low- and high-frequency types. The mean bone conductive hearing loss at 0.5, 1, and 2kHz was calculated, and this represented the low-frequency type. The high-frequency type comprised the hearing threshold at 4kHz alone. Clinically relevant, persistent SNHL was defined as an increase in the bone conduction threshold by >=15 dB (relative to the baseline reading) that persisted on at least two consecutive audiograms. Any two consecutive post-treatment hearing loss findings of >=30 dB was regarded as severe SNHL. The interval to the development of SNHL was defined as from the date of RT completion to the first consecutive reading of persistent SNHL. | 1336 |
| Is testing technique validated? No |  |
| Is equipment validated/calibrated? Yes – every 6 months | 1336 |
| Time points for testing: Baseline, 6, 12, 18, 24, 30 months post completion of RT |  |
| Is a reason given for time points of testing? No |  |
| Imputation of missing data: If yes – what method used. No |  |
| Is statistical analysis used appropriate: The probability of persistent SNHL was estimated using the Kaplan-Meier method, and the difference was compared using log–rank statistics. Multivariate analysis was performed using the forward stepwise logistic regression model to identify the prognosticators for the development of persistent SNHL. The dose–response relationship was estimated with logistic regression analysis using the mean cochlear dose and concurrent cisplatin dose as covariates. Finally, the two-sided t test was used to compare the percentage of SNHL in the population at different cut-offs of the mean cochlea dose to explore the best dose-constraint value. Method for assessing covariables is appropriate | 1336 |
### Have confounding factors been identified?

Yes – increasing age

### Have confounding factors been accounted for?

No - No adjustment of hearing loss with increasing age was made, assuming that the hearing deterioration with age was negligible in this relatively short study period.

### Notes

Some patients had chemotherapy after radiotherapy, so hearing loss for these patients (not identified) will be at different times to those who had RT alone.

### Risk of bias and validity

<table>
<thead>
<tr>
<th>Question</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was patient assignment randomised?</td>
<td>No randomisation. Pt's were allocated to different treatment as per protocol for the stage of cancer</td>
</tr>
<tr>
<td>Was blinding of participants and personnel done?</td>
<td>None mentioned</td>
</tr>
<tr>
<td>Blinding of outcome assessment:</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Incomplete outcome data:</td>
<td>No mention of attrition, of imputing missing data</td>
</tr>
<tr>
<td>Selective outcome reporting?</td>
<td>Not apparent</td>
</tr>
<tr>
<td>Other bias:</td>
<td>Not apparent</td>
</tr>
<tr>
<td>Notes: Data given with increase in time post treatment and mean hearing thresholds do not account for those who dropped out who may have characteristics that influence hearing change (e.g., stage of cancer)</td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Group 1

<table>
<thead>
<tr>
<th>Stage I or II cancer</th>
<th>Type of treatment: RT only</th>
<th>No. randomised to group: not randomised - 15</th>
<th>Description of intervention Patients with StageT1 or T2 disease received conventional [timing of] RT (2 Gy/daily fraction, five fractions weekly)</th>
<th>Duration of treatment period: Not clear</th>
<th>Timing: As above</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Group 2

<table>
<thead>
<tr>
<th>Stage III or IV cancer</th>
<th>Type of treatment: Induction chemo with CRT, or RT with CRT and adjuvant chemo</th>
<th>No. randomised to group: not randomised - 72</th>
<th>Description of intervention: Stage T3 or T4 disease received accelerated RT (2 Gy/daily fraction, six fractions weekly. Stage III and IV patients were treated with induction chemotherapy followed by concurrent chemoradiotherapy until late 2005. The induction chemotherapy regimen included cisplatin 100 mg/ m2 on Day 1 and 5-fluorouracil 1,000 mg/m2 on Days 1–5 every 3 weeks for three cycles, followed by concurrent cisplatin 100 mg/ m2 with RT for two to three cycles. Cisplatin was replaced by carboplatin (area under the curve, for patients with suboptimal renal function.)</th>
<th>Duration of treatment period: Between 5 and 7 weeks – not clear</th>
<th>Timing: As above</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Notes: The treatment groups were brought together for calculating hearing loss.
Cochlea dose (Gy)
Maximal dose range 36.6–73.8; Median 57.4; Mean dose range 33–71.7;
Median 48.9
Treatment regimen (ears): RT alone 30; Chemoradiotherapy 140
Chemotherapy
Concurrent cisplatin dose (mg/ m2); Median 160; Range 0–300
No concurrent cisplatin dose (mg/m2); Median 240; Range 0–300

Results 1 Hearing deterioration incidence/prevalence: SNHL >=15dB deterioration

<table>
<thead>
<tr>
<th>What were the No. of missing participants and reasons:</th>
<th>Treatment Group 1 Grouped data Low frequency (0.5, 1, 2kHz average)</th>
<th>Treatment Group 2 Grouped data 4kHz</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup:</td>
<td>N/A</td>
<td></td>
<td>1137</td>
</tr>
<tr>
<td>Time point: 6 months</td>
<td>16 out of 170 ears</td>
<td>83 out of 170 ears</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>23 / 168 ears</td>
<td>92/ 168 ears</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>17/ 152</td>
<td>78/ 152</td>
<td></td>
</tr>
<tr>
<td>24 months</td>
<td>12/ 98</td>
<td>42/ 98</td>
<td></td>
</tr>
<tr>
<td>30 months</td>
<td>4/ 18</td>
<td>9/ 18</td>
<td></td>
</tr>
<tr>
<td>Results:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results 2 Hearing deterioration severity/grade: SNHL>=30dB deterioration

<table>
<thead>
<tr>
<th>What were the No. of missing participants and reasons:</th>
<th>Treatment Group 1 Grouped data Low frequency (0.5, 1, 2kHz average)</th>
<th>Treatment Group 2 Grouped data 4kHz</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup:</td>
<td>N/A</td>
<td></td>
<td>1137</td>
</tr>
<tr>
<td>Time point: 6 months</td>
<td>3 out of 170 ears</td>
<td>34 out of 170 ears</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>2 / 168 ears</td>
<td>39/ 168 ears</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>2/ 152</td>
<td>36/ 152</td>
<td></td>
</tr>
<tr>
<td>24 months</td>
<td>3/ 98</td>
<td>17/ 98</td>
<td></td>
</tr>
<tr>
<td>30 months</td>
<td>1/ 18</td>
<td>2/ 18</td>
<td></td>
</tr>
<tr>
<td>Results:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes:</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Results and risk factors

Risk factors:
Gender, *age, pre-treatment hearing, *treatment dose and treatment regime
(“*” significant)
The log–rank test showed that the concurrent chemoradiotherapy group had a significantly
greater incidence of SNHL at a high frequency (55% vs. 33.3%, p = 0.02) compared with
the RT-alone group but not at a low frequency (7.9% vs. 16.7%, p = 0.17). The median
interval to the development of persistent SNHL (either high or low) was 12 months.
Univariate analysis was performed to identify the potential prognosticators determining the
development of SNHL. Gender, maximal cochlea dose, mean cochlea dose, concurrent
cisplatin dosage, non-concurrent cisplatin dosage, and baseline
hearing threshold were tested. The results are listed in Table 3. A correlation analysis was
performed, and age correlated significantly with the baseline hearing threshold at
both high and low frequencies (correlation coefficient, 0.536 and 0.499, respectively; p < 0.001 for both). Hence, only age was entered into the multivariate analysis. The concurrent cisplatin dosage (p < 0.01) and mean cochlea dose (p = 0.013) were important determinants of high-frequency SNHL, and age (p = 0.03) was significant in governing low-frequency SNHL. These factors remained statistically significant on multivariate analysis. Because no consensus has been reached regarding the percentage of hearing loss considered justifiable, we arbitrarily defined the percentage as <15% for severe persistent SNHL, resulting in a dose constraint of 47 Gy for patients receiving concurrent chemoradiotherapy. Odds ratio data is reported with confidence values given, but no explanation is given of what the odds ratio is comparing.

Quality assessment of results

**RCTs and Cohort studies**

How precise are the results? Percentages are given for incidence – ok. The log–rank test showed that the concurrent chemoradiotherapy group had a significantly greater incidence of SNHL at a high frequency (55% vs. 33.3%, p = 0.02) compared with the RT-alone group but not at a low frequency (7.9% vs. 16.7%, p = 0.17). The median interval to the development of persistent SNHL (either high or low) was 12 months. Univariate analysis was performed to identify the potential prognosticators determining the development of SNHL. Gender, maximal cochlea dose, mean cochlea dose, concurrent cisplatin dosage, non-concurrent cisplatin dosage, and baseline hearing threshold were tested. The results are listed in Table 3. A correlation analysis was performed, and age correlated significantly with the baseline hearing threshold at both high and low frequencies (correlation coefficient, 0.536 and 0.499, respectively; p < 0.001 for both). Hence, only age was entered into the multivariate analysis. The concurrent cisplatin dosage (p < 0.01) and mean cochlea dose (p = 0.013) were important determinants of high-frequency SNHL, and age (p = 0.03) was significant in governing low-frequency SNHL. These factors remained statistically significant on multivariate analysis. Because no consensus has been reached regarding the percentage of hearing loss considered justifiable, we arbitrarily defined the percentage as <15% for severe persistent SNHL, resulting in a dose constraint of 47 Gy for patients receiving concurrent chemoradiotherapy. Odds ratio data is reported with confidence values given, but no explanation is given of what the odds ratio is comparing.

**Do you believe the results?** Some mis-reporting here. Table 2 mentions 83 ears out of 170 at 6 months post RT with hearing loss (<50%), yet the text states 87 ears (>50%). Also, graphs shown in figure 2 show probability of SNHL loss development beyond 30 months, yet time of testing hearing after treatment was only up to 30 months, and there is no explanation of why these extended times are given in the text. The reporting of some data is not complete, e.g. the odds ratio data for concurrent chemoradiation is not given a comparator.

**Can the results be applied to the local population?** The % incidence values can be applied to a group of NPC patients who receive 3D-CRT or IMRT in a similar ratio, but as the 2 radiotherapy techniques differ in their actual dosing of the ear, the results cannot be applied to one or other of these groups. The results are compelling regarding the additive effect of chemotherapy to radiotherapy in creating hearing loss, but stage of cancer too needs consideration. However, RT only for Stage I/II NPC cancer persists as the treatment of choice as does CRT for Stage III/IV cancer. No accounting was made of the effect of carboplatin for those patients who had this instead of cisplatin.

**Do the results of this study fit with other evidence?** Yes, re HF loss with chemotherapy and radiotherapy. No accounting of increasing age, with increase in LF loss was given., but age was equated to (substituting) to baseline hearing level...perhaps raised LF pre-treatment levels indeed show hearing loss that is more susceptible to change than normal hearing before treatment. It was stated that most hearing loss occurred after 12 months,
but testing was done at 6-month time periods, with persistent loss deemed to be at 2 consecutive test periods. Earlier testing post treatment may show higher incidence of hearing loss, and even if this has a conductive element, reduced overall hearing will have an impact on patient experience. Also, some OME can persist and even preclude SNHL or permanent mixed HL.

**What are the implications of this study for practice?**

Notes: Results indicate that chemoradiotherapy produced statistically greater incidence and severity of hearing loss compared to RT alone. A dose constraint of 47Gy was suggested, but this was for combined 3D-CRT/ IMRT – perhaps this dosage would be different for IMRT alone.

**Other information**

<table>
<thead>
<tr>
<th>Have important populations been excluded from the study?</th>
<th>Yes/No/Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. All patients who should have been included, were.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Does the study directly address the review question?</th>
<th>Yes/No/Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes. It provided information on the % of patients who had SNHL development with RT with or without chemotherapy, what factors may contribute to SNHL, and a recommended maximum radiation dose to the cochlea</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key conclusions of study authors</th>
<th>Persistent high-frequency SNHL after chemoradiotherapy is common. The incidence and severity of high-frequency SNHL are significantly related to the mean cochlea radiation dose and the dose of concurrent cisplatin (synergistic effect). With the current treatment protocol, they recommend a mean cochlea radiation dose of &lt;47 Gy to control the ototoxicity of chemoradiotherapy for NPC patients.</th>
</tr>
</thead>
</table>
Appendix 2.2 Data extraction form – qualitative study

Review aim: “How many adult patients who have treatment for their head and neck cancer have hearing loss and what is their experience?”


