ANGLIA RUSKIN UNIVERSITY

AN INTERNET INTERVENTION FOR TINNITUS

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Soli Deo Gloria

DEDICATION

To my two very special angels, Heidi and Charlotte.

May you be inspired to seize opportunities where adversity lies, follow your dreams and continually help others along the way

ABSTRACT

Objectives: Creative approaches to improve access to evidence-based tinnitus interventions are required. The purpose of this thesis was to address this need by developing an Internet-based cognitive behavioural therapy intervention (iCBT) specifically for those with tinnitus in the United Kingdom (UK). A unique aspect was providing audiological, instead of psychological guidance for those undertaking the intervention. Further objectives were to evaluate whether audiologist-guided iCBT could reduce tinnitus distress and tinnitus-associated comorbidities in a UK population.

Method: Initially an innovative iCBT tinnitus intervention adapted for a UK population was developed. The intervention was assessed for functionality and acceptability by both tinnitus professionals (n = 5) and adults with tinnitus (n = 29). A three-phase audiologist-guided clinical trial followed to evaluate feasibility (n = 39), efficacy (n = 146) and effectiveness (n = 92). In addition, the longer-term outcomes and unwanted effects were investigated (n = 104). A process evaluation was conducted parallel to the efficacy trial. Standardised self-reported assessment measures for tinnitus distress, insomnia, anxiety, depression, hearing disability hyperacusis, cognitive failures and life satisfaction were included.

Results: The developed intervention was rated as acceptable by both professionals and adults experiencing tinnitus. In Phase I, feasibility was established in terms of recruitment potential, attrition and adherence rates. In Phase II, efficacy was evident as undertaking iCBT led to a significant reduction in tinnitus distress and tinnitus-related comorbidities (insomnia, depression, hyperacusis, cognitive failures and increase in life satisfaction). These results remained stable up to 1 year post-intervention. Unwanted treatment effects were reported by 11% of participants. Process evaluation identified intervention aspects that facilitated and hampered the outcomes obtained. Phase III results were comparable regardless of receiving iCBT or individualised face-to-face care.

Conclusion: An acceptable iCBT tinnitus intervention was developed for a UK population. Original research has been undertaken, which has indicated the acceptability, feasibility, efficacy and effectiveness of audiologist-guided iCBT in reducing tinnitus distress and tinnitus-associated comorbidities in a UK population.

Keywords
Tinnitus; Internet-intervention; cognitive behavioural therapy; telehealth, clinical trial, process evaluation

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RESEARCH OUTPUT ASSOCIATED WITH THIS THESIS

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LIST OF ABBREVIATIONS

ANOVA:	Analysis of variance
BTA:	British Tinnitus Association
CBT:	Cognitive behavioural therapy
CFQ:	Cognitive Failures Questionnaire
CI:	Confidence interval
CONSORT:	Consolidated Standards of Reporting Trials
ENT:	Ear Nose and Throat
F2F:	Face-to-face
GAD-7:	Generalized Anxiety Disorder
GCBT:	Group-based cognitive behavioural therapy
GP/s:	General Practitioner/s
HADS:	Hospital anxiety and depression scale
HHIA-S:	Hearing Handicap Inventory for Adults-screening version
HQ:	Hyperacusis Questionnaire
iCBT:	Guided Internet-based cognitive behavioural therapy
ISI:	Insomnia Severity Index questionnaire
ITT:	Intention to treat
M:	Mean
MCAR:	Missing completely at random
NHS:	National Health System
NIHR:	National Institute for Health Research
PHQ-9:	Patient Health Questionnaire
RCI:	Reliable Change Index
rTMS:	Reletitive transcranial magnetic stimulation
SD:	Standard deviation
SPSS:	Statistical Package for Social Sciences
SPIRIT:	Standard Protocol Items: Recommendations for Interventional Trials
SWLS:	Satisfaction with Life Scales
TFI:	Tinnitus Functional Index
THI:	Tinnitus Handicap Inventory
THI-S:	Tinnitus Handicap Inventory–screening version
TRQ:	Tinnitus Reaction Questionnaire
tDCS:	Transcranial direct current stimulation
UK:	United Kingdom
USA:	United States of America

1 INTRODUCTION

This initial chapter outlines the research context and purpose of this thesis. It concludes by providing an overview of the subsequent chapters.

1.1 RESEARCH CONTEXT

Chronic health conditions place a substantial burden on healthcare organisations (West, 2012). One such condition is tinnitus, described as the conscious perception of unwanted sounds in the absence of a corresponding external acoustic stimulus (McFadden, 1982). Tinnitus is a prevalent complaint and one of the most distressing and debilitating audiological symptoms (Cima, Vlaeyen, Maes, Joore, & Anteunis, 2011). As no cure has been identified, treating tinnitus remains challenging and costly. The estimated annual healthcare cost related to tinnitus is £750 million, with a resulting societal cost of £2.7 billion per year in the United Kingkom (UK; Stockdale et al., 2017). Although specialist tinnitus services are in high demand, geographical and service constraints result in limited access to these services (Hoare, Broomhead, Stockdale, & Kennedy, 2015). Moreover, although various tinnitus management approaches exist, evidence for their efficacy is scarce (Hoare, Kowalkowski, Kang, & Hall, 2011). To date, cognitive behavioural therapy (CBT) has the most evidence of efficacy in reducing tinnitus distress (see Hesser, Weise, Westin, & Andersson, 2011a for a systematic review). Despite positive outcomes, there is limited accessibility to CBT for tinnitus, largely due to a shortage of suitably trained clinicians (Hoare et al., 2015; McFerran & Baguley, 2009). Creative approaches to improve accessibility to evidence-based tinnitus treatments are required (Hall, Mohamad, Firkins, Fenton, & Stockdale, 2013). Telehealth is increasingly used to provide accessible healthcare (Weinstein et al., 2014). Advantages of telehealth over face-to-face (F2F) treatment include convenience, accessibility, higher cost-effectiveness and the possibility of larger scale interventions (Andersson & Titov, 2014). To improve access to evidence-based tinnitus care an Internet-based CBT (iCBT) tinnitus intervention was pioneered at Linköping University, Sweden, by Andersson and Kaldo (Andersson, Strömgren, Ström, & Lyttkens, 2002). As this intervention indicated efficacy in reducing tinnitus distress (Andersson, 2015), it has been incorporated into regular care in Sweden (Kaldo et al., 2013; Kaldo-Sandström, Larsen, & Andersson, 2004). Although this approach shows promise, few examples of large scale dissemination of iCBT for tinnitus exist worldwide (Jasper et al., 2014a).

.

1.2 PURPOSE OF THIS THESIS

Identifying effective alternative tinnitus management strategies has been recognised as one of the top 10 research priorities by the James Lind Alliance (Hall et al., 2013). The use of iCBT is a possible candidate intervention. A culturally and linguistically suitable iCBT intervention for tinnitus in the UK was, however, not available. A further obstacle is provision of suitable guidance to the individuals undertaking the intervention. Guidance in previous iCBT for tinnitus trials has been offered by clinical psychologists, due to expertise in provision of CBT. Guidance from psychologists would not be feasible in a UK context where tinnitus is largely treated within the audiology community (McFerran & Baguley, 2009). Whether audiologist-guided psychological interventions for tinnitus are effective remains unknown, and assessing this has been identified as a further research priority by the James Lind Alliance (Hall et al., 2013).

To address these knowledge gaps, two broad objectives with six specific research questions were identified. The first objective of this thesis was to develop an iCBT intervention for a UK population. The second purpose was to evaluate the effectiveness of audiologist-guided iCBT in a three-phase clinical trial. This research has furthered knowledge regarding the acceptability, feasibility, efficacy and effectiveness of audiologist-guided iCBT for tinnitus management in the UK. This original research is important as it is in line with the tinnitus community's research priorities (Hall et al., 2013). Its uniqueness lies in the systematic methodological framework followed to address the research questions.

1.3 THESIS OUTLINE

This research has been divided into separate interlinking sections to answer the research questions. A brief summary of subsequent chapters is provided below.

Chapter 2 forms the literature review. It focuses on providing and understanding of tinnitus and the implications for intervention delivery to adults with tinnitus. Gaps in the literature are identified and form the basis for the selected research questions.

Chapter 3 presents detailed information regarding the carefully chosen methodology for this thesis. Reasons for the selected conceptual and scientific framework are provided.

Chapter 4 describes the development of an iCBT intervention for a UK population together with the functionality and acceptability thereof. It addresses the first research question determining how to develop iCBT to be an acceptable intervention that leads to positive outcomes.

Chapter 5 explores the second research question regarding the feasibility of audiologist-guided iCBT in terms of recruitment potential, attrition and adherence in a UK population.

Chapter 6 focuses on three research questions evaluating the short- and longer-term efficacy of audiologist-guided iCBT in reducing tinnitus distress and related comorbidities.

Chapter 7 addresses the final research question by comparing the clinical outcomes obtained with iCBT to the standard face-to-face individualised tinnitus care provided in the UK in the context of an effectiveness trial.

Chapter 8 shares the contribution to knowledge this three-phase clinical trial has provided together with the identified limitations and suggestions for further research.

Chapter 9 concludes this thesis by summarising the main research findings and unique contribution to knowledge they have made.

In conclusion, this introduction serves as an outline of the overall thesis. This work was performed entirely by the author. Advice from other professionals was sought where required. Guidance during the research was provided in the form of monthly supervisory meetings. Chapter 2 follows with the literature review pertaining to the complexities surrounding tinnitus and tinnitus interventions.

2 LITERATURE REVIEW

This literature review aims to provide a deeper understanding regarding the complexities surrounding tinnitus. The evidence base for tinnitus interventions is explored. Restrictions in current tinnitus care models are identified, highlighting the need for innovative intervention approaches. Knowledge gaps in the literature are ascertained and form the basis for the research questions on which the subsequent chapters of this thesis are grounded.

2.1 TINNITUS PERCEPTIONS

Providing evidence-based, clinically and cost-effective diagnosis and intervention routes is at the heart of healthcare (Greenhalgh, 2017). Due to scientific and technical advances, many health-related conditions are successfully managed (Durrani, 2016). These advances have also increased the possibility of addressing many auditory-related pathologies, including profound hearing loss (Gaylor et al., 2013). Despite this progress, one intriguing auditory-related symptom that continues to challenge health professionals is tinnitus (Baguley, McFerran, & Hall, 2013b). Historically, tinnitus has been defined as the conscious perception of unwanted subjective auditory sensations in the absence of a related external stimulus (McFadden, 1982). Tinnitus consists of separable clinical characteristics, such as its loudness, pitch, location, and the type of sound heard, of which various descriptions are found (Baguley, Andersson, McFerran, & McKenna, 2013a). It is known to be related to most dysfunctions involving the auditory system, with hearing loss and noise exposure being the most common causes of tinnitus (Møller, 2003). For those with hearing loss, the pitch of the tinnitus generally corresponds to the region of hearing loss (Sereda et al., 2011) or within the neighbouring frequencies (Moore et al., 2010). Due to the strong association between tinnitus and noise exposure, it would be intuitive to assume that tinnitus is a symptom of modern-day living. Interestingly, this is not the case. There is evidence of experiences of and interventions for these internally generated sounds in many historical medical texts, including Egyptian papyruses and clay tablets, dating back centuries (Stephens, 2000).

Tinnitus has also been associated with various non-auditory aetiologies including head and neck injuries, ototoxic drugs, vascular and cerebrovascular disease and autoimmune disorders (Baguley et al., 2013a), as shown in Table 2.1. These clinical or auditory indicators are, however, not necessarily required to initiate tinnitus. Tinnitus-like auditory perceptions have been reported in a large proportion of a non-clinical adult population by placing them in a soundproof booth (Bo et al., 2008; Heller & Bergman, 1953; Tucker et al., 2005).

Table 2.1 Known direct and indirect risk factors for developing tinnitus

Category	Type
Otological, infectious	Otitis media, labyrinthitis, mastoiditis, infections, inflammation
Otological, neuroplastic	Vestibular schwannoma, meningioma
Otological, labyrinthine	Sensorineural hearing loss, Ménière's disease, vestibular vertigo, otosclerosis, sudden deafness
Otological, other	Impacted cerumen, otosclerosis, presbyacusis, noise exposure
Neurological	Meningitis, migraine, multiple sclerosis, epilepsy
Traumatic	Head or neck injury or trauma, loss of consciousness
Orofacial	Temporomandibular joint disorder
Cardiovascular	Hypertension, cardiovascular and cerebrovascular disease
Rheumatological	Rheumatoid arthritis
Immune-mediated	Systemic lupus erythematosus, systemic sclerosis
Endocrine and metabolic	Diabetes mellitus, hyperinsulinaemia, hyper- and hypothyroidism, hormonal changes during pregnancy
Psychological	Anxiety, depression, emotional trauma
Ototoxic medications	Analgesics, antibiotics, antineoplastic drugs, corticosteroids, diuretics, immunosuppressive drugs, non-steroidal anti-inflammatory drugs, steroidal anti-inflammatory drugs, salicylate analgesics, nonsteroidal anti-inflammatory drugs, cardiac medications, chemotherapeutic agents
Demographic	Age, loud noise exposure, alcohol consumption, familial inheritance

Adapted from: Baguley et al. (2013a) and Hoffman & Reed (2004)

Those experiencing tinnitus may feel isolated, although in fact it is one of the most highly prevalent global chronic conditions. Around 10–30% of the adult population have tinnitus as seen from studies across the globe, for example from Egypt (Khedr et al., 2010), Italy (Gallus et al., 2015), Japan (Fujii et al., 2011; Michikawa et al., 2010) Korea (Kim et al., 2015), New Zealand (Wu, Searchfield, Exeter, & Lee, 2015) Nigeria (Lasisi, Abiona, & Gureje, 2010), the UK (Davis & Rafaie, 2000; Dawes et al., 2014) and the United States of America (USA; Bhatt, Lin, & Bhattacharyya, 2016; Shargorodsky, Curhan, & Farwell, 2010). Inconsistent definitions and measurements of tinnitus across prevalence studies make it difficult to determine the exact global prevalence of tinnitus (McCormack, Edmondson-Jones, Somerset, & Hall, 2016). Furthermore, since tinnitus has many forms, putting a

single number on prevalence rates may not be realistic or appropriate (Møller, 2011). The incidence of tinnitus is likely to continue to rise, due to factors such as an increase in life expectancy and recreational noise exposure (Martinez, Wallenhorst, McFerran, & Hall, 2015).

The effects of gender and age differences on tinnitus are not straightforward. A systematic review (39 studies in 16 countries) found a general rise in prevalence of tinnitus as age increased (McCormack et al., 2016). This pattern was seen until approximately 70 years of age, above which the prevalence either became constant or decreased slightly (Møller, 2011). Tinnitus prevalence among men is generally higher (see Figure 2.1). This may be partly due to the greater likelihood of previous occupational noise exposure for this gender (Lindgren, Wieslander, Dammström, & Norbäck, 2009). However, from 75 years of age, this gender difference becomes small. Women have been reported to perceive more complex tinnitus sounds (Dineen, Doyle, & Bench, 1997). It has also been reported that women with tinnitus are more likely to be prone to anxiety and depression (Ahmed, Ammar Ahmed, Akhtar, & Salim, 2017), and to experience more tinnitus annoyance and sleep interference (Seydel, Haupt, Olze, Szczepek, & Mazurek, 2013). Tinnitus annoyance was reported to decrease in older men (over 60 years of age), but not in older women, who again reported more sleep disturbances than older men (Seydel, Haupt, Olze, Szczepek, & Mazurek, 2013).

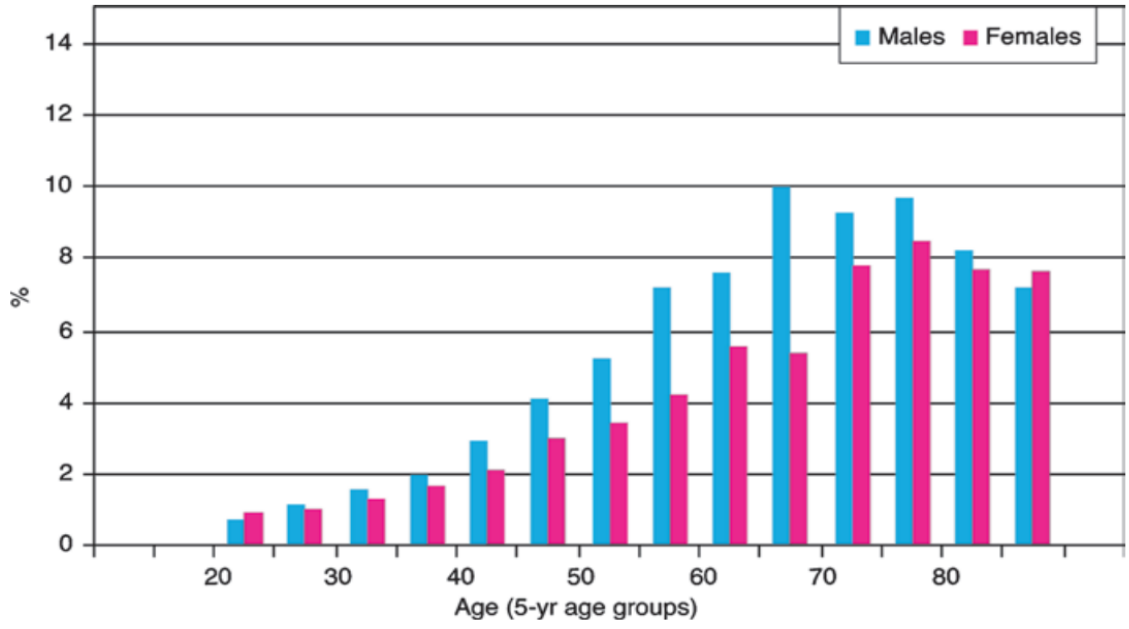


Figure 2.1 Age and gender prevalence data of chronic tinnitus. From: the 1994–1995 (n = 99,435) US National Health Interview Survey (Hoffman & Reed, 2004). Permission to reproduce granted by Decker Publications, November 2017.

The number of unanswered questions regarding tinnitus has caused major challenges for the tinnitus research and clinical practice communities. These include (i) understanding why

some people are distressed by tinnitus and others are not; (ii) determining why some develop tinnitus whereas others do not; (iii) finding a cure to eliminate tinnitus; and (iv) identifying how to manage tinnitus and the associated comorbidities. Each of these aspects will be explored in the subsequent sections.

2.2 REACTIONS TO TINNITUS

A tinnitus paradox often reported is the range of individual reactions following the onset of tinnitus (Andersson & Westin, 2008). The majority of people with tinnitus do not find having tinnitus problematic. Some, however, have strong reactions to tinnitus (Brüggemann et al., 2016). Results of a National Study of Hearing in England (n = 48,313) found 2.8% of the study population described their tinnitus as moderately annoying, 1.6% explained it was severely annoying and 0.5% were unable to lead a normal life due to the severity of the tinnitus (Davis & Rafaie, 2000). Those who were severely distressed reported an inability to work and a small minority may contemplate suicide (Pridmore, Walter, & Friedland, 2012), although there is a lack of evidence indicating a direct link between tinnitus and suicide (Jacobson & McCaslin, 2001). A higher prevalence of psychiatric disorders, especially anxiety and depression, has been noted in those with distressing tinnitus (Geocze, Mucci, Abranches, de Marco, & de Oliveira Penido, 2013; Hymowitz, 2016; Langguth, Landgrebe, Kleinjung, Sand, & Hajak, 2011; Pinto et al., 2014). Some factors have been identified as possible predictors to finding tinnitus distressing. These include an initially unpleasant perception of tinnitus, recent tinnitus onset, unilateral tinnitus, reduced well-being following the onset of tinnitus, lack of coping ability, sleeping difficulties, depressive disorder, older age, male gender, and social isolation (Alhazmi, Kay, Mackenzie, Kemp, & Sluming, 2016; Nondahl et al., 2011; Olderog, Langenbach, Michel, Brusis, & Kohle, 2004; Schmitt, Patak, & Kröner-Herwig, 2000). Those finding tinnitus debilitating report it has an impact on their quality of life (Henry, Dennis, & Schechter, 2005). Moreover, they explain that many aspects of daily life may be disrupted. These include sleep and concentration difficulties, and indirect psychosocial effects, such as feelings of hopelessness, irritability, frustration, anxiety, and depression (Holmes & Padgham, 2009; Langguth, 2011). The presence of insomnia has for instance been found to be present in 25%–76% of those with tinnitus (see Andersson, Lyttkens, & Larsen, 1999; Crönlein, Langguth, Geisler, & Hajak, 2007; Lasisi & Gureje, 2011; Schecklmann et al., 2015). Difficulties concentrating due to tinnitus can affect cognitive performance, reading competence and working memory (see Andersson, Eriksson, Lundh, & Lyttkens, 2000; Hallam, McKenna, & Shurlock, 2004; Rossiter, Stevens, & Walker, 2006). In addition, tinnitus is often accompanied by increased sound sensitivity (hyperacusis), misophonia (dislike of certain sounds) and phonophobia (fear of certain sounds) (Baguley & Andersson, 2008). Hyperacusis is reported in up to 40% of those with tinnitus, and 86% of those who

have hyperacusis also report tinnitus (Andersson, Lindvall, Hursti, Carlbring, & Andersson, 2002).

These comorbidities increase the burden of tinnitus and can affect relationships with significant others (Granqvist, Lantto, Ortiz, & Andersson, 2001). Tinnitus is consequently more than its psychophysical characteristics as it is often accompanied by great distress (Holmes & Padgham, 2009; Langguth, 2011). Tinnitus is a complex percept encompassing multiple separable clinical, cognitive and emotional aspects (De Ridder, Vanneste, & Freeman, 2014). This is often noticeable in people's descriptions of tinnitus such as "most of the time my tinnitus sounds like a ringing sound, but sometimes it changes to a rushing low-pitched sound. It drives me slowly crazy and is really quite depressing. I feel I can't cope with it."

2.3 WHY PEOPLE DEVELOP TINNITUS

A further tinnitus complexity is why some people develop tinnitus and others do not. This has led to an ongoing search for possible mechanisms and models of tinnitus. Current theories propose pathophysiology from the ear to wider cortical networks. An understanding of these mechanisms is fundamental as it forms the foundation for tinnitus management in terms of cures and interventions. For the purpose of this thesis, tinnitus mechanisms will be discussed in two broad categories: firstly, mechanism associated with tinnitus generation and perception, followed by mechanisms associated with not only the perception but also tinnitus reactions.

2.3.1 Mechanisms addressing tinnitus generation and perception

Initial models considered peripheral auditory system damage to cause tinnitus (Eggermont, 1990). Evidence was based on tinnitus being strongly linked with the presence of damaged hearing, as has been frequently reported (for example by Tan, Lecluyse, McFerran, & Meddis, 2013). Other models advocated that the reduced afferent input from auditory areas of damage led to reduced inhibitory responses and increased excitatory function within the central auditory pathways (Gerken, 1996). They proposed a surge in the spontaneous firing of auditory and central nerve fibres, a rise in cortical neural synchrony, and/or increased central gain (Eggermont, 2003). Further models associated tinnitus not only with the auditory system but also with non-auditory neural pathways. The prominent neurophysiological model (Figure 2.2) by Jastreboff (1990), was one of the earlier models to stress these associations. This model explained the emergence of tinnitus in three stages: generation, detection and tinnitus perception and evaluation. Generation was attributed to many different causes including discordant damage of outer and inner hair cells, crosstalk between auditory nerve fibres, ionic imbalance in the cochlea and dysfunction of cochlear neurotransmitter systems. Detection was explained to be based on a pattern recognition principle of decoding auditory information by neural network

mechanisms. The perception and evaluation process was proposed to involve memory, as well as cortical pathways and the limbic system. In the majority of cases, the abnormal activity that causes tinnitus is classified as a neural stimulus and thereby blocked from reaching conscious perception (habituation). However, when the abnormal activity is classified as important, the limbic and autonomic nervous systems are activated by such neural activity. The initial lack of auditory input results in a negative feedback loop as seen in Figure 2.2 (Jastreboff, 1990; Jastreboff & Hazell, 1993; Jastreboff, Hazell, & Graham, 1994; Jastreboff, Gray, & Gold, 1996). Although ground-breaking and instrumental in improving tinnitus management (Jastreboff & Hazell, 2008), some aspects of the model have been criticised, as they are not well supported. It does not, for instance, explain the temporal properties and actual moment when aversive reactions become conditioned (Mckenna, 2004). Personal attributes such as personality are also marginalised and the model cannot explain why tinnitus becomes bothersome to some and not to others, or why tinnitus may be resistant to habituation (Kröener-Herwig et al., 2000).

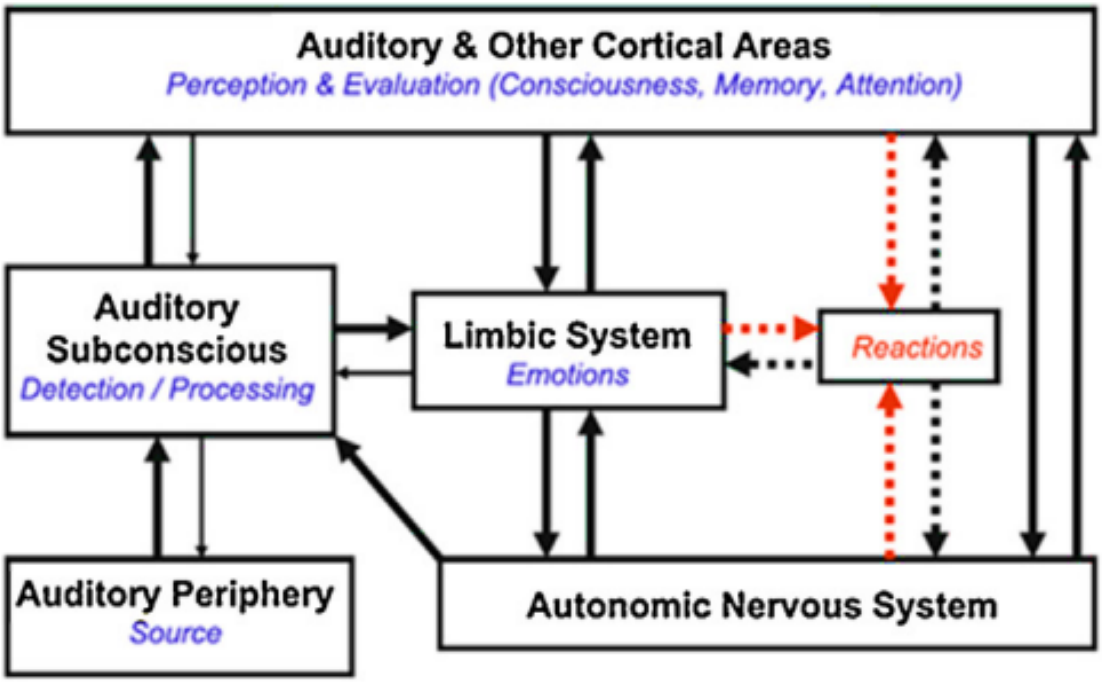


Figure 2.2 The neurophysiological model of tinnitus. Proposed and published in Jastreboff et al. (1996). Reproduced in De Ridder et al. (2014). Neuroscience & Biobehavioral Reviews, 44, 16-32. Permission to reproduce under licence number 4211861149103.

Animal models of tinnitus have contributed to the understanding of the neuroscience and pathophysiology of tinnitus (Brozoski & Bauer, 2016). Methodologies have broadly been either interrogative (using psychophysical procedures, generally based on conditioned behaviour) or reflexive (hearing based on an elicited reflex). Jastreboff and colleagues (1988), pioneered the first animal-based tinnitus model. Models such as those from Bauer

(2003) and Eggermont (2013) followed. Although an interaction between tinnitus and auditory attention has been modelled (Kalappa, Brozoski, Turner, & Caspary, 2014; Sametsky, Turner, Larsen, Ling, & Caspary, 2015), it has been difficult to identify emotional and cognitive factors associated with tinnitus when using animal models (Brozoski & Bauer, 2016).

More recently, it has been suggested that the brain actively fills in missing auditory information in a predictive way, using memory mechanisms to diminish auditory uncertainty (De Ridder et al., 2014). Furthermore, it has been proposed that the reduced afferent input focuses attention on the disparity of what is predicted to be heard and what acoustic information is in reality heard. This activates a system for auditory attention leading to neuroplastic changes (Roberts, Husain, & Eggermont, 2013). Based on this theory, an integrative model depicting a hierarchical organisation of neurons has been put forward (Sedley, Friston, Gander, Kumar, & Griffiths, 2016). This hierarchical organisation creates predictions of neural states and errors when there are deviations from these expected states. Within this integrative model, hearing loss is a tinnitus precursor. Tinnitus, however, emerges only when its level rises sufficiently to override the default percept of 'silence'. Perceptual inference mechanisms learn to expect tinnitus and thereby engage connections in the parahippocampal cortex. Once these connections are made, chronic tinnitus occurs.

Although these models have advanced understanding of tinnitus in relation to hearing loss and the auditory system, many unanswered questions remain. They do not account for the fact that tinnitus is not always associated with measurable hearing loss (Schaette & McAlpine, 2011) or that those with hearing loss do not necessarily have tinnitus (Martines, Bentivegna, Martines, Sciacca, & Martinciglio, 2010). These questions have led to examining those with tinnitus and no measurable hearing loss on traditional audiometry. Findings demonstrated possible reduced electrical responses (i.e. hidden hearing loss) to sound stimulation generated by the auditory nerve (Schaette & McAlpine, 2011). Hidden hearing loss has recently been theorised to be responsible for tinnitus generation (Paul, Bruce, & Roberts, 2017), although findings have not been consistent (Guest, Munro, Prendergast, Howe, & Plack, 2017). A prominent shortfall of all these models is that they only account for tinnitus generation and cannot explain the reactions to tinnitus.

2.3.2 Mechanisms addressing tinnitus reactions

Emotional reactions to tinnitus have been observed for many years (e.g. Fowler, 1948). In an attempt to explain the variation in peoples 'reactions' to tinnitus, the habituation model by Hallam and colleagues was proposed (Hallam, Rachman, & Hinchcliffe, 1984). This model considered tinnitus to arise from the auditory system at any point between the

periphery and cortex. The model suggests that, like any repetitive stimulus, hearing tinnitus should lose its novelty. This would lead to a process of habituation, defined as a decline in the reactions to, and the perception of, tinnitus over time. Habituation should occur naturally so that perceiving tinnitus no longer results in a negative emotional response and does not affect day-to-day functioning. Habituation may, however, be disrupted in certain situations leading to dishabituation. Dishabituation would result in persistence of tinnitus due to a reduced ability to filter out and ignore tinnitus-related information. This may occur when tinnitus is associated with high levels of arousal or stress. In these situations, the combined states of high central and autonomic nervous system arousal lead to emotional significance being associated with perceiving tinnitus. This results in chronically intrusive tinnitus.

Due to the proposed influence of stress in the habituation model, further models were based on tinnitus persistence involving not only auditory systems, but also wider non-auditory systems. The cognitive model by places emphasis on the role of cognitive processes in the reaction to tinnitus, in opposition to the unconscious conditioning of the neurophysiological model (McKenna, Handscomb, Hoare, & Hall, 2014). It suggests that the key components in maintaining tinnitus distress are negative appraisal of tinnitus, arousal and distress, selective attention and monitoring, erroneous beliefs, counterproductive safety behaviours and unfavourable perceptions of tinnitus (Figure 2.3).

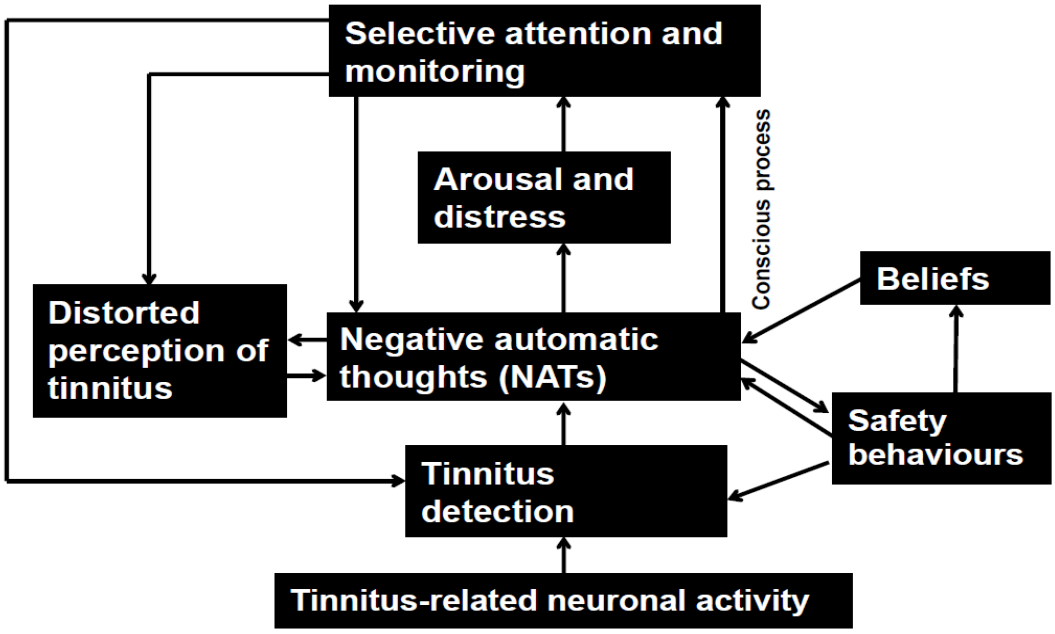


Figure 2.3 A cognitive model of tinnitus. Figure as originally published in McKenna et al. (2014). Frontiers in Neurology, 5. Unrestricted permission to reproduce obtained under Frontiers CC-BY 4.0 licence.