General information

<table>
<thead>
<tr>
<th>Date form completed: 1st Feb 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of person extracting data: Presanna Premachandra</td>
</tr>
<tr>
<td>Title: Communication Changes following non-glottic head and neck cancer management: The perspectives of survivors and carers</td>
</tr>
<tr>
<td>Date of publication: 2015</td>
</tr>
<tr>
<td>Country of Study: Australia</td>
</tr>
</tbody>
</table>

Population and setting

<table>
<thead>
<tr>
<th>Definition of Head and Neck cancer: Not stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub Type of cancer: oral cavity (4), nasopharyngeal (2), oropharyngeal (7) and hypopharyngeal (1) primaries</td>
</tr>
<tr>
<td>Histology: Not stated</td>
</tr>
<tr>
<td>Stage of cancer:</td>
</tr>
<tr>
<td>T1-2: 9</td>
</tr>
<tr>
<td>T3-4: 5</td>
</tr>
<tr>
<td>Histology: Not stated</td>
</tr>
<tr>
<td>Aetiology: HPV/smoking/alcohol intake</td>
</tr>
<tr>
<td>Inclusion criteria:</td>
</tr>
<tr>
<td>Group 1: Head and neck cancer survivors - Not clearly stated</td>
</tr>
<tr>
<td>Group 2: Carers – Not clearly stated</td>
</tr>
<tr>
<td>Exclusion criteria:</td>
</tr>
<tr>
<td>Group 1: Head and neck cancer survivors (non-glottic)</td>
</tr>
<tr>
<td>Participants were excluded from the study if they: (a) had received primary surgical management; (b) had pre-existing conditions associated with communication impairments (e.g. neurological conditions, moderate–severe cognitive impairments, degenerative conditions, hearing impairment); (c) were considered palliative; and/or (d) were not proficient in English.</td>
</tr>
<tr>
<td>Group 2: Carers</td>
</tr>
<tr>
<td>Carer participants were excluded if: (a) they had previously or were currently undergoing treatment for HNC; (b) had pre-existing conditions associated with communication impairments (e.g. neurological conditions, moderate–severe cognitive impairments, degenerative conditions, hearing impairment); (c) were not proficient in English; and/or (d) if their partner with communication changes had...</td>
</tr>
</tbody>
</table>
been excluded for the aforementioned reasons.

Method/s of recruitment: Maximum variation sampling (purposive)  

Was recruitment done in an acceptable way? Not clear how recruitment was done

Notes: Not clear how participants were recruited, if all those eligible to be recruited were approached (and reasons for non-inclusion were not given). Inclusion criteria not clearly stated.

### Methods

<table>
<thead>
<tr>
<th><strong>Aims of Study:</strong></th>
<th><strong>(P)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. to explore the views and experiences of communication changes following curative chemoradiotherapy for non-glottic HNC from the perspective of both the HNC survivor and their carer.</td>
<td>265</td>
</tr>
<tr>
<td>2. to understand the challenges faced by both HNC survivors and carers in regard to communication changes and elucidate the skills needed and support required, to adjust to these communication changes following treatment</td>
<td>265</td>
</tr>
</tbody>
</table>

Are aims clear? Yes

Design: Interview

Methodology: Qualitative - phenomenology

Start date: Not stated

End date: Not stated

Duration of participation: 20 minutes – 2 hours

Was research design appropriate to answer research question? Yes

Notes: Sampling method appears to be appropriate

### Participants

<table>
<thead>
<tr>
<th><strong>Total number of participants:</strong></th>
<th><strong>(P)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>265</td>
</tr>
</tbody>
</table>

(Or if no. of ears, can no. of participants be calculated? If so, what?):

People per cluster: 14 patients (Group 1) and 9 carers (Group 2)

Were there baseline imbalances between groups? N/A

Withdrawals and exclusions: Withdrawals not provided. No further exclusions stated from original criteria

Age:
- Group 1 (patients): 43-67 years (mean 56.1; SD 7.8)
- Group 2 (carers): 45-60 years (mean 52.4; SD 5.05)

Sex:
- Group 1 (patients): 12 males; 2 females
- Group 2 (carers): 8 females; 1 male

Co-morbidities: Not stated

Subgroups reported: Not provided

Notes: Male dominated patient group and female dominated carer group. All working age or near retirement age.
### Qualitative method checklist

<table>
<thead>
<tr>
<th>Interviewer/facilitator: Which author/s conducted the interview or focus group? Principal investigator</th>
<th>266</th>
</tr>
</thead>
<tbody>
<tr>
<td>Credentials: What were the researcher's credentials? <em>E.g. PhD, MD, PhD</em></td>
<td>263</td>
</tr>
<tr>
<td>Occupation: What was their occupation at the time of the study? Not clear</td>
<td></td>
</tr>
<tr>
<td>Gender: Was the researcher male or female? Assumed female</td>
<td>263</td>
</tr>
<tr>
<td>Experience and training: What experience or training did the researcher have? Not clear</td>
<td></td>
</tr>
<tr>
<td>Relationship established: Was a relationship established prior to study commencement? Not clear</td>
<td></td>
</tr>
<tr>
<td>Participant knowledge of the interviewer: What did the participants know about the researcher? <em>E.g. personal goals, reasons for doing the research</em> Not clear</td>
<td></td>
</tr>
<tr>
<td>Interviewer characteristics: What characteristics were reported about the interviewer/facilitator? <em>E.g. Bias, assumptions, reasons and interests in the research topic</em> Not clear</td>
<td></td>
</tr>
<tr>
<td>Methodological orientation and Theory: What methodological orientation was stated to underpin the study? <em>E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis</em> Phenomenology</td>
<td>265</td>
</tr>
<tr>
<td>Sampling: How were participants selected? <em>E.g. purposive, convenience, consecutive, snowball</em> Purposive (Maximum variation)</td>
<td>265</td>
</tr>
<tr>
<td>Method of approach: How were participants approached? <em>E.g. face-to-face, telephone, mail, email</em> Not clear</td>
<td></td>
</tr>
<tr>
<td>Sample size: How many participants were in the study? 23 (14 patients and 9 care givers)</td>
<td>265</td>
</tr>
<tr>
<td>Non-participation: How many people refused to participate or dropped out? Reasons? Not stated</td>
<td></td>
</tr>
<tr>
<td>Setting of data collection: Where was the data collected? <em>E.g. home, clinic, workplace</em> Not stated</td>
<td></td>
</tr>
<tr>
<td>Presence of non-participants: Was anyone else present besides the participants and researchers? Not clear</td>
<td></td>
</tr>
<tr>
<td>Description of sample: What are the important characteristics of the sample? <em>E.g. demographic data, date</em></td>
<td>265-266</td>
</tr>
<tr>
<td>Group 1: Head and neck cancer survivors (non-glottic) – April 2007 – April 2012 All participants had self-reported changes to their communication during and/or following treatment.</td>
<td></td>
</tr>
<tr>
<td>• curative treatment (chemoradiation)</td>
<td></td>
</tr>
<tr>
<td>• gender</td>
<td></td>
</tr>
<tr>
<td>• age</td>
<td></td>
</tr>
<tr>
<td>• geographical residence (major city/remote)</td>
<td></td>
</tr>
<tr>
<td>• months since treatment (&lt;3 months/&gt;3 months)</td>
<td></td>
</tr>
<tr>
<td>Participants were excluded from the study if they: (a) had received primary surgical management; (b) had pre-existing conditions associated with communication impairments (e.g. neurological conditions, moderate–severe cognitive impairments, degenerative conditions, hearing impairment); (c) were considered palliative; and/or (d) were not proficient in English.</td>
<td></td>
</tr>
<tr>
<td>Group 2: Carers</td>
<td></td>
</tr>
</tbody>
</table>
Carer participants were either in a de-facto relationship or were married to an individual with non-glottic HNC. Carer participants were also excluded if: (a) they had previously or were currently undergoing treatment for HNC; (b) had pre-existing conditions associated with communication impairments (e.g. neurological conditions, moderate–severe cognitive impairments, degenerative conditions, hearing impairment); (c) were not proficient in English; and/or (d) if their partner with communication changes had been excluded for the aforementioned reasons.

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interview guide Were questions, prompts, guides provided by the authors?</td>
<td>Yes, guides were given, but not stated if pilot tested</td>
</tr>
<tr>
<td>Repeat interviews Were repeat interviews carried out? If yes, how many?</td>
<td>Not stated</td>
</tr>
<tr>
<td>Audio/visual recording Did the research use audio or visual recording to</td>
<td>Audio recording</td>
</tr>
<tr>
<td>collect the data?</td>
<td></td>
</tr>
<tr>
<td>Field notes Were field notes made during and/or after the interview or</td>
<td>Not stated</td>
</tr>
<tr>
<td>focus group?</td>
<td></td>
</tr>
<tr>
<td>Duration What was the duration of the interviews or focus group?</td>
<td>20 minutes to 2 hours</td>
</tr>
<tr>
<td>Data saturation Was data saturation discussed?</td>
<td>No</td>
</tr>
<tr>
<td>Transcripts returned Were transcripts returned to participants for</td>
<td>Not stated</td>
</tr>
<tr>
<td>comment and/or correction?</td>
<td></td>
</tr>
<tr>
<td>Number of data coders How many data coders coded the data? More than 1</td>
<td>More than 1 – not clear - perhaps all 10 co-investigators?</td>
</tr>
<tr>
<td>- not clear - perhaps all 10 co-investigators?</td>
<td></td>
</tr>
<tr>
<td>Description of the coding tree Did authors provide a description of the</td>
<td>1. Open codes from participant statements were</td>
</tr>
<tr>
<td>coding tree? Yes:</td>
<td>2. Grouped into categories</td>
</tr>
<tr>
<td>3. Categories refined until consensus reached to created revised list</td>
<td>4. Transcripts recoded using revised list of categories</td>
</tr>
<tr>
<td>5. Themes were developed by considering relationship between categories</td>
<td></td>
</tr>
<tr>
<td>Derivation of themes Were themes identified in advance or derived from</td>
<td>Yes, as the quotations are used within the themes in the results</td>
</tr>
<tr>
<td>the data? Derived from data?</td>
<td></td>
</tr>
<tr>
<td>Software What software, if applicable, was used to manage the data?</td>
<td>NVivo10</td>
</tr>
<tr>
<td>Participant checking Did participants provide feedback on the findings</td>
<td>Not stated</td>
</tr>
<tr>
<td>Quotations presented Were participant quotations presented to illustrate</td>
<td>Yes and yes: “The biggest challenge is getting other people to adapt to</td>
</tr>
<tr>
<td>the themes / findings? Was each quotation identified? e.g. participant</td>
<td>your hearing. You get a bit offended from time to time when they won’t</td>
</tr>
<tr>
<td>number Yes and yes egg:</td>
<td>bother to talk to you because they think you can’t hear” [P012]</td>
</tr>
<tr>
<td>Data and findings consistent Was there consistency between the data</td>
<td>Yes, as the quotations are used within the themes in the results</td>
</tr>
<tr>
<td>presented and the findings? Yes, as the quotations are used within the</td>
<td></td>
</tr>
<tr>
<td>themes in the results</td>
<td></td>
</tr>
<tr>
<td>Clarity of major themes Were major themes clearly presented in the</td>
<td>Yes – 4 themes</td>
</tr>
<tr>
<td>findings? Yes</td>
<td></td>
</tr>
<tr>
<td>Clarity of minor themes Is there a description of diverse cases or</td>
<td>No</td>
</tr>
<tr>
<td>discussion of minor themes?</td>
<td></td>
</tr>
</tbody>
</table>
### Results 4 Hearing deterioration – patient experience

<table>
<thead>
<tr>
<th>No. of missing participants and reasons:</th>
<th>Treatment Group 1</th>
<th>Treatment Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not stated</td>
<td>Not stated</td>
</tr>
</tbody>
</table>

#### Theme 1: Impairments in communication sub-systems

HNC survivors spoke often of the physical changes resulting from treatment which had an impact on their communicative abilities (Table II). Many described experiencing changes to their voice for months and years following treatment. In particular, functional loss was noted in conversational exchanges: “[I need] to use so much more energy to be able to get the voice out” [P009]. Sometimes this led to the communicative intent being misinterpreted as aggression: “The response will come back ‘stop yelling’. I’ll say, ‘I’m not yelling, I have to use this voice so that you can hear me’” [P009]. Additionally, some participants reported pitch changes, hoarseness, vocal fatigue, a feeling of something in the throat and that their voice was often worse first thing in the morning. For half the participants, xerostomia (dry-mouth) had a substantial impact on everyday communication: “The dry mouth. It affects everything. It affects your throat, it affects your mouth, eating, swallowing, talking ... everything, it affects everything” [P009]. A few participants also spoke about the negative impacts of chemoradiotherapy-induced hearing impairment following treatment: “I’ve gone partly deaf and that is what makes it hard. I can’t hear what’s going on. I don’t know what’s going on” [P016].

#### Theme 2: The challenges of communicating in everyday life

Both HNC survivors and carer participants discussed a number of challenges they faced regarding communicating in everyday life (Table III). This theme was particularly relevant for the HNC survivors who had experienced hearing impairment as a result of their treatment. The most frequently reported challenge was the lack of understanding from others about their communication changes: “The biggest challenge is getting other people to adapt to your hearing. You get a bit offended from time to time when they won’t bother to talk to you because they think you can’t hear” [P012]. As a result of this lack of understanding, this participant noted that “you feel as if you’re left out quite often because people get frustrated and rather than say something to you they don’t bother” [P012].

Another frequent challenge, particularly for the HNC survivors with hearing impairment, was “the background noise, when that’s happening it is a lot harder for me” [P019]. Finally, both HNC survivors and carers faced challenges regarding support for communication during treatment from health professionals.
such as speech-language pathologists: “they were very good, but it [the sessions] was really not to do with communication, it was really to do with being able to swallow and what sorts of food I could eat. That was frustrating for me” [P009]. One of the carer participants summed up her experience

Theme 3: Broad ranging effects of communication changes

The physical changes to the communication sub-systems as a result of treatment, coupled with the challenges of communication in everyday life, resulted in broad ranging effects on communication interactions for both the HNC survivors and their carers (Table IV). The most dominant category was the impact of the communication changes on family life, particularly in regard to family relationships and roles and responsibilities within the family unit. One HNC survivor noted that: “My children tend to talk to my wife more now. I miss out on bits of information” [P012]. Conversely, one of the carer participants commented that: “He doesn’t like to read with [our daughter] anymore because he lisps a lot if he hasn’t got his teeth in properly” [C002]. These impacts were not confined to the family unit alone and both groups of participants commented on the impact of the communication changes on their social lives, as noted by this HNC survivor: “You might not go out as often as you should. It’s just much easier not to have to communicate” [P012]. Similarly, one of the carer participants stated that during treatment and in the acute recovery period that “it was a bit like life was on hold, we didn’t go out, we didn’t visit people and he preferred they didn’t visit us” [C005]. For the HNC survivors, the impact also extended into their work life: “I load trucks and I sent 20 tonnes of the wrong steel to Sydney because I couldn’t hear well. They [work] weren’t impressed” [P016].

As a result of these impacts, both the HNC survivors and the carers spoke about their emotional response to the communication changes including frustration and embarrassment for HNC survivors: “With communication it’s mainly [the] embarrassment. I’ve been [involved] in this [community organisation]. I’m seriously thinking of quitting because of [my communication changes]” [P011] and frustration, concern and sadness for carers. Despite these broad ranging effects, some HNC survivors and carers spoke about how they had not let the communication changes become a barrier: “it doesn’t stop you from talking, it might just slow me down for a couple of minutes” [P008].
| Theme 4: Adaptations as a result of communication changes | The fourth theme to emerge from the interviews related to the comments made by both HNC survivors and carers regarding the necessary adaptations required to adjust and cope with the communication changes (Table V). To facilitate successful communication interactions and adapt to changes in their communication, the HNC survivors used a number of p such as ensuring they always carried a bottle of water “to be able to talk to people” [P009]. A couple of HNC survivors also discussed the use of chewing gum, artificial saliva and oral sprays to increase moisture in the mouth.

In order to adapt to the changes to hearing, HNC survivors discussed a number of strategies including moving closer to their communication partner, asking them to speak louder and confirming the message to ensure what they heard was correct. Survivors who experienced voice changes improved their communication by performing vocal hygiene strategies such as drinking hot water with honey, using steam and, in the case of a professional voice user, ensuring she completed a proper warm up before performing. They also discussed other strategies such as avoiding communication interactions if possible, using non-verbal communication such as lip reading and exploring the use of different technologies such as earphones for the television and hearing aids. Carer participants reported using similar strategies to the HNC survivors, such as encouraging their partner to drink water to relieve their dry mouth, answering the phone for their partner so that they didn’t have to talk, repeating themselves to ensure their partner had received the correct message, pursuing Auslan classes to learn sign language and conducting their own research into technology that could assist with communication changes. Some HNC survivors and carers reported participating in regular sessions with a speech-language pathologist and dietitian. However, these interactions when discussed by participants were focused on mealtime difficulties and not the management of their communication changes.

Emotional adaptation was also paramount to adjusting to the changes to communication for both survivors and carers. A number noted that “it’s just an acceptance thing” [P019] and that the change “is what it is ... you just deal with it” [P019]. Others remained hopeful that their communicative function (or their partner's communicative function) would one day return to normal. Finally, HNC survivors and carers both discussed the importance of support from their family and friends, as well as from other HNC survivors and carers as part of their adjustment. |
Quality assessment of results

**Qualitative studies**

<table>
<thead>
<tr>
<th>Description</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptive validity: <em>How factually accurate is the account?</em> Accurate: Verbatim quotes were used following audio recording</td>
<td>266</td>
</tr>
<tr>
<td>Interpretive validity: <em>How well do findings represent meanings from the participants’ perspective?</em> It was not clear how many interviewees were represented in each theme</td>
<td></td>
</tr>
<tr>
<td>Theoretical validity <em>How do the findings of the study support underlying theory?</em> The premise of a negative impact following communication change (p264) was upheld with not only the patient, but also the carer (p265)</td>
<td>264, 265</td>
</tr>
<tr>
<td><em>How generalisable are the results?</em> Not very! Not clear how representative this is of the HNC patient population</td>
<td></td>
</tr>
<tr>
<td><em>How reproducible are the results?</em> Very - Method for creating themes from categories/ quotes clearly given</td>
<td></td>
</tr>
<tr>
<td><em>Has the researcher minimised their bias?</em> This was not addressed</td>
<td></td>
</tr>
<tr>
<td><em>Have ethical issues been taken into consideration?</em> Yes - Consent for participation was stated. Ethics committee clearance stated</td>
<td>266</td>
</tr>
</tbody>
</table>

**Other information**

<table>
<thead>
<tr>
<th>Description</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have important populations been excluded from the study?</td>
<td>Yes/No/Unclear</td>
</tr>
<tr>
<td>Yes, patients who have pre-existing hearing loss; they may have a greater impact on their loss with treatment Paper did not include those who had radiotherapy only, or those with nasal or salivary gland HNC, or consider hearing perspective of patient with laryngeal cancer.</td>
<td></td>
</tr>
<tr>
<td>Does the study directly address the review question/ aims?</td>
<td>Yes/No/Unclear</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Key conclusions of study authors</td>
<td></td>
</tr>
<tr>
<td>Health professionals should consider the impact of communication changes on the everyday lives of HNC survivors and their carers and provide adequate and timely education and management to this population. Providing interventions which adopt a holistic and family-centred approach to communication management may be most beneficial to achieve positive long-term outcomes for a whole family unit living with the effects of HNC management.</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 2.3 CASP quality rating form - quantitative studies

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Did the study address a clearly focused issue?</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>2. Was the cohort recruited in an acceptable way?</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>3. Was the exposure accurately measured to minimise bias?</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>4. Was the outcome accurately measured to minimise bias?</td>
<td>Y</td>
<td>N</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>5. (a) Have the authors identified all important confounding factors? *</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
</tr>
<tr>
<td>(b) Do/does design and/or analysis account for confounding factors?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>6. (a) Was the follow up of subjects complete enough?</td>
<td>C</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>(b) Was the follow up of subjects long enough?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>7. What are the results of this study?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. How precise are the results?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Do you believe the results?</td>
<td>C</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>N</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>10. Can the results be applied to the local population?</td>
<td>Y</td>
<td>C</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>11. Do the results of this study fit with other available evidence?</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>C</td>
<td>C</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>12. What are the practical implications?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall quality rating</td>
<td>H</td>
<td>M</td>
<td>L</td>
<td>H</td>
<td>H</td>
<td>M</td>
<td>L</td>
<td>H</td>
<td>M</td>
<td>H</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>

Key: Y —yes; N - no; C - Can’t tell; * see below; H – high quality; M – medium quality; L - low quality

*Question 5 b * Important risk factors: radiotherapy type, radiotherapy dose, chemotherapy dose, treatment regime, age, time of testing (Yes: 5-6/6; Can’t tell: 3-4; No: <3)

Other factors: Gender, stage of cancer, aetiology, pre-treatment hearing, pre-treatment middle ear status, post-treatment middle ear status, diabetes mellitus, hypertension

Quantitative study quality assessment scoring: Each yes response = 1. High quality: scores >7; Medium quality: scores 5-7; Low quality: scores <5
### Appendix 2.4 CASP quality rating form – qualitative study

<table>
<thead>
<tr>
<th>Question</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Was there a clear statement of the aims of the research?</td>
<td>Y</td>
</tr>
<tr>
<td>2. Is a qualitative methodology appropriate?</td>
<td>Y</td>
</tr>
<tr>
<td>3. Was the research design appropriate to address the aims of the research?</td>
<td>Y</td>
</tr>
<tr>
<td>4. Was the recruitment strategy appropriate to the aims of the research?</td>
<td>Y</td>
</tr>
<tr>
<td>5. Was the data collected in a way that addressed the research issue?</td>
<td>Y</td>
</tr>
<tr>
<td>6. Has the relationship between researcher and participants been adequately considered?</td>
<td>C</td>
</tr>
<tr>
<td>7. Have ethical issues been taken into consideration?</td>
<td>Y</td>
</tr>
<tr>
<td>8. Was the data analysis sufficiently rigorous?</td>
<td>C</td>
</tr>
<tr>
<td>9. Is there a clear statement of findings?</td>
<td>Y</td>
</tr>
<tr>
<td>10. How valuable is the research?</td>
<td>H</td>
</tr>
</tbody>
</table>