These models have transformed the notion of tinnitus being associated only with the peripheral and central auditory system. They suggest additional involvement of non-auditory

areas, such as areas associated with awareness and salience detection. De Ridder and colleagues (2014) suggested that higher perceptual overlapping networks are involved in tinnitus generation, localisation, tinnitus type and tinnitus-related distress. These areas have been mapped onto the neurophysiological model, as seen in Figure 2.4. Cortical areas representing distress and mood such as the amygdalae, anterior cingulate and anterior insula have been shown to be more active in those with chronic tinnitus (Vanneste, van de Heyning, & De Ridder, 2011). This may partly account for why some people with hearing loss develop tinnitus whereas others do not (De Ridder et al., 2014).

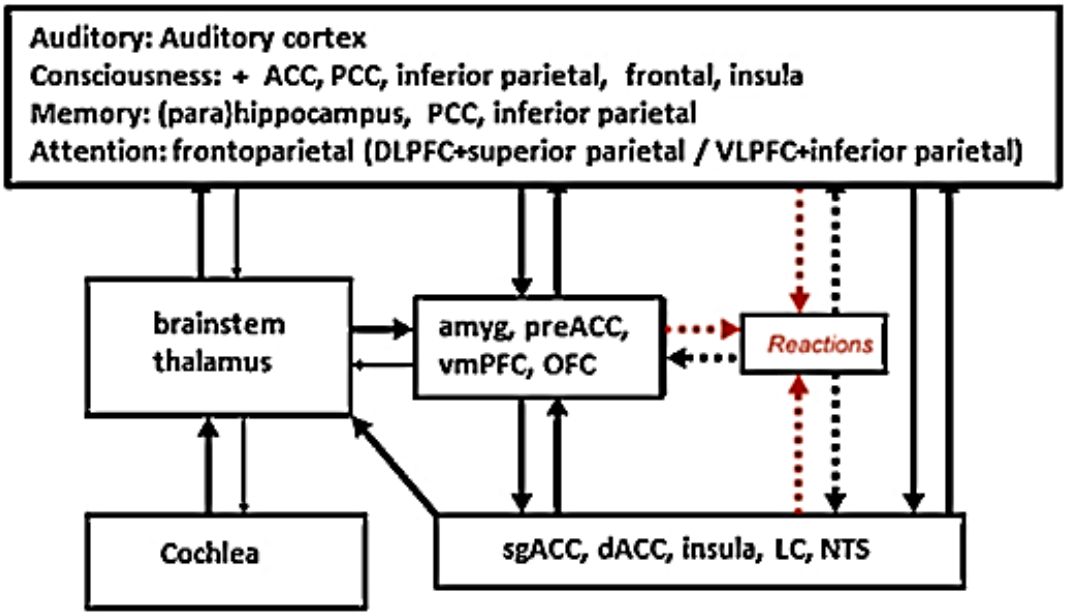


Figure 2.4. Brain areas associated with tinnitus. Originally published by De Ridder et al. (2014). Neuroscience & Biobehavioral Reviews, 44, 16-32. Permission to reproduce under licence number 4211861149103.

Acronyms: *ACC: Anterior Cingulate Cortex, PCC: Posterior Cingulate Cortex, DLPFC: Dorsolateral Prefrontal Cortex, VLPFC: Ventrolateral Prefrontal Cortex, Amyg: Amygamygdala, PreACC: Pregenual Anterior Cingulate Cortex, vmPFC: Ventromedial Prefrontal Cortex, OFC: Orbitofrontal Cortex, LC: Locus Coeruleus, and NTS: Nucleus Tractus Solitarius.*

Functional and anatomical changes in the audiotry cortex and non-auditory areas in people experiencing tinnitus (see Figures 2.5 and 2.6), have been supported by some imaging studies, although contradictory results exist (see Allan et al., 2016; Meyer et al., 2016; Schneider et al., 2009, Yoo, De Ridder, & Vanneste, 2016). There have been indications of tinnitus-related gender differences in imaging studies (Shlamkovich, Gavriel, Eviatar, Lorberboym, & Aviram, 2016; Vanneste, Joos, & De Ridder, 2012). Differences include

increased functional connectivity in females between the auditory cortex and areas such as the orbitofrontal cortex, insula, subgenual anterior cingulate and parahippocampal areas (Vanneste et al., 2012). In men, increased uptake in the upper temporal gyrus has been found. Moreover, many analogies between tinnitus and central neuropathic pain have been identified (Møller, 2007). This has led to a model of tinnitus being generated as a consequence of a dysfunctional noise-suppressing mechanism, which could be limbically driven (Leaver et al., 2011). This model proposes that the limbic system may be responsible for the generation and reaction towards tinnitus, as both loudness percept and distress are modulated by the limbic system. Thus, emotional state can influence loudness perception of tinnitus and vice versa.

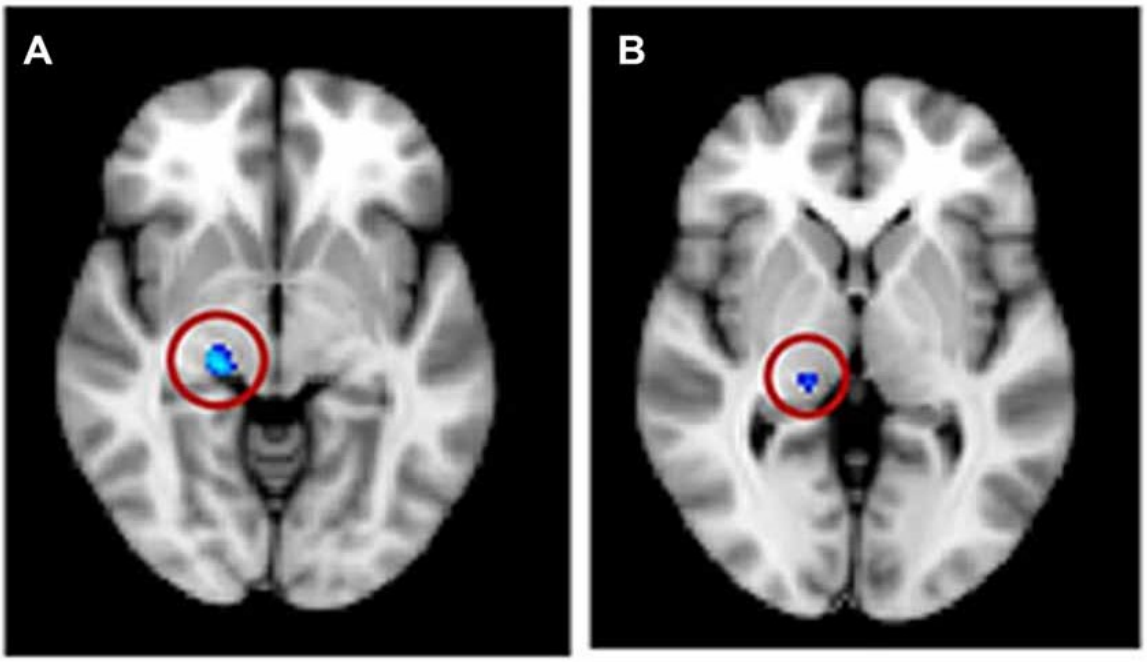


Figure 2.5 Functional changes due to tinnitus. Reduction in white matter for tinnitus participants (B) compared with controls (A) found in the medial geniculate nucleus (MGN). Figure originally published in Allan et al. (2016). Frontiers in Aging Neuroscience, 8. Unrestricted permission to reproduce obtained under Frontiers CC-BY 4.0 licence.

In summary, current tinnitus models focus on both the 'perception of and the 'reaction to' the tinnitus. Tinnitus generation appears to be an emergent property of multiple, parallel, dynamically changing and partially overlapping subnetworks encoding specific aspects of the tinnitus percept (De Ridder et al., 2014). The presence of a prominent signal (the tinnitus) creates focus and commands attentional resources feeding into non-sensory cognitive processes strongly associated with tinnitus distress (Vanneste et al., 2011). Emotional centres of the brain are activated and responsible for maintaining the tinnitus and defining the 'reaction' to hearing tinnitus. Some models suggest that variations in reactions to tinnitus are not directly related to the psychophysical characteristics of the tinnitus such

as loudness or pitch (Andersson et al., 1999; Wallhäußer-Franke et al., 2012), but instead to the psychological interpretation of the tinnitus (Henry & Wilson, 2001).

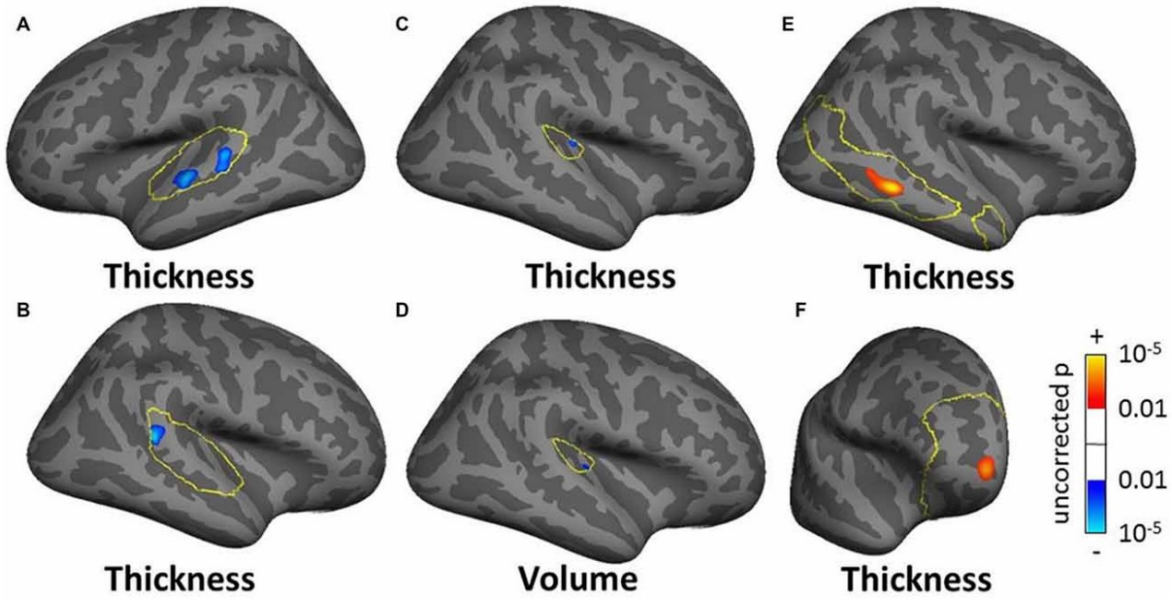


Figure 2.6 Anatomical changes due to tinnitus. Changes due to tinnitus in the auditory cortex (A), superior temporal sulcus (B), Heschl's gyrus (C and D), middle temporal gyrus and pre-frontal cortex (E and F). Blue areas correspond to a decrease in thickness or volume for the tinnitus group vs. the control group) and red areas to a positive effect (increasing thickness for increasing tinnitus severity). Figure originally published in Allan et al. (2016). Frontiers in Aging Neuroscience, 8*. Unrestricted permission to reproduce obtained under Frontiers CC-BY 4.0 licence.*

2.4 FINDING WAYS OF ELIMINATING TINNITUS

Finding a way to fully eliminate tinnitus is the ultimate goal of tinnitus research. The search for both pharmaceutical and non-pharmaceutical cures is ongoing. When investigating tinnitus cures, tinnitus related to otological pathologies and non-pathological tinnitus are considered separately.

Otological pathologies giving rise to tinnitus include otosclerosis, conductive hearing loss, Ménière's disease, pulsatile tinnitus, cerebellopontine angle and vestibular schwannoma lesions, superior semicircular canal dehiscence and myoclonus (Baguley et al., 2013a). Treatments may target different subtypes of tinnitus, such as pulsatile tinnitus (rhythmic pulsating in time with heartbeat) or somatosensory tinnitus (modulated by physical contact or movement) (Haider et al., 2017). Medical, surgical and pharmacological interventions associated with these pathologies may be indicated and sometimes they remove or reduce tinnitus perception (Allman, Schormans, Typlt, & Lobarinas, 2016). Unfortunately, in many

cases tinnitus is found to persist despite surgical interventions including auditory nerve section and vestibular schwannoma resection (Bell, Anderson-Kim, Low, & Leonetti, 2016).

For non-pathological tinnitus, pharmacological interventions have been used to attempt to eliminate tinnitus. As they can modulate neural activity, it is logical to reason that they could be effective at removing tinnitus (Allman et al., 2016). Furthermore, the similarities between the phantom nature of tinnitus and neurological pain suggest that some of the same agents might work to alleviate tinnitus. A wide range of pharmacological agents including vasodilators, calcium antagonists, antidepressants antispasmodic drugs, local anaesthetics, anticonvulsants, and benzodiazepines have been tested unsuccessfully on those with tinnitus (Beebe Palumbo, Joos, De Ridder, & Vanneste, 2015). Some placebo-controlled double-blind studies report improvements in tinnitus distress, but a reduction in tinnitus was found for both the pharmaceutical and placebo, with no difference between the treatments (for example Lee et al., 2017a). Although taking a tablet would be the intervention of choice for the majority of those with tinnitus, there is as yet no licensed pharmacological drug to eliminate non-pathological tinnitus (Langguth & Elgoyhen, 2012). This is possibly related to its heterogeneous aetiology, its varied clinical presentation and the incomplete understanding of its mechanisms and pathophysiology (Elgoyhen et al., 2015). The fact that an increasing number of pharmaceutical companies are developing compounds for tinnitus is encouraging.

Where medical interventions are not applicable or effective, tinnitus needs to be managed as a chronic condition. Many non-medical interventions are directed towards alleviating or managing the accompanying symptoms, making the tinnitus less intrusive or distressing.

2.5 TINNITUS MANAGEMENT

At the onset of tinnitus, most people search for a means to permanently alleviate this bothersome symptom (Fackrell, Hoare, Smith, McCormack, & Hall, 2012). Hopes are often shattered following Internet searches or initial contact with health professionals explaining that no such cure exists. People fail to realise there are various ways to help them manage tinnitus and its associated comorbidities. They, therefore, often revert to safety or avoidance behaviours to minimise the perceived threat of altering or exacerbating tinnitus. These behaviours are often associated with greater distress and poorer long-term outcomes (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996; McKenna et al. 2014).

The challenge of tinnitus interventions is to address its multidimensional nature, encompassing clinical, cognitive and emotional aspects. Although tinnitus mechanisms are still not completely understood, it is generally thought that different dynamic overlapping brain networks should be considered as targets for tinnitus interventions. Integral to most

interventions is a core involving directive counselling to educate and provide reassurance, as recommended in most current tinnitus practice guidelines (Fuller et al., 2017). New therapeutic options, based on increased knowledge of tinnitus mechanisms are constantly being explored. These include electrical, magnetic, sound, vibration and laser stimulation modalities. In addition, complementary approaches to managing tinnitus, including mind-body therapies, biofeedback and acupuncture are increasingly available (Wolever et al., 2015). The next sections search for evidence-based ways of managing tinnitus, among the more widely used approaches.

2.5.1 Medical interventions

Pharmaceuticals are often prescribed to reduce the effect of tinnitus and/or its associated comorbidities. These are intended either to help directly or to have a secondary effect of improving associated difficulties. In the UK, 49% of general practitioners (GPs) and 19% of ear nose and throat (ENT) specialists prescribe pharmaceuticals for acute tinnitus (Hall et al., 2011). Fewer professionals recommend pharmaceuticals for chronic tinnitus (Hall et al., 2011). Pharmaceuticals used include sleep medication, muscle relaxants and antidepressants (Baldo, Doree, Molin, McFerran, & Cecco, 2012). Herbal supplements such as zinc, vitamin B12, melatonin and ginkgo biloba are sometimes suggested for their perceived benefits for sleep, emotional states, concentration and tinnitus reduction. Although they could have a positive outcome in some cases, robust evidence of their effectiveness is lacking (Coelho et al., 2016). Therefore, current practice guidelines (where in existence in Europe and the USA) do not recommend the use of medication or herbal supplements to treat tinnitus itself (Fuller et al., 2017).

Various forms of stimulation targeting one or more (bimodal) modalities have been suggested as a possible intervention. Bimodal stimulation using sound together with trigeminal nerve (Hamilton et al., 2016), vagus nerve (De Ridder, Kilgard, Engineer, & Vanneste, 2015; Shim et al., 2015) and somatosensory (Jonsson, Bohman, Shekhawat, Kobayashi, & Searchfield, 2016) stimulation has been trialled. Much research interest has also been focused on repetitive transcranial magnetic stimulation (rTMS) (see Soleimani, Jalali, & Hasandokht, 2016 for a meta-analysis) and transcranial direct current stimulation (tDCS) (see Hoare, Adjamian, & Sereda, 2016 for a scoping review). Studies are varied, as they explore important questions such as the optimum site and duration of the intervention and the effects of bimodal stimulation including muscle stimulation (Schecklmann, Poeppl, Kreuzer, & Langguth, 2017) or counselling in the form of CBT (Richter, Acker, Lence Miloseva, & Niklewski, 2017). Although some moderate benefit has been indicated, especially regarding repetitive transcranial magnetic stimulation, numerous concerns remain. These include the quality of the methodologies followed and possible auditory system damage, as loud clicks are currently generated (peak levels greater than 140dB SPL) (Peterchev, Murphy, & Goetz, 2015). Current practice guidelines, from Germany, The

Netherlands and the USA, therefore, caution that there is insufficient evidence to recommend the use of rTMS and tDCS at present (Fuller et al., 2017).

2.5.2 Sound-based interventions

Sound-based interventions refer to the clinical use of sound to alter tinnitus perception and/or the reactions to tinnitus in a clinically meaningful way. The use of sound to change the intrusiveness of tinnitus was first mentioned in the medico-scientific literature in 1821 by Jean-Marie Itard (Stephens, 2000). Sound-based interventions encompass a heterogeneous range of intervention strategies. In addition to counselling, sound-based interventions are at the core of many tinnitus management programmes. They aim to make the tinnitus less noticeable, provide immediate relief, promote control, lead to habituation and shift attention from the tinnitus. The neurophysiological mechanisms associated with use of sound are presumed to promote plastic change in the central auditory system (Hoare, Searchfield, El Refaie, & Henry, 2014b). The main sound-based therapeutic approaches are discussed below.

2.5.2.1 Masking

Sound therapy devices with the purpose of 'masking' the tinnitus with a more acceptable sound were introduced by Vernon in 1976 (Vernon, 1987). This technique was later replaced by partial masking, using sound at a level low enough to maintain the usual perception of tinnitus (Jastreboff, 2007). Both table-top and ear-level sound generators can be used as a means of masking using sound enrichment. Various sounds have been suggested, ranging from white noise to nature sounds and music. A preference for some form of natural sound, such as running water, has been reported in some smaller-scale studies (Barozzi et al., 2016; Handscomb, 2006). Despite these accounts, little evidence exists for the efficacy of sound-based masking approaches on tinnitus (Hoare, Kowalkowski, Kang, & Hall, 2011).

2.5.2.2 The use of amplification

As tinnitus is often accompanied by hearing loss, some interventions aim to address both symptoms simultaneously (Searchfield, Kaur, & Martin, 2010). Hearing aids have been used to treat tinnitus as early as the 1940s (Saltzman & Ersner, 1947). Hearing aids amplify external sounds, lowering the contrast between tinnitus perception and the external sounds, thereby diminishing the relative salience of tinnitus. Moreover, they refocus attention on sounds that are different from the tinnitus sound. Additionally, they can improve hearing function and communication, which can assist in diminishing the effects of tinnitus. They act as a form of sound enrichment, decreasing sensory deprivation and neuroplastic changes within the central auditory system contributing to tinnitus generation. It is uncertain to what extent hearing aids produce a change in reactions to tinnitus (Hoare, Edmondson-Jones, Sereda, Akeroyd, & Hall, 2014a). Combination devices are also available, providing both

amplification and sound-enrichment. A few trials, (for example Henry et al., 2017a), have started to compare the effects of hearing aids with more sophisticated combination devices. Technological advances in smartphones have enabled apps that adjust hearing aids according to the needs of both tinnitus and hearing loss. Sound or music can also be streamed to the hearing aids wirelessly via Bluetooth connection.

Those with tinnitus, often report that hearing aids are beneficial (Aazh, Moore, Lammaing, & Cropley, 2016; Zarenoe, Hällgren, Andersson, & Ledin, 2017). Despite these accounts, little evidence exists for their efficacy for tinnitus reduction (Hoare et al., 2011). This is partly due to a lack of clinical trials, difficulty separating the various components of therapy, and the heterogeneity of the available devices and how these are fitted. In current practice guidelines, the use of hearing aids is only recommended for patients experiencing hearing loss, and not for those with tinnitus in isolation (Fuller et al., 2017)

Cochlear implantation also holds the potential to reduce the percept of tinnitus in some patients, although more evidence is required (Blasco & Redleaf, 2014; van Zon, Peters, Stegeman, Smit, & Grolman, 2015). Questions remain regarding the specific domains of tinnitus-related burden that implantation is likely to address, the type of stimulation to use and who is most likely to benefit. While cochlear implantation holds potential, it may not always be a cost-effective, feasible and acceptable intervention for many individuals at present.

Some therapies use a mixture of directive counselling and sound therapy. One is tinnitus-retraining therapy (TRT), which has its roots in the neurophysiological model of tinnitus (Jastreboff & Hazell, 1993). This structured approach uses continuous sound enrichment below the level of the tinnitus (below the mixing point) together with counselling. Questions remain as to the effectiveness of the different components of TRT in the absence of large-scale randomised controlled trials at present (Phillips & McFerran, 2010). A simplified version of TRT, for instance, was shown to be as effective as traditional TRT, indicating that the duration and type of counselling in TRT do not play critical roles in outcomes (Aazh & Moore, 2016).

2.5.2.3 Novel sound therapies

Various innovative sound therapies are currently being developed, such as nocturnal sound stimulation (Drexler et al., 2016). Neuromonics tinnitus treatment is another sound-based therapy built on the principles of systematic desensitisation. This approach uses spectrally-modified music to acoustically desensitise the tinnitus percept. Comparison of these devices with ear-level sound generators have found similar outcomes (Newman & Sandridge, 2012). Ear-level devices are currently the preferred choice as they are the least expensive option. A further innovative approach is altering the frequency spectrum of music but filtering out sound energy (using notched filters) at the frequencies corresponding to the tinnitus pitch.

This spectrally alters music with the rationale of reversing maladaptive cortical reorganisation of the frequency range surrounding the tinnitus. Much research in this area is still required. Some small studies suggest promise (Kim et al., 2017; Lee, Choi, Chang, & Cho, 2017b; Li, Bao, & Chrostowski, 2016) although tinnitus distress was not reduced in a larger controlled trial (Stein et al., 2016).

A further unconventional approach is the use of acoustic co-ordinate reset neuromodulation that attempts to counter the disruption of pathological neural synchrony thought to be responsible for tinnitus generation. It involves listening to a sequence of tones around the frequency corresponding to the tinnitus pitch for up to eight hours a day. The rational is to force the asynchronous firing of neurons (Tass, Adamchic, Freund, von Stackelberg, & Hauptmann, 2012). A systematic review (Wegger, Ovesen, & Larsen, 2017) indicated that robust evidence for this approach is lacking.

The request for sound-based interventions from GPs and ENTs is common, particularly in the UK. Referral rates from GPs and ENTs are 14% and 38% respectively for TRT and 14% and 43% respectively for acoustic devices for acute tinnitus (Hall et al., 2011). In cases of chronic tinnitus these percentages increase. Despite this, there remains much debate regarding the usefulness of sound-based interventions for tinnitus (Hobson, Chisholm, & El Refaie, 2012; Mckenna & Irwin, 2008). Regrettably, there are few large-scale controlled studies to support or refute many of the sound-based therapeutic options currently in use, amounting to considerable gaps in our evidence base (Hoare et al., 2011). A Cochrane review (an independent systematic review) evaluating the effectiveness of sound-generating devices concluded that although sound therapy appears to be a useful approach, the heterogeneity in the evaluations precludes meta-analysis of data (Maldonado Fernández, Shin, Scherer, & Murdin, 2015). The absence of conclusive evidence should, however, not be interpreted as evidence of lack of effectiveness (Hobson et al., 2012).

2.5.3 Psychological interventions

Psychological interventions were introduced, due to the high prevalence of psychological distress (including anxiety and depression) among those with significant tinnitus (Fagelson, 2007; Goebel & Floezinger, 2008; Langguth et al., 2007a; Marciano et al., 2003). Cognitive models of tinnitus imply that addressing negative automatic thoughts, reducing sympathetic autonomic nervous system activity, diminishing selective attention, and correcting distorted perception and inaccurate beliefs surrounding tinnitus are important to reduce the reactions to tinnitus (Andersson, 2002). This belief has led to the rise of psychological interventions that target unhelpful thoughts about tinnitus and thereby change an individual's reaction towards their tinnitus. These originate from cognitive therapy that was developed by Aaron Beck in the 1960's. This followed his clinical observations and some systematic clinical studies identifying a thinking disorder at the core of psychiatric problems such as depression

and anxiety (Beck, 1976). Distorted, negative cognition (primarily thoughts and beliefs) and a systematic bias in the individual's interpretation of particular experiences were identified. Cognitive therapy then aimed to modify maladaptive behaviours and cognitions, and propose alternatives. Cognitive therapy is seen as a first-wave psychological treatment from which CBT, often described as a second-wave psychological intervention, developed. CBT is directed towards altering maladaptive responses to tinnitus (inaccurate and/or unhelpful thinking) through behaviour modifications. It addresses the emotional reaction and problems related to having tinnitus and not the tinnitus itself. Third-wave interventions such as mindfulness-based stress reduction (MBSR) and acceptance and commitment therapy (ACT) were later introduced for tinnitus. The evidence base for psychological approaches for tinnitus is described in the subsequent sections.

2.5.3.1 Cognitive behavioural therapy (CBT)

CBT has been effectively used for many psychological conditions related to tinnitus, such as anxiety, depression and insomnia, as well as for related conditions such as chronic pain and chronic health conditions (see systematic reviews by Cuijpers et al., 2013; Hind et al., 2014; Hutton & Taylor, 2014; Jauhar et al., 2014; Trauer, Qian, Doyle, Rajaratnam, & Cunnington, 2015). Due to the relationship between tinnitus and psychological distress (McCormack et al., 2015), CBT has been applied as an integrative and pragmatic treatment approach for tinnitus for decades (see Hallam, Jakes, & Hinchcliffe, 1988; Scott, Lindberg, Lyttkens, & Melin, 1985; Sweetow, 1986; Sweetow, 1995). It is a structured approach incorporating goal setting, a timeframe for completion (generally 6–10 weeks), active participation, relapse prevention and assignments between sessions (Beck, 2011). Individuals are generally supported by a clinician. It is a comprehensive collaborative approach encompassing various components, as shown in Table 2.2. To reduce physiological arousal associated with stress, relaxation techniques are included. Cognitive restructuring strategies are incorporated to overcome maladaptive cognitions and fears related to tinnitus (Dobson, 2009). Habituation is further fostered by gradual exposure to feared situations, for example, hearing tinnitus in silence. Clinicians differ in what components they emphasise, such as relaxation (Lindberg, Scott, Melin, & Lyttkens, 1988) or cognitive therapy (Henry & Wilson, 2001). CBT for tinnitus incorporates techniques derived from audiology settings such as sound enrichment, although their added effectiveness has been questioned (Hiller & Haerkötter, 2005).

CBT for tinnitus has been researched over a number of years in controlled trials and longitudinal studies reported by independent research groups. A meta-analysis on psychological interventions for tinnitus (18 studies, 700 participants) indicated that the use of CBT led to the most favourable results in terms of reducing tinnitus distress (Andersson & Lyttkens, 1999). A further meta-analysis (15 studies, 1,091 participants) (Hesser et al.,

2011a) and Cochrane review (8 studies, 468 participants) (Martinez-Devesa, Perera, Theodoulou, & Waddell, 2010) also indicated the efficacy of CBT in reducing tinnitus distress. Results from the extensive range of studies highlight the effectiveness of CBT at decreasing tinnitus distress, annoyance, anxiety and improving daily life functioning. Effects are not as clear on tinnitus loudness and insomnia.

Table 2.2 Summary of CBT for tinnitus (Andersson, 2002)

CBT component	Description
Information	Knowledge is broadened regarding tinnitus, potential causes and moderating factors. Audiometric assessments are also included.
Functional analysis	Factors influencing tinnitus annoyance are addressed. These include medical, as well as psychosocial, factors.
Advice regarding hearing loss	This may include referral for amplification as well as behavioural advice in the form of hearing tactics.
Use of environmental sound enrichment strategies	Sound enrichment is used to facilitate habituation to tinnitus. The risks associated with trying to mask the tinnitus are outlined.
Applied relaxation	A method of gradually being taught to quickly relax and to use self-control over bodily and mental sensations such as stress. The aim is not to reduce tinnitus, but to control the effects of tinnitus. The goal is to obtain a balanced state of mind. In association with the relaxation training, imagery techniques are introduced.
Cognitive restructuring	The individual is helped to identify the content of thoughts and taught ways to challenge or control those thoughts usually described as unhelpful or even inaccurate. Reinterpretation of tinnitus into something more pleasant is furthermore addressed.
Emotional reactions	Fear and avoidance in relation to tinnitus are dealt with.
Problems with concentration and sleep	Methods for improving concentration are used. Sleep hygiene, bedtime and worry-time restriction, relaxation, and cognitive restructuring to address sleep problems are introduced
Relapse prevention	In the event of a relapse, a plan is devised for what to do should the tinnitus become worse.

In summary, research has indicated the efficacy of CBT for tinnitus. This does not, however, suggest that other habituation-promoting techniques are ineffective (McFerran & Baguley, 2009). There is, however, agreement in current practice guidelines that specialised CBT for tinnitus should be offered to patients for tinnitus or in the context of co-morbid anxiety or depression (Fuller et al., 2017).

2.5.3.2 Mindfulness-based stress reduction (MBSR)

The psychotherapeutic intervention of mindfulness has also been adopted in the management of tinnitus after indications of its helpfulness in managing a range of other health-related conditions in systematic reviews (Chiesa & Serretti, 2011; Fjorback, Arendt, Ørnbøl, Fink, & Walach, 2011; Piet & Hougaard, 2011). Mindfulness involves paying attention to the present moment on purpose and non-judgementally, relaxing control, tolerating discomfort and staying with negative emotions (Demarzo, 2015). It is built on the premise that by allowing feelings to be as they are, the individual makes them less threatening and reduces their impact. Mindfulness has been developed to improve well-being (see meta-analysis by Bohlmeijer, Prenger, Taal, & Cuijpers, 2010; Hofmann, Sawyer, Witt, & Oh, 2010) and, more recently, for tinnitus. Preliminary results have indicated that mindfulness reduces the impact of tinnitus (Gans, O'Sullivan, & Bircheff, 2014; Philippot, Nef, Clauw, Romrée, & Segal, 2012; Roland et al., 2015). Due to the similarities between mindfulness and relaxation, these disciplines have been compared. Initial clinical trials have indicated that mindfulness may be more effective than relaxation at improving outcomes related to tinnitus (Arif, Sadlier, Rajenderkumar, James, & Tahir, 2017; Marks, McKenna, Hallsworth, & Schaette, 2017). Although larger-scale studies are required, this is a further technique showing promise in minimising the impact of tinnitus.

2.5.3.3 Acceptance and commitment therapy (ACT)

ACT focuses on the functional usefulness of thoughts and actions (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). A key element of ACT is decreasing avoidance behaviour by increasing awareness of how thoughts and emotions can create distress. Like MBSR, ACT focuses on awareness of the present moment and observation in a non-judgmental way to decrease worry and contemplation. Both these approaches contrast with CBT in that they accept the existence of negative thoughts and emotions rather than trying to modify them. ACT has shown promise in a meta-analysis of various health conditions (Öst, 2014; Powers, Zum Vorde Sive Vording, & Emmelkamp, 2009; Veehof, Oskam, Schreurs, & Bohlmeijer, 2011). Trials determining its effectiveness for tinnitus are emerging, such as those comparing ACT to TRT (Westin et al., 2011).

2.5.4 Doing nothing

A trend has been identified through longitudinal studies that without treatment those with tinnitus do not get worse and tinnitus appears to naturally improve over time (Andersson, Vretblad, Larsen, & Lyttkens, 2001; Nondahl et al., 2002; Nondahl et al., 2010). The same trend has been found in meta-analysis of no-intervention periods in controlled trials (Hesser, Weise, Rief, & Andersson, 2011b; Phillips, McFerran, Hall, & Hoare, 2017). Although this is reassuring, the effect is highly variable across individuals (Phillips et al., 2017). Those distressed by tinnitus often prefer to seek professional help during the acute stage due to the effect the tinnitus has on their quality of life and the distress experienced. They can be reassured by these findings, but may in addition require further support to manage tinnitus, particularly during the acute phase.

In summary, in most cases, there is no effective cure for tinnitus. Current tinnitus interventions hence pursue symptoms of and reactions to tinnitus. Although a large number of management strategies have evolved, many lack empirical support (Martinez-Devesa et al., 2010). Psychological interventions, such as CBT, currently have the most evidence of efficacy in reducing tinnitus distress (Hesser et al., 2011a). Due to the complexities surrounding tinnitus, a single disciplinary approach is unlikely to fully address the broad context of individuals with tinnitus. Distressing tinnitus is best dealt with by focusing on individual needs in a collaborative multidisciplinary manner, encompassing the disciplines of neuroscience, psychology, medicine, and audiology (Baguley et al. 2013b).