**Overall quality rating**

**Key:** Y – yes; N - no; C - Can’t tell; * see below; H – high quality; M – medium quality; L - low quality

**Quantitative study quality assessment scoring:** Each yes response = 1. High quality: scores >7; Medium quality: scores 5-7; Low quality: scores <5
<table>
<thead>
<tr>
<th>1st Author (year)</th>
<th>Focus</th>
<th>Why rejected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhide (2007)</td>
<td>Otological toxicity after postoperative radiotherapy for parotid tumours</td>
<td>Review</td>
</tr>
<tr>
<td>Crabb (2017)</td>
<td>COAST (Cisplatin ototoxicity attenuated by aspirin trial): A phase II double-blind, randomised controlled trial to establish if aspirin reduces cisplatin induced hearing-loss</td>
<td>Multi-cancer trial with HNC results not separated in analysis</td>
</tr>
<tr>
<td>Dias (1966)</td>
<td>Effects on the hearing of patients treated by irradiation in the head and neck area</td>
<td>Review</td>
</tr>
<tr>
<td>Dunphy (2014)</td>
<td>Intensity modulated radiation therapy (IMRT) in head and neck cancer</td>
<td>Poster presentation at conference</td>
</tr>
<tr>
<td>Evans (1988)</td>
<td>Assessment of permanent hearing impairment following radical megavoltage radiotherapy</td>
<td>Hearing loss in the irradiated ear was compared with the non-irradiated ear of each patient, therefore not using same ear as a baseline reference.</td>
</tr>
<tr>
<td>Gaze (1992)</td>
<td>Routine nasopharyngeal biopsy in adult secretory otitis media</td>
<td>Presenting symptoms</td>
</tr>
<tr>
<td>Gibb (2000)</td>
<td>The role of radiation in delayed hearing loss in nasopharyngeal carcinoma</td>
<td>Case study</td>
</tr>
<tr>
<td>Glazer (1980)</td>
<td>Audiologic management of head and neck carcinoma patients</td>
<td>Hearing aids</td>
</tr>
<tr>
<td>Harrison (2017)</td>
<td>Active surveillance management of head and neck paragangliomas: case series and review of the literature</td>
<td>Non HNC</td>
</tr>
<tr>
<td>Hyde (2000)</td>
<td>Hearing loss associated with maxillectomy</td>
<td>Using obsolete treatment (radiotherapy prior to 2004); includes children</td>
</tr>
<tr>
<td>Jolly (2017)</td>
<td>A case of pulsatile tinnitus</td>
<td>Case study</td>
</tr>
<tr>
<td>Jones (2006)</td>
<td>Auditory toxicity after parotid irradiation</td>
<td>Comment on an article</td>
</tr>
<tr>
<td>Matz (1968)</td>
<td>Nasopharyngeal cancer</td>
<td>Presenting symptoms or disease</td>
</tr>
<tr>
<td>Rackley (2017)</td>
<td>Unilateral radiotherapy for surgically resected lateralized squamous cell carcinoma of the tonsil</td>
<td>Pre-treatment hearing check not done</td>
</tr>
<tr>
<td>Singh (1991)</td>
<td>Late audiovestibular consequences of radical radiotherapy to the parotid</td>
<td>Pre-treatment hearing tests not done</td>
</tr>
<tr>
<td>Author</td>
<td>Title</td>
<td>Type</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Symonds (1992)</td>
<td>Late audio-vestibular consequences of radical radiotherapy to the parotid</td>
<td>Comment on an article</td>
</tr>
<tr>
<td>Thomson (2016)</td>
<td>Indications for Salivary Gland Radiotherapy</td>
<td>Review</td>
</tr>
<tr>
<td>Watson (2016)</td>
<td>Diagnosis and management of a tympanic membrane hemangioma</td>
<td>Non HNC</td>
</tr>
<tr>
<td>Yardley (1998)</td>
<td>Use of transient evoked otoacoustic emissions to detect and monitor cochlear damage caused by platinum-containing drugs</td>
<td>Patient disease type not reported</td>
</tr>
</tbody>
</table>

Key: HNC – head and neck cancer
Appendix 4.1 Pilot study

The author had conducted a pilot study to assess hearing deterioration of patients having head and neck cancer treatment. A retrospective assessment was conducted of hearing thresholds conducted at the author’s audiology department between May and October 2013. A comparison was made of pre-treatment testing to post-treatment testing of head and neck patients. Intra-patient comparison was not performed as not all of the patients assessed had the pre and post treatment hearing tests. Consequently, a comparison was made of the hearing of grouped ear thresholds.

Post-treatment hearing testing was performed on patients between the ranges of 2 months and 5 years after treatment, with the results shown below:

<table>
<thead>
<tr>
<th></th>
<th>Number of ears</th>
<th>Mean age</th>
<th>Frequency (kHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of ears</td>
<td>Mean age</td>
<td>0.25</td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>86</td>
<td>60</td>
<td>19.07</td>
</tr>
<tr>
<td></td>
<td>17.06</td>
<td>17.83</td>
<td>17.87</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>48</td>
<td>58</td>
<td>21.77</td>
</tr>
</tbody>
</table>

It can be seen that hearing thresholds at 6 and 8kHz are most affected by this pooled ear comparison. The average deterioration for each of these frequencies is approximately 15dB and this is classed as a clinically significant difference as Grade 1 change according to CTCAE criteria. This data was used to determine the study sample size, for intra-patient and intra-group comparison.
## Ear and labyrinth disorders

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing impaired</td>
<td>Adults enrolled in a Monitoring Program (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of 15–25 dB averaged at 2 contiguous test frequencies in at least one ear.</td>
<td>Adults enrolled in Monitoring Program (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of &gt;25 dB averaged at 2 contiguous test frequencies in at least one ear.</td>
<td>Adults enrolled in Monitoring Program (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of &gt;25 dB averaged at 3 contiguous test frequencies in at least one ear (absolute threshold &gt;60 dB HL at 2 kHz and above); non-removable hearing.</td>
<td>Adults not enrolled in Monitoring Program: hearing loss with hearing aid or intervention indicated; limiting instrumental ADLs and self-care ADLs.</td>
<td>Adults: Decrease in hearing to profound bilateral loss (absolute threshold &gt;80 dB HL at 2 kHz and above).</td>
</tr>
<tr>
<td></td>
<td>Adults not enrolled in Monitoring Program: subjective change in hearing in the absence of documented hearing loss.</td>
<td>Adults not enrolled in Monitoring Program: hearing loss but hearing aid or intervention not indicated; limiting instrumental ADLs.</td>
<td>Adults not enrolled in Monitoring Program: hearing loss with hearing aid or intervention indicated; limiting self-care ADLs.</td>
<td>Adults not enrolled in Monitoring Program: hearing loss sufficient to indicate therapeutic intervention, including hearing aids; threshold shift &gt;25 dB at 3 kHz and above in at least one ear; additional speech-language related services indicated.</td>
<td>-</td>
</tr>
<tr>
<td>Pediatr (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift &gt;20 dB at 8 kHz in at least one ear.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Pediatr: Audiologic indication for cochlear implant and additional speech-language related services indicated.
Appendix 4.3 Interview questions

1: Can you tell me about your experience of hearing loss (can include deterioration) since being diagnosed with head and neck cancer?
   Before, during and after treatment?
   Impact on life?

2: What information or support did you receive to help you understand and manage your hearing deterioration?

3: How do you think we can support people with hearing deterioration having had cancer treatment?
Appendix 4.4 Study approval documents

Approval for the original study (Phase 1) was obtained from:

- NRES Committee London Westminster: 08 January 2015 (Reference 14/LO/2249);
- Faculty of Health and Medical Science Ethics Committee: University of Surrey 23 January 2015 (Reference EC 2015 05);
- Research and Development Department Guys and St Thomas’ NHS Foundation Trust: 21 January 2015 (Reference RJ115/N025).

Approval was based upon the following documents:

- Evidence of Sponsor insurance or indemnity (non-NHS Sponsors only);
- GP/consultant information sheets or letters: v1 (15 December 2014);
- IRAS Checklist XML: [Checklist_01122014];
- IRAS Checklist XML: [Checklist_06012015];
- Supervisor CV_Roma Maguire;
- Participant demographics: v1 (28 November 2014);
- Checklist: v2 (06 January 2015);
- Reply to REC: (06 January 2015);
- Participant consent form: v1 (28 November 2014);
- Participant consent form: v2 (18 December 2014);
- Participant information sheet: (PIS) v1 (28 November 2014);
- Participant information sheet: (PIS) v2 (18 December 2014);
- REC Application Form [REC_Form_01122014];
- Research project protocol proposal: v1 (28 November 2014);
- Summary CV for Chief Investigator (CI) [CV_Presanna] - (28 November 2014);
- Summary CV for supervisor (student research) [Professor Kearney].
Approval for substantial amendment (Phase 2) was obtained from:

- NRES Committee London-Westminster: 03 May 2016 (Reference 14/LO/2249);
- Faculty of Health and Medical Science Ethics Committee: University of Surrey 04 May 2016;
- Research and Development Department Guys and St Thomas’ NHS Foundation Trust – 21 January 2015 (Reference RJ115/N025).

Documents that were granted Ethics and Research approval for Phase 2 included:

- Interview schedules or topic guides for participants: v1 (08 April 2016);
- Notice of Substantial Amendment (non-CTIMP): v1 (08 April 2016);
- Email clarification: 12 April 2016;
- Participant consent form: v8 (08 April 2016);
- Participant information sheet (PIS): v9 (28 April 2016);
- Research protocol or project proposal: v8 (08 April 2016)
- Summary CV for supervisor (student research) [Professor Emma Ream]

The study project protocol proposal included a statement that the study had been conducted in compliance with the Research Governance Framework for Health and Social Care, and the guidelines produced by Good Clinical Practice (GCP).

**Compliance and non-Compliance**

The author ensured that the trial was conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework, the Guys and St Thomas’s Trust Research Office policies and procedures, and any subsequent amendments.
A noted systematic lack of adherence to standard operating protocols, the study protocol, or the GCP by either the author or the study staff, which could have led to prolonged collection, deviations, breaches or suspected fraud, would constitute non-compliance. Such non-compliances would be identified in a variety of different ways such as monitoring visits, CRFs, communications and updates.

In the case of any non-compliance, the sponsor maintained a log of such non-compliances to ascertain if there were any trends developing which needed to be investigated. The sponsor would assess the non-compliances and specify a time frame in which they should be dealt with. Each action would be given a different time-frame dependent upon the nature and severity of the non-compliance. If the non-compliances were not dealt with according to the specifications, the sponsor and the R&D Office would agree appropriate action, including an on-site audit. If compliance with recommendations following the on-site audit were not adhered to, the study could be invalidated.

**Monitoring and Audit**

This study was subject to audit by any method listed below. By:

- The risk assessment process;
- An individual investigator or department requesting an audit;
- Being identified via an allegation of research misconduct or fraud or a suspected breach of regulations;
- Being selected at random. The DH states that Trusts should audit a minimum of 10% of all research projects;
- Being randomly selected for audit by an external organisation;
- Internal audits conducted by a sponsor’s representative.
Appendix 5.1 Participant characteristics – tested at 3-month follow-up after treatment

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Hearing deterioration Grade</th>
<th>Gender</th>
<th>Age</th>
<th>Location</th>
<th>Stage</th>
<th>Aetiology</th>
<th>Treatment type</th>
<th>Pre-treatment hearing level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>3</td>
<td>F</td>
<td>52</td>
<td>Hypopharynx</td>
<td>IVA</td>
<td>None</td>
<td>CRT</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0</td>
<td>F</td>
<td>81</td>
<td>Parotid</td>
<td>II</td>
<td>S</td>
<td>RT</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1</td>
<td>M</td>
<td>59</td>
<td>Tongue</td>
<td>III</td>
<td>S A</td>
<td>RT</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>3</td>
<td>F</td>
<td>56</td>
<td>Nasopharynx</td>
<td>III</td>
<td>V</td>
<td>CRT</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>3</td>
<td>M</td>
<td>46</td>
<td>Tongue</td>
<td>IVA</td>
<td>None</td>
<td>CRT</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>1</td>
<td>M</td>
<td>61</td>
<td>Tongue</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>3</td>
<td>M</td>
<td>51</td>
<td>Tonsil</td>
<td>IVA</td>
<td>V</td>
<td>CRT</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>1</td>
<td>M</td>
<td>52</td>
<td>Tongue</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
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<td>3</td>
<td>M</td>
<td>59</td>
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<td>IV</td>
<td>S A</td>
<td>CRT</td>
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<td>Tongue</td>
<td>IVA</td>
<td>A</td>
<td>CRT</td>
</tr>
<tr>
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<td>M</td>
<td>55</td>
<td>Tonsil</td>
<td>IVA</td>
<td>S A</td>
<td>CRT</td>
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<td>3</td>
<td>M</td>
<td>65</td>
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<td>IIIA</td>
<td>S A V</td>
<td>CRT</td>
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<td>3</td>
<td>F</td>
<td>67</td>
<td>Gingiva</td>
<td>III</td>
<td>None</td>
<td>RT</td>
</tr>
<tr>
<td>30</td>
<td>1</td>
<td>1</td>
<td>M</td>
<td>64</td>
<td>Tongue</td>
<td>IVA</td>
<td>A</td>
<td>CRT</td>
</tr>
<tr>
<td>35</td>
<td>1</td>
<td>1</td>
<td>F</td>
<td>86</td>
<td>Lip</td>
<td>III</td>
<td>None</td>
<td>RT</td>
</tr>
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<td>0</td>
<td>1</td>
<td>M</td>
<td>73</td>
<td>Tonsil</td>
<td>IVA</td>
<td>S A V</td>
<td>CRT</td>
</tr>
<tr>
<td>40</td>
<td>3</td>
<td>3</td>
<td>F</td>
<td>52</td>
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<td>IVA</td>
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<td>CRT</td>
</tr>
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<td>1</td>
<td>F</td>
<td>72</td>
<td>Nasal cavity</td>
<td>II</td>
<td>S</td>
<td>RT</td>
</tr>
<tr>
<td>49</td>
<td>3</td>
<td>1</td>
<td>M</td>
<td>62</td>
<td>Vallecule</td>
<td>IVA</td>
<td>S A V</td>
<td>CRT</td>
</tr>
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<td>3</td>
<td>3</td>
<td>F</td>
<td>55</td>
<td>Tonsil</td>
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<td>S</td>
<td>CRT</td>
</tr>
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<td>3</td>
<td>3</td>
<td>M</td>
<td>65</td>
<td>Glottis</td>
<td>III</td>
<td>S</td>
<td>CRT</td>
</tr>
</tbody>
</table>