2.6 RESTRICTIONS IN CURRENT TINNITUS CARE MODELS

This literature review has explored tinnitus perceptions and paradoxes. Considering the distress often associated with tinnitus, appropriate clinical care pathways are crucial. Unfortunately, these are not always available, due to obstacles preventing delivery of appropriate interventions. A clear understanding of these limitations is required prior to considering potential solutions to address them. The main restrictions include access to tinnitus care, provision of evidence-based interventions and the costs associated with intervention delivery.

2.6.1 Lack of access to specialist care

Accessing specialist health services largely depends on geographic location. Despite proven benefits, audiological services are unavailable to many of the world's population (Swanepoel & Hall, 2010). It is estimated that in more developed countries there is one audiologist per 20,000 people. This ratio decreases to one audiologist per 0.5 to 6.25 million people in less developed countries (Goulios & Patuzzi, 2008). Reasons for this poor ratio include shortage of resources, lack of trained professionals, poor infrastructure and a greater focus on basic healthcare. In the UK, medical care is provided by the publicly funded National Health Service (NHS) and is largely free at the point of use. GPs provide primary

healthcare and refer patients to specialist services as required. In England alone, a staggering estimated 750,000 people a year visit their GP with tinnitus as their primary complaint (El-Shunnar et al., 2011). Of these, only an estimated 33% (Hall et al., 2011) to 37% (El-Shunnar et al., 2011) are referred to specialist services by their GPs. The majority of referrals involve medical examinations from ENT specialists. What is also required by those who are distressed by tinnitus is the provision of management strategies. Of those seeing ENT's, 21% are referred to specialist services providing strategies to manage tinnitus. The majority of this 21% are referred to audiologists (68%), followed by psychotherapists (13%), neurologists (9%) and hearing therapists (10%) (Hall et al., 2011). This is partly due to specialist service being available only at certain clinical settings. Even with the extensive NHS healthcare in the UK, tinnitus services are not readily available, particularly in remote geographical regions (Hoare et al., 2015). This leaves many with troublesome tinnitus without access to beneficial educational and psychological interventions. While definitive information about what would be an optimal rate of referral to secondary care for tinnitus is not available, there is evidence of an unmet need in the tinnitus population (Gander, Hoare, Collins, Smith, & Hall, 2011).

The NHS is experiencing challenges due to funding constraints together with an ever-growing demand for its services (Smith, McKeon, Blunt, & Edwards, 2014). This has led to an inevitable increase in appointment waiting times. This delay in intervention has been associated with poorer outcomes for a variety of health issues (Pizer & Prentice, 2011; Smith et al., 2014). For patients experiencing significant levels of health-related distress, such as those with chronic tinnitus, overcoming these barriers by maximising access to care and minimising the waiting times should be prioritised (Gander et al., 2011).

2.6.2 Limited provision of evidence-based interventions

In terms of evaluation of tinnitus management, a significant barrier is the lack of standardisation of approaches (Hoare & Hall, 2011). There is no standard procedure for the diagnosis or management of tinnitus (Maldonado Fernández et al., 2015). Existing practice guidelines and approaches to clinical management of tinnitus typically reflect differences between clinical specialisms and country-specific resources (Hall et al., 2011; Hoare & Hall, 2011). In addition to the complexity of tinnitus, its severity may not be related to the loudness or tinnitus characteristics, but rather to the psychological complaints thereof (Andersson, 2002). Tinnitus interventions targeting the tinnitus sound itself, are, therefore, often less effective than psychological interventions which focus on improving functionality and minimising tinnitus-related effects (Hoare, Kowalkowski, Kang, & Hall, 2011). In a study based at a specialised audiology department, patients rated counselling, education and CBT as more valuable than sound-based therapies (provision of bedside generators, hearing aids, ear-level sound generators) received for tinnitus and hyperacusis (Aazh et al.,

2016). The discrepancy exists that the management routes most frequently offered to patients are often those with least evidence of efficacy (Landgrebe et al., 2012). The intervention with most evidence in reducing tinnitus distress at present is CBT (Grewal, Spielmann, Jones, & Hussain, 2014; Hesser et al., 2011a). A study by Cima and colleagues (2012), is one example indicating that including CBT and tinnitus counselling in addition to standard audiological care (audiometry, basic information, hearing aid/s or sound generator/s) can significantly reduce tinnitus severity and improve health-related quality of life. An economic evaluation related to this study indicated that those receiving CBT and tinnitus counselling gained 0.015 quality-adjusted life years (Maes et al., 2014).

Despite the known efficacy of CBT in reducing tinnitus-related distress and the fact that it is one of the most researched tinnitus management interventions, it is rarely offered in clinical practice, particularly in the UK (Gander et al., 2011; Hall et al., 2011; Hoare et al., 2015). This is largely due to a shortage of suitably trained psychologists and psychotherapists in the UK (Hall et al., 2011; McFerran & Baguley, 2009). Similarily, Bhatt and colleagues (2016) reported that doctors in the USA recommended CBT only 0.2% of the time. Hall et al. (2011) found higher referral rates for psychological treatments in France, Spain and Germany of 16–20%. An additional barrier to CBT is the high cost, estimated to be £471 for three sessions in England in 2013 (Department of Health, 2013).

Within the UK, the bulk of tinnitus interventions are delivered by audiologists and hearing therapists. The principles of the neurophysiological model form the backbone of the interventions offered. These generally include a mixture of patient education, relaxation therapy, various counselling techniques and sound therapies (Hoare et al., 2015). Due to the non-standardised approaches to tinnitus care in the UK, improving access to quality care has been attempted through good practice guidelines for tinnitus (Department of Health, 2009). These guidelines promote self-help interventions and CBT. Self-help interventions are those that can be undertaken independently with or without some support from clinicians. Self-help CBT interventions for tinnitus have been shown to reduce tinnitus distress, as evidenced by effect sizes of Cohen's d = 0.48, when compared with a passive control (Nyenhuis, Golm, & Kröner-Herwig, 2013b). Service delivery models should not only attempt to improve access to tinnitus services but should also focus on increasing provision of evidence-based care.

2.6.3 The costs associated with intervention delivery

Provision of healthcare cannot be considered without evidence of the cost-effectiveness of these interventions. Good practice guidelines for the commissioning of tinnitus services in the UK (Department of Health, 2009) outline the routes for tinnitus care. They involve a sequential approach with initial management of tinnitus starting with primary care (GPs), local tinnitus services (audiologists and hearing therapists) and specialist centres which

include multidisciplinary teams involving ENT specialists, hearing therapists, audiologists and clinical psychologists (Department of Health, 2009). This process can be extensive and often encompasses a number of appointments with various disciplines (Cima et al., 2009). The average cost of a tinnitus pathway journey in the UK was calculated at £1,051 in 2017 (Stockdale et al., 2017). For some, untreated tinnitus can result in a complex set of complaints resulting in indirect psychological and psychosocial effects (Bartels, Middel, van der Laan, Staal, & Albers, 2008). As there is a strong relationship between tinnitus and hearing difficulties, this combination adds to the distress experienced (Langguth, Kreuzer, Kleinjung, & De Ridder, 2013). These concurrent effects contribute to the healthcare burden, as further input may be required from various health professionals (Cima et al., 2012).

An economic evaluation of the healthcare cost of tinnitus management in the UK in 2017 (Stockdale et al., 2017) indicated that the annual cost of tinnitus interventions was £750 million in total, or £717 per tinnitus patient. This is equivalent to 0.6% of annual healthcare spending. It is not only healthcare costs that need to be considered. The annual societal costs related to tinnitus were calculated to be £2.7 billion per year in the UK (Stockdale et al., 2017), although higher costs have been quoted (for example €6.8 billion in the Netherlands by Maes et al., 2013). Work production losses related to work absences due to tinnitus account for a large proportion of this cost. Significant predictors of both healthcare and societal costs included higher levels of tinnitus severity and depression, and shorter durations of tinnitus. A further significant predictor of higher societal costs was younger age (Maes et al., 2013).

Considering that the prevalence of tinnitus is predicted to increase, this will place further financial constraints on already pressurised healthcare systems. Innovative planning is required to ensure systems are able to meet these additional demands and challenges such as poor patient-to-health professional ratios. Lack of accessibility to evidence-based tinnitus interventions needs addressing.

2.7 OVERCOMING BARRIERS

Innovative ways of providing effective and sustainable tinnitus care is evident worldwide and not isolated to the UK (Andersson, 2016). Technological advances have changed our lives in many ways and can assist innovations in healthcare. Examples of the use of digital interventions for both rehabilitative and diagnostic telehealth are shown in Figure 2.7 (Sternberg, 2004). Automation and transferability of digital healthcare provide unique opportunities to overcome barriers and improve cost-effective clinical care for numerous health-related conditions (Polisena, Coyle, Coyle, & McGill, 2009). Telehealth encompasses a range of alternative formats of healthcare delivery such as use of the Internet, computer-based technologies, videoconferencing and smartphone applications.

As the Internet is such a powerful tool, many telehealth self-help interventions are Internet-based (Reavley & Jorm, 2011). An Internet-based treatment has been defined as “A primarily self-guided intervention program that is executed by means of a prescriptive online program operated through a website and used by consumers seeking health- and mental-health related assistance. The intervention program itself attempts to create positive change and or improve/enhance knowledge, awareness and understanding via the provision of sound health-related material and use of interactive web-based components.” (Barak, Klein, & Proudfoot, 2009, p.5). One prominent form of telehealth that has developed is providing CBT via the Internet (iCBT). This form of treatment has been shown to be effective for a range of conditions, including auditory-related conditions (Thorén, Öberg, Wänström, Andersson, & Lunner, 2014), anxiety (Tulbure, 2011), mood disorders, depression (Johansson & Andersson, 2012), headaches, insomnia, and somatic problems such as chronic pain (see meta-analysis and systematic reviews by Arnberg, Linton, Hultcrantz, Heintz, & Jonsson, 2014; Cuijpers, van Straten, & Andersson, 2008; van Beugen et al., 2014). A systematic review and meta-analysis indicated equivalence between iCBT provided with therapeutic support (guided) and F2F CBT for a range of psychiatric and somatic disorders, although only a few studies for each condition were investigated (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014).

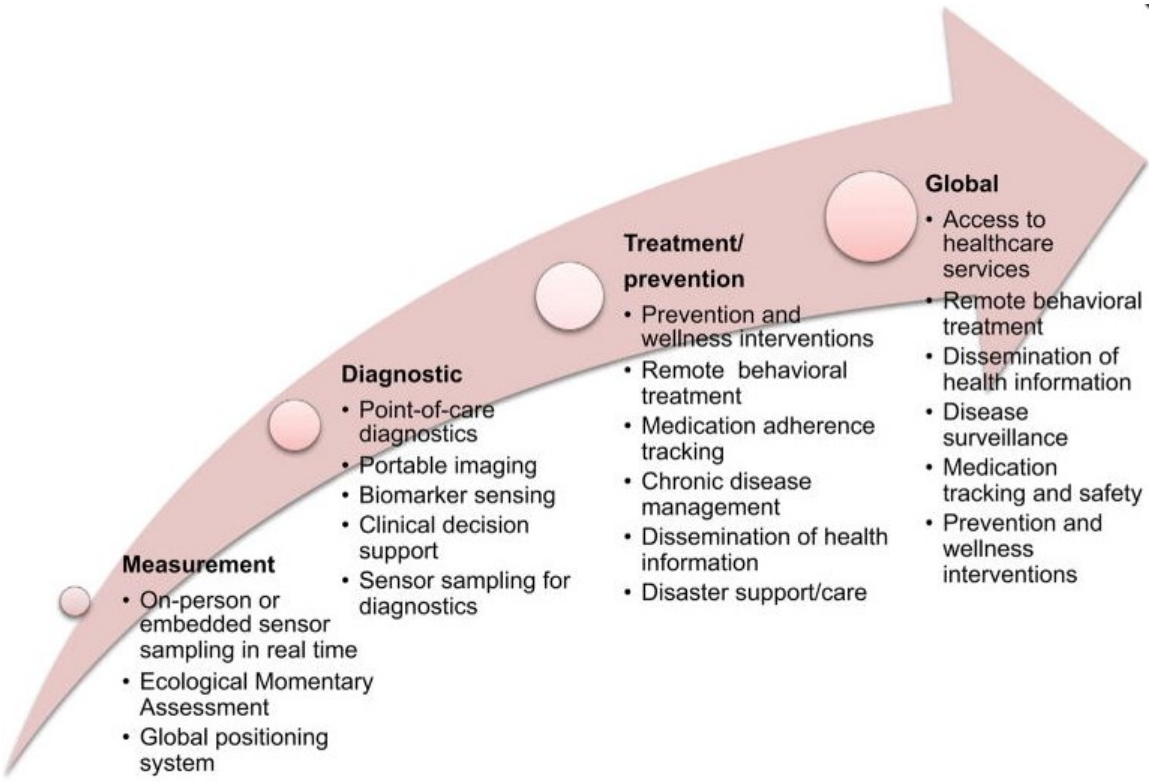


Figure 2.7 Continuum of telehealth tools. Originally published in Kumar et al. (2013). American Journal of Preventive Medicine, 45(2), 228-236. Permission to reproduce under licence number 4211851078218.

The potential of iCBT was considered by Andersson and colleagues in Sweden (2002) and led to the development of iCBT for tinnitus. Examples of the webpages of such an intervention are shown in Figure 2.8. Results of an initial efficacy randomised control trial (RCT) with a waiting-list control group indicated a reduction in tinnitus-related distress, anxiety and depression for those undergoing the intervention (Andersson et al., 2002). Although small effect sizes were reported (d = 0.26), results were maintained 1 year post-intervention. A series of iCBT studies in Sweden followed, as summarised in Appendix A. The second study was a non-randomised effectiveness trial in a clinical setting (Kaldo-Sandström et al., 2004). Medium effect sizes at post-intervention (d = 0.66) and at the 3 month follow-up (d = 0.68) period were found. In addition, significant within-group effects were reported for anxiety, depression and insomnia. Although attrition rates were better (30%) than for the first trial (51%), there was further room to improve these. With the aim of addressing high attrition and low compliance, the intervention underwent improvements by Andersson and Kaldo (2004), and Kaldo and colleagues (2007). These included expanding the text, making participants define their own treatment goals and setting priorities for the time needed for the treatment.

The third study used the standard form of tinnitus care, namely group-based CBT (GCBT) as the active control (Kaldo et al., 2008). The same treatment manual (Andersson & Kaldo, 2004) was used for the two treatment arms. Tinnitus reduction was evident in both groups, more so for the iCBT group (Cohen's d = 0.73 and d = 0.64, respectively). Improvements were also reported for insomnia and anxiety in both groups, and depression in the iCBT group post-intervention. At 1 year follow-up, improvements were maintained for insomnia and depression for only the GCBT group. Attrition rates were lower than for the earlier studies, at 4% post-intervention and 13% at 1 year follow-up. A further study by Hesser et al. (2012) found both iCBT and Internet-delivered acceptance and commitment therapy to be effective when compared with a discussion forum control group (d = 0.70 and d = 0.68, respectively). Those in the iCBT treatment group also improved more than the control group for anxiety (d = 0.68) and quality of life (d = 0.45). Furthermore, iCBT was again shown to be effective (d = 0.58) when implemented in Sweden for a larger group of sequential patients (Kaldo et al., 2013) than previously used (Kaldo-Sandström et al., 2004). Reductions in depression, anxiety, insomnia and hyperacusis were evident post-intervention. In this trial, a low-intensity intervention with less therapeutic input and fewer homework assignments was offered to those with less tinnitus distress. This low-intensity intervention yielded small within-group effect sizes (d = 0.26).

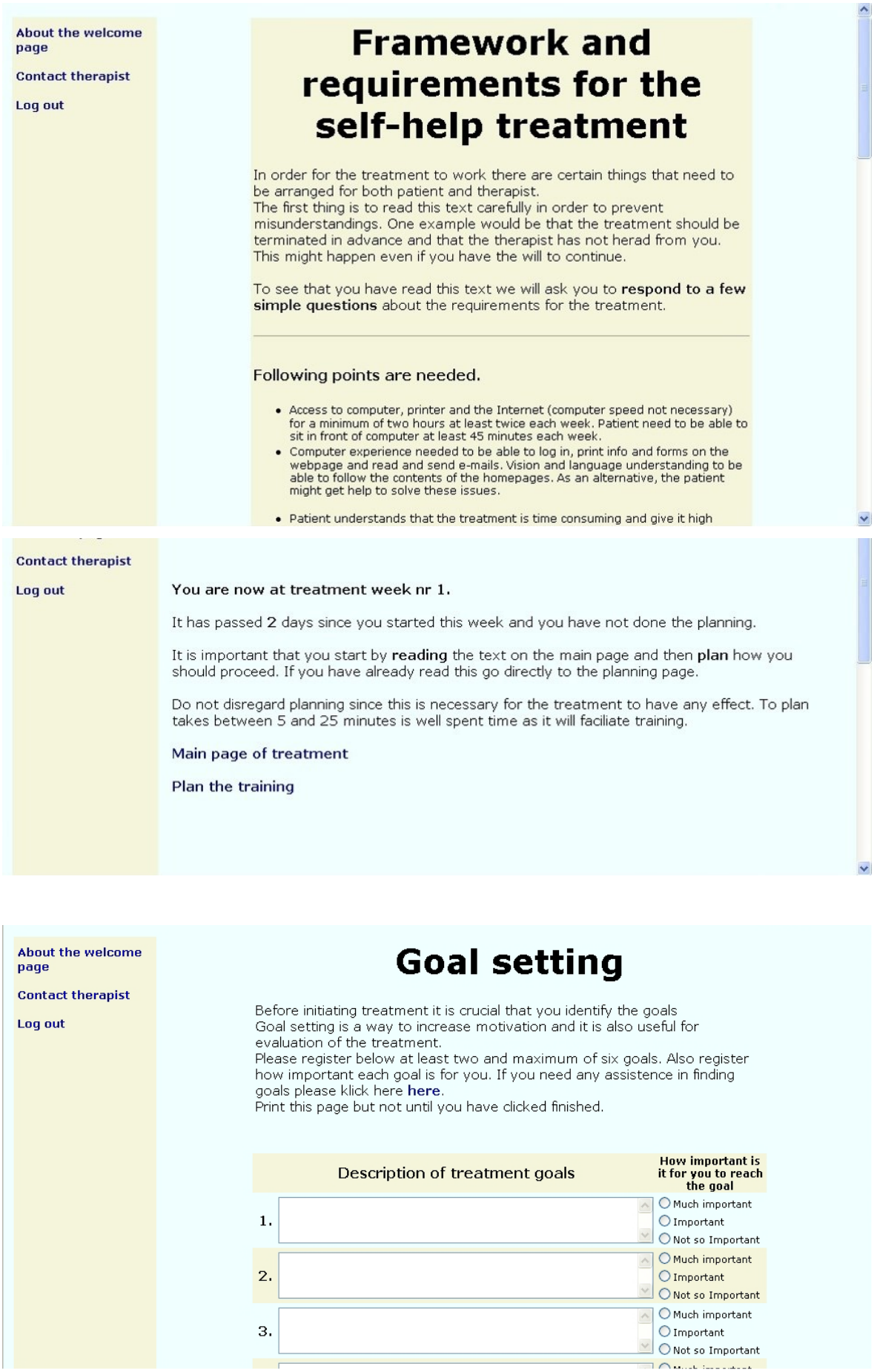


Figure 2.8 Screenshots from the original iCBT for tinnitus intervention.

Following the success of these Swedish-based studies, the materials were translated into both English and German. Evaluations of the Germany iCBT version indicated efficacy for tinnitus distress, depression and insomnia (Jasper et al., 2014a; Weise, Kleinstauber, & Andersson, 2016). The active treatment groups were iCBT, GCBT and an Internet-based discussion forum. The English version was trialled in Australia on a commercial website by Abbott et al. (2009). No statistically significant benefit was found when comparing iCBT to an information-only control program (without CBT content). This was partly due to a relatively low level of baseline tinnitus distress and possible cultural differences in attitudes towards text-based learning. Moreover, attrition rates were high, as half of the participants discontinued the trial.

Nyenhuis and colleagues (2013a) evaluated the effectiveness of iCBT for tinnitus using an iCBT programme that differed from those for the previously mentioned studies. They used a nine chapter manual adapted from the CBT-oriented Tinnitus Coping Training manual (Kröner-Herwig, Frenzel, Fritsche, Schilkowsky, & Esser, 2003). Andersson (2015), reported that the pooled effect size of previous iCBT controlled efficacy studies (Abbott et al., 2009; Andersson et al., 2002; Hesser et al., 2012; Jasper et al., 2014a; Nyenhuis et al., 2013a) was Hedges g = 0.6, although the study by Weise et al. (2016) was not included. This study found large effect sizes for tinnitus distress (g = 0.83), medium effect sizes for tinnitus acceptance (g = 0.76) and insomnia (g = 0.66) and small effect sizes for anxiety (g = 0.35) and depression (g = 0.36). Results further improved at 1 year follow-up. These trials across Sweden and Germany have had indicated promising results for iCBT for tinnitus.

In the UK, there are no national Internet-based interventions. There is, however, an Internet-delivered tinnitus programme (http://www.tinnituseprogramme.org), developed by a hearing therapist. It consists of downloadable educational materials, relaxation exercises, brief cognitive restructuring skills training, optional social support in the form of a moderated online discussion forum, and information about books and other useful websites. The programme is undertaken without any therapeutic support. It runs over 6 weeks, followed by a 4-week maintenance period (Greenwell et al., 2015). Since its inception in 2009, it has not been widely used, which may be linked to the fact that this intervention has never been formally evaluated, although a protocol to assess the intervention effects has been proposed (Greenwell et al., 2016b). The evidence base for this intervention is, therefore, not established and it is not CBT-based.

What is clearly limited in availability in the UK, is accessible CBT self-help interventions for people with troublesome tinnitus. The additional treatment option of iCBT for tinnitus distress in the UK would complement existing tinnitus pathways and self-help information by providing a more cost-effective, evidence-based, accessible, comprehensive and

standardised intervention. This intervention has clear service delivery advantages, including widespread access to tinnitus services particularly in underserved communities, but application is not restricted to those with reduced clinical access. It can also be accessed easily by those who may find attending hospitals difficult due to mobility issues, needing take time off work, reliance on others for transport or poor health (Chiang, Chen, Dai, & Ho, 2012). Additional intervention routes ensure that distressed patients can be treated in a more timely manner, which, in turn, can reduce the anxiety and distress often associated with waiting for an intervention. Health professionals can also be freed up to see patients who require urgent care. Service delivery costs are always an important factor. A delivery model including an Internet intervention could be more cost-effective than F2F interventions, as fewer resources are required (Hedman et al., 2014). The Internet is a viable alternative for people who are unable to access F2F care for reasons such as a long travelling time, the stigma of seeing a therapist, communication difficulties due to hearing impairment or walking problems (Cuijpers et al. 2008). Another advantage is the ability to access an intervention at home, at a comfortable pace and when individuals are in the right emotional state to absorb new information (Griffiths & Christensen, 2007; Muñoz, 2010). Learning and retention can be facilitated as the information can be revised at any stage. Ferguson & Henshaw (2015), for instance, found improved knowledge of hearing aids for those patients who obtained information online as opposed to those only receiving instructions in a clinical setting. This mode of intervention may also suit those who find it hard speaking to someone F2F about personal problems due to reduced stigma and online anonymity (Griffiths, Lindenmeyer, Powell, Löwe, & Thorogood, 2006). Outcome monitoring can be embedded in the intervention, allowing closer monitoring of progress, easier data management and time-saving capabilities. It can improve efficiency in healthcare as interventions can be standardised regardless of the therapist or clinic attended. Changes in health care behaviours towards more self-management have been evident following the use of self-monitoring fitness and health-related apps and devices (Chiauzzi, Rodarte, & DasMahapatra, 2015). An Internet-based intervention can empower individuals to take responsibility and promote self-efficacy (Bendelin et al., 2011; Williams & Whitfield, 2001).

The positive effects of self-help for long term health-conditions have been indicated (for example Macea, Gajos, Calil, & Fregni, 2010; van Straten & Cuijpers, 2009). In the UK, self-help methods for tinnitus management are advocated in the Good Practice Guidelines for tinnitus management (Department of Health, 2009). Self-help interventions require individuals to work though materials as a means of increasing knowledge of managing tinnitus (Nyenhuis, Golm & Kröner-Herwig, 2013b). Various formats of self-help for tinnitus exist. These encompass books, smartphone applications and information provided by Tinnitus charities, support groups, and GPs. A systematic review and meta-analysis by Nyenhuis and colleagues (2013b), indicated a positive impact of self-help CBT interventions

for tinnitus. On the other hand, a systematic review by Greenwell and colleagues (2016a) indicated insufficient evidence to support self-help for tinnitus. This does not stop people searching for self-help methods for their tinnitus. Due to the heterogeneous nature of tinnitus, having a variety of intervention options to suit different needs is important. By the nature of an Internet-based intervention, those undertaking it need access to a computer and the Internet, and should have the ability to read, write and understand text. There will be people who do not have the available resources or language skills to undertake such interventions, and alternative intervention formats should still be made available. Having iCBT could complement existing services, but should by no means replace existing tinnitus care.

2.8 UNMET RESEARCH NEEDS PERTAINING TO INTERVENTIONS FOR TINNITUS

Fewer than 10% of governmental and charitable investments in the UK have been for treatment evaluations (Chalmers & Glasziou, 2009). This is particularly found in tinnitus research, which has been focused on underpinning neurophysiological mechanisms (Hall et al., 2013). Consequently, aspects of tinnitus management are often overlooked and not prioritised. The James Lind Alliance Tinnitus Priority was established to identify and prioritise unmet research needs (Hall et al., 2013). One of the top 10 research priorities identified was investigating management strategies that are more effective than the usual model of audiological care in improving outcomes for people with tinnitus. This thesis aims to provide more information on this unmet research need by investigating a model using iCBT for tinnitus. As discussed in Section 2.7, iCBT could be a promising approach within stepped care tinnitus models in the UK. Despite the potential of iCBT, many unanswered questions remain.

Firstly, it is not known how acceptable such an intervention would be to a UK population. As the original intervention was largely text-based, such a format may not be appealing to a UK population and in itself be a barrier to usage. An iCBT intervention for a UK population had to be developed and deliverd in a way that would improve outcomes and promote acceptability of such an intervention in the UK.

Secondly, the feasibility of an Internet-delivered intervention is unknown a UK culture where people are accustomed to receiving F2F healthcare.

Thirdly, previous iCBT interventions have been provided by clinical psychologists, trained to provide CBT interventions. A tinnitus service based on the provision of iCBT could create a major manpower issue due to a dearth of psychologists who are audiologically literate

and prepared to participate in the management of tinnitus patients (McFerran & Baguley, 2009). In addition, it is costly seeing a clinical psychologist, at £268 for two hours, as the proposed 2013 rate (Personal Social Services Research Unit, 2013). Audiological professionals are the profession currently delivering tinnitus treatments. They understand the auditory system and have the expertise to address comorbidities such as hearing disability and hyperacusis that often co-occur with tinnitus (Nelson and Chen, 2004). An advantage of using audiologists is that they are not as costly as clinical psychologists, with the 2016 national tariffs (NHS England, Office of the Chief Scientific Officer, 2016) for an audiological assessment being £53 an hour, and the hourly rates of a specialist audiologist who could treat tinnitus being £18.76 per hour.

Studies published on the outcomes of the efficacy of CBT on tinnitus have been undertaken by psychologists with an international reputation for managing this condition. Although the literature is clear that CBT provided by psychologists is effective, it is not known whether CBT for tinnitus provided by audiologists would also be effective (Thompson, Hall, Walker, & Hoare, 2017). Interest in this question is developing with a recent study protocol (Tin Man study) being developed (Taylor et al., 2017). Audiologists have skills in counselling potentially anxious patients presenting with hearing-related or balance disorders (Searchfield & Baguley, 2011), but are not trained to provide CBT during their basic training. There are short CBT courses available, but these cannot compare to a degree in psychology. Determining whether an audiologist can effectively provide iCBT to reduce tinnitus distress is required. This knowledge gap has also been identified as one of the top 10 tinnitus research priorities of the James Lind Alliance (Hall et al., 2013), namely whether CBT or psychological therapy, delivered by audiology professionals, is effective for people with tinnitus. This research, is therefore, in line with the tinnitus community's research priorities.

Fourthly, tinnitus can be accompanied by many comorbidities. Past iCBT interventions have generally investigated the effects of iCBT on anxiety, depression and insomnia (see Appendix A). The effects on a larger range of comorbidities such as hyperacusis, hearing disability, cognitive failures and life satisfaction are unknown.

Fifthly, assessment of the longer-term effects of audiologist-guided iCBT for tinnitus distress and this range of comorbidities using is required. Possible unwanted effects of such an intervention have also not been previously empirically explored.

Lastly, previous effectiveness studies by Kaldo-Sandström et al. (2004) and Kaldo et al. 2013) have not been controlled trials. Furthermore, iCBT has been compared with GCBT in active-controlled efficacy trials (Jasper et al., 2014a; Kaldo et al., 2008; Nyenhuis, Zastrutzki, Weise, Jäger, & Kröner-Herwig, 2013a). Most of the UK tinnitus services provide

individualised tinnitus care. Determining how effective iCBT is compared with the usual individualised F2F audiological care in the UK is unknown.

This research has never previously been attempted in the UK, probably due to restrictions in audiologists providing CBT and general healthcare provision being largely F2F. Access to psychological therapies such as CBT for tinnitus is limited (Gander et al., 2011, Hoare et al., 2015) and the use of iCBT in the UK is untried. This research has challenged expectations from the tinnitus-community regarding healthcare provision and professional boundaries. These barriers were expected, and strategies to address them were required to be incorporated alongside this research. Including the tinnitus community at each stage of the research journey was thus as important as undertaking this research.

2.9 RESEARCH QUESTIONS TO ADDRESS KNOWLEDGE GAPS

This research aims to provide an original contribution to knowledge by improving an existing intervention and applying it to a new population. To investigate the identified research gaps the following research questions have been formulated:

Research question 1

Can an acceptable iCBT be developed that can lead to positive outcomes and inspire recipients to complete the programme?

Null hypothesis: *Redeveloping iCBT is unable to lead to positive outcomes*

Alternative hypothesis: *Redeveloping iCBT is able to lead to positive outcomes*

Research question 2

Is audiologist-guided iCBT feasible for treating adults with tinnitus in the UK?

Null hypothesis: *Audiologist-guided iCBT is not a feasible intervention for tinnitus*

Alternative hypothesis: *Audiologist-guided iCBT is a feasible intervention for tinnitus in the UK*

Research question 3

What is the efficacy of audiologist-guided iCBT in reducing tinnitus distress in the UK?

Null hypothesis: *There is no efficacy in audiologist-guided iCBT in reducing tinnitus distress in the UK*

Alternative hypothesis: *There is efficacy in audiologist-guided iCBT in reducing tinnitus distress in the UK*

Research question 4

Can iCBT for tinnitus reduce the impact of some of the comorbidities associated with tinnitus?

Null hypothesis: *iCBT for tinnitus is unable to reduce the impact of some of the comorbidities associated with tinnitus*

Alternative hypothesis*: iCBT for tinnitus is able to reduce some of the comorbidities associated with tinnitus*

Research question 5

Are the iCBT intervention effects maintained 1 year post-intervention when delivered by an audiologist?

Null hypothesis: *iCBT intervention effects cannot be maintained 1 year post-intervention when delivered by an audiologist*

Alternative hypothesis: *iCBT intervention effects can be maintained 1 year post-intervention when delivered by an audiologist*

Research question 6

Are clinical outcomes with iCBT comparable to the outcomes obtained when providing standard individualised F2F tinnitus care in the UK?

Null hypothesis: *Outcomes are worse with iCBT for tinnitus when compared with standard tinnitus care*

Alternative hypothesis: *Outcomes with iCBT for tinnitus are comparable to standard tinnitus care*

The next chapter outlines the methodological approach selected to answer these research questions.

3 METHODOLOGICAL APPROACH

The purpose of this chapter is to provide detailed information regarding the carefully selected methodology applied to answer each research question. This is presented within the conceptual framework. Justification is provided for the choice of intervention features, study design and outcome measures selected.

3.1 CONCEPTUAL FRAMEWORK

The conceptual framework conceived for this research was based on identifying an innovative way to provide sustainable cost- and clinically effective tinnitus care to complement existing provision in the UK. This framework proposes an additional tinnitus intervention to minimise the current burden of tinnitus on affected individuals and healthcare systems. From the literature review three key factors acting as intervention barriers in the UK were identified. These were high costs, limited efficacy of, and access to tinnitus interventions. This conceptual framework attempts to address these restrictions by providing evidence-based content, offering an accessible intervention tool and using a suitable healthcare professional to guide individuals. Justification for the selected components is detailed in sections 3.1.1 to 3.1.3.

3.1.1 Providing an intervention using evidence-based content

There are various approaches to tinnitus management currently in use as outlined in Chapter 2. The objective for this proposed intervention was to provide only evidence-based, informative, accurate and interesting content. CBT was shown in Chapter 2 to have the most evidence of efficacy in minimising the effects of tinnitus distress (Hesser et al., 2011a). It also has longer-term efficacy and was selected as the most clinically and cost-effective approach presently available (Hesser et al., 2012; Weise et al., 2016). CBT principles were therefore selected to form the evidence base of the intervention to improve the chances of reducing tinnitus distress.

3.1.2 An accessible intervention tool

There were various formats this Intervention could take. Considering which format would enhance the user's engagement and interaction was important. A blended approach was an option, but including F2F contact would increase the intervention costs. A smartphone app-based delivery was another option, but this could again act as an access barrier for those with dexterity or visual problems. The Internet is a versatile platform and increasingly used to promote healthcare and provide interventions (Samoocha, Bruinvels, Elbers, Anema, & van der Beek, 2010; van der Eijk et al., 2013). It provides numerous ways for

users to interact with the intervention (Webb, Joseph, Yardley, & Michie, 2010). In terms of tinnitus, the Internet has become a means for many people to connect, as is seen with the increasing specific online tinnitus forums and online support groups (Kaplan, Salzer, Solomon, Brusilovskiy, & Cousounis, 2011). The Internet is also a familiar vehicle used widely by patients who seek information about health conditions (Madathil, Rivera-Rodriguez, Greenstein, & Gramopadhye, 2015). Use of the Internet to search for information on tinnitus has indicated an upward trend in the UK since 2004 (Google Trends, 2017). Remarkably, there are over 11 million webpages devoted to tinnitus information, treatment, self-help, and discussion forums (Fackrell et al., 2012). The Internet is therefore a familiar and frequently used means of obtaining more information about tinnitus.

It was important to determine whether using the Internet as the delivery platform was viable. Although use of the Internet holds much advantage, its effectiveness is highly dependent upon whether the target population has both the access to and the skill set required to use the associated technology. Interestingly, it has been found that hearing-impaired adults aged 50–74 years, had greater computer skills and Internet use than those without hearing loss (Henshaw, Clark, Kang, & Ferguson, 2012). An Internet-based intervention may, therefore, be particularly suited to those with hearing problems. As many people with tinnitus have hearing loss, an Internet-based intervention may be well received. It is important to ensure access to the Internet if this is to be used for the intervention delivery. The UK Office of National Statistics (2017) report showed that 89% of adults in the UK use the Internet at least weekly and 78% use the Internet on-the-go, most frequently for emailing purposes. The Internet is part of daily life for the majority of adults. There are, however, certain age groups with less access. Those under 35 years of age have 99% access and this decreases to 41% for those over 75 years of age (Office for National Statistics, 2017). Although this ratio is not optimal for older adults, the UK Office of National Statistics (2017), indicated a trend of increased Internet access for all age groups, as seen in Figure 3.1. In view of this increasing trend, the Internet was selected due to its advantages of providing a means to a standardised, comprehensive, accessible intervention empowering end-users to be actively involved.

Although many would have access to this intervention, it would not suit everyone. By nature of the intervention, those undertaking it need access to a computer, the Internet, and require the ability to read, write and understand English text. There will be people who do not have the available resources or language skills to undertake an Internet-based intervention. It is therefore proposed as an additional intervention and not a substitute for existing interventions. Due to the heterogeneous nature of tinnitus, having a variety of intervention options to suit different needs, remains important.

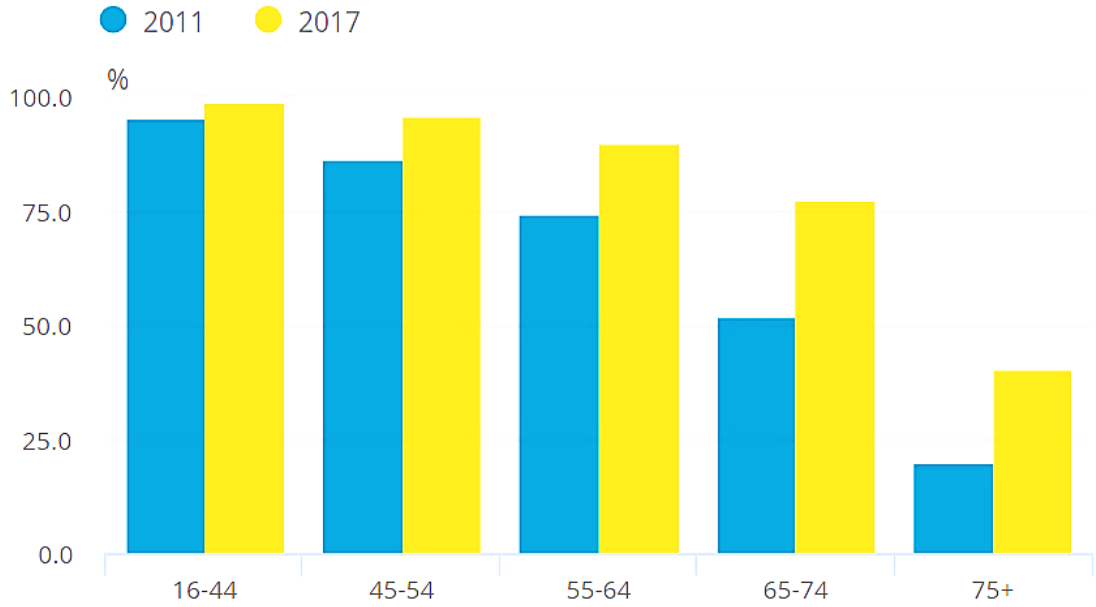


Figure 3.1 Recent Internet use by age groups. From the Office of National Statistics (2017). Permission to reproduce under the Open Government Licence v3.0.

3.1.3 Suitable intervention guidance

Internet interventions are either independent of professional support (unguided) or offer some form of support (guided). Guidance is a mechanism whereby individuals can obtain external information about themselves and their progress (Barak, Klein, & Proudfoot, 2009). Guidance can be synchronous (such as real-time chats), asynchronous (such as emailing) or a blended approach combining various means. As better outcomes have been reported for guided interventions (see Baumeister, Reichler, Munzinger, & Lin, 2014; Richards & Richardson, 2012 for systematic reviews), a guided intervention was selected. Using an Internet-support system further differentiated this programme from other information-only programmes in existence. The guidance format in terms of the communication mode, quantity (dose-response relationship) and quality (who provides the guidance) was debated, as discussed in sections 3.1.3.1 to 3.1.3.3.

3.1.3.1 Communication mode

Little is known regarding the effect of communication mode on intervention outcomes (Berger, 2017). No difference was found for outcomes when comparing support using either telephone calls without advice compared with support via an Internet forum for an Internet intervention for social phobia (Titov et al., 2009). Asynchronous support studies showed larger pooled effects (g = 0.70) than studies with synchronous support (g = 0.28) for Internet interventions for depression (Richards & Richardson, 2012). These differences may, however, reflect dissimilarities in technological developments and study designs across studies. For this intervention a blended approach was selected to incorporate the

advantages of both synchronous and asynchronous guidance. Synchronous guidance offers the opportunity to speak to a health professional whereas asynchronous guidance makes continuous support available during the intervention. Telephone interviews were conducted prior to starting the intervention. This telephone call provided the opportunity to further screen participants and give them the opportunity to ask questions. Not all previous iCBT trials have included these telephone interviews. In the iCBT trial done in Australia, these interviews were not undertaken. As a result the participants selected may not have been suitable, which may have contributed to the poor outcomes (Abbott et al., 2009).

Following completion of the post-intervention outcomes, participants were again telephoned to discuss their outcomes and experiences with the intervention. In addition, an encrypted email-type messaging system was incorporated to enable the health professional and participants undertaking the intervention to freely communicate. This system is more secure than unencrypted emails and all previous communications could be accessed in one place. This written form of asynchronous communication was used to introduce weekly modules, support, encourage engagement, provide feedback, and answer queries.

3.1.3.2 Quantity of guidance

The dose-response relationship regarding guidance has not been the focus of many studies. A study on Internet-based treatment for panic disorder reported that there was no difference in outcomes using a higher dose of guidance compared with provision of a lower dose of guidance (Klein et al., 2009). As no definite guidance exists, recommendation about protocols used by many previous Internet-based interventions for tinnitus (such as those by Hesser et al., 2012; Kaldo-Sandström et al., 2004; Weise et al., 2016) were followed to add an element of consistency. The quantity of guidance was set to a minimum of 10 minutes per week per participant, with additional time if required.

3.1.3.3 Quality of guidance

Therapeutic alliance is defined as achieving collaboration between a client and a therapist (Bordin, 1979). A systematic review indicated that only 11 (1.3%) of 840 studies investigated the therapeutic relationship in Internet interventions (Sucala et al., 2012). Therapeutic alliance during Internet interventions has been rated highly by participants, when previously investigated (Ruwaard, Lange, Bouwman, Broeksteeg, & Schrieken, 2007; Ruwaard et al., 2009). Although positive reports, such as not missing face-to face contact and that contact was pleasant and personal have been reported from the participants' perspective, much is still to be discovered regarding the role of online guidance (Sucala et al., 2012). Previous studies for other health conditions have unexpectedly indicated that the level of qualification and experience of the e-Health therapist does not appear to affect treatment efficacy (Baumeister et al., 2014). Outcomes have, for instance, been comparable using a psychologist versus a technical assistant for depression (Titov et al., 2010), social phobia

(Titov et al., 2009) and anxiety (Robinson et al., 2010). Likewise no significant difference in outcomes was found when comparing guidance by a psychologist versus a student psychologist for social anxiety (Andersson, Carlbring & Furmark, 2012). Similarly, no difference was found when comparing guidance between psychologists with and without specialist training for anxiety (Johnston, Titov, Andrews, Spence, & Dear, 2011). As outlined in Chapter 2, previous research has not determined whether delivering iCBT for tinnitus by a non-psychological professional is feasible. Determining whether audiology professionals without CBT training can provide effective iCBT needs to be explored. To investigate outcomes using guidance provided by an audiologist, the author was selected to guide participants, due to her suitability as an experienced audiological scientist, being registered with the Health and Care Professions Council and being appropriately trained to master's level in audiology. Although she had past experience of managing tinnitus patients, no formal CBT training had been undertaken.

In summary, the conceptual framework was built on the three key principles illustrated in Figure 3.2. By providing audiologist-guided iCBT, the impact of tinnitus on healthcare systems and individuals was hypothesised to decrease. The aim of the intervention was to empower the individual to achieve behavioural and cognitive change using fewer resources required than for F2F clinical care.

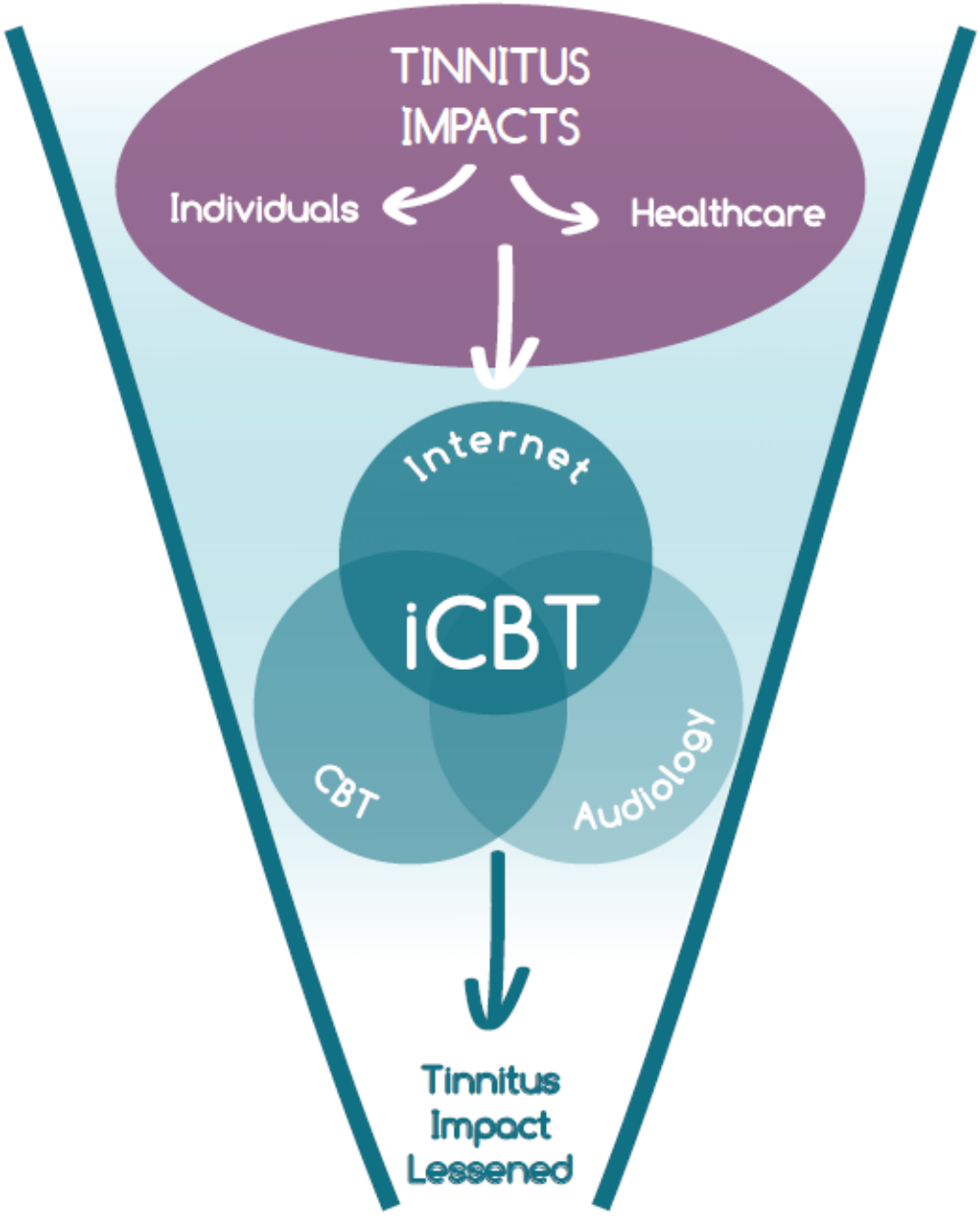


Figure 3.2 Conceptual framework of the research.

3.2 THEORETICAL FRAMEWORK

Barriers are often encountered during the translation of health-related research into clinical practice and policies (Grol, 2001). These barriers led to discrepancies in evidence-based practice and to the public failing to benefit optimally from advances in healthcare (Grimshaw, Eccles, Lavis, Hill, & Squires, 2012). Overall, tinnitus studies vary in design and there is significant heterogeneity in the evaluation of tinnitus perception and the questionnaires used (Landgrebe et al., 2012). This jeopardises comparison between trials and precludes meta-analysis of intervention effects. The lack of long-term results in addition to the common use of combined approaches in the management of tinnitus are in part responsible for the lack of conclusive evidence (Landgrebe et al., 2012). It is likely that the differences reported in efficacy and effectiveness of individual Internet-interventions are due

to sub-optimal designs for the intervention development and evaluation used (Morrison, Yardley, Powell, & Michie, 2012). Ensuring that experimental designs include sequential phases of development and evaluation minimise these hurdles (Craig et al., 2008).

At the heart of this research was the aim of providing an effective intervention route for those with tinnitus. The research started out with the proposal to evaluate the intervention in a non-randomised manner. This was feasible within the time available for this doctorate. Together with this proposal was the desire to ensure that the research contributed to the field of Internet interventions and healthcare. The research strategy was thus rethought as it became clear that the first priority was to follow the most rigorous methodology possible. The hierarchy of evidence assigned to studies (Figure 3.3), based on the methodological quality of their design was considered. Higher quality was achievable by implementing well-designed randomised control trials (RCT) (Evans, 2003). This led to changing the proposal to the planning of a RCT. In parallel, literature about evaluating complex interventions was studied (Craig et al., 2008).

	Effectiveness	Appropriateness	Feasibility
Excellent	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies
Good	• RCT • Observational studies	• RCT • Observational studies • Interpretive studies	• RCT • Observational studies • Interpretive studies
Fair	• Uncontrolled trials with dramatic results • Before and after studies • Non-randomized controlled trials	• Descriptive studies • Focus groups	• Descriptive studies • Action research • Before and after studies • Focus groups
Poor	• Descriptive studies • Case studies • Expert opinion • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality

Figure 3.3 Hierarchy of evidence to evaluate healthcare interventions from (Evans, 2003). Reproduced with permission by John Wiley and Sons licence number 4211331192262.

It was realised that a full clinical trial woud add further value. Looking through the published literature there was very little on intervention development and feasibility. It became clear that developing and evaluating this intervention systematically and sequentially using appropriate theoretical underpinnings was paramount. Although this meant a lot more to do in the timeframe, the approach would minimise inconclusive results due to a non-optimal methodology. Neglect of any of these steps would make it less probable that the intervention could later be implemented successfully. In addition, publications of the process of

development and evaluation were prioritised for transparency and to promote best practice in the field of Internet-based intervention development.

3.3 SCIENTIFIC STRATEGY

The theoretical framework therefore led to a three-phase clinical trial methodology to increase the quality of evidence. Justification of the phases included is provided in sections 3.3.1 to 3.3.4.

3.3.1 Intervention development

Ensuring that an intervention was delivered with suitable content and presentation formed the first part of the scientific strategy and addressed the first research question. The intervention development needed to be shaped to be suitable for a UK population to account for linguistic and cultural differences. Evaluations of the technical functionality and acceptability of the intervention were required. Only once the intervention was acceptable could the feasibility and efficacy of its use be assessed.

3.3.2 Phase I Feasibility

Prior to larger scale trials, a feasibility study was considered an important pre-requisite to identify barriers and guide planning of larger-scaled investigations, as suggested by the Medical Research Council framework for the evaluation of complex interventions (Campbell et al., 2000). The feasibility of this intervention format was the focus of the second research question and was of particular importance in a culture accustomed to having individualised F2F healthcare. This proof-of-concept evaluation would ensure that efficacy testing had the best chance of success by troubleshooting potential issues early on.

3.3.3 Phase II Efficacy

Determining the efficacy of an intervention is an essential step during intervention evaluation. The design selected is crucial to ensure that sound methodological principles are incorporated and bias is minimised. Efficacy trials prioritise internal validity and therefore include a control group in the study design. They evaluate whether an intervention can work under ideal circumstances (Cochrane, 1972). The use of RCTs is a central component in evaluating new interventions. Participants are randomised into groups with the aim of obtaining an unbiased and reliable comparison of these groups. Randomisation is important as it ensures that participants are objectively similar with regard to demographic and prognostic factors in the selected groups. Randomisation achieves this, as each participant has a known chance of being given a treatment in an allocation that cannot be predicted (Altman & Bland, 1999). To ensure that rigorous methods are selected, the Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed (Schulz, Altman, &

Moher, 2010) as well as the CONSORT-eHealth guidelines (Eysenbach, 2011). These guidelines set standards to adhere to, such as ensuring enough power to produce statistically valid results. The Standard Protocol Items: Recommendation for Interventional Trials (SPIRIT) checklist were used to ensure comprehensive reporting of methods and results (Agha, Altman, & Rosin, 2015; Chan et al., 2013). Efficacy for tinnitus distress and the associated comorbidities was investigated to answer the third and fourth research questions. A further important evaluation was determining longer-term intervention effects, both wanted and unwanted. The fifth research question addressed stability of treatment effects 1 year post-intervention.

3.3.3.1 Process evaluation

In parallel to the efficacy trial, a process evaluation was run. This had the aim of identifying factors that can facilitate or hamper the outcomes obtained (Saunders, Evans, & Joshi, 2005). Three process evaluation models used widely in healthcare interventions are the Reach, Efficacy, Adoption, Implementation and Maintenance framework (RE-AIM) (Dzewaltowski, Glasgow, Klesges, Estabrooks, & Brock, 2004; Glasgow, Vogt, & Boles, 1999) and the components suggested by Baranowski & Stables (2000) and Steckler, Linnan, & Israel (2002). Although each model is unique, there is some overlap. The RE-AIM model includes five dimensions namely: (i) reach, investigating the extent to which the intervention was received by the targeted group; (ii) effectiveness, related to the impact of the intervention measured by the selected outcome measures; (iii) adoption, associated with delivering the intervention; (iv) implementation, investigating whether the protocol was followed as planned and assessing the delivery of the intervention; and (v) maintenance, related to the degree the intervention and whether the results and involvement can be sustained over time. The 11 components suggested by Baranowski and Stables (2000) covered: (i) recruitment procedures; (ii) maintenance; (iii) the specific context; (iv) resources required; (v) implementation of the programme; (vi) reach; (vii) barriers encountered; (viii) exposure to the intervention; (ix) initial use; (x) continued use; and (xi) contamination related to the extent to which additional treatments were received. Linnan and Steckler (2002) suggested inclusion of seven components namely: (i) context; (ii) reach; (iii) dose delivered related to the intended intervention components to be provided; (iv) dose received indicating engagement with the intervention on an individual level; (v) fidelity investigating the extent to which the intervention was delivered as planned; (vi) implementation; and (vii) recruitment. The current study selected parameters from these models to identify processes that facilitated or hindered the outcomes obtained during Phase II of this research.

3.3.4 Phase III Effectiveness

It is not always clear whether results from efficacy trials can be generalised into normal clinical practice. A limitation of efficacy research is that intervention effects are not contextualised, as they are not applicable in typical intervention settings (Glasgow,

Lichtenstein, & Marcus, 2003). As a follow-up from these, effectiveness studies examine whether a treatment works in real-world clinical settings and in situations that health professions encounter in their daily routine practice (Lutz, 2003). This type of study emphasises the external validity of the research findings.

Effectiveness trials can take various forms. For this phase, this new intervention was compared with the usual clinical care, as this is regarded as the gold standard of evaluating new interventions. This phase addressed the final research question. The objective was to show that a new intervention is not inferior to an existing intervention. The CONSORT guidelines were followed for running non-inferiority and equivalence randomised trials (Piaggio et al., 2012).

3.4 MEASURING THE IMPACT

As highlighted in Chapter 2, experiencing tinnitus involves both the percept of the sound and the impact on daily functioning such as difficulties listening or concentrating (Langguth, 2011). Quantifying the severity of this impact and how this effect changes as a result of an intervention is difficult. An International Classification of Functioning, Disability, and Health (ICF) conceptual framework has been proposed by the World Health Organisation (WHO) within the biopsychosocial model for evaluating health-related quality of life issues (World Health Organization, 2001). This has been applied to tinnitus, as shown in Figure 3.4 (Newman, Sandridge, & Jacobson, 2014). Ths model should be considered when selecting assessment measures for tinnitus-related research.

A number of different broad approaches have traditionally been used to evaluate the impact of tinnitus (Newman et al., 2014). These include psychoacoustic tests, rating scales, diaries, open-ended questions, questionnaires describing functional effects and global perception of intervention-related changes (Hall et al., 2016). Objective assessment measures for tinnitus are desirable but challenging. Psychoacoustic measures such as measurements of tinnitus loudness, pitch or character matching bear no consistent relationship to the severity or perceived loudness of tinnitus (Henry & Meikle, 2000) and are thus not ideal to use to evaluate intervention effects. Global rating methods are not uniform and the limited information on the reliability and validity of such ratings limits their applicability (Meikle, Stewart, Griest, & Henry, 2008). Diaries and open-ended questionnaires have advantages, but their responses are difficult to quantify across participants (Reja, Manfreda, Hlebec, & Vehovar, 2003). Rating scales and questionnaires are more commonly used in both the management of tinnitus patients and in tinnitus research to assess tinnitus distress and the associated difficulties that may be present (Meikle et al., 2008). They can generally be completed relatively rapidly with little examiner involvement and can be psychometrically

tested for reliability and validity. The importance of selecting the most appropriate assessment measures cannot be over-emphasised. Some assessment measures are discriminative (designed to evaluate differences between individuals at a single point in time) whereas others are evaluative (measuring change over time) (Kirshner & Guyatt, 1985). When evaluating intervention effects the assessment measures selected need to be evaluative and designed specifically to have high sensitivity to treatment-related changes that are important to the individual (Newman et al., 2014). The psychometric construct of assessment measures should be carefully reviewed (Hyde, 2000). Considerations regarding the appropriateness, test-retest reliability, validity, precision and interpretability, acceptability to the individual, and administrative feasibility are important to consider (Hyde, 2000). In addition, selecting assessment measures that are applicable for the selected research methodology is crucial (Kumar et al., 2013).

Figure 3.4 Interaction of the domains of the WHO-ICF schema. How each domain relates to tinnitus and overall health-related quality of life within the context of personal and environmental factors is shown. Originally published in Newman, C.W., Sandridge, S.A. and Jacobson, G.P. (2014). Journal of the American Academy of Audiology, 25(1), 76-105. Permission granted to reproduce under licence number: 4211850586108.

Acronym HRQoL: Health related quality of life.

For purposes of this research, the following six priorities were set to aid selection. Firstly, to obtain cross-sectional information regarding the participants. Secondly, to have a responsive assessment measure for change in tinnitus distress. This would form the main outcome measure. Thirdly, to screen for hearing difficulties to ensure these could be acted upon. Fourthly, to measure the impact on the numerous comorbidities associated with tinnitus. These would form the secondary outcomes. Fifthly, to monitor tinnitus distress during the intervention as a way of quality control. Lastly, to evaluate post-intervention satisfaction. Due to the identified need for consensus on assessment measures (Langguth et al., 2007b), there has recently been a strong focus on putting together a set of global assessment measures for tinnitus (Fackrell et al., 2017; Hall, Londero, & Schlee, 2015; Hall et al., 2015). Identifying the core outcome domains of such measures is currently being investigated (Fackrell et al., 2017). This will improve comparison amongst clinical trials. The decisions regarding the assessment measures selected were based on the information available when embarking on this research at the end of November 2014. The thought process behind the decisions will be discussed.

3.4.1 Cross-sectional data

A demographic questionnaire was used to obtain information related to gender, age, tinnitus duration, hearing aid use, medical examinations related to tinnitus, past or current tinnitus treatments, health and/or mental health conditions and employment (See Appendix B). This information served to ensure that participants met the eligibility criteria and to provide a means of collecting cross-sectional data.

3.4.2 Measuring the impact of tinnitus distress

Due to the multi-dimensional nature of tinnitus, self-reported questionnaires are generally used to quantify tinnitus severity and/or assess intervention-related change over time. Numerous such questionnaires have been developed (see Fackrell, Hall, Barry, & Hoare, 2014, for a review). For the purposes of this clinical trial the primary outcome selected was a reduction in tinnitus distress after undergoing the intervention. Selecting the most appropriate measure for this was challenging. In a systematic review of instruments used in tinnitus clinical trials, the Tinnitus Handicap Inventory (THI; Newman, Jacobson, & Spitzer, 1996) (at 15%) and tinnitus loudness rating scales (at 8%) were used most frequently (Hall et al., 2016). In previous iCBT tinnitus trials, the THI (Newman et al., 1996) and Tinnitus Reaction Questionnaire (TRQ; Wilson, Henry, Bowen, & Haralambous, 1991), were the most commonly used measures (Andersson, 2015). These measures have, however, been developed as diagnostic tools with defined categories of severity and have been criticised for lacking sensitivity to changes (Meikle et al., 2007). They are, therefore,

not ideally suited to assess intervention effects for the present clinical trial. A more recently developed assessment measure, the Tinnitus Functional Index (TFI; Meikle et al., 2012), was designed to measure tinnitus severity and indicate responsiveness to treatment. It provides a comprehensive coverage of the broad range of symptoms associated with tinnitus. Although further validations are still required, the TFI is increasingly being used internationally (for example Henry, Frederick, Sell, Griest, & Abrams, 2015; Scherer et al., 2014) and is being validated for these purposes (Fackrell, Hall, Barry, & Hoare, 2016; Henry et al., 2016a; Rabau, Wouters, & van de Heyning, 2014). It has been translated into at least 14 languages (Henry et al., 2016a), has adequate psychometric properties as seen in Table 3.1 and a test-retest reliability of 0.8 (Meikle et al., 2012). A reduction in TFI score shows improvement in tinnitus distress with meaningful change occurring when the score is reduced by 13 points or more (Meikle et al., 2012). Due to its validation for assessing treatment responsiveness, it was selected for the present clinical trial as the main outcome measure (Appendix C). Permission to use the TFI for this research was obtained.

3.4.3 Identifying hearing loss

As there is a strong relationship between tinnitus and hearing difficulties (Langguth et al., 2017), there may be adults with tinnitus and unidentified hearing loss (Akeroyd, Foreman, & Holman, 2014). Including a screening measure of hearing could identify those that need more in-depth hearing assessment (Chou, Dana, Bougatsos, Fleming, & Beil, 2011; Yueh, Shapiro, MacLean, & Shekelle, 2003). Various options to provide such a measure were considered. One route was getting participants to undergo formal audiometry and upload the results electronically. This could potentialy put people off participating and not be a cost-effective option (Davis, Smith, Ferguson, Stephens, & Gianopoulos, 2007). The other option was to include a hearing screening online (Smits, Merkus, & Houtgast, 2006). This initially appeared feasible. However, it became clear that this was very difficult. Many of the online tests that exist did not have the required validation (Yueh et al., 2003). Those that were possibilities could not be linked to the intervention website. The participants would have to log into two websites and send their hearing screening test results by taking a screen shot. Again, this was considered too complicated. Organisations such as Action on Hearing Loss, the University of Southampton and Nottingham's National Institute for Health Research (NIHR), who had done previous work on online hearing testing, were contacted (see Vlaming, MacKinnon, Jansen, & Moore, 2014). Many of the tests were no longer in use. The NIHR, however, offered use of their sound-wave files. Adding these to the intervention was attempted, but establishing normative data using these was outside the scope of this doctorate. The next best option was to use a self-reported measure of hearing disability. The Hearing Handicap Inventory for adults screening version (HHIA-S; Newman, Weinstein, Jacobson, & Hug, 1991) was selected (Appendix E) to assess hearing difficulty, which in

this context may be related to the penetrating nature of tinnitus or the presence of hearing loss, commonly found in those with tinnitus (Langguth et al., 2017). If scores were high, this was discussed with participants and they were advised according to their needs (for example to have existing hearing aids adjusted locally).

3.4.4 Measuring the impact of tinnitus-related comorbidities

As outlined in Chapter 2, experiencing tinnitus may negatively affect many aspects of daily life, including sleep, mood, and concentration (Langguth, 2011). It can, therefore, be debilitating and reduce quality of life. It would be valuable to determine whether the intervention was effective in alleviating some of these commonly experienced comorbidities. The range of assessment measures for each option was evaluated. Previous trials of iCBT for tinnitus had not used an extensive range of assessment measures and focused on tinnitus distress, insomnia, anxiety and depression (see Jasper et al., 2014a; Kaldo et al., 2008; Weise et al., 2016). One of the difficulties faced in selecting secondary assessment measures was considering the additional time it would take participants to complete the associated questionnaires. Although lengthy questionnaires may be more informative, having a questionnaire battery taking a few hours to complete would not be feasible. The assessment measures selected were the most valid short measures available. Information about each is given below. They can be accessed in Appendix F-K and are summarised in Table 3.1

i) The Insomnia Severity Index (ISI; Bastien, Vallières, & Morin, 2001) was used to assess the presence of insomnia, as sleep difficulties are prevalent amongst those with tinnitus (Crönlein et al., 2016). A legal contract to use the ISI was set up.

ii) The Generalised Anxiety Disorder (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006) was selected to quantify the level of anxiety, as the prevalence of anxiety is high in those with severe tinnitus (Pinto et al., 2014).

iii) The Patient Health Questionnaire (PHQ-9; Spitzer, Kroenke, Williams, & Patient Health Questionnaire Primary Care Study Group, 1999) was chosen to assess symptoms of depression, as depression amongst those with severe tinnitus is often reported (Pinto et al., 2014).

iv) The Hyperacusis Questionnaire (HQ; Khalfa et al., 2002) was administered to assess the presence of reduced tolerance of everyday sounds, otherwise known as hyperacusis, as there is a large overlap in the prevalence of tinnitus and hyperacusis (Schecklmann, Landgrebe, Langguth, & TRI Database Study Group, 2014).

v) The Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, FitzGerald, & Parkes, 1982) was administered to assess cognitive functions, as tinnitus may

impact the control of attention, leading to cognitive slips and errors in task completion (Tegg-Quinn, Bennett, Eikelboom, & Baguley, 2016). Although longer than ideal, it was challenging finding a more appropriate measure.

vi) The Satisfaction with Life Scales (SWLS; Diener, Emmons, Larsen, & Griffin, 1985) was administered as a quality of life measure assessing global life satisfaction as opposed to quality of life measures related to self-care and mobility, which was not relevant in this context.

For these assessment measures, a low score signified fewer problems than a high score and a reduction in score indicated improvement for all these measures except for the SWLS. For the SWLS a higher score showed more life satisfaction than a lower score and an increase in score revealed improved life satisfaction.