Key: Aetiology (S-smoker or ex-smoker; A-alcohol drinker (> 14 units/week); V-virus confirmed); Pre-treatment hearing status (N-Normal; Mod-Moderate) BSA guidelines; RT – radiotherapy; CRT - chemoradiotherapy
Appendix 6.1 Transcript from Interview 1

Initial categories

<table>
<thead>
<tr>
<th>Continuous Tinnitus</th>
<th>In vivo codes (INT – Interviewer; P – Participant 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced pitch</td>
<td>Date: 5th–June 2016</td>
</tr>
<tr>
<td>hearing</td>
<td>INT - Thank you for agreeing to participate in this study that is part of a doctoral thesis. I wish to seek your views of the extent of impact of hearing loss following treatment for head and neck cancer, which currently is not known. The interview should take no longer than an hour.</td>
</tr>
<tr>
<td>Combination of aural symptoms</td>
<td>INT - So first of all please can you tell me about your experience of hearing loss or deterioration since being diagnosed with head and neck cancer?</td>
</tr>
<tr>
<td>Difficulty with hearing</td>
<td>P51 - What as in now that I have the tinnitus since I have had the treatment which I have never had before and my only problem is I have not got general deafness problems it is purely a certain pitch level that I cannot hear. Other people are fine and there is no rhyme nor reason to it, it is not deep voices, high voices, male, female, television is my worst problem and I do struggle with TV. Once I have got my hearing aids in, in general conversation I am fine in a room of people, absolutely fine</td>
</tr>
<tr>
<td>TV</td>
<td>INT - How was your hearing before you started–treatment?</td>
</tr>
<tr>
<td>Benefit of hearing aids for hearing</td>
<td>P51 - Perfect absolutely spot on in fact I had a left sphenoid wing meningioma back in February 2014 and my hearing after having that removed actually increased, it became I could hear a pin drop So all of a sudden to now have these hearing problems has taken me, you know, I have really found a difference.</td>
</tr>
<tr>
<td>Pre-treatment hearing ok</td>
<td>INT - How did it make you feel to have a change in your hearing after the treatment?</td>
</tr>
<tr>
<td>Awareness of aural change with treatment</td>
<td></td>
</tr>
<tr>
<td>Not bothered with hearing aids, or by hearing change</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Difficulty with hearing: in social gatherings; hearing TV; in cinema; in social gatherings with background noise (music)</td>
<td></td>
</tr>
<tr>
<td>Problems still with hearing aids</td>
<td></td>
</tr>
<tr>
<td>Hearing in context of cancer</td>
<td></td>
</tr>
</tbody>
</table>

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**P51** - I do not mind the fact that I have to wear hearing aids, I do not mind the fact that there are certain people I cannot hear, main thing is it is the social side of things, as well as TV, it is going to the cinema. You cannot hear some things that happen at the cinema but if you put the hearing aids in, obviously when you have got the music and that, it is really loud. It is more of the social side of it. I struggle in a crowded bar or a pub or anything like that that has also got music that I do struggle with because then I cannot wear my hearing aids because everything is just way too loud and then if I am with a table full of people I then do struggle with them. But generally, I am fine with it; fine with it compared to some of the other problems I have been left with.

---

**INT** - Please let me know a little bit more about when you first noticed a change in your hearing.

**P51** - It was immediately after, I had day 1 and 29 of Cisplatin and it was immediately after day 29. When I had the first on day one chemo, day two I woke up and it was like I was under water. My hearing was very like I had got water in my ears and I sort of was not shouting at people but I could not hear myself talk. Well after about a week that improved, it went, and my hearing went back to normal until I did the day 29 Cisplatin and then after that, that is when I was suddenly getting the high-pitched tinnitus and I did notice I was struggling to hear people. Because I was quite ill with the treatment it was not until I had finished my radiotherapy that then I really, and I started to feel better in myself, that I really realised I had a problem with hearing.

---

**I** - How has the hearing change made you feel about yourself?

**P51** - I am fine with it, I am fine with the fact that I have got a hearing problem. I think it helps that my parents wear hearing aids. My father-in-law wears hearing aids, you know so I have no, whenever I talk to someone that I do not know or if I am in a room with people I tell people that I have got a hearing problem so you
<table>
<thead>
<tr>
<th>Not bothered with hearing aids</th>
<th>know so I might going excuse me, excuse me, pardon, you know sort of. I am fine with it; it has not made me self-conscious or anything like that and I mean I have got long hair but I wear my hair up and when I have got my hearing aids in and I really do not mind if people see them or not</th>
</tr>
</thead>
<tbody>
<tr>
<td>Others have to repeat themselves</td>
<td>INT - How have your friends and family taken to you wearing the aids?</td>
</tr>
<tr>
<td>Frustration by partner</td>
<td>P51 - Again with my family there is not much change because they are used to like my mum and dad not being able to hear and having to like repeat everything they say. My husband gets a bit, every now and again, he goes oh you know he gets quite agitated by it at times because I cannot hear him because I do not wear my hearing aids all the time. But that I think is because my hearing was so good before the treatment he never had to repeat himself and that but he is realising that's how it is or just does not talk to me.</td>
</tr>
<tr>
<td>Withdrawal by partner from communication</td>
<td>INT - And with the treatment, the second dose of chemo, you noticed that things were deteriorating and treatment finished. What happened to your hearing after that?</td>
</tr>
<tr>
<td>Maintained hearing loss</td>
<td>P51 - It did not get any worse. It stayed how it was the minute I had had the second lot of treatment, within the couple of days after that is exactly how it is now. It has not. I do not think, I mean it might have done with the tests you did, but I do not think it has deteriorated any more or changed, you know within the pitches or anything like that.</td>
</tr>
<tr>
<td></td>
<td>INT - Okay so today is the 3rd of June and can you remember when you finished your treatment?</td>
</tr>
<tr>
<td></td>
<td>P51 - 2nd of October.</td>
</tr>
<tr>
<td></td>
<td>INT - That's about 8 months now. That is from the hearing side of things so just to clarify from the hearing perspective you are noticing difficulty in what circumstances specifically?</td>
</tr>
<tr>
<td>Difficulty hearing: TV; social gatherings with background noise – music and people</td>
<td>P51 - With the TV definitely, and it is loud noisy social events. If there was four of us out for a meal at a table that is fine but when you are in a pub or anywhere with a lot of music and there is a group of you, because the music is then so loud I do not put the hearing aids in but then I cannot necessarily hear people talk because there is a lot of noise around you from other people. You know what is the lesser of two evils? You are either really loud with the music and that or you cannot hear people. They are the big ones, big social gathering events.</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>Difficulty hearing in social gatherings</td>
<td>INT - In those circumstances what do you do?</td>
</tr>
<tr>
<td>Others speak louder</td>
<td>P51 - I do not wear the hearing aids but I tell my friends that you know that I have not got them in so basically, they either have to shout at me or, they have all been good, because they know that I wear them they know I have got problems that if I ignore them they do not take offence by it they just nudge me and go ‘I was talking to you.’ You know.</td>
</tr>
<tr>
<td>Others need to gain attention</td>
<td>INT - Has there been much change to your life as a consequence to the hearing change?</td>
</tr>
<tr>
<td>Withdrawal from going to cinema</td>
<td>P51 - No, it is silly things like I used to go to the pictures, I do not go to the pictures anymore because the noise because obviously you do not get subtitles in the cinema, and the noise is so, you know there is no in between with the hearing, it is either really, really, loud because you have got your hearing aids in or again there are some voices you cannot hear even though a cinema is a loud place, you know there is still certain pitches I cannot, it is like they are mumbling and I cannot hear them. Other than that, no I still go out, I still socialise, I still you know, see people, do things, no it has not changed it. I think if anything it has changed my husband a bit more because he does get annoyed indoors when I have to have the telly louder because for him that is too much for him and he says, ‘turn it down, it is really, really, loud I cannot listen to it, it is too loud’. So, if anything, I think it has affected him a bit.</td>
</tr>
<tr>
<td>Difficulty hearing in the cinema</td>
<td>INT - Right.so there’s been an effect on your immediate circle?</td>
</tr>
<tr>
<td>Others annoyed by hearing change</td>
<td></td>
</tr>
<tr>
<td>Increase in TV volume</td>
<td></td>
</tr>
<tr>
<td>Others bothered by hearing change</td>
<td></td>
</tr>
</tbody>
</table>
Others not bothered by hearing change
Others have to repeat themselves
Others annoyed by hearing change

Difficulty hearing in environmental noise

Lip-reading
Unaware on need to lip-read
Others need to speak clearer

P51 – Yes other than that no-one else minds because as I say mum and dad wear hearing aids so they do not mind coming around to a loud telly or anything. And as I said [my husband] when he has to keep repeating himself sometimes he gets a bit, you know, flustered by it.

INT - Right with the repetition?

P51 - Yes.

INT - With your husband. In the one to one is it any specific circumstance with the one to one or if you are doing a particular activity?

P51 - No - I mean it is silly things like I can be in the kitchen and if the washing machine on, the tumble dryer, the dishwasher or whatever then I cannot hear him if he is in the front room and talks to me where I used to be able to.

INT - so please could you just continue with what circumstances in the one to one that you are finding particularly difficult.

P51 - If I am in a different room to somebody and they talk to me, if I have got say, I do not know, the tumble dryer or washing machine, anything like that, I now cannot hear them whereas I used to be able to. Sometimes my husband has a habit of sitting with his laptop on his lap and obviously the screen is right in front of him so sometimes I cannot hear him. I know it sounds silly, it is as though it has been blocked by the screen but literally only on the other settee opposite the room from him, things like that. He forgets sometimes that he has to talk a bit clearer to me. That is another thing, it is weird, because sometimes his voice is perfectly clear and other times it is not but he does not change his pitch greatly in how he's talking.

INT - I am wondering whether in those circumstances, is he facing you or is he turning aside maybe?
| Others need to face listener to be heard | P51 - No he is not facing me so he is either turning to side or as I say he is in a different room but before I used to be able to hear it, it was not a problem. But it is things like that with one to one but if I am actually sitting like this, across a table from him I am fine with it, absolutely fine. |
| Continuous tinnitus Whistle sound Not bothered by tinnitus Ignore tinnitus Benefit of hearing aids for tinnitus Not bothered by tinnitus | INT – Good. Noises - tell us about noises |
| Sudden tinnitus | P51 - It is like a very high-pitched whistle in my head constantly but it does not affect my sleeping and I have sort of learnt to sort of ignore it during the day. It is only if I am sitting and it is silent and then you can that you hear it but then every now and again if I put my hearing aids in it goes. So, it is like nice to have some peace and quiet. It does not affect anything I do; it does not affect the sleeping or anything like that |
| Acceptance of hearing loss | INT—- That is good - and when did the high pitch come about? |
| P51 - Literally as soon as I had the second lot of chemo–on day 29 |
| INT - So you have had the change, and if I am correct in understanding you have been able to take that on board and you have noticed alterations to circumstances but in terms of how it has made you feel about yourself, from what I understand it has not really made that much of an impact? |
| P51 - No - it has not made me self-conscious or I am not embarrassed by it or anything like that. You know how many people have hearing problems in this day and age? You know it does not upset me, it does not embarrass me, it does not worry me, no, I am fine with it. |
| INT - That is good. Moving on to another question what information or support did you receive to help you understand and manage your hearing deterioration? |
| Pre-treatment, made aware that hearing may change | P51 - I knew from, it is a lot to take on board, when you are first told that you have got cancer and this is what is going to happen they do briefly explain that this is possible what could happen from having chemo-radiotherapy so they talk about your loss of taste buds, saliva, the mouth ulcers, loss of hearing, they talk about it but to be perfectly honest with you, you do not take it in. You hear is the word cancer and then that is it. And then literally you are in the start of the tests you know week long of tests to make sure you are okay for the treatment and then you are starting so you do not really get time to think about it because my problem for the hearing did not click in until day 29 so I was like 4 or 5 weeks in by that time and by that time I have got the saliva problems, the phlegm problems, the taste buds, the ulcers and I was really ill. So, it was not until I think I came back to you at the end of my treatment and then you explained to me look that this is what has happened, it has not got any better, these are your options. So, you really did not get much to start with because they were more concerned with giving you how you were physically going to feel and cope with it for 6 weeks. |
| Hearing in context of cancer | | |
| Shock of cancer diagnosis | INT - So a lot to take on board? |
| Hearing in context of cancer treatment | P51 - Absolutely. Because you are given hundreds and hundreds of leaflets and pamphlets and booklets, I came out with a wad like that, you know, but the thing they emphasise on when you are first told you have got cancer, this is your treatment plan, this is what is going to happen, the things they really concentrate on are what are actually going to physically affect you whilst you are having your treatment. How you are going to get through it. What is going to happen. And obviously the hearing I do not think they see that as a physical problem at that time. And as I say it was when I came to see you at the end of my treatment and you did the re-test and you said this is the situation and you went through it all and explained it and what my options were, you know, and everything like that. |
| Hearing test explanation clear | INT - Yes, it is a lot to take on board. |
| Hearing in context of cancer | |
P51 - Yes.