Table 3.1 Assessment measures administered

Outcome Measures. Reference: validation used	**Items**	**Scale used**	**Range of scores**	**Internal consistency (Cronbach's alpha)**	**Levels of significance**
Tinnitus Functional Index (Fackrell et al., 2016;Meikle et al., 2012)	25	1–10	0–100	0.97/ 0.8	<25: mild 25-50: significant 50+: severe
Tinnitus Handicap Inventory-screening (Newman, Sandridge, & Bolek, 2008)	10	1–3	0–40	0.87	>6: tinnitus handicap
Insomnia Severity Index (Bastien, Vallières, & Morin, 2001)	7	0–4	0–28	0.74	0–7: Not clinically significant 8–14: Sub-threshold Insomnia 15–21: moderate Severity 22–28: severe
Generalised Anxiety Disorder (Löwe et al., 2008)	7	0–3	0–21	0.89	0-4: minimal anxiety 5-9: mild anxiety 10-14: moderate anxiety 5-21: severe anxiety
Patient Health Questionnaire (Spitzer et al., 2006)	9	0–3	0–28	0.83	5-9: mild depression 10–14: moderate 15–19: moderately severe 20–18: severe depression
Hearing Handicap Inventory-screening (Newman et al., 1990, 1991)	10	1–3	0–40	0.93	0–8: 13% probability of HI, 10–24: 50% probability of mild-moderate HI

					26–40: 84% probability
Hyperacusis Questionnaire (Fackrell, Fearnley, Hoare, & Sereda, 2015; Khalfa et al., 2002)	14	0–4	0–42	0.66 /0.88	>28: strong hypersensitivity
Cognitive Failures Questionnaire (Broadbent et al., 1982)	25	0–4	0–100	0.89	Higher scores indicate more difficulties
Satisfaction with Life Scales (Diener et al., 1985)	5	1–7	0–35	0.87	0–9: Extremely dissatisfied 10–14: Dissatisfied 15–19: Below average satisfaction 20–24: Average satisfaction 25–29: High satisfaction 30–35: highly satisfied

3.4.5 Weekly monitoring during the intervention

Monitoring individuals during the intervention was imperative as a safety precaution. A weekly measure of tinnitus distress was hence sought. Using the TFI or THI would not be feasible, as this was too long and may have become too familiar and affect post-intervention results. Using an extract from the TFI was considered, but advised against following analysis by Fackrell et al. (2016), as not all subscales contribute equality to the composite measure of the TFI. Using a visual analogue scale to rate tinnitus annoyance and loudness was a possibility. However, such ratings do not correlate strongly with either psychoacoustic or multi-item questionnaire measures of tinnitus (Adamchic, Langguth, Hauptmann, & Tass, 2012). Due to the difficulty of trying to create such a measure online it was decided against using it. The best option was the screening version of the THI (THI-S), due to its concise nature, consisting of only 10 questions (Newman et al., 2008). This would differentiate it from the post-intervention assessment and not be too taxing to complete weekly. This weekly measure would be an effective way of easily monitoring tinnitus distress by both the

participants and the researcher during the eight week period (Appendix L). The scores obtained are comparable (r = 0.90) with those for the full version of the THI (Newman et al., 2008). Good convergent validity (0.86) has been found between the TFI and full version of the THI (Meikle et al., 2012), indicating some overlap between the TFI and THI-S scores.

3.4.6 Intervention satisfaction questionnaire

Assessing post-intervention satisfaction was important. Existing standardised questionnaires are aimed at service satisfaction with questions such as: How would you rate the quality of service you have received? (from the Client Satisfaction Questionnaire; Attkisson & Zwick, 1982). This wording was not appropriate to assess intervention satisfaction. As an appropriate measure was not found, one was designed to determine the suitability, content, usability, presentation and exercises on the platform. The questionnaire consisted of 15 five-point Likert-type scaled questions (Appendix M). The scale was from low to high, with 1 representing strongly disagree and 5 representing strongly agree. Four additional open-ended questions were posed. These sought to identify the best aspects of the intervention, how much time was spent on each module, what required attention and any suggestions. The drawback of this approach was that the assessment measure was not validated.

3.5 DATA COLLECTION

All data were collected online within the intervention platform, due to its efficiency and cost effectiveness. Accuracy should not be affected as it has been established that online data collection does not compromise the psychometric characteristics of responses (Ritter, Lorig, Laurent, & Matthews, 2004; Thoren, Andersson, & Lunner, 2012). The assessment measures were implemented on the intervention platform, and could be automatically or manually assigned to users. A further advantage is minimising the risk of missing items, as users are alerted when this is the case. Responses were verified where required by telephone interview as a follow-up to the online questionnaire completion. Immediate clarification, especially regarding open-ended questions was, however, not possible. Online collection may have reduced the diversity of the participants, as not all individuals have access to technology or feel confident using the Internet.

To minimise attrition reminders and encouragement were provided throughout for participants who had not completed questionnaires or worksheets on time. Three reminders were automatically and electronically sent on the three consecutive days following the release of the questionnaire. Further reminders were sent if required up to a maximum of seven, as well as a reminder phone call, over a period of three weeks.

Data were collected at baseline (T_0), at post-intervention (T_1) for phase I and at follow-up (T_2) in Phases II and III. For Phase II further outcome data were obtained 1 year post-intervention (T_3). At post-intervention participants were telephoned to discuss their progress and further needs. The assessment schedule is shown in Table 3.2.

Table 3.2 Measurement schedule for data collection

STUDY PERIOD	**Enrolment**	**Intervention**	**Post-intervention**	**Follow-up**	**1 year follow-up**
Measurement time point	***T_0: baseline***	***8-weeks***	***T_1 (post-intervention)***	***T_2 (2 months post-intervention)***	***T_3 (12 months post-intervention***
ENROLMENT					
Informed consent	X				
Online screening questionnaire	X				
Telephone screening	X				
Intervention allocation		X			
ASSESSMENTS					
Tinnitus Functional Index (TFI; Meikle et al., 2012)	X		X	X	X
Insomnia Severity Index (ISI; Bastien et al., 2001)	X		X	X	X
Generalised Anxiety Disorder (GAD-7; Spitzer et al., 2006)	X		X	X	X
Patient Health Questionnaire (PHQ-9; Spitzer et al., 1999)	X		X	X	X
Hearing Handicap Inventory-screening (Newman et al., 1990)	X		X	X	X

Hyperacusis Questionnaire (HQ; Vernon, 1987)	X		X	X	X
Cognitive Failures Questionnaire (CFQ; Broadbent et al., 1982)	X		X	X	X
Satisfaction with Life Scales (SWLS; Diener et al., 1985)	X		X	X	X
Tinnitus Handicap Inventory-screening (THI-s; Newman et al., 2008)	X	Weekly for 8 weeks	X		
Post-intervention satisfaction questionnaire and telephone call			X		

3.6 Ethical considerations

The following ethical considerations were addressed during the trial:

3.6.1 Data management

One of the main concerns surrounding Internet interventions is the security of stored personal data. The appropriate technical and organisational measures to safeguard user privacy and confidentiality were put in place. The central electronic online data capturing system was held in Linköping University (Sweden), due to their expertise in Internet interventions. Information was added and procedures were put in place to ensure that the webportal complied with the following UK legislation: The Data Protection Act (UK Parliament, 1998) and The Privacy and Electronic Communications (EC Directive) Regulations (Riach, 2003). Appropriate technical and organisational measures were taken to safeguard the security of the webportal. These included locking the servers in a computer room to which only authorised personnel had access, using cards and keys. It was also not possible to establish a link between the data and individual users through access to the database. Data were kept on the secure webportal and archived when no longer required.

All data communication between servers and users was encrypted (via TLS/https) and all sensitive data were stored encrypted in the database, using algorithms such as

HMAC/sha256/secret keys. Only two administrators had access to the servers and encryption key.

3.6.2 Participant data

Participants were informed of how collected information might be used and shared. This included information about Cookie usage and opting out of the programme. Multiple backups were made so that data were never lost due to system failure. All personal data were kept confidential. Each participant was assigned a random user code (four digits followed by four letters), used by health professionals to identify the participant during the trials.

3.6.3 Clinical monitoring

Protocols to minimise the risks to participants and the researcher were put in place. The outcome data, together with any other spontaneously reported adverse events during the intervention were reported. If any participants were identified as requiring additional support, a letter was sent to their GP, so that this care could be arranged (Appendix P).

All participants were monitored on a weekly basis during the course of the study by means of the THI-S. Participants undertaking the online intervention were monitored by their assigned audiologist evaluating their worksheets and communications via a secure online messaging system. This therapeutic alliance allowed for feedback and assistance if participants had any difficulties. Participants allocated to receive F2F care (Phase III) were monitored by their designated local audiologist. GPs were notified when participants completed the trial (Appendix Q).

3.6.4 Trial registration

Prior to obtaining ethical approval the clinical trials had to be registered on a clinical trials database. They were registered with Clinical Trials.gov. The registration for Phases I and II was NCT02370810 on 05/03/2015. The registration for Phase III was NCT02665975 on 22/01/2016.

3.6.5 Ethical approvals

For phase I and II, ethical approval was granted by the Faculty Research Ethics Panel of Anglia Ruskin University (FST/FREP/14/478, Appendix R).

For Phase III, ethical approval was granted by the East of England-Cambridge South Research Ethics Committee (REC reference: 16/EE/0148, Appendix S) and Health Research Authority (IRAS project ID: 195565, Appendix T) following a meeting with 20

board members. The Research and Development departments for all participating centres provided permission for the study to take place within the three selected hospitals following capability and capacity approvals.

Participants provided informed consent online if they were interested in participating (Appendix O). Any trial modifications were communicated with all relevant parties. The study sponsor was Anglia Ruskin University.

3.7 PARTNERSHIPS

This research sought to create the opportunity for the general public, clinicians and researchers to work together. A service public-patient partnership with the Cambs Tinnitus Support Group was included. They were involved in this research from the development stage, and assisted with functionality testing and evaluation of the developed iCBT intervention. They ensured that the materials provided were patient-friendly. This group also served as an independent point of contact for participants for impartial advice about the trial. Both professionals and the general public were thus involved in this research from the outset and skills were developed to manage these partnerships. The partnership with Linköping University, Sweden involved working with multidisciplinary professionals. Other multidisciplinary teams were formed during the design of the intervention, such as with a learning technologist. Assistance from these experts in running Internet interventions from psychological and information technology perspectives was of immense benefit.

3.8 FUNDING

This project was feasible due to a generous offer from Linköping University, Sweden, who allowed use of their ePlatform and related resources free of charge. Additional expenses associated with the research had to be covered by external sources of funding. After numerous applications, one small charity, The Basil Brown Trust, provided a donation to pay initial costs. Grant applications were unsuccessful to the British Tinnitus Association, Action on Hearing Loss, and the British Society of Audiology during 2015, although the experience of grant application was of value. In April 2016, a small grant was obtained from the British Society of Audiology to fund Phase III of the clinical trial (E Beukes, principal investigator).

3.9 TIMELINE

This research was formalised and conducted over a three year period. This was possible due to use of an established ePlatform and working on different aspect of each research phase simultaneously. The broad research timelines are outlined in Figure 3.5.

3.10 DATA ANALYSIS

The Statistical Package for Social Sciences (SPSS) versions 20–23.0 was used for statistical analysis (IBM Corp, 2013). Descriptive statistics such as means, standard deviations and percentages, were used to evaluate the sample characteristics. A *p*-value of < 0.05 was considered statistically significant for all subsequent chapters. An assessment of normality was a prerequisites to statistical testing. The required assumptions were checked for each statistical test. Generic data analysis is described below, and specific data analysis can be found for each trial in the corresponding chapter.

3.10.1 Missing data analysis strategy

An intention-to-treat (ITT) paradigm was used, as this method is less susceptible to bias than complete case analysis techniques. Missing value analysis was conducted to determine how to account for missing data using Little's "missing completely at random" test (Little, 1988). This indicated that missing values were likely to be randomly distributed across all observations and that there was no systematic pattern to the missing data, missing data could be imputed through the multiple imputation procedure offered by SPSS using the Markov Chain Monte Carlo method which uses five imputation runs (Asendorpf, van de Schoot, Denissen, & Hutteman, 2014). All preintervention assessment measures results were used as predictors. Pooled results were obtained by averaging the five imputation runs. For some of the statistics, a pooling algorithm was not available. When this was the case, the first imputed set of results was reported. These results were compared with those obtained when performing a per-protocol analysis, which includes only data from participants who completed the assigned intervention.

3.10.2 Sample characteristics

Descriptive statistics were used to evaluate the sample characteristics and ratings provided. These included measures of central tendency and the spread of data to summarise the data in a meaningful way and to identify patterns emerging from the data.

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
	2014											
Designing study protocol												
	2015											
Ethical application Phase I, II												
Intervention content development												
Acceptability trial												
Recruiting Phase I												
Running Phase I												
Recruiting Phase II												
	2016											
Running Phase II												
Ethical application for phase III												
Setting up for Phase III												

Recruiting and running Phase III												
	2017											
Continuing Phase III												
1 year outcomes phase II												

Figure 3.5 The broad research timescales.

3.10.3 Pre-post treatment comparison

Significance testing

Statistical methods to test the significance of results were selected to be appropriate for each study design. Type I errors may have occured due to multiple testing. Previously mechanisms to counter this have included Bonferroni corrected *p*- values (which would have been $p < 0.005$ in most cases for this methodology). These methods have, however, lost appeal due to being too conservative (Armstrong, 2014). To counter these errors a main outcome was selected (for tinnitus distress). In addition, emphasis was placed on reporting effect sizes and not only significance results.

Effect sizes

Effect sizes and the 95% confidence intervals at post-intervention were calculated by dividing the mean differences by the pooled standard deviations. Effect sizes below $d = 0.5$ are small, those from 0.5 to 0.79 are medium effect sizes and those equal or greater than $d = 0.8$ are large (Cohen, 1992).

Clinically significant Change

The statistical significance of differences in group means is the standard outcome measure in trials. Supplementing this with an evaluation to determine whether the change in scores is clinically meaningful is a further indicator of the value of the intervention. The reliable change index (RCI; Jacobson & Truax, 1991) is a way to determine whether an individual's pre-post intervention difference score indicates a clinically significance change. It is calculated using the standard deviation and means at T_0, the means at T_1, and the test-retest reliability coefficient or Chronbach's alpha (from Table 3.1) where this was not available. For the primary outcome measure the RCI was calculated using the baseline standard deviation and means, post-intervention means, and a test-retest reliability coefficient of 0.78 for the TFI, as reported in the TFI validation study (Meikle. et al., 2012). Individual's pre-post intervention difference scores were compared with the calculated RCI to determine whether the change was considered a clinically significant change.

It is important to consider that, due to regression to the mean, those with poor initial scores are more likely to show larger changes on assessment measures than those with less poor initial scores (Campbell & Kenny, 1999).

3.11 PARTICIPANTS

Information about the research was given on the study website and printed participation information sheets (Appendix N). Those interested in participating registered on the study website (http://www.tacklingtinnitus.co.uk). They were informed of their right to withdraw at any stage without penalty. Reasons for withdrawal were obtained where possible. Eligibility for the study was determined in a two-stage process. Initially, participants completed the baseline assessment measurements online. Following completion, a telephone screening was arranged. This was done to ensure that participants fulfilled the study requirements, which were as follows:

Inclusion Criteria

i) Aged 18 years and over and living in the UK (England, Wales, Scotland, and Northern Ireland).
ii) Computer and Internet access and the ability to use these
iii) The ability to read and type in English
iv) Experiencing tinnitus for a minimum duration of three months

Exclusion Criteria

i) Mentioning any major medical, psychiatric or mental disorder which may hamper commitment to the programme
ii) Reporting pulsatile or unilateral tinnitus, which had not been investigated medically
iii) Tinnitus as a consequence of a medical disorder, still under investigation
iv) Undergoing any tinnitus therapy concurrently with partaking in this study

3.12 CONCLUSIONS

Rehabilitative tele-audiology holds potential in bridging barriers evident in audiology and tinnitus healthcare provision (Swanepoel et al., 2010). This potential will not be realised if new interventions are not systematically developed and evaluated. This chapter has outlined the reasons and evidence for the selected methodology. The methods outlined were included in the subsequent clinical trials. For brevity, methodological aspects outlined in this chapter are not again repeated. Where specific methods were followed these are discussed in the context of subsequent experimental chapters. The next chapter addresses the first research question regarding how iCBT was developed for a UK population.

4 DEVELOMENT AND ACCEPTABILITY OF ICBT

This chapter explains how iCBT was adapted for a UK population and assessed for suitability. It addresses the first research question determining whether an acceptable iCBT intervention can be developed to improve positive outcomes.

4.1 INTRODUCTION

The use of iCBT could complement existing tinnitus management routes and improve access to evidence-based tinnitus care in the UK. To date no such UK based intervention is in existence. The Swedish CBT self-help programme for tinnitus was translated into English, but only used in one study by Abbott and colleagues (2009). In this trial no statistically significant difference in tinnitus distress was found compared with an information-only control program (without CBT content) and attrition rates were high. It was noted that for many people the programme was not engaging enough to promote adherence and retention. Cultural differences have been reported regarding computer literacy (Pflug, 2011). It is possible that cultural differences in attitudes towards text-based learning, were present between the Swedish samples of the general public and the industrial sample in Australia. It is, thus important to ensure that interventions are adapted for the intended population. Moreover, new interventions need to be accepted as an effective intervention within the tinnitus community. As healthcare in the UK is largely F2F, an Internet intervention would need to be specifically created to overcome potential barriers to usage and be appealing. Internet interventions should ensure flexibility within the design in order to adapt to technological advances and the progression of new knowledge (Andersson, 2016). Considering the flexibility and functionality of the intervention platform is important. Selecting an adaptable platform with the level of technical sophistication required is vital. The Australian trial was for instance run on a commercial company's website. Furthermore, determining the credibility of new interventions from both clinical experts and end users is important.

This chapter aims to address the need for an evidence-based iCBT intervention for tinnitus distress, specifically for a UK population. Specific objectives were as follows:

i) Developing iCBT for tinnitus to improve outcomes and behavioural change
ii) Identifying technical functionality concerns causing barriers to the usability of iCBT in the UK

iii) Evaluating the acceptability of the intervention in terms of content, presentation, and suitability

4.2 METHOD

The methodology was divided into two parts. Firstly, the intervention was designed to be suitable for a UK population in terms of cultural and linguistic requirements. Secondly, the functionality and acceptability of the intervention was assessed.

4.2.1 The development process

Guidance on developing complex interventions (those with a number of interacting components) was followed (Craig et al., 2008). The fundamental premise was based on proven conceptual models (Campbell et al., 2000). The theoretical models of Ritterband and colleagues (2009), were used to guide the development of this intervention. The key features known to add to the effectiveness of Internet interventions, from Andersson and colleagues article 'What makes Internet therapy work?' (Andersson, Carlbring, Berger, Almlöv, & Cuijpers, 2009), and insights from Morrison et al. (2012) were applied. There were eight principles selected and incorporated into the design, as discussed in sections 4.2.1.1 to 4.2.1.8.

4.2.1.1 Suitable functionality of the platform

This intervention was created on the *Iterapi* (https://www.iterapi.se/) purpose-built web-based platform (Vlaescu, Carlbring, Lunner, & Andersson, 2015; Vlaescu, Alasjö, Miloff, Carlbring, & Andersson, 2016) designed by academic staff at the Department of Behavioural Sciences and Learning, Linköping University, Sweden. This platform has excellent functionality, following experience in providing interventions for conditions such as depression, anxiety and hearing loss. It is designed to be easily adaptable following technological advances and the progression of new knowledge, as recommended by Webb and colleagues (2010). The platform has the required security features in place for data protection. It is flexible and responsive, transparently adapting to screen size to provide a fully functional experience regardless of whether the platform is accessed using a desktop computer (PC and Mac), laptop, tablet, or smartphone. The webmaster, George Vlaescu, assisted with settingup the intervention. Varying levels of access to different aspects of the intervention was possible by assigning users different roles and privileges. This included what materials, therapeutic contact and discussion forums individuals had access to. Data logging was available to record the frequency of login, modules read, worksheets completed, and the number of messages sent.

The website consisted of two parts, a general information part for the public (Figure 4.1) and a separate section for those undertaking the intervention who required a secure login. The recruitment section was comprehensive and included segments detailing the intervention, what happens during the study, who the study is suitable for, and contact details if more information was required. There was a link on the website to register for the study. Those registered were invited to complete the screening questionnaire after the trial commenced.

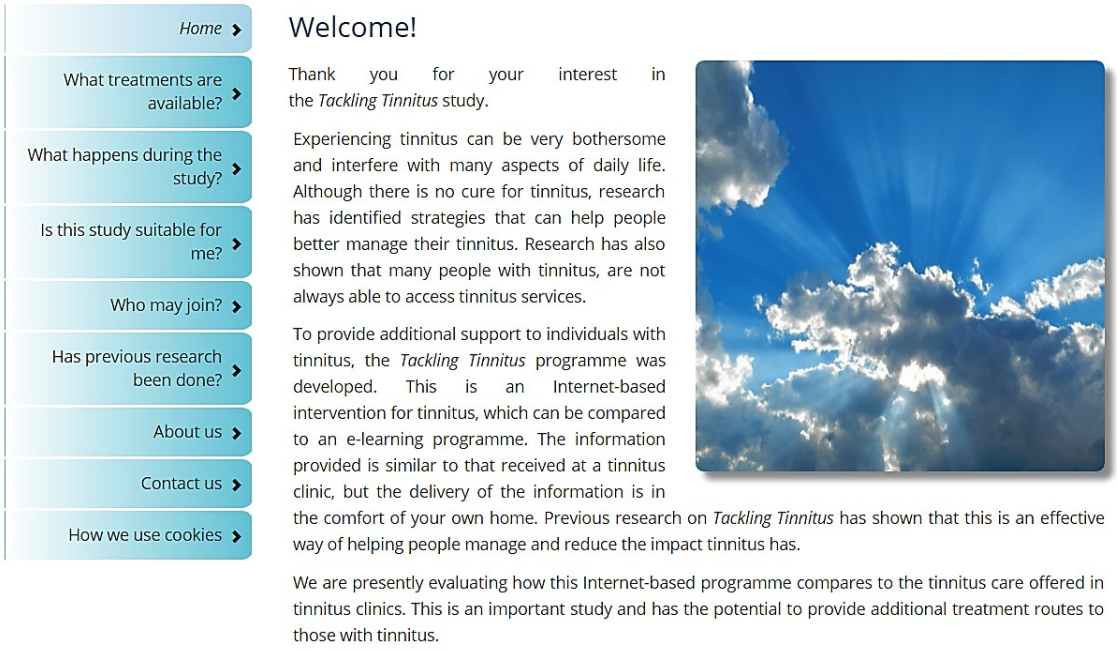


Figure 4.1 General information section of the website for the public.

4.2.1.2 Evidence-based content

The objective was to present only evidence-based, informative, accurate and interesting content. CBT principles formed the evidence base for the intervention, as these presently have the most robust evidence of effectiveness in reducing the effects of tinnitus, particularly in the long term (Hesser et al., 2011a). The CBT self-help programme, designed by Kaldo and colleagues (2007) specifically for tinnitus, was selected, due to its strong theoretical base. The programme combines a cognitive rationale (Henry & Wilson, 2001) and a learning theory approach (Hallam et al., 1984). Audiological principles formed from clinical experience and research and found to be effective for tinnitus informed the theoretical base. Theoretical resources were incorporated to ensure the content was accurate and tailored to those with tinnitus. To emphasise the theoretical base, individual modules were organised into a clear structure, including an overview, explanation and rationale, step-by-step instructions and a further help section, covering possible difficulties that may have been experienced, as shown in Figure 4.2.

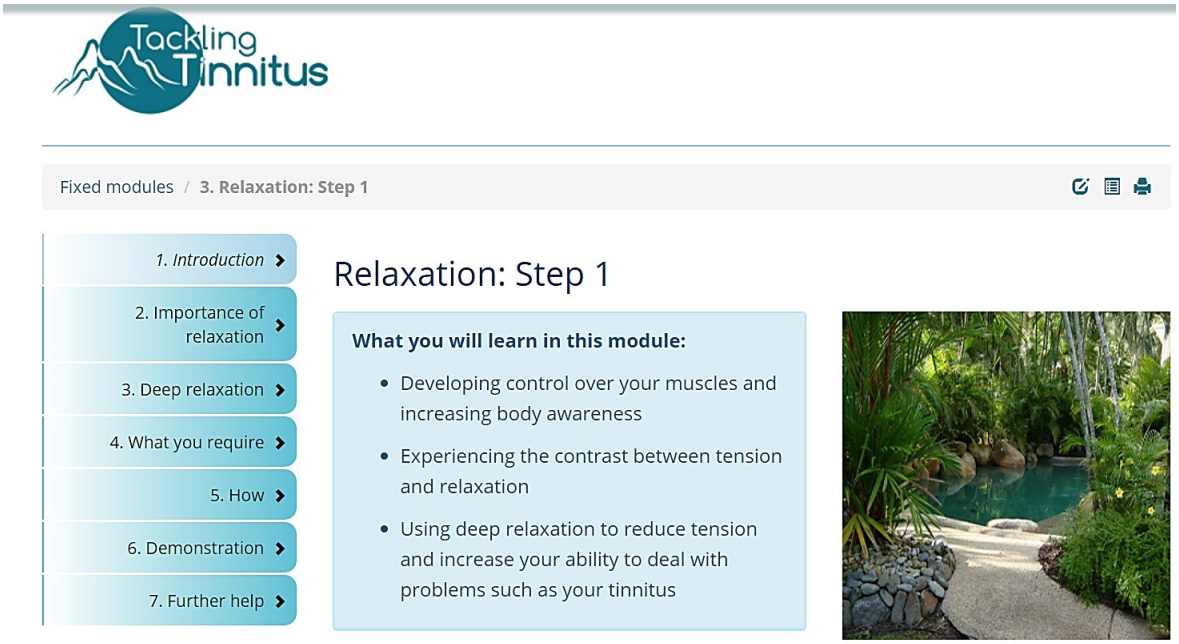
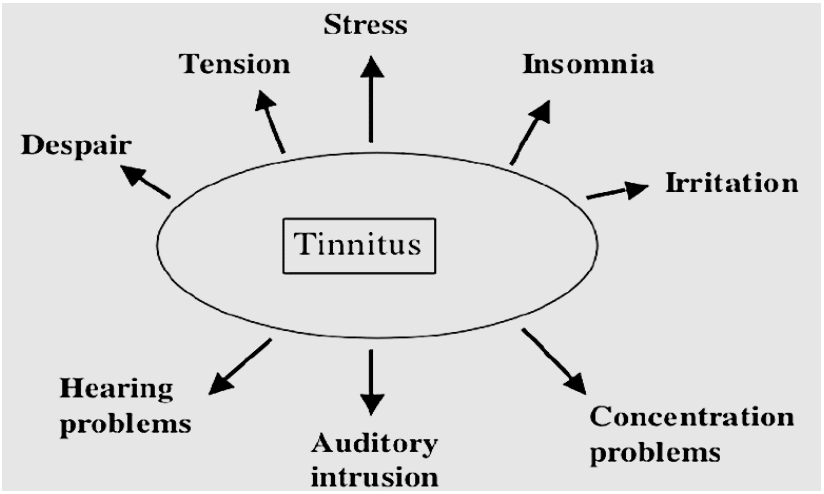


Figure 4.2 Illustration of the structure of content provided by the intervention.

4.2.1.3 Comprehensiveness

The intent was to promote behavioural change by offering various techniques focussing on addressing the physical, emotional and daily effects of experiencing tinnitus. Figure 4.3 illustrates some techniques suggested to minimise these effects. To target the emotional aspects of tinnitus and transform unhelpful thought patterns, key CBT techniques such as negative automatic thought analysis, cognitive restructuring and exposure techniques (Andersson, 2002) were included. Emotional, physiological and behavioural reactions to tinnitus can be alleviated through stress management techniques (Weber, Arck, Mazurek, & Klapp, 2002). Ways of promoting stress reduction are important in any tinnitus approach. Relaxation and breathing-focused and meditation-based approaches have been introduced in clinical medicine with demonstrated efficacy in the treatment of many stress related disorders (Klainin-Yobas, Oo, Suzanne Yew, & Lau, 2015; Manzoni, Pagnini, Castelnuovo, & Molinari, 2008), including tinnitus (Arif et al., 2017; Davies, McKenna, & Hallam, 1995; Jakes, Hallam, Rachman, & Hinchcliffe, 1986; Weber et al., 2002). A progressive relaxation programme, together with techniques such as positive imagery, were included to deal with the physical aspects of tinnitus and promote behavioural change (see Andersson & Kaldo, 2005).



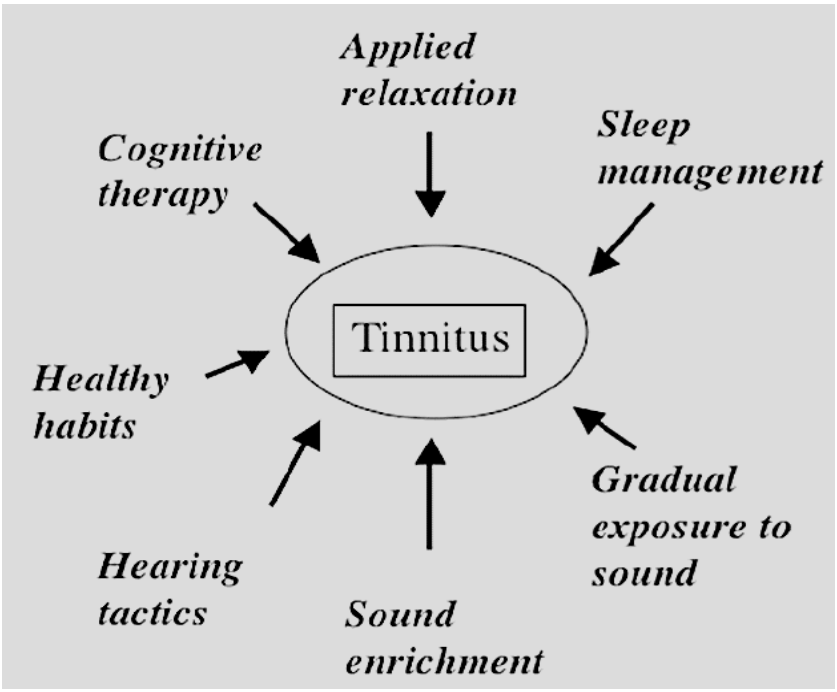


Figure 4.3 Model of the consequences of tinnitus.

Top: consequences of tinnitus, bottom: how using a comprehensive treatment may help reduce these consequences impact (bottom). From Andersson & Kaldo (2005). In Tyler, R (Ed). Tinnitus Treatment Clinical Protocols. New York: Thieme New York.

Key audiological approaches to the treatment of tinnitus such as the use of sound enrichment, hearing tactics and advice about sound sensitivity (Department of Health, 2009) were included to ensure a fully comprehensive intervention. Sound therapy on its own is of unproven benefit, but it is a suggested component of any clinical programme of tinnitus management (Hoare, Searchfield, El Refaie, & Henry, 2014b). The intervention therefore covered a broad and comprehensive spectrum, consisting of the 21 modules shown in Table 4.1, following the version developed by Kaldo and colleagues (2007). Due to the extent of information, 8 weeks was selected as the length for the intervention.

Table 4.1 An overview of the iCBT intervention modules and intervention load

Time line	**Intervention content**	**Short worksheets or quizzes**	**Intervention load**	
			Weekly Reading	**Daily practising**
Week 1	Programme rationale and outline	3	15 minutes	
	Understanding tinnitus	5	15 minutes	
Week 2	Deep relaxation	2	10 minutes	10 minutes
	Positive imagery	2	10 minutes	5 minutes
	Sound enrichment*	3	10 minutes	As required
Week 3	Diaphragmatic breathing	4	10 minutes	10 minutes
	Reinterpreting tinnitus	5	10 minutes	5 minutes
	Sleep management*	6	15 minutes	As required
Week 4	Entire body relaxation	2	10 minutes	5 minutes
	Focusing techniques	2	10 minutes	5 minutes
	Concentration management*	7	10 minutes	As required
Week 5	Rapid relaxation	1	10 minutes	3 minutes
	Thought analysis	3	15 minutes	3 x 15 minutes
	Reducing sound sensitivity*	7	15 minutes	Daily
Week 6	Relaxation in daily routines	1	10 minutes	3-5 situations
	Cognitive restructuring	1	15 minutes	3 x 15 minutes
	Communication tactics*	5	15 minutes	As required
Week 7	Relaxation in stressful situations	2	10 minutes	As required
	Gradual exposure (listening to and not avoiding) tinnitus	4	10 minutes	3 x 5 minutes
Week 8	Reviewing helpful techniques	8-13	20 minutes	Evaluation
	Maintenance and relapse prevention	5	20 minutes	Future plan

*Optional modules

4.2.1.4 Interactive approach

Active intervention involvement is a key component in deriving benefit (James, 2013), particularly for Internet interventions (Webb, Joseph, Yardley, & Michie, 2010). As many sources of information for those with tinnitus in the UK are provided passively and in written form, an interactive approach, to differentiate this intervention from others, was considered essential. In order to address the use of different learning styles (Cassidy, 2004) multimedia formats including a variety of materials, such as videos, quizzes, diagrams, and pictures were combined in the intervention. Thirteen videos specifically for the intervention were filmed, either demonstrating techniques, or providing expert opinions or explanations. There were 33 quizzes asking questions such as 'how many people do you think have tinnitus, select A, B, C or D' and 50 worksheets with questions to think about such as 'how do you view your tinnitus?' An example of a worksheet is given in Figure 4.4.