INT - When do you think it would have been helpful for you to have received information about the hearing? When do you think you would have been ready to receive that?

P51 - I think it was right actually how I got it to be honest with you because I did have such a rough time getting through the treatment and there are so many other physical things that affect you a lot more and it is not as though you have lost your hearing, it is just that it has deteriorated. It has changed a bit, you know, you have not lost it and there are a lot worse things could have happened coming out of it you know. So, believe it or not I actually think I am quite lucky with how I have come out the end of it because I was really, really ill because I ended up in hospital for 2 weeks at the end of my treatment. I had serious eating difficulties and so the hearing side of it, you know what, it is what it is.

INT - It is what it is.

P51 - That is how I have unfortunately looked at it and I think I have still got my hearing, I am not deaf, you know I still have my hearing it has just changed a bit and people have got to realise that.

INT - So that was in terms of information and support. We were able to, at the end of your treatment re-test your hearing and explain that there has been a change. In terms of any further action to help you with your hearing when do you think you would have liked that to have happened? So, you had the explanation of your change in hearing at the end of treatment, in terms of when were you ready to actually receive help, when would that have been?
| Hearing support timing | P51 - No, I think that was right as well because I would not have wanted any help from you while I was having the treatment because quite honestly getting through the treatment is bad enough, it is not until you have the re-test and you start to feel a bit better in yourself and all the other symptoms start calming down that you can deal with. I know hearing is not trivial, but in compared to whatever else you are going through then it is quite a trivial one. So, you know I think that was quite right. INT - Okay. |
| Hearing in context of cancer | P51 - Definitely would not want to suddenly be told ‘would you like hearing aids’ or whatever when you get to day 29 and have the problem, definitely would not want them doing that then. INT - So from what I understand certainly at the end of treatment? Any time after that? P51 - I do not know. I think that depends on the person. INT - As for you it was though at what time? P51 - It was right for me but it might not be for somebody else, like somebody a bit older because I think you have got to be able to cope. I think it is the person as well, I mean there were certain things that they were trying to do me and I had to put my foot down and say I cannot do it because I was so ill with my stomach PEG and everything like that and I lost 4 stone in the space of like about 8 or 9 weeks and I was so ill that for me I got to the end of my treatment, I started feeling right, I thought now okay this is it I have got to get myself back, fighting fit, and so that is when I just wanted to get it done. I did not want to wait. If you had said to me get everything else done and come back to me in another 3 months and then we will talk about the hearing aids, then we will talk, no. I am through the treatment, that is it; I have beat it now I have to get myself back as I was. But not everybody is like that. |
Hearing support timing
Pre-treatment, made aware that hearing may change
During treatment, patient alerted clinician of aural problem
Hearing support to be by audiology
Disappointment at return of symptoms

Uncertainty with progression of aural symptoms

INT - Absolutely. What further support do you think we could offer to people who have experienced hearing deterioration after cancer treatment?

P51 - You see I am quite happy with it. I feel that I was, I knew from the word go I was going to have some hearing problems. Admittedly it was when I had the second lot of chemo treatment, when I actually spoke to the oncology team and explained that I had the hearing problem, they were very much, oh that is standard, that is going to happen, but do not worry you are under audiology. So, they did not go into it at all then. I did not know, I suppose really, I thought it was going to get better like it did on day one when I had the first lot of chemotherapy and within a week or so it got better but no I as quite happy with how it was explained and what happened and everything like that.

INT - Thank you. I just want to go back. You said that you knew that the hearing might change? Earlier you said that you were given a whole lot of information. When was it that you remembered that ‘I knew my hearing was going to change?’ Or what state did you think to remember?

P51 - When they actually said to me when I went after the second lot of chemo and they said to me what problems are you experiencing, blah, blah, blah, and I said I have got this hearing thing, that is when they said yes but your hearing will change, that is how it is, and then all of a sudden you remember when you had your first lot of chemo, oh yes it did change but then you assume, or I assumed oh perhaps it will go back like it did before so I will be okay. I did not realise it was going to be as definite as it was. But it is not that bad, I know that is a bit of a contradiction in what I am saying really, the fact that I did not know it was going to be permanent but you know what, I am ok with it.

INT - You have been quite accepting in other words?
<table>
<thead>
<tr>
<th>Hearing loss in context of cancer</th>
<th>P51 - Yes, you know I think you have to look at it, that it is cancer, it could have ended a lot differently. So, to have a minor hearing problem to me is nothing in comparison to other situations.</th>
<th>INT - Surely. Who was it that you spoke with when you noticed after day 29, which were the specialists? Which were the specialities?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P51 - You see on a Wednesday in outpatient oncology, you see one of the chief radiographers, I cannot remember her name but you actually see her and she is the one that prescribes your medicines and she is the one that goes through you know like what other problems you have got and she give you a list of medication and that is when I said to her about it.</td>
<td>INT - So it was not actually with one of the oncologists it was actually with one of the paramedical staff.</td>
</tr>
<tr>
<td></td>
<td>P51 - Yes, because every Wednesday you see them, you only see the oncologist every, I cannot remember, it is not very Wednesday you see the oncologist but you do see this, what as her name, I do not know she is one of the chief radiographers, and you see her every Wednesday and she goes through everything with you. Like your eating, your symptoms, your illnesses, your sickness, everything like that.</td>
<td>INT - And that list is a pretty comprehensive list?</td>
</tr>
<tr>
<td></td>
<td>P51 - Yes.</td>
<td>INT - Within that is there a specific one on hearing or …?</td>
</tr>
<tr>
<td></td>
<td>P51 - No</td>
<td>INT - There is not. So just a comprehensive list and do you have anything else?</td>
</tr>
</tbody>
</table>
During treatment, no discussion of aural problems prompted by clinician

P51 - Yes. At no point throughout it do they ask you how your hearing is. They just say to you any other things and I just happened to mention about the hearing. But they never actually say have you noticed any hearing problems, difficulty, noises, tinnitus, anything like that. Never do they mention that.

INT - Okay. Well here is an opportunity for us to try to perhaps change this. Do you have any other questions about your hearing at all?

P51 - No, I mean I am, as I say now that you have tweaked to give me a second programme for telly and that I think I am going to go and try that and hopefully that is good but I did not realise that I could have a second programme put in, I thought that was how the hearing aids were. I must admit. I did not realise you could have like a second programme.

INT - Right so just to clarify for the purposes of the interview. We have provided hearing aids after your 3-month check, yes and how has that experience been for you?

P51 - Fine, I mean the nice thing, the one thing I will say that was really nice was the fact that you have always accommodated me as in whenever I have had to come you have always said right let us know when you are in here already and we will fit you in on that day. You know what, that is really helpful, really nice because when you feel so ill, so rough and you have to come up by train and that and you are the one department that does that which is really nice, I must say that.

INT - Thank you. In terms of the hearing aids, what problems had you after treatment that have been improved with the hearing aids and which situations are still a problem for you? Shall I re-phrase that?
<table>
<thead>
<tr>
<th>Benefit of hearing aids for hearing</th>
<th>P51 — Yes sorry.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems still with hearing aids</td>
<td>INT - You are having difficulties with some one-to-one circumstances, cinema, TV so which of the situations has been improved with hearing aiding and which situations are still a bit problematic for you?</td>
</tr>
<tr>
<td>Benefit of hearing aids for hearing</td>
<td>P51 - The ones that have improved are definitely one-to-one because even before I had the hearing aids there are some people that, you know, silent room one to one I still have trouble hearing them because of the pitch of the voice. With the hearing aids, I do not have that problem at all now. Concerns still are with the telly which hopefully the second programme will now rectify but it is when you are in a crowded, noisy environment and you have to take the hearing aids out and then you struggle with anybody that even if they are sitting opposite you, I struggle with that. They are the ones I struggle with, but general day to day has improved greatly with the hearing aids.</td>
</tr>
<tr>
<td></td>
<td>INT - That is very good to hear, very good to hear. Okay I think we have finished now, thank you very much participating in the interview.</td>
</tr>
</tbody>
</table>
Appendix 6.2 Themes, subthemes and initial categories

# - Interview number; P – Participant number

**Theme 1 – Sensation of impairment**

**Subtheme – Hearing Change**

Reduced pitch hearing #1/P51, #2/P11, #6/P53, #11/P7, #13/P7

General deafness #5/P12, #13/P17

Dull ear sensation #11/P7

No change from pre-treatment hearing #3/P5, #4/P9, #10/P42

Sensation of wax #3/P5

Blocked ear #2/P11

Pressure in ear #2/P11

Fluid in ear #1/P51, #11/P7

Aware of hearing problems before treatment #9/P2, #4/P9, #10/P42, #13/P17

Pre-treatment hearing ok #1/51, #7/P6, #8/P29, #12/P30

Sudden hearing loss #1/P51

Awareness of aural change with treatment #1/P51, #5/P12, #8/P29, #6/P53, #7/P6, #11/P7, #12/P30

Gradual hearing loss #5/P12, #7/P6, #13/P7

**Subtheme – Tinnitus**

Combination of aural symptoms #1/P51, #5/P12, #7/P11, #7/P6,

High hum sounds #2/P11

Tinnitus hovers over ears #5/P12

Tinnitus in ear #6/P53

Ringing sensation #6/P53, #13/P17

White noise #11/P7
Whistle sound #1/P51, #11/P7

“shh” sound #11/P7

Tinnitus in head #11/P7

High pitch sound #1/P51, #7/P6

Sea sound #8/P29

Tinnitus continuous #7/P6

Tinnitus in the background #5/P12, #2/P11

Buzzing sound #13/P17

Tinnitus and noise #11/P7

Hyperacusis #11/P7

Ear pain #11/P7

No tinnitus #3/P5, #4/P9, #9/P2, #12/P30, #10/P42

Sudden tinnitus #1/P51, #11/P7

Gradual tinnitus #7/P6

**Subtheme – Progression of aural change**

Deterioration in hearing #11/P7, #9/P2,

Temporary hearing loss #1/P51, #11/P7

Fluctuating hearing loss #2/P11, #6/P53, #7/P6, #3/P5 (wax), #5/P12

Maintained hearing loss #1/P51, #2/P11, #12/P30

Unsure if hearing change has altered #5/P12

Improved hearing #6/P53, #7/P6

Continuous tinnitus #1/P51, #5/P12

Reduction in tinnitus #5/P12, #6/P53, #13/P17, #7/P6

Fluctuating tinnitus #8/P29

Change in tinnitus #11/P7, #5/P12
Theme 2 – Functional changes

**Subtheme – Communication difficulties**

Reduced hearing clarity #5/P12, #6/P53

Difficulty with hearing in shops #6/P53

Difficulty with hearing in social gatherings #1/P51, #5/P12, #9/P2, #13/P17

Difficulty with hearing in restaurants #5/P12

General communication problems #6/P53, #7/P6, #9/P2, #13/P17

Difficulty with hearing on the phone #6/P53, #7/P6, #13/P17

Difficulty with hearing in background noise (people) #1/P51, #6/P53, #8/P29,

Difficulty with hearing due to tiredness #11/P7

Difficulty with fast talking #11/P7

Difficulty with high pitched talkers #11/P7

No hearing difficulties #3/P5, #4/P9

1:1 ok #6/P53, #7/P6, #8/P29, #9/P2

Tinnitus made worse with stress/tiredness #11/P7

Unaware of need to lip-read #1/51

**Subtheme – Problems with entertainment**

Difficulty with hearing music #2/11, #11/7

Difficulty with hearing TV or radio #1/51, #6/53, #9/2, #11/7, #12/30, #7/6

Difficulty hearing in the cinema #1/51, #11/7

Difficulty hearing in social gatherings in background noise (music) #1/51, #2/P11, #13/P17