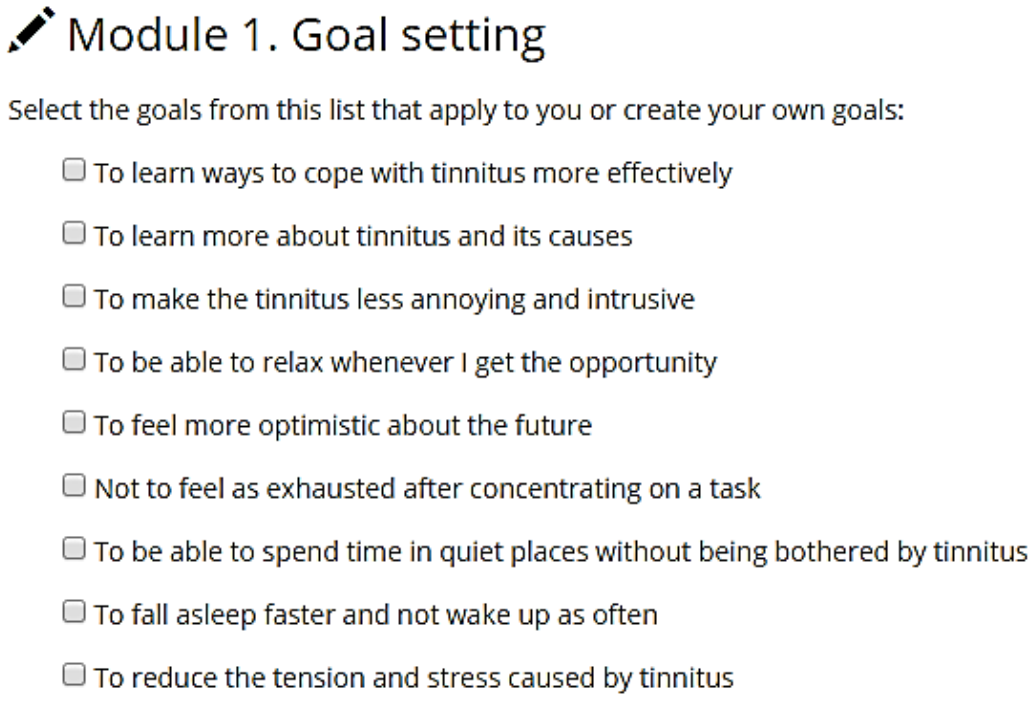


Figure 4.4 Example of a worksheet.

4.2.1.5 Support

As those with tinnitus often feel isolated, peer support in group therapy can facilitate coping with tinnitus (Mo & Coulson, 2008; Thompson, Pryce, & Refaie, 2011). Internetinterventions can incorporate many forms of support such as a closed discussion forum (allowing recipients to only read about peer experiences) or open forum (allowing users to communicate with each other, with or without moderation). A closed forum was selected to minimise the possibility of a negative influence and ensure that the intervention was a platform to grow and develop. Some of the topics on this forum are shown in Figure 4.5. In

addition, guidance by an audiologist was provided, as discussed in Chapter 3. The audiologist was alerted when worksheets were completed or messages were sent, so that feedback could be provided in a timely manner.

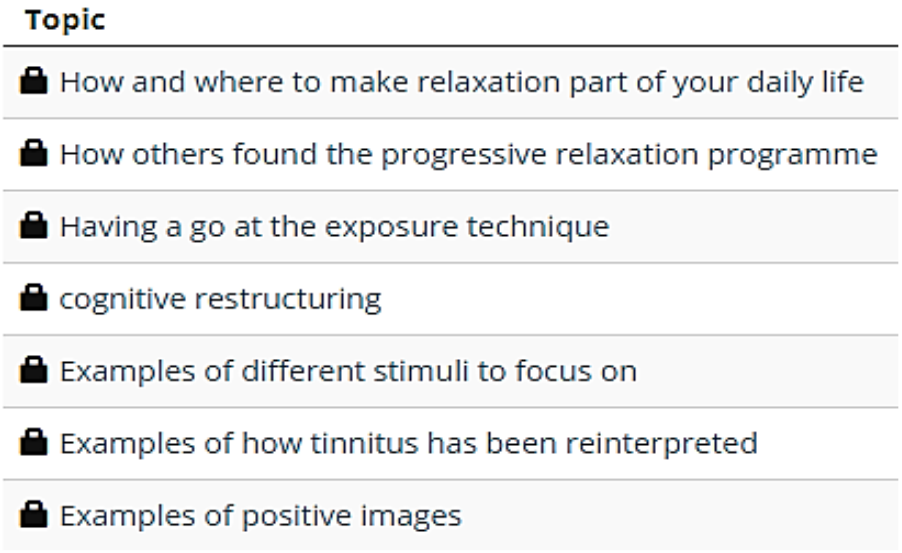


Figure 4.5 An example of the closed-forum discussion topics.

4.2.1.6 Minimising technological barriers

User-friendly Internet interventions can improve outcomes (Andersson et al., 2009). Minimising technological barriers was considered imperative. Ensuring that information was clear, straightforward to read, and all features were easily accessible was a priority. This would increase the application of the intervention to those with varying levels of computer literacy. The first module included navigational instructions to explain the site layout. An option to print and download information was incorporated to provide off-line use of the programme. To ensure linguistic appropriateness, the Fletcher reading ease (ease of reading on a scale of 0−100) and Flesch-Kincaid Grade Level (the years of education required to understand the writing) of the intervention was assessed. The target was the generally recommended levels of around 60−70 and seven on each scale, respectively (Laplante-Lévesque, Brännström, Andersson, & Lunner, 2012). Careful attention was given to the website appearance to ensure it was aesthetically pleasing, did not appear cluttered, and had a calming effect. A catchy logo was designed to define the intervention (see Figure 4.2). The background was white to facilitate reading ease. The theme colour selected was blue, due to its known calming effect from colour psychology. Attractive and visually stimulating diagrams and pictures were included to enhance the appearance of the intervention. An example is shown in Figure 4.6.

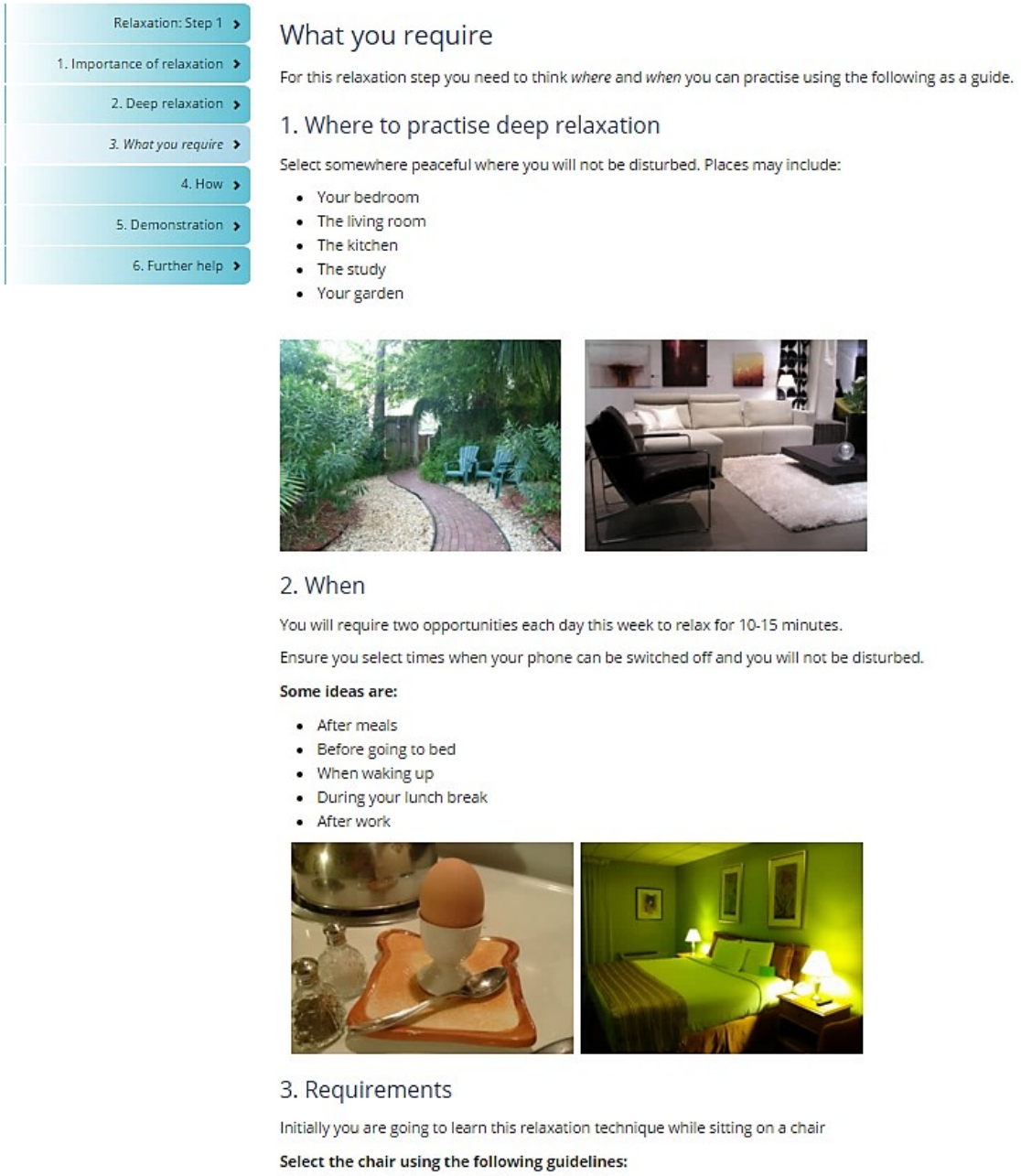


Figure 4.6 Illustration of the way in which the intervention was presentation.

4.2.1.7 Tailoring

Interventions can be fully standarised or tailored by developing specific aspects based on individual characteristics (Kreuter, Strecher, & Glassman, 1999). This may be personalised communication and/or the ability to select certain therapeutic aspects of the intervention. Providing a tailored intervention aligns the intervention with specific difficulties individuals may be experiencing. Andersson & Kaldo (2004) included tailoring aspects in their tinnitus programme, such as personal treatment goals and receiving individualised weekly feedback. Due to the heterogeneous nature of tinnitus, a tailored intervention, with the flexibility to address individual needs and preferences, appeared more appropriate than a

standardised approach. For this intervention, 16 recommended and 5 optional modules targeting specific symptoms (insomnia, hyperacusis, concentration and hearing difficulties) were included, as suggested by Andersson and colleagues (2011). An example of the module selection is given in Figure 4.7. If initial baseline scores for the ISI indicated at least subthreshold insomnia (≥ 8), undertaking the optional sleep module was recommended. If the HHIA-S scores indicated a 50% probability of hearing disability (≥ 26) the hearing tactics module was suggested and if scores were ≥ 30 on the CFQ the module covering concentration guidelines was suggested. The sound sensitivity module was recommended if scores were ≥ 28 on the HQ.

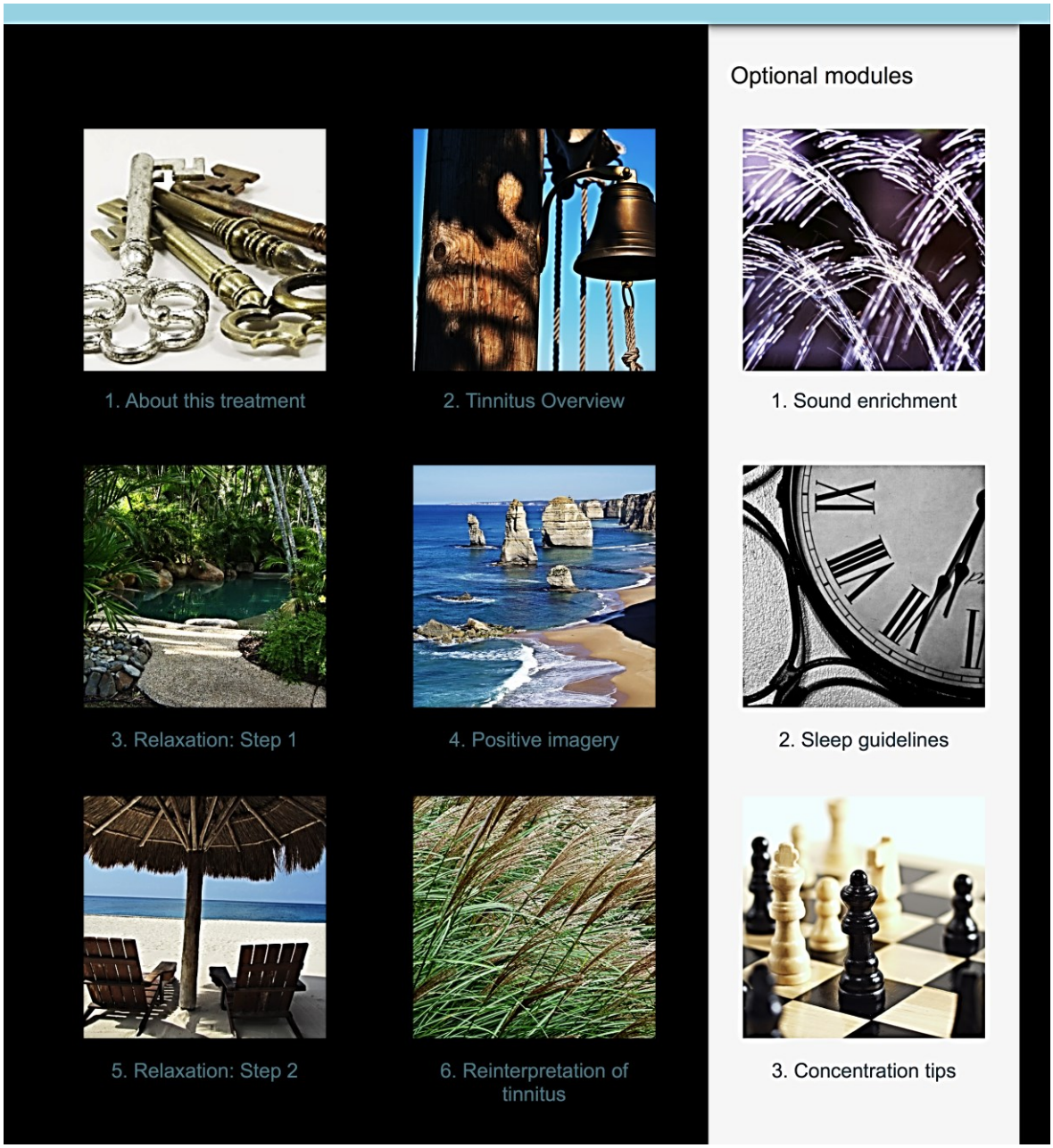


Figure 4.7 Tailored intervention modules.

4.2.1.8 Monitoring progress

Monitoring progress during and after undertaking an intervention is important. All assessment measures were integrated on the platform and could be automatically or manually assigned to users. Reminders to complete questionnaires and graphical progress indicators were included.

In summary, a comprehensive intervention was designed as illustrated in Figure 4.8. Many difficulties were encountered during this development process. Alternative ways of delivering the material were experimented with before the final version was established. The usability of worksheets, quizzes, and diaries, were adjusted to adapt to various browsers whilst maintaining ease of navigation.

4.2.2 Functionality and acceptability of the intervention

4.2.2.1 Research design

An independent measures research design was used to evaluate the suitability, content, usability, presentation, and monitoring aspects of the intervention. To ensure the intervention was of a high standard and appropriate to those with tinnitus, the intervention was rated by two user groups: an expert reviewers group and a group of adults with tinnitus. Both professionals and the general public were therefore involved in the intervention from the outset. Participants were provided login information and full access to the intervention, including the quizzes and worksheets. The purpose of the evaluation was explained and participants had a two-month period to complete the intervention evaluation questionnaire.

4.2.2.2 Participants

Expert reviewers group

Expert reviewers (n =10) with an established background in tinnitus management from both a clinical perspective and supportive background were individually selected using convenience sampling and invited to evaluate the intervention. Eight specialised audiologists and hearing rehabilitationists were approached, as involving practitioners enables translation of practice to research (Glasgow et al., 1999). Two committee members from the Cambs Tinnitus Support Group were also invited to obtain a diverse level of expertise.

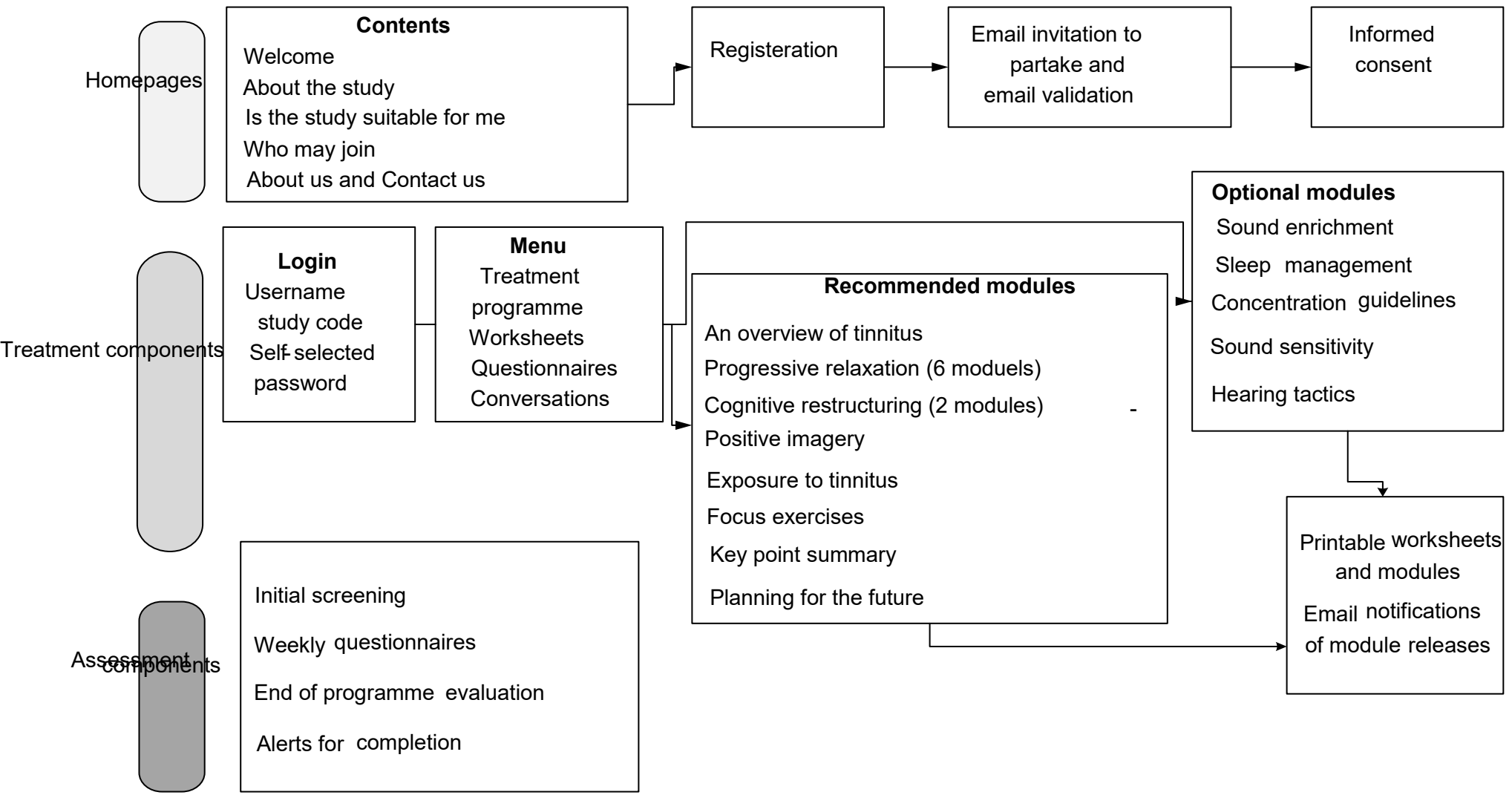


Figure 4.8 Outline of the components used in the intervention.

Adults with tinnitus group

This study was advertised UK-wide at tinnitus support groups (for example Birmingham, Canterbury, Norfolk), hearing and tinnitus charities and forums (for example British Tinnitus Association (BTA), Action on Hearing loss) and in audiology departments (for example Cambridge, Northampton, Windsor). Those meeting the eligibility criteria were invited to register for the study on the research website (http://www.tacklingtinnitus.co.uk). Due to the heterogeneous nature of tinnitus, the aim was to attract a range of participants (n = 25–30) with varying demographical backgrounds.

4.2.2.3 Data Analysis

Independent samples *t*-tests were used to compare the evaluations from expert reviewers and participants. Levene's test for equality of variances was performed to compare the variances in the two groups.

4.3 RESULTS

4.3.1 Participant characteristics

4.3.1.1 Expert reviewer group

The iCBT intervention evaluation questionnaire was completed by five expert reviewers, consisting of two specialised audiologists, one hearing rehabilitationist and two members of the tinnitus support group (2 males, 3 females). This yielded a 50% response rate, which is low, but reflects the heavy workload that clinicians experience.

4.3.1.2 Adults with tinnitus group

The target number of adults with tinnitus was obtained, as 29 completed the iCBT intervention evaluation questionnaire. The demographic profile of the participants (see Table 4.2) demonstrated that the desired range of participants with different educational and employment backgrounds, as well as varying tinnitus experiences were drawn to the study. The average tinnitus severity score was 58 (SD 18) indicating a severe level of tinnitus within this group. The majority of participants had tinnitus for between 1 and 5 years (45%), although tinnitus duration varied greatly from 3 months to more than 10 years. 72% of participants reported a co-existing hearing loss. This group was consequently familiar with the challenges that the typical combination of hearing loss and tinnitus presents. They were well read and around half of the group had undergone previous tinnitus treatments. As a whole the group had the appropriate demographic background to evaluate the intervention.

Table 4.2 Demographical characteristics of the adults with tinnitus

DEMOGRAPHIC INFORMATION	**Number (%)**
Gender	Male: 14 (48%) Female: 15 (52%)
Mode of age	60–69 years: 12 (41%)
Tinnitus Functional Index average	58.12 out of 100 (SD: 18)
Tinnitus duration	3–12 months: 2 (7%) 1–5 years: 13 (45%) 5–10 years: 5 (17%) 10+ years: 9 (31%)
Location of tinnitus	Both ears: 15 (52%) Right ear: 3 (10%) Left ear: 6 (21%) Head/ unsure: 5 (17%)
How often tinnitus is heard	Constant: 17 (59%) Most of the time: 11 (38%) Without hearing aids: 1 (4%)
Tinnitus characteristics	High pitched: 13 (45%) Low pitched: 6 (22%) Pulsating: 6 (22%) Clicking: 4 (4%)
Seen a GP/ENT regarding tinnitus	28 (97%)
Previous tinnitus treatments received	14 (48%)
Highest Educational level	School: 6 (21%) College/vocational training: 8 (28%) Undergraduate degree: 12 (41%) Postgraduate degree: 3 (10%)
Employment	Manager/professional: 9 (31%) Skilled tradesman/technical: 4 (14%) Homemaker/service occupation: 2 (7%) Retired: 12 (41%) Unemployed: 2 (7%)
Read up about tinnitus	27 (93%)
Hearing loss reported	21 (72%)
Hearing aids used	10 (35%)

4.3.2 Functionality testing

A participant's login username was sent via the participant's email address. Some of the emails sent from the platform did not reach the recipients. It was found that the emails were treated as spam. Rectifications included changing the programme name from Conquering Tinnitus to Tackling Tinnitus, as the latter wording was less likely to be analysed as spam by email systems. In addition, the initial login, requiring a high-security password, was too difficult for some users, despite onscreen instructions.

4.3.3 Acceptability evaluations

The expert reviewers and adults with tinnitus completed online evaluations using a five-point Likert scale of the intervention suitability, content, usability, presentation, and monitoring aspects, as seen in Figure 4.9. Mean scores are shown in Table 4.3. Overall, the intervention was highly rated, with an average score of 4.3 (SD: 0.8) out of 5 (range 3 to 5). The rating for each question is shown in Figure 4.10, which compares ratings between the two groups. Areas with the lowest ratings were those associated with the monitoring aspects.

With one exception, the ratings of expert reviewers' and adults with tinnitus for the different questions were not significantly different, as seen in Table 4.3. The expert reviewers mean rating for iCBT was 4.5 (SD: 0.3), while the mean tinnitus group rating was 4.3 (SD: 0.3). The only significant difference was for how informative the materials were, which the expert reviewers rated significantly higher than the tinnitus group.

Table 4.3 Intervention ratings

Category	**Expert reviewers Mean (SD)**	**Adults with tinnitus Mean (SD)**	**Mean difference (95% CI)**	***t*-test**
USABILITY				
Straightforward to use	4.8 (0.45)	4.4 (0.78)	0.42 (-0.98 to 0.14)	$t(8.9) = -1.71$; $p = 0.12$
Easy to navigate	4.6 (0.89)	4.4 (0.73)	0.22 (-0.96 to 0.52)	$t(32) = -0.61$; $p = 0.55$
Appropriate module length	4.4 (0.89)	4.4 (0.77)	0.06 (-0.83 to 0.72)	$t(32) = -0.15$; $p = 0.89$

CONTENT				
Suitable level of information	4.2 (0.84)	4.5 (0.78)	0.25 (-0.53 to 1.03)	$t(32) = 0.65$; $p = 0.52$
Informative materials	5 (0.00)	4.6 (0.73)	0.41 (-0.69 to -0.14)	$t(28) = -3.04$; $p = 0.005$*
Interesting materials	4.8 (0.45)	4.6 (0.68)	0.18 (-0.82 to 0.46)	$t(32) = -0.57$; $p = 0.57$
PRESENTATION				
Content was well-structured	4.2 (0.84)	4.2 (0.79)	-0.04 (-0.74 to 0.82)	$t(32) = 0.11$; $p = 0.92$
Suitable presentation	4.2 (0.84)	4.4 (0.72)	-0.14 (-0.58 to 0.87)	$t(32) = 0.41$; $p = 0.69$
Ease of reading	4.0 (1.00)	4.6 (0.56)	0.62 (-0.62 to 1.85)	$t(4.45) = 1.35$; $p = 0.24$
SUITABILITY				
Suitable for those with tinnitus	4.8 (0.45)	4.3 (1.03)	0.5 (-1.12 to 0.07)	$t(13.13) = -1.89$; $p = 0.81$
Appropriate range of modules	4.8 (0.45)	4.4 (0.45)	0.4 (-0.98 to 0.14)	$t(9.52) = -1.67$; $p = 0.13$
Beneficial topics covered	4.8 (0.45)	4.3 (1.03)	0.5 (-1.12 to 0.07)	$t(13.13) = -1.89$; $p = 0.82$
MONITORING ASPECTS				
Worksheets appropriateness	4.6 (0.55)	3.0 (1.08)	0.7 (-1.72 to 0.31)	$t(32) = -1.41$; $p = 0.17$
Clear instructions how to practice	4.0 (0.71)	4.1 (0.95)	0.1 (-0.78 to 1.05)	$t(32) = 0.31$; $p = 0.76$
Motivation to do the exercises	3.6 (0.55)	3.4 (1.27)	-0.2 (-1.40 to 0.96)	$t(32) = -0.38$; $p = 0.71$

* *Significant at* $p < 0.05$

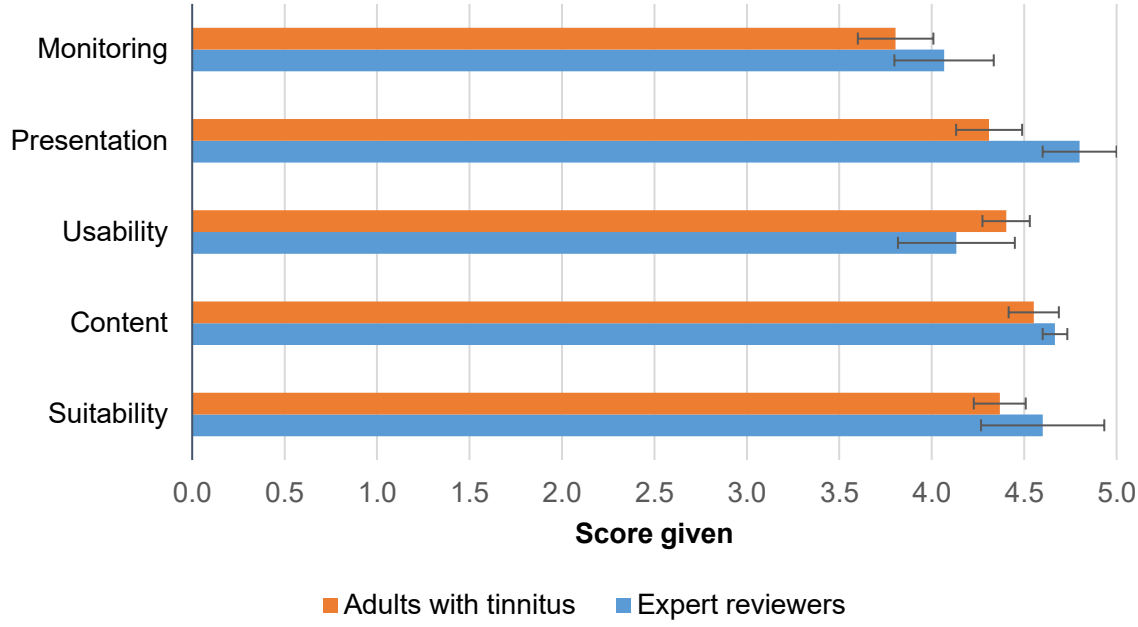


Figure 4.9 Ratings for various aspects of the intervention. Error bars represent the ±1 standard error of the mean.

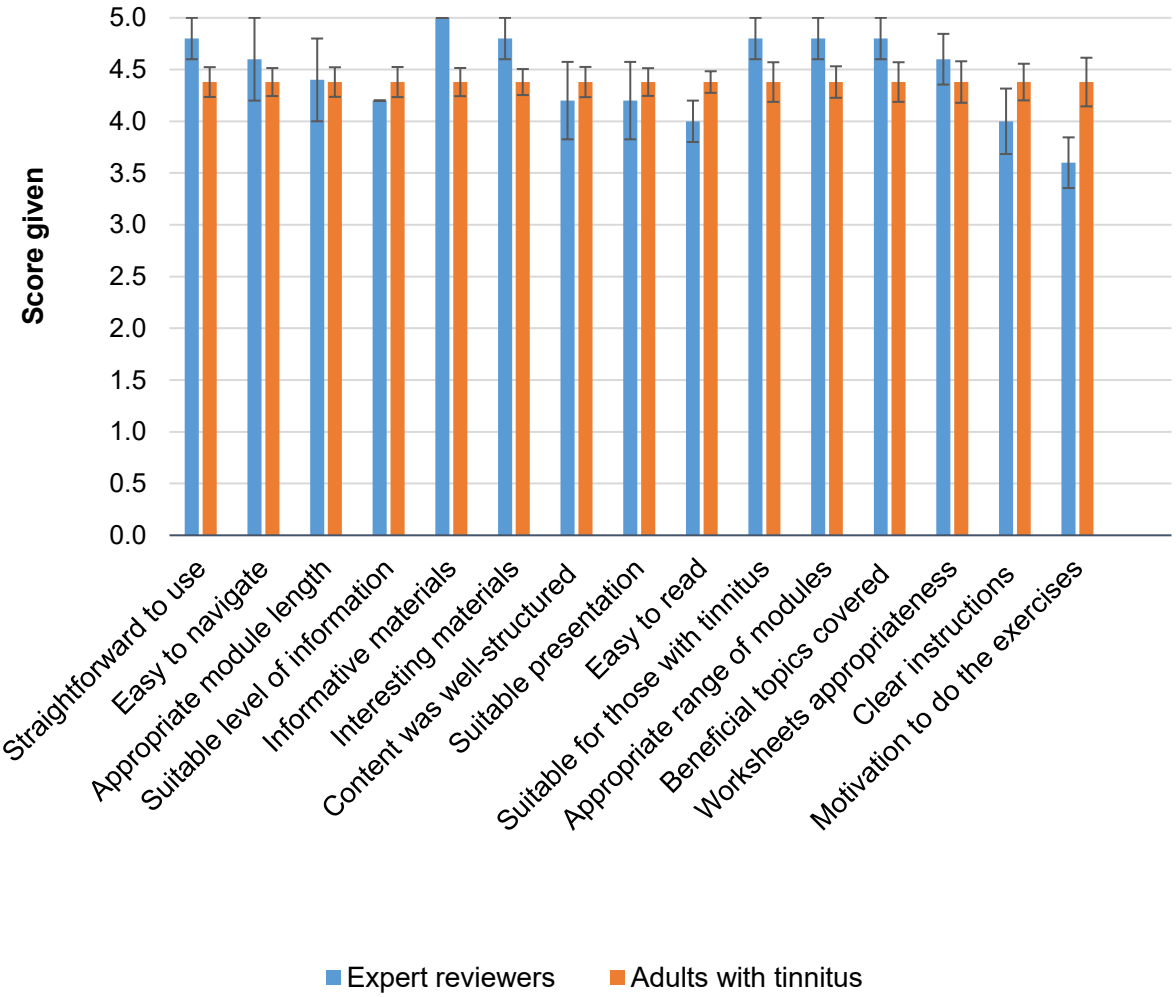


Figure 4.10 Graphical representation of the ratings. Error bars represent the ±1 standard error of the mean.

4.3.4 Intervention refinements suggested

Suggestions made by the two groups included simplifying the login process and vocabulary used. More questions were recommended in the frequently asked questions sections at the end of each module. Subtitles were requested for the videos.

4.4 DISCUSSION

In this chapter, the development and technical functionality evaluation of an Internet-based intervention for tinnitus as adapted for a UK population are described. This discussion focuses on the development process and findings from the evaluations undertaken.

4.4.1 Development of iCBT for tinnitus

The intervention was aimed to promote user engagement, improve positive outcomes and inspire recipients to complete the programme. Important theoretical principles were incorporated into every aspect of the intervention. The strength of the design was the multi-disciplinary collaboration at each phase of development. The final version was comprehensive, attractive, easy to navigate and interactive. A high level of adaptability was integrated into the design to ensure it could be revised and altered if further refinements were required.

The intervention was tailored, enabling participants to select optional modules that would be of benefit. The evidence base supporting tailoring remains inconclusive. In a meta-analysis reviewing 40 studies, Lustria and colleagues (2013) found that tailored interventions resulted in significantly greater improvement in health outcomes than non-tailored interventions. On the other hand, Păsărelu and collegues (2017), did not find that tailored interventions resulted in improved outcomes in a meta-analysis reviewing 19 Internet-based CBT studies for anxiety and depression. As experiences of tinnitus are heterogeneous, a tailored approach was judged to be appropriate for a tinnitus intervention.