**Subtheme – Problems with environmental sounds**

Problems with the computer #5/12

Missing doorbell sound #5/12, #11/7

Difficulty hearing in environmental noise #1/51
Theme 3 – Coping mechanism

Subtheme – General strategies

Asks speaker to repeat/ others have to repeat themselves #1/51, #13/17, #5/12, #9/2
Asks speaker to speak louder/others speak louder #1/51, #7/6, #13/17
Asks others to speak clearer/Others need to speak clearer #1/51, #11/7
Lip-reading/ Others need to face listener to be heard #1/51, #11/7, #13/17, #7/6
Unaware of need to lip-read: #1/51
Tells others there is a hearing problem #1/51
Others need to gain attention #1/51
Others not aware of need to alter communication #12/30
Need to concentrate more to listen #9/2, #13/17
Reduction in background noise #13/17
Change in listening to music #2/11, #11/7
Increase in TV volume #1/51, #5/12, #9/2, #12/30, #11/7
Reduction in TV volume #11/7
Need to concentrate more to listen to TV #7/6,
Use subtitles #11/7
Tell others to slow down their speech #11/7
Pretend to hear #5/12
Make out that they are stupid #6/53
Ignore tinnitus #7/6, #2/11, #1/51

Subtheme – Use of assistive devices

Use headphones/earphones #11/7, #5/12
Benefit of hearing aids for hearing #1/51, #6/53, #8/29
Benefit of hearing aids for tinnitus #1/51
Cover ears #11/7
Problems still with hearing aids #1/51
Change doorbell frequency #11/7

Obtain auto-inflation balloon for OME #11/7

**Theme 4 – Emotional response to aural change**

**Subtheme – Attitude to hearing deterioration**

Not bothered by hearing change #1/51, #5/12, #6/53, #7/6, #9/2, #13/17

Acceptance of hearing loss #1/51, #2/11, #6/53, #5/12

Not bothered with hearing aids #1/51

Not bothered by tinnitus #1/51, #5/12, #2/11, #8/29, #13/17

Acceptance of tinnitus #2/11, #5/12, #13/17

Try to overcome difficulties #1/51, #7/6, #11/7

Hearing in context of cancer treatment #1/51, #5/12, #13/17

Possible denial of hearing loss #5/12

**Subtheme – Downplaying of symptoms**

Uncertainty with progression of aural symptoms #1/51, #11/7

Disappointment at return of symptoms #1/51

Frustration with hearing loss #7/6

Irritation with hearing loss #11/7

Annoyance in having a hearing loss #2/11

Annoyance with tinnitus #7/6, #11/7, #5/12

Irritation with tinnitus #11/7

Distraction by having tinnitus #11/7

Tinnitus a terrible sensation #6/53

Guilt in causing inconvenience to others #7/6

Others annoyed by hearing change #1/51, #7/6

Others not bothered by hearing change #1/51, #6/53, #13/17, #3/5, #4/9, #5/12,
Others bothered by hearing change #1/51, #11/7, #5/12, #7/6

**Subtheme – Sense of loss**
Disappointment with having hearing aids #8/29
Reduced confidence with having hearing aids #8/29
Stigma with hearing loss #7/6

**Subtheme – Social isolation**
Other reduce amount that is said #11/7
Withdrawal by partner from communication #1/51
Withdrawal from phone use #13/17
Withdrawal from going to cinema #1/51

**Theme 5 – Information and support**

**Subtheme – Pre-treatment information**
Pre-treatment, made aware that hearing may change #1/51, #4/9, #5/12, #6/53, #9/2, #11/7
Shock of cancer diagnoses #1/51

**Subtheme – Discussion of aural changes**
During treatment, patient alerted clinician of aural problem #1/51, #11/7
During treatment, no discussion of aural problems prompted by clinician #1/51
Change in treatment #11/7
Hearing test explanation clear #1/51, #2/11, #11/7, #7/6,
No explanation of hearing #13/17, #5/12
No explanation of tinnitus #5/12, #7/6
Management options for aural care #2/11, #3/5, #13/17, #11/7
Management options for a change in hearing #5/12, #8/29, #11/7, #13/17, #6/53, #10/42, #12/30
Delay in seeking hearing support #5/12, #8/29
Hearing support to be by audiology #1/51

**Subtheme – Further support**

Greater awareness of potential change in hearing #6/53

Tinnitus explanation and management #7/6, #5/12

Support depends on individual circumstances #1/51, #8/29, #11/7

Hearing support timing #1/51

Hearing test timing #2/11, #3/5, #4/9, #5/12, #8/29, #11/7, #9/2, #10/42, #13/17
Section B Research log

A research log is used to document progress of a study project from its inception to completion. It serves to identify areas of development for the individual conducting the study. It also points up influences that may have altered the direction of the study. The following account will detail how the research question itself, and the nature of the research enquiry, developed during the five years of study (2012-2017) within the Doctorate of Clinical Practice (DClinPrac) programme undertaken by the author of this log.

Background – identifying and clarifying the research question

The researcher is an audiologist with experience in paediatric habilitation of hearing and adult hearing rehabilitation, as well as in the clinical assessment of balance disorder. The project being logged began in January 2012 as an evaluation of a novel balance system assessment tool that was being developed in his host department. However, a year and a half into the course, in June 2013, it was realised that the assessment tool was already being evaluated, and his supervisors advised that while further investigation may complement findings, it would not necessarily add to research knowledge, a critical determinant for doctoral research enquiry.

In a previous post, the researcher had been involved in the systematic assessment and monitoring of hearing for children receiving cancer treatment. However, in his current position, the monitoring of hearing was not standard procedure in the service provision for adults receiving cancer treatment, although patients who had received treatment for HNC were requesting support and advice when they discovered they had experienced hearing loss – sometimes as much as up to two years after treatment.
In order to address this situation, the researcher, in consultation with oncologists specialising in the treatment of patients suffering from HNC, set up a monitoring protocol to assess patients' hearing before and after treatment. At this point the researcher agreed with his supervisors to use the evaluation of this protocol as a new subject for his research study. It therefore seemed appropriate to make the evaluation of this hearing monitoring protocol the subject of one of the course assignments, on service development and leadership. Information from this assignment then became the basis of the proposal submitted to the necessary ethics committees.

In July 2014, with the appointment of a new team of supervisors, who were both specialists in cancer care, it was decided to review the aims of the study. As the monitoring protocol was already in place, it was felt by the new supervisors that an evaluation of the protocol would be of limited value, and therefore there would be insufficient originality for a research project at doctoral level.

It was then decided to shift the focus of the project, and conduct a quantitative assessment to determine how many people experienced psychoacoustic change following treatment for cancer in the UK. The researcher advised his supervisors that to his knowledge at the time, the incidence of hearing loss in relation to HNC treatment had not previously been measured in a UK population.

**Literature review**

The review of literature within the subject area of the project enables the student to evaluate current knowledge and experience within the field and to discover gaps in that knowledge which would warrant investigation suitable for doctoral research. Such a review also provides an insight into the appropriate methods and methodology for this particular area of enquiry. The first stage of the literature review entails the development of a search strategy to identify literature strictly relevant to the subject to be identified; the second stage involves
the critical appraisal of the material to enable the student to assess the quality of the studies being reviewed.

In order to develop the skills required to conduct a comprehensive search of the literature available, throughout the course the researcher has taken advantage of a number of training sessions made available at both the University of Surrey and King's College Hospital Library. It was also helpful to discuss the research process with a post-doctoral researcher who had experience in creating frameworks for systematic reviews. The ‘advanced research methods’ module of the DClinPrac programme, while giving attention to the critical appraisal of papers identified in the search, also provided opportunities for a further stage in the literature review process, namely the application of the knowledge obtained to the student’s own particular study project.

In consultation with his supervisors, the researcher revised his search strategy several times. Initially, the strategy was found to be too broad and the results included too many irrelevant articles. However, when the strategy was narrowed, it was found that important relevant studies failed to appear. This meant a third adjustment was necessary. At this point the supervisors noted that in papers being identified there was considerable overlap with the subject area of the researcher’s project. It was therefore suggested that the project did not offer sufficient novelty for doctoral research. The matter was resolved by modifying the research question to include a qualitative element, to assess patient experience of the wider implications of hearing deterioration following HNC treatment. The search strategy was modified accordingly and this resulted in only one article being identified, a study that dealt with general communication difficulties following cancer treatment. A way was therefore open for the researcher to pursue an in-depth study of issues particularly related to patient experience of hearing deterioration.

Over a period of four years the scope of the literature review was changed at least four times. This brought home to the researcher the importance of clearly identifying the
research question, and of selecting appropriate search terms for reviewing the literature – a process that may require revision a number of times.

**Study design**

Throughout this study project, the researcher has come to appreciate the relative value and appropriateness of both quantitative and qualitative methods of enquiry.

From experience as an undergraduate in biochemistry, and as a post graduate student working on an MSc in audiology, his studies had tended to draw on deductive methodology with its emphasis on quantitative enquiry. It was perhaps natural therefore, that the researcher began the current study as a quantitative enquiry, using hearing tests pre and post treatment to determine the incidence and severity of hearing deterioration, although the qualitative element of patient experience was always present in his thinking.

The 'community of practice' module of the course, and specifically the philosophy of science element within the module, was particularly valuable in helping the researcher to recognise how different scientific paradigms contribute to the understanding of phenomena. The 'advanced research' module discussed how phenomena are explored using different methodologies and methods. Relating this understanding of scientific enquiry to his own study, the researcher adopted a critical realist stance, using mixed methods methodology, to view and explore the phenomenon of hearing deterioration in patients who had received treatment for HNC.

This first phase of the research project (the quantitative enquiry) led to a second phase in which participants from phase one who had measurable hearing deterioration were interviewed to explore patient experience of hearing deterioration – thus introducing a qualitative element, and a mixed methods methodology into the study.
The course was therefore instrumental in enabling the researcher to see how both quantitative and qualitative enquiry was appropriate in his specific study to explore the phenomenon of hearing deterioration following treatment of patients with HNC. The final study design consequently made use of mixed methods methodology, with the phases arranged in a sequential explanatory pattern.

**Research governance**

At the outset of the study, the researcher undertook the ‘good clinical practice researcher training’ course, which is mandatory for undertaking NHS UK research. This course included an examination of the principles of the Declaration of Helsinki (2008), which sets out ethical principles relating to clinical trials on humans. The declaration obliges researchers to act in the best interest of study participants and to ensure that accessible information is made available to potential participants so that they can make informed decisions prior to and during the study. These requirements were met in the online IRAS application form which contains questions covering every aspect of the research project, and requires submission of copies of participant information sheets and consent forms.

The IRAS form, necessary for NHS ethics approval, in order to ensure adequate governance of the project by all relevant supervisory bodies, required identification of the sponsor of the study (in this case the University) who was responsible for ensuring a proper framework was in place for the study to be conducted. The sponsor is also responsible for the covering of indemnity and monitoring arrangements.

As there was no change in the usual treatment provision of participants involved in the study, the application was submitted for ‘proportionate review’ by the London-Westminster NHS ethics committee. The application was given a provisional favourable opinion, subject to minor amendments being made. The amendments were made and the application was duly approved by the NHS committee in January 2015. This led to approval by the University
ethics committee and the Research and Development Department of the host hospital, enabling the study to start in February 2015.

As the study progressed however, it became evident, as discussed in the literature review section above, that expansion of the project was required to fully capture the qualitative assessment of patient experience. The study was adapted to include the second phase, a qualitative element (exploring patient experience in interviews), and this necessitated a change from a purely quantitative enquiry to a mixed methods methodology. The host hospital’s Patients Experience Manager gave helpful advice on how to ask questions for the interviews now being included. Because of the change in the research methodology, a ‘substantial amendment’, to the study protocol was submitted in April 2016 to the NHS ethics committee. This submission included updated consent and participant information sheets. The amended application was successful, and so the second phase of study commenced in June 2016.