The intervention was designed to enable users to engage with the content visually. This may reinforce information retention, which is known to be poor following provision of information verbally, as is usually done in clinical appointments (Doherty and Desjardins, 2012). Guidance was provided by an audiologist to aid and encourage participation and completion of the programme. These features were included to promote positive outcomes for the specific culture it was intended for.

4.4.2 Technical functionality of iCBT for tinnitus

Technical functional difficulties can prevent individuals completing the intervention. To minimise these barriers the developed iCBT intervention was thoroughly tested by both expert reviewers and adults with significant levels of tinnitus. Some initial technical difficulties were experienced, as a few emails sent from the webplatform were not accepted by certain email accounts. Changes were required to ensure the smooth running of the intervention. Some users found the initial login difficult and needed assistance from the therapist. Often the on-screen instructions regarding the password requirements were not followed and participants did not always use their study user name to login. As login was challenging for some, it was simplified as much as possible, without compromising data protection. More technical difficulties were found when compared with those experienced by populations in Sweden and Germany. Further problems with some navigational aspects, hyperlinks, interactive components, media clips and media links were detected and rectified. Functionality testing was useful in identifying hindrances to usage of the intervention.

4.4.3 Acceptability of the intervention

Key strategies to help new interventions to be translated into routine practice are suggested by guidance from the Medical Research Council (Craig et al., 2008). These include removing barriers associated with data security, cost, acceptance and operational barriers (Hill & Powell, 2009). The acceptability of an intervention has always been regarded as one of the key features required to translate research into practice (Kaltenthaler et al., 2008). Lack of acceptability may influence take up, increase dropout rates and affect the overall effectiveness of an intervention. Acceptability is required not only by individuals undertaking the intervention but also by professionals and non-professionals who have an interest in the condition being treated. Acceptance of new interventions is largely based on health professionals' attitudes toward them (Perle et al., 2013). Much work is still required to improve these perceptions (Eikelboom, 2016). Unfounded fears, such as concerns that clinical intervention routes will no longer be required, need to be addressed. Additional treatment routes are designed as a complement to existing interventions by improving access to provision of care. Approaching these fears in a culturally sensitive manner is important (Hadjistavropoulos, Thompson, Klein, & Austin, 2012).

The public and patient's perceptions of Internet interventions are also important. Musiat and colleagues (2014) found that perceptions in the UK of computerised interventions were poor and a greater acceptance was found for F2F interventions. Obtaining acceptability ratings from experts (n = 5) and adults (n = 29) with tinnitus in terms of the suitability, content, usability, presentation and monitoring aspects were therefore important. On average, the intervention was well rated. Ratings did not differ significantly between expert reviewers and

adults with tinnitus apart from one subsection, namely how informative the materials were. Although both ratings for this were high, expert reviewers rated the intervention as significantly more informative than the adults with tinnitus. This may be related to participants in the tinnitus group being well read regarding tinnitus and to the fact that half of this group had undergone previous tinnitus therapies. This prior knowledge meant that not all the information presented was new.

The most poorly rated area in the intervention was that relating to motivation to complete the worksheets. The worksheets were subsequently revised to ensure that they were user-friendly. A shortcut to accessing the worksheets from the main menu was installed to enable participants to navigate to these more easily.

Previous trials have found variable results regarding the credibility and acceptability of iCBT. In Australia, the iCBT intervention was given a rating of 32.6 out of 50 (SD: 6.7) by participants (Abbott et al., 2009). Kaldo and colleagues (2008), compared treatment credibility ratings for those experiencing significant levels of tinnitus. They found that GCBT was rated as more credible than iCBT pre-intervention. On the other hand, Kaldo-Sandström et al. (2004) did not find a difference in credibility ratings between iCBT and GCBT. Nyenhuis and colleagues (2013c), investigated the acceptance of iCBT versus GCBT for tinnitus by presenting both groups with the same CBT manual. They found that participants were as satisfied with the iCBT as they were with GCBT and the dropout rate was similar for the two at 35% for the iCBT and 35% for GCBT. However, more people in the iCBT group did not complete the programme, at 64% opposed to 55% for GCBT. They found that satisfaction was affected by the age of participants, as older participants preferred GCBT. Similar results were obtained by Weise and colleagues (1998), who reported that satisfaction with GCBT training increased with age while it decreased with age for iCBT. Lower levels of initial tinnitus distress were associated with higher satisfaction for iCBT, a trend not found for the GCBT group. Clearly much work is still required in this area before Internet interventions will be viewed as credible by patients, health professionals and stakeholders alike, particularly in a UK context. Involving both professionals and adults with tinnitus from the onset of this research was one strategy to minimise these barriers and add treatment credibility.

4.4.4 Revising the intervention

Suggestions made following the evaluations by the adults with tinnitus were implemented where possible into a revised version. This included simplifying the vocabulary, and adding subtitles for the videos. Additional frequently asked questions were added.

4.4.5 Study limitations

The required sample size was not estimated prior to the study. A standardised satisfaction outcome measure was not used, as one was not identified that was specific enough. Although this is a drawback, the designed outcome measure was tailored to this particular intervention.

4.5 CONCLUSIONS

The first research question, determining whether an acceptable iCBT intervention could be developed was addressed. The intervention was developed to be engaging by including interactive components. A sound theoretical base and evidenced-based materials were used. Encouraging completion of the programme was achieved by including monitoring aspects, empowering participants to identify their own intervention goals and by providing guidance throughout.

Evaluations by both expert reviewers and adults with tinnitus showed high satisfaction regarding the content, suitability, presentation, usability and monitoring aspects provided in the intervention. These evaluations provided confidence that this intervention was ready to be used during further clinical trials. The next chapter describes the experimental results regarding the feasibility of iCBT for tinnitus in a UK population.

5 CLINICAL TRIAL PHASE I: FEASIBILITY OF ICBT

This chapter explores the second research question focusing on the feasibility of audiologist-guided iCBT for adults with tinnitus in the UK.

5.1 INTRODUCTION

An iCBT intervention for a UK population was developed to address the need to increase access to evidence-based tinnitus interventions for this population (see Chapter 4). Although iCBT holds potential, it may not be realised if it is not systematically evaluated, as discussed in Chapter 3. A feasibility study was considered to be an appropriate starting point. Feasibility studies can identify barriers and guide planning of subsequent randomised controlled trials (Campbell et al., 2000). Various feasibility aspects surrounding iCBT warrant investigation. As iCBT for tinnitus has not been used in the UK before, the recruitment potential needs to be ascertained (McDonald et al., 2006). Attrition rates should to be established with this population, as variable rates have been reported in previous iCBT for tinnitus trials (see Appendix A). Moreover, determining adherence using a self-help intervention format is important (Donkin et al., 2011; Kelders, Kok, Ossebaard, & van Gemert-Pijnen, 2012). The feasibility of using an audiologist, as opposed to psychologist, to guide iCBT needs assessment, as lack of experience in applying CBT techniques may affect the outcomes obtained. This trial formed Phase I of a clinical trial regarding the feasibility of audiologist-guided iCBT in the UK. Specific objectives were as follows:

i) Establishing the feasibility of iCBT in terms of recruitment potential, attrition and adherence rates
ii) Determining the feasibility of audiologist-guided iCBT with regard to the outcomes obtained for tinnitus distress and tinnitus-related comorbidities
iii) Identifying the need for further refinements to the iCBT intervention and the protocol for implementation during subsequent randomised control trials

5.2 METHOD

5.2.1 Study design

As a feasibility study, a large randomised study design was not sought. A single-group open trial design was selected. The same protocol as for Phase II was used (see Chapter 6), to identify whether any alterations were required. The only difference was that no control group or long-term evaluations were incorporated.

5.2.2 Recruitment and enrolment

The intended population were those with significant levels of tinnitus and who were underserved with tinnitus interventions. The recruitment period was set to 1 month. Recruitment was UK wide, using a variety of approaches. The British Tinnitus Association (BTA) provided information about the study in their magazine, Quiet. Tinnitus support groups (n = 30), tinnitus forums (n = 2) and audiology departments (n = 5) shared the study details. Those interested were directed to the study website (http://www.tacklingtinnitus.co.uk) where they could read more about the study and register interest in partaking. Participants meeting the inclusion criteria after completion of the baseline assessment measures and the telephone screening were given login information to enable access to the intervention.

5.2.3 Statistical analysis

5.2.3.1 Missing data analysis

An Intention to treat (ITT) paradigm was used as described in Section 3.10.1. Results from Little's "missing completely at random" test (Little, 1988) indicated that the data were likely to be MCAR (missing completely at random; (χ^2= 12.37, p = 0.19). In other words, missing values were likely to be randomly distributed across all observations and that there was no systematic pattern to the missing data. Missing values were thus imputed, as described in Section 3.10.1 for data analysis. Results were compared with per-protocol analysis (including only data from participants who completed the assigned intervention). As there was no difference, the ITT results are reported.

5.2.3.2 Pre- and post-intervention comparisons (T_0–T_1)

The primary study outcome was a change in TFI score at post-intervention (T_0–T_1). Secondary study outcomes were changes in the scores of secondary assessment measures between T_0 and T_1. Paired-samples *t*-tests were used to compare pre- and post-intervention scores (T_0–T_1) for all assessment measures. Effect sizes (Cohen's *d*) were calculated by dividing the differences in pre- and post- intervention means by the pooled standard deviations. The Reliable Change Index (RCI) was calculated to assess whether clinically significant changes in the TFI were obtained, as described in chapter 3.

5.2.3.3 Monitoring intervention effects between T_0 and T_1

A one-way repeated measures ANOVA was used to copare the weekly THI-Scores with the within-subject factors of time (weeks 1-8). The main effects were followed up by Bonferroni-corrected post-hoc testing.

5.2.3.4 Predictors of outcome

To help define participant criteria for future trials, predictors of outcome were calculated. This was done using partial correlations to determine the relationship between post-intervention scores and specific predictors while controlling the effects of additional variables. The predictors considered were initial TFI score, level of education, employment type, tinnitus duration, age and gender. For each correlation, five variables were partialled out.

5.3 RESULTS

5.3.1 Recruitment potential and participant characteristics

Participants who had registered on the study website over the recruitment period were invited to participate (n = 44). Of those invited, 37 provided online consent, completed the online questionnaire and were eligible to participate. Participants had a range of TFI scores (22–94), including two participants who had scores below 25, which is considered to be 'mild' tinnitus. All participants were included, regardless of their TFI scores. The reason for this was to assess what criteria should be set for TFI scores in subsequent clinical trials. The demographic profile of the participants is shown in Table 5.1. Participants with varying clinical and demographical backgrounds were drawn to the study. Participants were spread across the UK, with the majority based in England and a few in Wales, Scotland and Northern Ireland.

5.3.2 Attrition

The number of participants who completed the assessment measures at each time point is shown in Figure 5.1. Of the 37 participants who started the study, two developed major health problems. A further three withdrew, one due to login and navigation difficulties. The other two participants withdrew as their tinnitus had improved and they no longer required the intervention. One of these participants had a baseline score of 52, indicating severe tinnitus. The other had a low initial TFI score of 24 and felt that their tinnitus was not significant enough to require the level of support provided by the intervention. Those withdrawing did so within the first 2 weeks of the intervention. The post-intervention assessments were completed by 29 participants, yielding a completion rate of 78%. The attrition rate was 22%.

Table 5.1 Demographic characteristics of the participants: Phase I

Category	Number (%) or mean (SD)
Gender	Male: 18 (489%) Female: 19 (51%)
Mode of age	60–69 years: 12 (32%)
Mode of tinnitus duration	1–5 years: 16 (43%)
Hearing loss reported	26 (70%)
Hearing aids used	10 (27%)
Location of tinnitus	Both ears 17 (46%) Left ear: 7 (19%) Right ear: 6 (16%) Head/unsure: 7 (19%)
Frequency of tinnitus	Constant: 22 (60%) Most of the time: 14 (38%) Without hearing aids: 1 (3%)
Seen a GP/ ENT due to tinnitus	35 (95%)
Previous tinnitus treatments	16 (43%)
Read up about tinnitus	34 (92%)
Educational level	School: 11 (30%) College/vocational training: 10 (27%) Undergraduate degree 14 (38%) Postgraduate degree: 2 (5%)
Employment status	Manager/professional: 10 (27%) Skilled tradesman/technical: 5 (14%) Homemaker/service occupation: 4 (11%) Retired: 16 (43%) Unemployed: 2 (5%)
Reduced working due to tinnitus	Stopped working: 8 (22%) Reduced hours: 1 (3%)

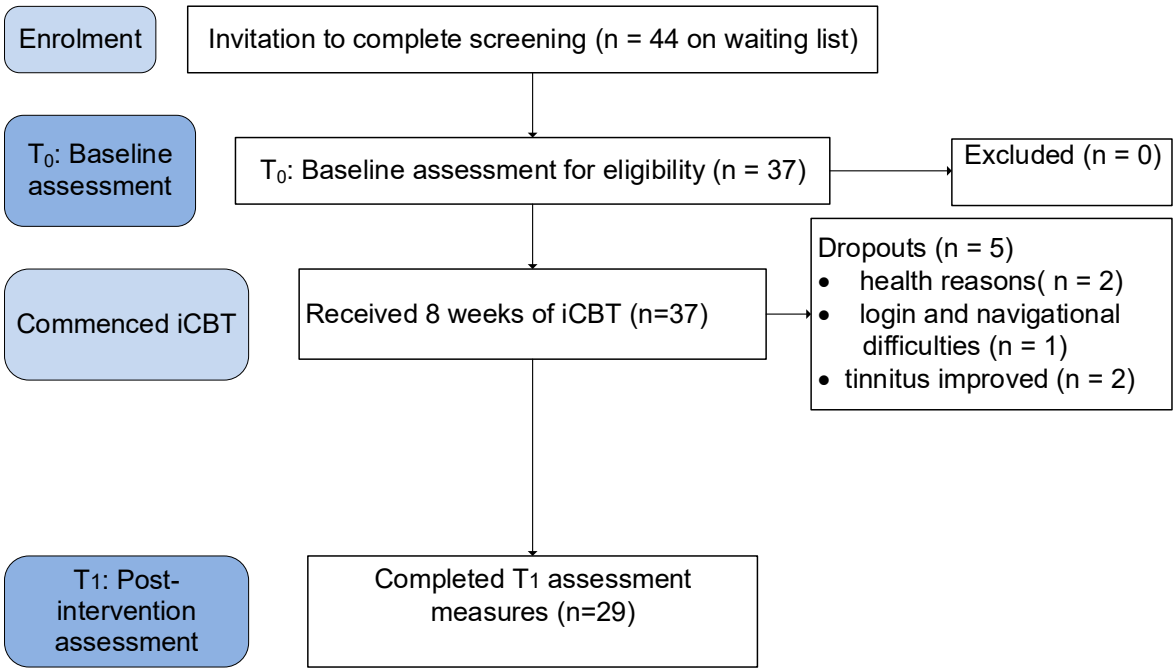


Figure 5.1 The CONSORT study profile for Phase I.

5.3.3 Intervention adherence

The extent to which participants actively engaged and interacted with the resources provided by this iCBT intervention is shown in Table 5.2. Participants (excluding those who withdrew) logged into the programme an average of 18 times during the 8 week period of the intervention. An average of 78% of the recommended modules and 68% of the optional module were read. Overall 43% of the worksheets were completed. In many cases participants who were not engaging explained this was due to a bout of ill health or lack of time. Some participants commented that they valued being able to do the intervention at their home or when out without requiring a hospital appointment. Furthermore, working at their own pace was reported to be an advantage.

5.3.4 Guidance

The audiologist spent at least 10 minutes per week providing written feedback to each participant. Feedback was also provided during the week as and when worksheets were completed. There were 413 tailored messages to individual participants (13 per user, excluding those who withdrew), with a minimum of one message per week. These messages aimed to add encouragement, to maintain involvement and provide feedback on worksheets completed. Messages were sent to all participants on a weekly basis to introduce the new modules. Those not logging on were telephoned by the audiologist to see if they required assistance. In open questioning about the study, some participants (n = 11) spontaneously mentioned that the guidance received was of value.

Table 5.2 Intervention adherence: Phase I

	Participants n = 32 (excluding those who withdrew)	**Mean per participant**
Logins	572	18
Modules read	475	15
Worksheets completed	684	21
Messages sent	119	4
Reported time spent on the module content on average	21 minutes (SD: 18)	(range 10–60 minutes)

5.3.5 Feasibility of audiologist-guided iCBT for tinnitus distress

At post-intervention (T_1) the mean TFI score was 19 points lower (SD: 19) than baseline (Table 5.3). There was a significant improvement (T_0–T_1), with a large effect size (d = 1.18) for the change in TFI score. The RCI indicated that a change of 24 in the TFI score was required post-intervention to be considered clinically significant. This was reached by 38% of participants (n = 14).

5.3.6 Monitoring intervention effects

Differences were found in tinnitus distress as measured by the THI-S across the 8 time points between T_0–T_1 [$F(7, 35) = 7.73$, $p = 0.001$] (see Figure 5.2). Follow-up analysis indicated significant difference between week 1 through to week 8 of this period.

Table 5.3 Pre- and post-intervention assessment measures comparisons

Assessment measure	T_0 Mean (SD)	T_1 Mean (SD)	Effect size, (Cohen's *d*)	*t*-test
TFI	56 (18)	37 (20)	1.18	$t(36) = 6.26$; $p = 0.001$*
ISI	12 (5)	7 (5)	1.20	$t(36) = 5.54$; $p = 0.001$*
GAD-7	8 (5)	6 (5)	0.10	$t(36) = 3.74$ $p = 0.07$
PHQ-9	7 (6)	6 (5)	0.37	$t(36) = 1.73$; $p = 0.09$
HHIA-S	15 (12)	13 (10)	0.06	$t(36) = 1.32$; $p = 0.20$
HQ	19 (10)	16 (10)	0.29	$t(36) = 1.71$; $p = 0.10$
CFQ	36 (15)	34 (15)	0.16	$t(36) = 0.68$; $p = 0.50$
SWLS	16 (7)	17 (7)	0.28	$t(36) = -1.22$; $p = 0.25$

* Significant at $p < 0.05$

Acronyms: *SD: Standard Deviation, T_0: pre-intervention, T_1: post-intervention, THI-S: Tinnitus Handicap Inventory-screening version, TFI: Tinnitus Functional Index, ISI: Insomnia Severity Index, GAD: Generalised Anxiety Disorder, PHQ: Patient Health Questionnaire, HHIA-S: Hearing Handicap Inventory for Adults-screening version, HQ: Hyperacusis Questionnaire, CFQ: Cognitive Failures Questionnaire, SWLS: Satisfaction with Life Scales*

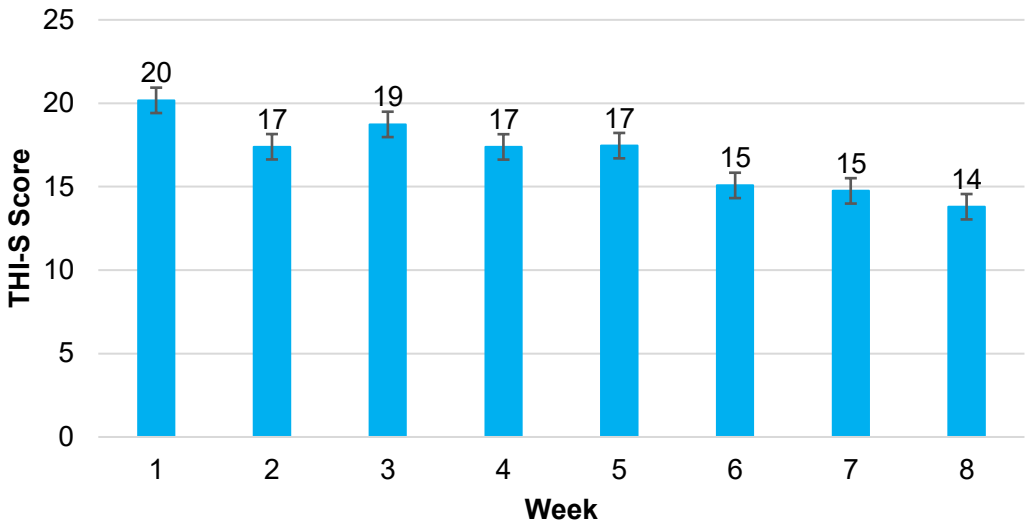


Figure 5.2 Weekly Tinnitus Handicap Inventory-Screening scores: Phase I. Error bars represent the ±1 standard error of the mean.

5.3.7 Feasibility of audiologist-guided iCBT for tinnitus-related comorbidities

Pre-intervention scores for many of the secondary assessment measures were below the level of clinical significance. As a result, post-intervention improvements would be unlikely. Only the ISI showed a significant difference post-intervention (T_1), with the mean severity changing from 'sub-threshold significance' to 'non-significant' results. This represented a large-sized effect. No significant T_0–T_1 changes were found for questionnaires related to anxiety, depression, hearing disability, hyperacusis, satisfaction with life and cognitive failures.

5.3.8 Sample size and target population for larger clinical trials

Sample size estimations for future trials were established from these results. Calculations indicated that 19 participants would be required per group, based on achieving a significant between-group change of 19 points at a significance level of 0.05 and effect size of 0.9, when using G*Power version 3.1.6 (Faul, Erdfelder, Lang, & Buchner, 2007). To ensure that the required power is achieved, additional participants would need to be recruited to account for possible drop-outs at a rate estimated at 22% from this trial.

To help identify the target population for such an intervention, pre-intervention factors that were correlated with post-intervention TFI scores were sought. The only significant moderate positive correlation was between pre- and post-intervention TFI scores [$r(31) = .533$, $p = 0.001$]. The strength of the relationship was weak between post-intervention TFI

outcome and other variables, including level of education, employment status, duration of having tinnitus, age or gender (Table 5.4).

Table 5.4 Factors influencing post-intervention tinnitus severity

Comparison	Pearson's Correlation (r)	Confidence interval of the correlation	*p*-value	R^2	% of variance accounted for
Initial tinnitus severity	0.59	0.32 to 0.80	0.001*	0.35	34.8%
Gender	0.27	-0.11 to 0.60	0.16	0.07	7.3%
Age	-0.16	-0.47 to 0.19	0.41	0.03	2.6%
Educational level	-0.12	-0.40 to 0.19	0.54	0.01	1.4%
Employment status	-0.27	-0.58 to 0.10	0.51	0.07	7.3%
Tinnitus duration	0.23	-0.32 to 0.80	0.24	0.05	5.3%

5.3.9 Refinements required for larger clinical trials

Refinements to the demographic questionnaire were required as the categories for certain questions were too broad. For example, when identifying how long participants had had tinnitus, pre-formed categories were provided, such as 1–5 years, 5–10 years. Participants indicated that these categories were too broad and self-selecting the exact time would be better. A further suggestion was to personalise messages, instead of anonymising them. The participants remarked that the weekly questionnaire options of 'yes, sometimes, no' were too general, and a questionnaire with more defined options would be preferred. An indication of modules already read would be of value. The sound quality of some of the video's was not optimal, making it difficult to hear what was said.

5.4 DISCUSSION

This chapter has evaluated the feasibility of an Internet-based CBT intervention for tinnitus in the UK, using guidance from an audiologist in an open trial design. The study was of value in preparing for future controlled trials in the UK. The results obtained for each objective are discussed.

5.4.1 Feasibility of iCBT in the UK

5.4.1.1 Recruitment potential

Take-up rates for the study were low. Recruitment was largely through tinnitus support group networks, hospitals and tinnitus charities, therefore targeting those more familiar with strategies to manage tinnitus. This may have partly attributed to these low rates. Another possible reason for low take-up rates, is related to public views of Internet interventions. Musiat and colleagues (2014) found that perceptions of computerised interventions were poor in the UK, with more acceptance for F2F interventions. To increase recruitment rates, improvement in public perception of such interventions within the UK is required (Gul & Ali, 2010). In addition, a clearer understanding of who viewed the recruitment website may guide future recruitment strategies. Web analytic tools should be incorporated in the recruitment website to monitor website traffic during future trials.

5.4.1.2 Attrition rates

A concern regarding Internet-delivered interventions is the possibility of a high dropout rate, especially in unguided interventions (Eysenbach, 2005). In previous iCBT studies for tinnitus, attrition rates have varied greatly between 5 and 57% (see Appendix A). Attrition rates for the present study fell toward the middle of this range at 22%. Such attrition rates are acceptable, as they are similar to those found for traditional GCBT interventions for tinnitus (Kaldo et al., 2008). Previous research has demonstrated that drop-out rates for iCBT were no greater than in traditional psychological therapy (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Lewis, Pearce, & Bisson, 2012). Strategies to minimise attrition rates in future trials need to be prioritised. Ensuring post-intervention questionnaire completion should be a key element in improving attrition in further trials. One strategy would be to schedule post-intervention telephone calls. This set telephone appointment may serve as a motivator to encourage post-intervention questionnaire completion. Sample size calculations need to account for anticipated missing data in future trials (Dziura, Post, Zhao, Fu, & Peduzzi, 2013). Overall the obtained attrition rates indicate the feasibility of iCBT within the UK, and an effectiveness trial is warranted.

5.4.1.3 Adherence to iCBT

There was a variability degree of engagement in the programme. Despite regular encouragement, some participants struggled to engage with the intervention. Time constraints, work pressures and poor health restricted engagement. Kaldo and colleagues (2008) found that 43% of participants did not complete the full iCBT programme. Although not directly comparable, this was similar to the percentage of sessions actually attended by those receiving GCBT. Donkin & Glozier (2012), investigated factors contributing to Internet

intervention adherence. Key factors were perseverance, intrinsic motivation, identification with the intervention, experiencing improvements and having more control. Additional factors were active involvement, a positive attitude, the ability to work independently, taking responsibility, and identifying the link between the effort made and the resulting success (Bendelin et al., 2011; Heinrich et al., 2016; Macea et al., 2010). Active intervention involvement should to be encouraged, as this is likely to lead to improved behavioural change (James, 2013). It is possible that guidance provided by an audiologist, as opposed to a psychotherapist, contributed to the variability in engagement. Exploring and comparing the nature of the guidance provided is therefore important. Yardley and colleagues (2016), argued that effective engagement promotes adherence. Ways of promoting effective engagement should be sought.

5.4.2 Feasibility of audiologist-guided iCBT on the outcomes obtained

5.4.2.1 Feasibility of audiologist-guided iCBT for tinnitus distress

Tinnitus distress was lowered by the intervention, as measured by the TFI. The large effect size of 1.18 exceeded the effect sizes from two previous single-group effectiveness trials (Cohen's *d* = 0.56 and 0.58) by Kaldo-Sandström and colleagues (2004), and Kaldo and colleagues (2013), respectively. These discrepancies may be related to the different assessment measures (Tinnitus Reaction Questionnaire (TRQ; Wilson et al., 1991) versus TFI) and populations (clinical versus research volunteers) used in these studies. Guidance from an audiologist appears feasible for iCBT for tinnitus. This is plausible, as previous Internet-based studies for depression, anxiety and social phobia have found comparable results regardless of whether guidance was provided by a clinician or a technical assistant (Robinson et al., 2010; Titov et al., 2009; Titov et al., 2010).

To assess clinical significance, the RCI was calculated. The T_0–T_1 TFI score change of 24 was regarded as clinically significant. This RCI value is similar to the meaningful difference found by Fackrell and colleagues (2016), studying a group of research volunteers, although it differs from the 13 point difference found by Meikle and colleagues (2012) for a clinical population. This may be partly due to research volunteers being included in both the present research and the study by Fackrell and colleagues (2016). In the present study, only 38% of participants achieved a clinically significant change. Ways of improving this rate need to be sought.

5.4.3 Protocol refinements

Protocol refinements were identified. These included asking participants for their names, although this was still optional, so that personalised messages could be sent during correspondence. The screening questionnaire was adjusted to yield more specific results.

This was achieved by including an open response opportunity for certain categories such as age and duration of tinnitus. Although the weekly questionnaire was found not to be specific enough, alternative options were less specific or too long for a repetitive measure. To help participants monitor which modules had been read, ticks were automatically placed next to read modules. The videos required re-recording to improve their sound quality.

Participants valued the Internet intervention due to the ability to access help in the comfort of their own homes. They appeciated not needing to take time from work for hospital appointments. Furthermore, working at their own pace was an advantage. Participants also found it useful to access the information when they were out, such as on a train. Weekly monitoring indicated that intervention effects were evident after 6 weeks. The 8-week period selected for the intervention appeared suitable.

An intervention such as this has potential as a useful supplement to standard clinical tinnitus care in the UK. As such, it is essential to determine for which populations of those with tinnitus this may be a suitable intervention. Besides high pre-intervention TFI scores, which may be an artefact, no additional predictors of outcome were identified. Previous studies also suggested that gender, age, educational level and computing skills did not affect outcomes (Andersson, 2009). These results suggest that initial TFI scores may have implications for the inclusion criteria. This is in line with findings by Kaldo and colleagues (2013) that significant levels of tinnitus distress are required to serve as motivation to complete CBT programmes. If severity is mild, participants may not feel the need to commit to such a programme. A score of 25 or higher was suggested by the developers of the TFI to be indicative of the need for clinical intervention (Meikle et al., 2012). Of the two participants with TFI scores lower than 25, one withdrew, indicating thattheir tinnitus was not severe enough to undergo an intervention. The other participant with low TFI score continued to participate due tobenefitting from undertaking the intervention. When this participant completed the post-intervention questionnaire, the scores were higher than baseline TFI scores, despite indicating that his tinnitus distress had reduced. Although speculative, this may have been potentially attributed to having filled in his initial questionnaire in a guarded manner (thus possibly not indicating the true level of difficulty). From this experience, the telephone interview should be used to help decide whether initial scores are too guarded. The inclusion criteria of a TFI score of 25 or higher is recommended for further trials.

5.4.4 Study limitations

Numerous study limitations were identified which should to be addressed prior to the planned RCT. As no control group was present, regression towards the mean cannot be

discounted and has implications for result interpretation. The demographical questionnaire was not specific enough, as questions related to age and tinnitus duration were categorised into broad groups. Adjustments to this questionnaire are required to ensure that more accurate information is obtained during future studies. Wider recruitment strategies in subsequent trials are required to reach the target population of those underserved with tinnitus interventions..

5.5 CONCLUSIONS

This chapter has addressed the second research question investigating the feasibility of iCBT for tinnitus in the UK. The null hypothesis was rejected and the alternative hypothesis accepted that iCBT in the UK is feasible in terms of recruitment, attrition, adherence and the outcomes obtained using guidence from an audiologist. The next chapter investigates the efficacy of iCBT compared with weekly monitoring in a UK population.

6 CLINICAL TRIAL PHASE II: EFFICACY OF ICBT

This chapter investigates the efficacy of iCBT for tinnitus in a UK population. It addresses research questions regarding the post-intervention and longer-term efficacy of audiologist-guided iCBT in reducing tinnitus distress and its comorbidities.

6.1 Introduction

To increase access to evidence-based tinnitus intervention, a comprehensive, user-friendly iCBT intervention tailored for a UK population was designed (see Chapter 4). The easibility of iCBT in the UK was determined in terms of recruitment, attrition, and adherence, as outlined in Chapter 5. The clinical efficacy of this iCBT intervention for a UK population remains unknown. In addition, evaluation of the efficacy of using audiologist guidance for this intervention in terms of both post-intervention and in the longer-term outcomes is required. Moreover, unwanted events from such an intervention arepossible. Unwanted events are defined as all events of negative quality occurring alongside interventions (Linden, 2013). The incidence of these events does not imply a causal relationship between the intervention and the events, adversities as circumstances unrelated to treatment, such as personal or vocational issues, may contribute. As little is known about the occurrence or characteristics of unwanted events in iCBT trials, these need to be investigated (Boettcher, Rozental, Andersson, & Carlbring, 2014). Toidentify factors contributing to the results, a process evaluation (see Chapter 3) was run in parallel to thes efficacy trial. This trial formed Phase II of a clinical trial regarding the efficacy of audiologist-guided iCBT in the UK. Specific objectives were as follows:

i) To evaluate the efficacy of audiologist-guided iCBT in reducing tinnitus distress compared with weekly monitoring
ii) To ascertain the efficacy of iCBT for tinnitus-related comorbidities
iii) To assess the stability of iCBT intervention effects 2 months and 1 year post-intervention
iv) To assess any unwanted events associated with the intervention
v) To investigate the processes that contributed to the outcomes obtained

6.2 METHOD

6.2.1 Study design

Selecting the most appropriate study design was challenging. As there are established ways of treating tinnitus, a waiting list control group without intervention was not regarded as ethical. Comparison with a different form of intervention would not answer the research questions. A weekly monitoring control withdelayed intervention for the control group was selected.. This was a prospective, two-arm RCT. The experimental group (iCBT) received the iCBT intervention for 8 weeks, while the control weekly check-in group (WCI) were monitored weekly. Once the experimental group completed the intervention, the control group underwent the same iCBT intervention. The study design provided the opportunity to evaluate intervention effects in two independent groups at two time points. Although the control group had a delay of 8 weeks before undertaking theintervention, this time scale was likely to be shorter than the possible 18 weeks wait on standard intervention pathways within the NHS.