As part of the governance procedure, the host hospital’s Research and Development Team required notification when the collection of study data was completed. The collection of data for Phase 1 (the quantitative element – hearing testing) was completed in February 2016, and data for Phase 2 (the qualitative element – participant interviews) was completed in July 2016, and notification given at each stage.

Data collection

Phase 1 of the project took one year to complete. Hearing test data was collected at three time points: before treatment, at the end of treatment and three months post treatment. Liaison with oncology and radiography colleagues was essential to co-ordinate testing, as participants often had altered hospital appointment dates that required alteration to the hearing testing schedule. As the researcher was working full-time at his hospital post,
involvement of team members within the audiology department was also essential for booking appointments and assisting with performing the tests.

Phase 2 was completed over two months and was more manageable to arrange than Phase 1. As with the hearing tests for Phase 1, the interviews were conducted on dates that participants were coming to hospital for other appointments, although this was not always possible, and some came voluntarily to attend for interview only.

Results and writing up

Support from the in-house statisticians at the host hospital was essential for formulating relevant statistical data analysis for the quantitative phase of the study. As the researcher lacked experience in qualitative research prior to the study commencement, he drew heavily on reading material around the subject and on the knowledge and support of his study supervisors in analysing the mass of material contained in the transcripts of interviews.

Study chapters were regularly submitted in draft form for review by the course supervisors who constantly encouraged the researcher to adopt a more critical approach to his material and avoid the descriptive style that characterised much of his earlier writing. In order to address this issue, and to develop his written communication skills more generally, the researcher participated in two writing-group workshops, provided by the Researcher Development Programme at the host University.

Communication

The researcher gave presentations on the study to a PhD writing group at the host university and to hospital research groups (audiology and oncology). Following the presentation to the oncology research group, the researcher was invited to give a presentation on audiology
support at a well-being event provided by the host hospital for survivors of HNC treatment and their carers and family members. Audiology support is now regularly featured in this survivorship programme.

The researcher also participated in the ‘23 Things for Publication Programme’ web-based course that offered guidance in writing journal articles. Skills learned on this course assisted the researcher in writing a paper on Phase 1 results. This paper, intended for publication in an academic journal was submitted together with the study as required by the DClinPrac degree programme.

**Summary**

The researcher has benefited from all aspects of the research process and has learned much throughout this journey. He has a much greater understanding and appreciation of the rigour required to undertake academic research, and through the various amendments required by the applications for approval by the ethics committees, realises the necessity for regular evaluation and where necessary, for alteration to an original research design. This can even involve the redefining and rewording of the research question.

The researcher now also understands that social science research requires good teamwork, communication, and cross-discipline co-operation to ensure that the process progresses smoothly.

Having concluded this study, the researcher hopes that more will be learned about the inter-relationship between treatment for cancer and hearing, that the medical disciplines involved will discover new opportunities for professional co-operation, and most importantly, that in future patients will receive the support and service provision they require for their more complete well-being. (Word count: 2283).
Introduction

The DClinPrac course offers an opportunity for researchers to develop an understanding of organisational and scientific knowledge, and of what shapes and influences health policy. It also provides an opportunity for involvement in translational research by the formulating of a project to enhance human health and well-being. The course was well suited for clinicians in managerial and clinical responsibility not only for their personal development, but also for the enhancement of their specific health discipline and others that relate to it.

The researcher is an audiologist with twenty years of NHS experience. On commencing the course, the researcher was new to the role of clinician-manager with leadership responsibilities. Prior to the course, the researcher attended a leadership-management training seminar organised by an audiology department: ‘Steer ing a true course’ (South Tees Hospitals NHS Foundation Trust, 2015). This course focussed on the practicalities of influencing change within audiology teams, however, its remit did not include the application of research. The researcher is aware of the apparent paucity of translational research in audiology within the UK, and was therefore attracted to the DClinPrac course with its emphasis on developing researcher skills within the context of health policy and leadership.

The taught elements of the course included the following modules: communities of practice; politics, policy and power; advanced research methods; and service development and leadership. Each of these modules will be discussed in turn.

Communities of practice

This module exposed the researcher to different types of knowledge, including organisational, embodied and scientific. Organisational knowledge is that which is known
and shared, such as from national standard frameworks and NICE. Lectures on the course suggested that NHS provision can be improved by drawing upon embodied knowledge, which is held by individuals within and without the organisation. Involvement of patient groups and external monitoring can help in the development of holistic health policy by applying relativist knowledge that recognises and accepts different perspectives on a situation.

The philosophy of science lectures showed how in scientific knowledge phenomena are viewed in different ways. The researcher found it of value to be made aware of these different layers of knowledge within ‘communities of practice’ which are often self-selecting individuals and groups who wish to share knowledge, solve problems and implement change for service improvement.

**Policy, politics and power**

The importance of communities of practice was carried through the policy, politics and power module. Health policy is influenced by different ideologies, economic evaluations and ethics. The researcher considered all these aspects in the module assignment on the white paper, ‘Any Qualified Provider’ (NHS, 2012a) particularly with its application to audiology (NHS, 2012b). In an attempt to address the request for patient choice in health provision, and to reduce the expenditure of public services, the Government initially rolled out the policy as ‘Any Willing Provider’. However, this was conducted without consulting relevant health professionals and with limited public involvement. Following considerable public outcry, the policy was revised and re-named ‘Any Qualified Provider’ in order to ensure that appropriate clinical and operational standards were met. When these standards were applied to audiology, it meant that private competitors were also accountable to the same levels of clinical expertise and moral code of conduct as usual NHS health providers. The module was valuable in that it highlighted the different perspectives on commissioning of services,
and it also underlined the importance of involving all relevant stakeholders at the outset, in the hope that transparent operation would result in effective policy acceptable to all parties concerned.

**Advanced research methods**

Different methodologies and methods were discussed within this module. The assignments for this module included doing a critique of existing evidence for formulating a research question; they also required students to create a structure of research design, which drew upon both qualitative and quantitative methodologies. These exercises were useful for the researcher’s own study project which had itself employed both quantitative and qualitative data collection phases.

**Service evaluation and leadership**

The principle of conceptual frameworks underpinning research was introduced in this service evaluation and leadership module to enable the evaluation of policies and procedures. One such framework was the Medical Research Council (MRC) model for evaluating complex health interventions. The researcher employed this particular model in his module assignment: ‘Audiology assessment of patients undergoing chemo-radiotherapy for treatment of head and neck cancer’. He used this assignment in preparing the proposal on the evaluation of a monitoring protocol for hearing to be submitted to the various ethics committees.

The leadership aspect of the course discussed different models of leadership, and offered a critique of various models, from individual (‘Great Man’) leadership to group (distributed) leadership. These lectures described the evolution of these different styles, from leadership focussed in one individual to an understanding of leadership as the activity of a team. Good leadership requires good communication and transparency. Distributed leadership was
chosen as most applicable for the leadership assignment, as involvement of different stakeholders was required for the monitoring programme to be adopted and implemented.

**Research project**

The researcher used elements from each of these course modules in shaping his ideas for the research study of the DClinPrac programme. The communities of practice module highlighted the advantages of sharing knowledge from different perspectives in order to ensure holistic care. Drawing on principles learned from this module, the researcher attended multidisciplinary team meetings where ENT surgeons, oncologists, speech therapists, dentists, dieticians, physiotherapists, clinical nurse specialists and radiographers discussed treatment plans for patients with HNC. It was valuable to see the different approaches made by each specialty on patient care, but there was no discussion of audiological issues.

The researcher was aware that a recent UK health policy document on cancer care (DH, 2011) stressed the importance of advocating the most suitable treatment regimen and the need to provide appropriate support to enhance survivorship, but this document did not mention support for patients with hearing loss following treatment. However, the researcher was aware of patients who were attending his audiology clinic two or more years following the end of cancer treatment.

Subsequently, the researcher met with oncologists who specialised in HNC care to discuss a process for monitoring hearing loss in patients receiving treatment. This discussion brought forth a positive response from the oncologists and the suggestion that co-operation between oncologists and audiologists would be beneficial for more comprehensive patient care. Consequently, the research enquiry for this study began with an evaluation of the monitoring programme, drawing on the responses obtained from interviews with different stakeholders: patients, oncologists and staff of the audiology department, in order to gain different
perspectives. A cost-benefit analysis was also to be included as part of the study, in order to determine if there was a difference in overall costs if audiological intervention were to be made soon after treatment completion rather than the current practice of intervention at two years or more from the end of treatment.

As mentioned above in the discussion of the service evaluation and leadership module of this course, the MRC model for evaluating complex health interventions was to be used as the conceptual framework for the study. However, the focus of the researcher’s project was then changed when new study supervisors suggested that as a monitoring protocol was already in place, an evaluation of the protocol would be of limited value and of insufficient originality for a research project at doctoral level. This shift of focus involved research into determining how many people experienced hearing change following treatment for cancer in the UK. This required developing different research methods and methodologies discussed in the advanced research methods module. The change of perspective enabled the researcher to appreciate how a phenomenon (in this case, the study of hearing deterioration) can be approached in different ways depending upon the knowledge, training, expertise and conceptual or theoretical perspective of the researcher and/or supervisors.

In summary, the change in the direction of the study meant drawing upon different types of knowledge in the investigation. Viewing human health from an economic perspective (the cost-benefit analysis) drew upon organisational knowledge; the change of focus to viewing patient experience from a clinical perspective has involved investigating scientific knowledge. Information acquired from each of the modules in the study programme has not only assisted the researcher throughout the entire project, it has also deepened and enriched his overall academic experience and personal development.
Personal development

The researcher has greatly enjoyed his participation in this course. By having the opportunity to explore different scientific paradigms and to acquire new knowledge in the investigation of the subject area for the research project, he found himself changing his mind-set, and thus developing both personally and professionally. There were seminal moments for the researcher in each area. During the community of practice module, he found the introduction of qualitative enquiry confusing at first; it simply did not register as being relevant in a scientific study. The researcher still tends to favour quantitative methodology, but as a result of this course he is more open to the consideration of the validity of individual experience and the recognition of the importance of feelings. The inclusion of qualitative methods in this study has thus contributed to a deepening of his personal growth in his approach to scientific study.

In the area of professional growth, the researcher was aware of feeling discomfort in the leadership module of the course, during a lecture on clinician-manager roles. The lecturer was drawing upon discussions in a series of seminars he had conducted with clinicians and managers on the subject of patient care. In general, clinicians tend to focus on individual benefit, having a more immediate responsibility for the care and well-being of patients, whereas managers tend to have a larger perspective, being responsible for the overall governance and day-to-day running of a particular department, and on the service as a whole. When these two groups are brought together within a work environment, tensions can arise if there is not a recognition that both views have their place and both need to understand how their roles inter-relate in service provision. The researcher realised that he was experiencing this tension within himself as a clinician-manager, a peculiar role, which he had not understood and certainly had not been prepared for when he took up the role. Consequently, the researcher believes that specialist training is needed to help clinicians
prepare for embarking on this dual role and responsibility. A course such as the DClinPrac is well suited to meet this need.

**Summary**

The DClinPrac course is ideal for clinician-managers undertaking research that involves evaluation of processes and the formulation of policy within healthcare. It is particularly suitable for those wishing to develop an understanding of the influences on health care provision, and how services within the NHS are organised.

Learning with students from other health disciplines enabled the researcher to obtain a broader perspective of health care generally and service delivery in particular. In addition, having supervisors from different disciplines of health care meant that when the study project changed from an exercise in monitoring service evaluation to a more clinical examination of patient experience, the different perspectives of the various teams of supervisors was advantageous in assisting the researcher in formulating the changes in the proposals.

The University of Surrey no longer offers the DClinPrac, but has replaced it with the Integrated PhD course which, while still maintaining core modules on leadership and health policy, allows more time for students to undertake research. It is also open to nurses and allied health professionals to enable inter-disciplinary learning. In addition, within the Government's Modernising Scientific Careers framework there is the Higher Specialist Scientific Training Scheme, which offers a Doctorate in Clinical Science (DClinSci) programme specifically for audiology clinicians (DH, 2015). Of these two new courses, the Integrated PhD appears to be more suited to audiologists who wish to develop managerial skills and contribute to health policy. But for those audiologists who wish to have more in-depth training in specialist audiology fields and to promote clinical research, it would seem that the DClinSci may be the more suitable option. (Word count: 2020).
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