6.2.2 Recruitment

Recruitment was UK-wide. The recruitment strategy was modified for Phase II following experiences from Phase I. To improve coverage, a press release was written which provided information about tinnitus, the study and how to register for the trial. To target those who were underserved with tinnitus interventions, the study information was published in newspapers and magazines (for example Mature Times, People's Friend, Musicians Union bulletin, New Scientist, National Federation of Occupational Pensioners Magazine, and Cambridge News). To target those who use the Internet, Twitter (BTA), forums, Facebook (such as Action on Hearing loss, Thyroid UK) and websites containing information about clinical trials (for example the NHS Choices and clinicaltrials.gov websites) were used to share the study information. Recruitment ran for a 2-month period to attract more interest than was received during Phase I. Those interested registered on the study website (http://www.tacklingtinnitus.co.uk).

An additional inclusion criterion incorporated following the feasibility trial, was that a score of 25 or above on the TFI (Meikle et al., 2012) was required to participate. This score or higher was suggested to indicate the need for tinnitus care during the development of the TFI (Meikle et al., 2012).

6.2.3 Enrolment and randomisation

Participants meeting the inclusion criteria after completing baseline assessment measures and the telephone screening were randomly assigned in the ratio of 1:1 to either the experimental or control group. Allocation was based on a randomisation sequence generated by computer algorithm (http://www.randomizer.org/). To prevent an unequal distribution among groups, participants were pre-stratified on the factors of age (≤ 60 or >60

years) and tinnitus severity (TFI 25 ≤ 50 or >50). Block randomisation, with blocks of four, was applied to ensure equal groups sizes within each stratum. Participants were informed when the intervention would commence, but not which group they had been assigned to. The trial design resulted in the investigator not being blinded to the assignment of interventions during the running of the trial. During the initial telephone screening, it was explained that the trial would start once registration was full and all participants were telephoned and randomised. Participants expected a delay before the trial onset as no time period was given. Participants may have realised their group assignment, but this was never explicitly stated.

6.2.4 Assessment measures

In addition to the generic assessment methods used in each phase, the following assessment measures wereobtained:

i) Module ratings: participants were asked to score how valuable each module was on a Likert scale of 1–5.

ii) To assess unwanted intervention effects, the following questions were included:
   - Did you experience any unwanted effects/events associated with the Internet intervention you undertook? (yes/no)
   - If yes, please list all the unwanted affects you experienced associated with undertaking this intervention (open question)
   - What was the negative impact of the event/s at the time of the event? (select from a range of minimal to very severe)
   - What is the negative impact of the event/s at present? (i.e. 1 year post-intervention (select from a range of minimal to very severe)

6.2.5 Process evaluation parameters

The process evaluation parameters used were selected from the three models widely applied to intervention delivery, namely the RE-AIM model (Glasgow et al., 1999) (Dzewaltowski et al., 2004), those of Baranowski & Stables (2000) and the framework of Steckler and colleagues (2002) (see Chapter 3). The processes selected covered a broad spectrum and addressed the specific research objectives of this study, as outlined in Table 6.1.

Table 6.1 Processes selected and how these were assessed

Process	Description	Assessment measure
Processes related to the research context		
Recruitment	Procedures used to approach and attract participants	Monitoring traffic on the recruitment website via Google analytics
Reach	The extent to which the intervention was received by the targeted population of those with distressing tinnitus who were underserved with previous interventions for tinnitus	Demographic questionnaire
Context	The social, demographic and socio-economic characteristic of the participants that may affect generalisability of the outcomes	Demographic questionnaire and baseline levels on assessment measures
Processes related to the intervention delivery		
Treatment (dose) delivered	Intervention components actually provided to participants	Nature of the guided-intervention
Treatment (dose) received	The extent to which participants engaged in and adhered to the intervention	Data logging
Processes related to the outcomes obtained		
Barriers affecting the outcomes obtained	Barriers that may affect the outcomes obtained	Post-intervention satisfaction questionnaire
Factors facilitating effectiveness	Intervention's effectiveness from the participant's perspective	A benefit questionnaire was used to rate the iCBT modules

6.2.6 Statistical analysis

6.2.6.1 Sample size calculations

The required sample size estimation was estimated calculated using G*Power version 3.1.6 (Faul et al., 2007) based on achieving a clinically relevant change between baseline and post-intervention using the primary assessment measure, the TFI. A more conservative sample size estimate was obtained using data from Meikle et al. (2012) than using data

from Phase I (Chapter 5) and that of Fackrell et al. (2016). The 13 point difference suggested by Meikle et al. (2012) was thus incorporated into sample-size calculations. This indicated that 58 participants were required per group, to achieve a two-sided significance level of 0.05, with an effect size of 0.50 and 80% power. An additional 30 participants were recruited to ensure sufficient power during per-protocol analysis and to allow for possible dropouts (estimated to be 22% from Phase I). Therefore, 73 participants were recruited to each group (n = 146).

6.2.6.2 Missing data analysis

An ITT paradigm was used (see Section 3.10.1). Little's "missing completely at random" test (Little, 1988) indicated that the data were likely to be MCAR (missing completely at random (χ^2= 21.70, p = 0.75), i.e. missing values were likely to be randomly distributed across all observations withs no systematic pattern to the missing data. Missing data could thus be imputed. Results were compared with per-protocol analysis. As there was no difference, the ITT results are reported.

6.2.6.3 Baseline group differences

Baseline group differences were analysed using independent samples *t*-tests for continuous variables and Chi-square tests for categorical variables.

6.2.6.4 Group differences

Mixed 2x3 analyses of variance (ANOVA) for repeated measures with the between-subject factor of group (experimental and control) and within-subject factorof time (T_0, T_1, T_2) were carried out to compare assessment measure results across the three time points. The Greenhouse-Geisser correction for non-sphericity was applied. The main effects were followed up by paired-samples *t*-tests to compare within-group differences at individual time points. Independent samples *t*-tests were used to compare results between the two groups at each time point. Effect sizes (Cohen's *d*) were calculated by dividing the differences in pre- and post- intervention means by the pooled standard deviations.

6.2.6.5 Clinically Significant Change

The RCI criterion (see Chapter 3) was used to estimate clinically significant changes. The mean difference scores for those completing the intervention from the experimental group at T_1 and from the control group at both T_1 and T_2 were evaluated against the RCI criterion for the TFI.

6.2.6.6 Monitoring intervention effects between T_0 andT_1

A mixed 2x8 ANOVA for repeated measures was used to compare the results of the weekly THI-S scores was conducted with the between-subject factor of group (experimental and control) and within-subject variable of time (weeks 1–8). The main effects were followed up by Bonferroni-corrected post-hoc testing.

6.2.6.7 Long term outcomes

As both the control and experimental groups had undertaken the same intervention at T_3, group comparison at T_3 did not provide valuable insights. To evaluate the longer-term outcomes, results were pooled between the groups and analysed as one group. Repeated measures ANOVA with the independent variable of time [T_0, T_2 (after both groups completed the intervention), T_3), was carried out to compare the assessment measure across the three time points. The main effects were followed up by paired samples *t*-tests to compare within-group differences for each assessment measure at individual time points. Effect sizes (Cohen's *d*) were calculated by dividing the differences in pre- and post- intervention means by the pooled standard deviations. The RCI was calculated for the TFI results at 1 year post-intervention.

6.2.6.8 Unwanted events

Unwanted events, reported in an open format question, were coded according to the checklist for unwanted events and adverse treatment reactions (UE-ATR) (Linden, 2013). Two raters independently coded the events, namely the author and a second rater, experienced in using the UE-ART. Both raters judged whether these events were related to the intervention using the UE-ATR categories of unrelated, probably unrelated, possibly related, probably related and related. The inter-rater reliability for the categorisation was calculated using Cohen's Kappa (Cohen, 1960). The kappacoefficient indicated perfect agreement (100%) between the two raters (K = 1.0).

To determine the relationship between reporting or not reporting unwanted events and demographic and clinical variables, Spearman rank correlationcoefficient was performed.

6.2.6.9 Process evaluation

For comparison purposes, individual scores for each assessment measure were converted to percentages. Baseline group differences were analysed using independent samples *t*-tests for continuous variables and Chi-square tests for categorical variables.

6.3 RESULTS

6.3.1 Participant Characteristics

Baseline assessment measures were completed by 169 of the 244 adults on the trial waiting list. A total of 146 adults met the eligibility criteria and were randomly assigned to the experimental (n = 73) and control (n = 73) groups, as shown in the CONSORT diagram (Figure 6.1). The mean age of the participants was 56 years (SD: 13). There were more male than female participants (57%). The groups were well matched, with no geographical or clinically meaningful differences, as shown in Table 6.2. The ranges of baseline TFI scores were similar at 28–97 for the experimental group and 25–95 for the control group. The intention to recruit mainly those who had already had a medical examination due to tinnitus was fulfilledas 93% had seen their GP and 71% reported having seen an ENT specialist. It was also found that mostt (77%) had not had previoustinnitus interventions. Past treatment included: audiological interventions (14%), tinnitus retraining therapy (2%), medical interventions (4%), psychological treatments (2%) and complementary therapies (1%). The majority (89%) had not attended tinnitus support groups.. Most participants were from England, as shownin Figure 6.2. The reach included adults across the UK, although there were fewer from Scotland, Wales and Northern Ireland. Permission was granted for one additional participant to participate who resided in the Irish Republic.

Analysis of the recruitment processes indicated that there were around 2,300 views from 1,003 users on the recruitment website during the recruitment period. The majority of the views were from the UK. The average session duration was 10 minutes, indicating that those interested spend some time looking at the information about the trial.The majority of visitors (60%) returned to the recruitment pages.

6.3.2 Attrition

Four participants (5%) from the experimental group and three participants (4%) from the control group withdrew, due to time pressures or health problems. Significantly more participants [χ^2 (1, n = 146) = 5.8, p = 0.02] from the control group (99%) completed the assessment measures at T_1 thanfrom the experimental group (86%). There was no significant difference [χ^2 (1, n = 146) = 2.1, p = 0.16] in completion rates at T_2, which were 74% for the experimental group and 82% for the control group. Completion rates were also not significantly different at T_3, with 68% from the experimental group and 74% from the control group completing.

No significant baseline differences in terms of age, gender, employment status, level of education, tinnitus severity, insomnia, anxiety or depression were found between those who completed the assessment measures and those who choose not to complete them.

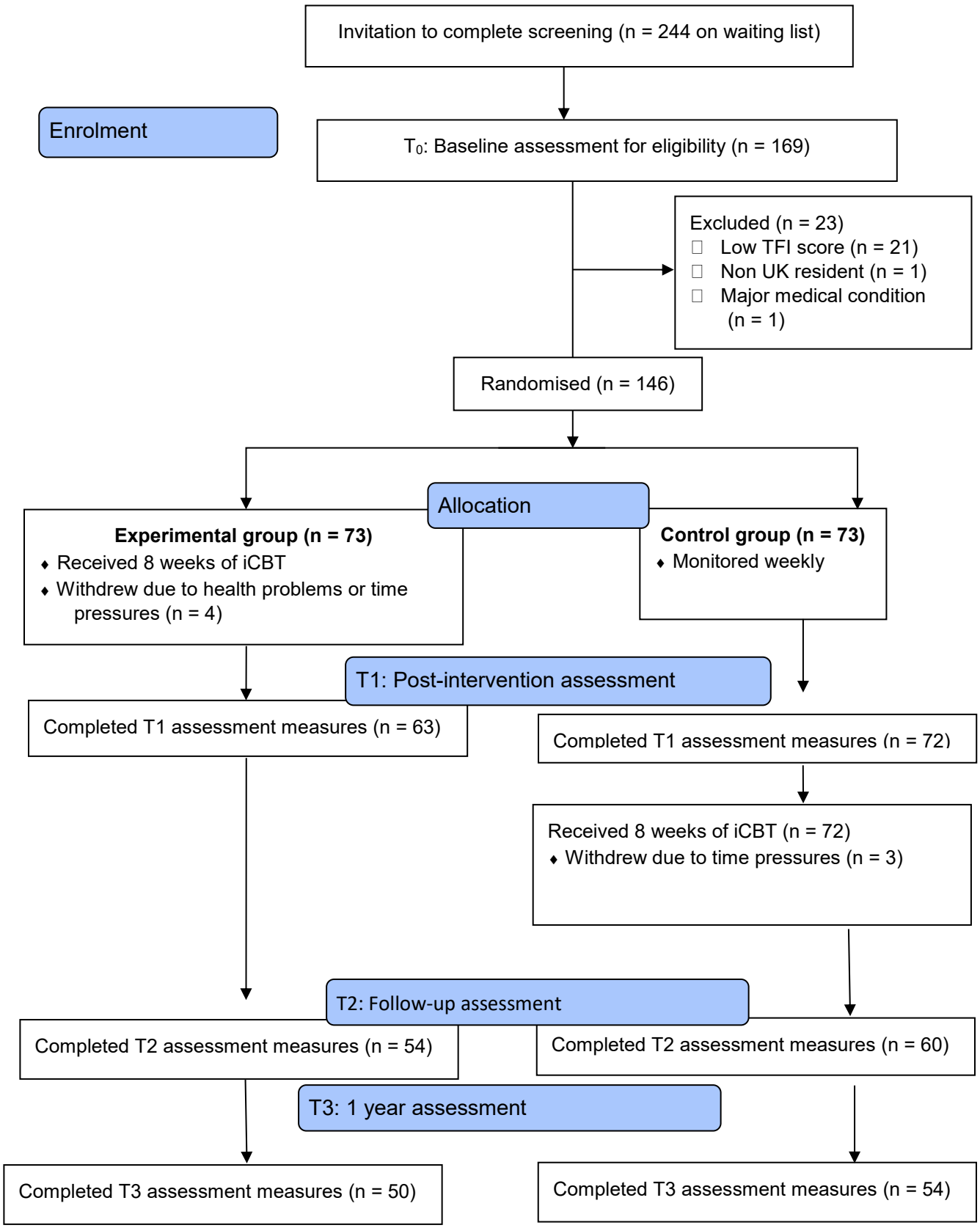


Figure 6.1 The CONSORT study profile for Phase II.

Table 6.2 Demographic characteristics of the participants: Phase II

Category	Description	Experimental group (n = 73)	Control group (n = 73)	Overall (n =146)	Group Differences (*= significant)
Gender	Male	43 (59%)	40 (55%)	83 (57%)	$\chi^2(1) = 0.25$, $p = 0.62$
	Female	30 (41%)	33 (45%)	63 (43%)	
Age	Mean years (SD)	57 (SD: 12.2)	54 (SD: 13.5)	56 (SD: 12.9)	
	Range	24–79 years	22–83 years	22–83 years	$t(144) = 1.18$, $p = 0.24$
Tinnitus duration	Mean years (SD)	12 (11.5)	12.5 (12.91)	11.63 (12)	
	Range	3 months–52 years	3 months– 56 years	3 months–56 years	$t(144) = -0.69$, $p = 0.49$
Using hearing aids	No	46 (63%)	46 (63%)	92 (63%)	
	Yes	27 (37%)	27 (38%)	54 (37%)	$\chi^2(1) = 1.12$, $p = 0.38$
Reduced working hours due to tinnitus	Reduced hours	3 (4%)	3 (4%)	6 (4%)	$\chi^2(2) = 4.32$, $p = 0.23$
	Stopped work	12 (16%)	11 (15%)	23 (16%)	
	Disability allowance	2 (3%)	4 (6%)	6 (4%)	
Seen GP	No	6 (8%)	4 (6%)	10 (7%)	
	Yes	67 (92%)	69 (95%)	136 (93%)	$\chi^2(1) = 0.43$, $p = 0.51$
Seen ENT specialist	No	23 (32%)	20 (27%)	43 (30%)	
	Yes	50 (69%)	53 (73%)	103 (71%)	$\chi^2(1) = 0.30$, $p = 0.59$

Figure 6.2 Spread of participants for Phase II.

6.3.3 Efficacy of iCBT versus weekly monitoring for tinnitus distress

Differences between the two groupswere not constant over time (Table 6.3). Pre-intervention (T_0) means were similar. At post-intervention (T_1) the mean TFI score was 21 points lower (SD: 15) thanbaseline forthe experimental group. For the control group, the mean TFI score was 5.5 points lower (SD: 3.9) thanbaseline. Although both groups exhibited reduced mean scores, the magnitude of the reduction in mean score was greater for the experimental group than forthe control group, and this difference was statistically significant (p = 0.001) with a medium effect size (Cohen's d = 0.69).

Figure 6.3 shows that the majority of the experimental group had a T_0–T_1 difference score between 10 and40 points, with a maximum reduction of 81 points. There were 55 participants (75%) with difference scores between 10 and81 points., The majority of the control group had smaller improvements.. The maximum improvement for the control group was 29 points. The two groups had similar means at follow-up (T_2), indicating that the control group improved further after completing the intervention, as summarised in Table 6.3.

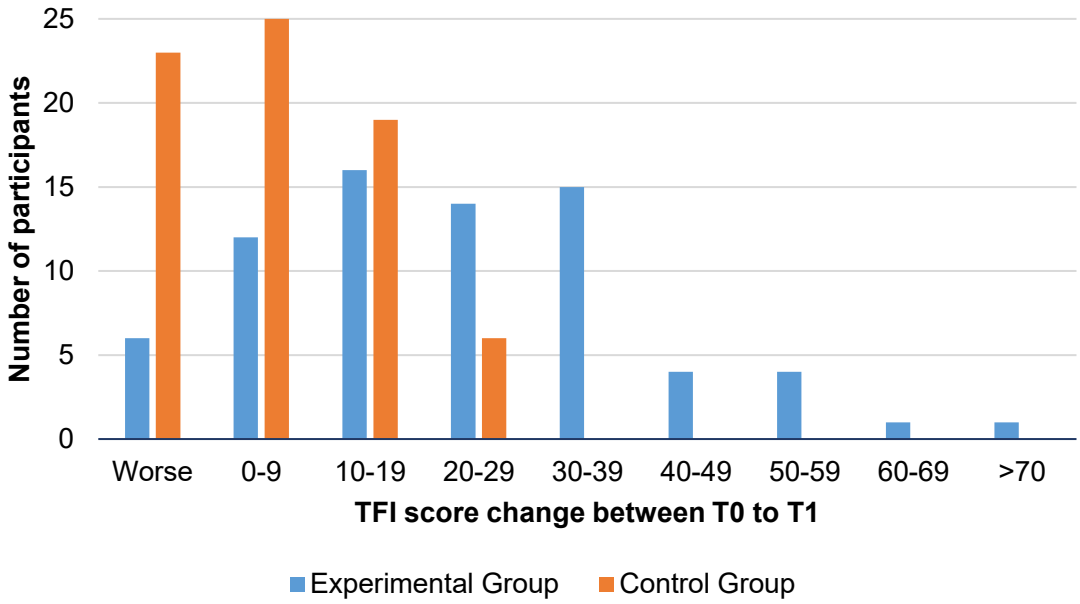


Figure 6.3 Distribution of Tinnitus Functional Index score changes between T_0 and T_1.

The calculated RCI criterion was a change of 23 points in the TFI score (1.96 times the standard error of 11.9). Assessed against this score change, clinical significance was achieved by 51% of the experimental group and 5% of the control group at T_1. A clinically significant change was found for 47% of the control group at T_2 after they undertook the intervention. At $T_1$41% of the experimental group and 1% of the control group hadTFI scores below the level requiring intervention (< 25) and also had a reliable change of 23.34 points difference in TFI score after they completed the intervention. At T_2 there were 38% of the control group with TFI scores below the level requiring intervention who also had a reliable change of 23.34 points difference in TFI score..

Table 6.3 Group comparisons over time: Phase II

Measure	Group (n = 73 for each group)	Mean (Standard deviation)			Group comparison T_0–T_1: *F*-Statistic			Follow-up analysis: *t*-statistic	Cohen's *d* (95% CI)
		T_0	T_1	T_2	Time by group interaction	Within-group time effect	Between-group effect	Between-group at T_1	Between-group at T_1
TFI	**iCBT**	60 (18)	39 (24)	38 (25)	15.76, *p* = 0.001*	97.53, *p*= 0.001*	3.91, *p* = 0.05*	4.34, *p* = 0.001*	0.69 (0.35–1.02)
	WCI	60 (19)	54 (19)	41 (23)					
ISI	**iCBT**	12 (7)	9 (7)	8 (7)	5.32, *p* = 0.006*	47.55, *p* = 0.001*	5.39, *p* = 0.02*	3.30, *p* = 0.001*	0.55 (0.21–0.87)
	WCI	14 (7)	12 (7)	11 (7)					
GAD-7	**iCBT**	8 (6)	6 (5)	5 (5)	3.06, *p* = 0.05	11.62, *p* = 0.001*	0.50, *p* = 0.55	1.84, *p* = 0.07	0.27 (0.06–0.60)
	WCI	8 (6)	7 (5)	6 (5)					
PHQ-9	**iCBT**	8 (6)	6 (6)	6 (5)	3.67, *p* = 0.03*	17.83, *p* = 0.001*	1.05, *p* = 0.31	2.10, *p* = 0.04*	0.33 (0.00–0.65)
	WCI	8 (6)	8 (5)	6 (6)					
HHIA-S	**iCBT**	17 (12)	15 (12)	15 (11)	1.73, *p* = 0.18	12.22, *p* = 0.001*	0.67, *p* = 0.42	0.63, *p* = 0.53	0.23 (0.10–0.55)
	WCI	18 (11)	18 (10)	15 (10)					
HQ	**iCBT**	19 (8)	16 (10)	17 (10)	3.12, *p* = 0.046*	5.88, *p* = 0.003*	1.23, *p* = 0.27	2.10, *p* = 0.038*	0.33 (0.00–0.65)

	WCI	19 (9)	19 (10)	18 (9)					
CFQ	**iCBT**	40 (15)	38 (17)	38 (16)	4.22, p = 0.019*	1.12, p = 0.32	1.81, p = 0.18	2.22, p = 0.028*	0.37 (0.04–0.69)
	WCI	41 (17)	45 (18)	42 (19)					
SWLS	**iCBT**	17 (6)	18 (7)	19 (7)	3.13, p = 0.046*	12.00, p = 0.001*	1.37, p = 0.24	2.33, p = 0.021*	0.34 (0.00–0.65)
	WCI	17 (6)	16 (6)	18 (6)					

***** Significant at $p < 0.05$

Acronyms: *CI: Confidence Interval, iCBT: Internet-delivered CBT intervention experimental group, WCI: weekly check in control group, M: means, SD: Standard Deviation, T_0: pre-intervention, T_1: post-intervention, T_2: follow-up, TFI:Tinnitus Functional Index, ISI: Insomnia Severity Index, GAD: Generalised Anxiety Disorder, PHQ: Patient Health Questionnaire, HHIA-S: Hearing Handicap Inventory for Adults-screening version, HQ: Hyperacusis Questionnaire, CFQ: Cognitive Failures Questionnaire, SWLS: Satisfaction with Life Scale*

6.3.4 Monitoring intervention effects between T_0 and T_1

Differences between the two groupswere not constant across the 8 time points between T_0 and T_1. The experimental group had a greater weekly reduction in tinnitus distress, as evidenced by the significant interaction [$F(7, 1008) = 19.5$, $p = 0.001$*; Cohen's $d = 0.90$]. Follow-up analysis examining this main effect week-by-week indicated no group differences in weeks 1 to 2 of this period. From week 3 to 8 there were significant differences, as the experimental group's tinnitus distress was significantly lower than that of the control group, as shown in Figure 6.4.

The two groups had similar means at follow up (T_2), indicating that the control group had improved to the level of the experimental group after completing the intervention, as summarised in Table 6.3.

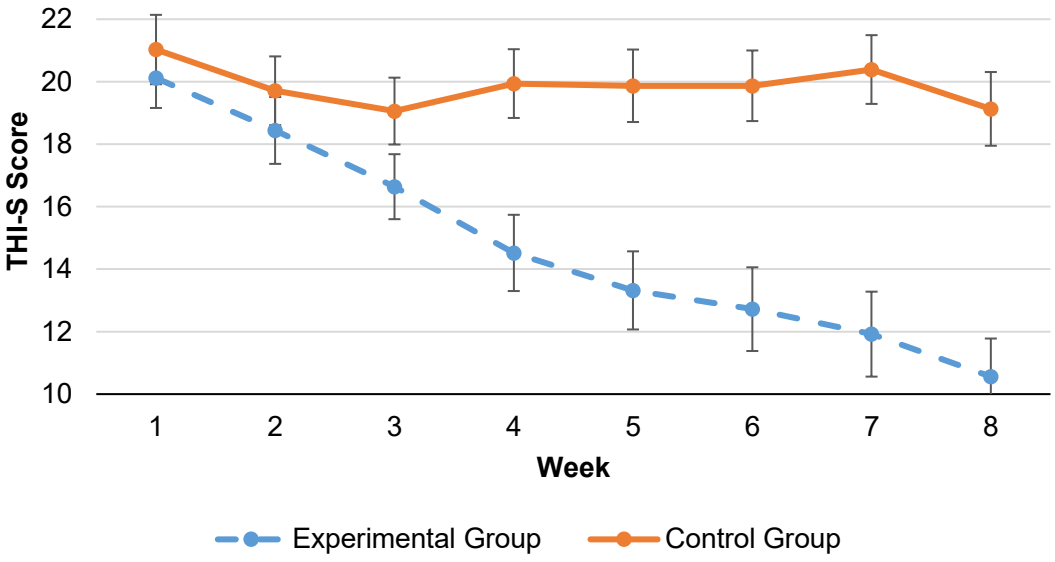


Figure 6.4Weekly Tinnitus Handicap Inventory-screening scores: Phase II. Ratings were obtained during the first 8-week active intervention period between T_0 and T_1. Error bars represent the ±1 standard error of the mean.

6.3.5 Efficacy of iCBT versus weekly monitoring for tinnitus-related comorbidities

Differences between the secondary assessment measures were not constant over time for the two groups(Table 6.2). Pre-intervention (T_0) means were similar. At post-intervention (T_1), the experimental group had significantly greater reductions in insomnia, depression, hyperacusis, cognitive failures and improvement in life satisfaction thanthe control group. For anxiety and hearing disability, significant within-group differences were found post-intervention, but no significant interaction between time and group was found.

Clinical significance for the secondary assessment measures was only achieved by a few participants at T_1. For the ISI, clinical significance (score change >9.75) was reached by 22% of the experimental group and 4% of the control group. For the PHQ-9, clinical

significance was reached by 16% of the experimental group and 4% of the control group (score change of 6.4). For the HQ, clinical significance (score change of 14.3) was reached by 11% of the experimental group and 4% of the control group. For the CFQ clinical significance was reached b 17% and 5% of the groups, respectively (score change of 14.1) whereas it was reached by 14% and 3% of the respective groups for the SWLS (score change of 6.3). The ISI had the highest percentage of participants showing a clinically significant change amongst the secondary assessment measures.

The two groups had similar means at follow-up (T_2), indicating that the control group had improved to the level of the experimental group after completing the intervention, as summarised in Table 6.3.

6.3.6 Stability of intervention effects

6.3.6.1 Stability of effects at T_2

There were no significant differences in the TFI scores between T_1 andT_2 for the experimental group, as shown in Figure 6.5. Likewise, improvements were maintained for all secondary assessment measures, as no statistically significant differences were found between T_1 and T_2. Intervention effects were, therefore, maintained 2 months post-intervention for the experimental group.

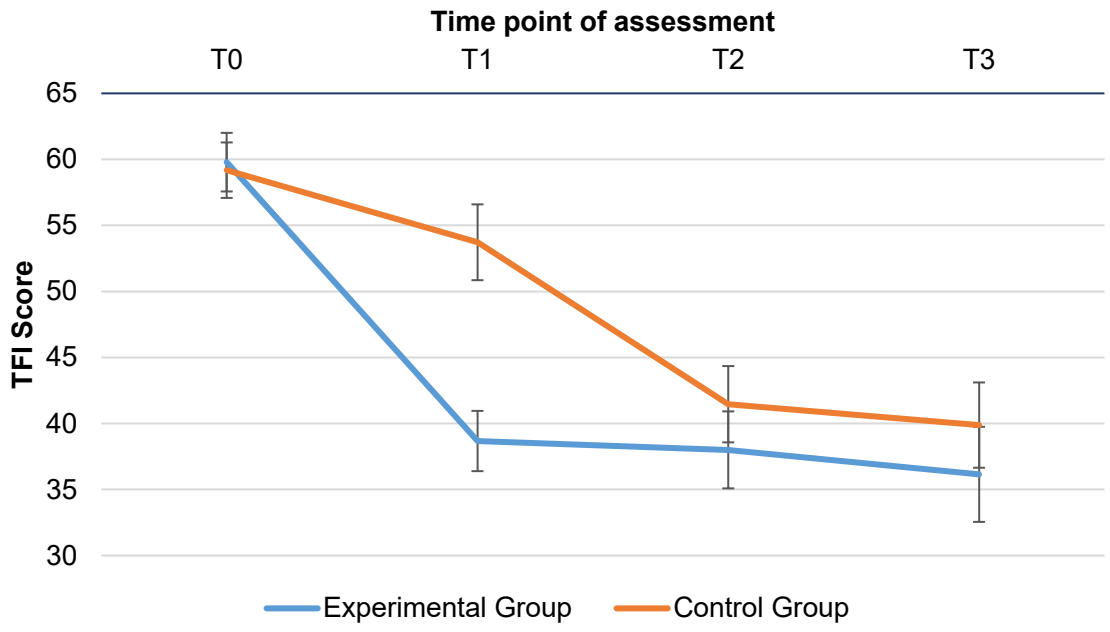


Figure 6.5 Change in tinnitus distress over time as measured by the Tinnitus Functional Index (TFI): Phase II. Error bars represent the ±1 standard error of the mean.

Table 6.4 Within-group comparisons of the assessment measures over time.

Combined pooled data from both groups (n =104) were used to investigate the effects 1 year post-intervention

Measure	**Mean score at each time point (Standard deviation)**			**Difference in means (SD)**		**F-Statistic repeated measures ANOVA**	***Follow-up analysis t*-statistic pairwise comparison**			**Cohen's *d* (95% CI)**
	T_0	**T_2**	**T_3**	**T_0–T_2**	**T_0–T_3**	**T_0–T_2–T_3**	**T_0–T_2**	**T_0–T_3**	**T_2–T_3**	**T_0–T_3**
TFI	59 (17)	36 (22)	36 (25)	23 (22)	-0.30 (14)	F = 100.75, p = 0.001*	t = 11.56, p = 0.001*	t = 10.66, p = 0.001*	t = -0.14, p = 0.89	1.07 (0.78–1.36)
ISI	12 (7)	9 (7)	9 (7)	4 (6)	-0.07 (4)	F = 32.35, p = 0.001*	t = 7.28, p = 0.001*	t = 5.83, p = 0.001*	t = -0.16, p = 0.89	0.53 (0.25–0.80)
GAD-7	8 (6)	5 (5)	5 (5)	2 (6)	-0.28 (3)	F = 15.47, p = 0.001*	t = 5.05, p = 0.001*	t = 3.65, p = 0.001*	t = -0.84, p = -0.84	0.40 (0.13–0.68)
PHQ-9	8 (5)	5 (5)	6 (6)	2 (5)	-0.63 (3)	F = 19.98, p = 0.001*	t = 6.34, p = 0.001*	t = 3.75, p = 0.001*	t = -1.96, p = 0.05	0.33 (0.06–0.61)

HHIA-S	17 (12)	14 (12)	16 (11)	10 (1)	-1.29 (8)	F = 5.39, p = 0.006*	t = 3.40, p = 0.001*	t = 2.25, p = 0.03*	t = -1.75, p = 0.08	0.14 (-0.14–0.41)
HQ	19 (9)	16 (9)	17 (10)	3 (10)	-1.10 (5)	F = 10.24, p = 0.001*	t = 4.50, p = 0.001*	t = 2.50, p = 0.01*	t = -1.90, p = 0.06	0.21 (-0.07–0.48)
CFQ	40 (16)	39 (18)	40 (18)	2 (13)	-2.3 (11)	F = 2.26, p = 0.11	NA	NA	NA	-0.01 (-0.28–0.26)
SWLS	17 (6)	19 (6)	18 (7)	-2 (5)	0.61 (4)	F = 14.55, p = 0.001*	t = 5.09, p = 0.001*	t = 3.61, p = 0.001*	t = 1.46, p = 0.147	0.28 (0.00–0.55)

***** Significant at $p < 0.05$

Acronyms: *SD: Standard Deviation, T_0: pre-intervention, T_1: post-intervention, T_2: follow-up, TFI: Tinnitus Functional Index, ISI: Insomnia Severity Index, GAD: Generalised Anxiety Disorder, PHQ: Patient Health Questionnaire, HHIA-s: Hearing Handicap Inventory for Adults-screening version, HQ: Hyperacusis Questionnaire, CFQ: Cognitive Failures Questionnaire, SWLS: Satisfaction with Life Scale*

6.3.6.2 Stability at T_3

Long term assessment measures were completed by 104 participants. The pooled T_3 mean for the TFI was 36 (SD: 25) lower than the pre-intervention (T_0) means of 59 points. This difference was statistically significant [F = 100.75, p = 0.001*] with a large effect size (Cohen's d = 1.09) shownin Table 6.4. This was a clinically significant change for 51% of participants**.** The T_3 means was similar to that at T_2, indicating that the results were maintained 1 year post-intervention. There was one participant who had not show a change in TFI score and 14 (13%) who had a deterioration in score (average 9.4 points). There were statistically significant changes for all secondary assessment measures between T_0 andT_3 except for the CFQ, for which scores were not significantly different across the three time points..

6.3.7 Effectiveness of the modules

Participants rated how useful different modules within the intervention were. The pooled results from both groups are shown in Figure 6.6. The relaxation modules were rated as most usefull, while the hearing tactics module was rated the least useful.

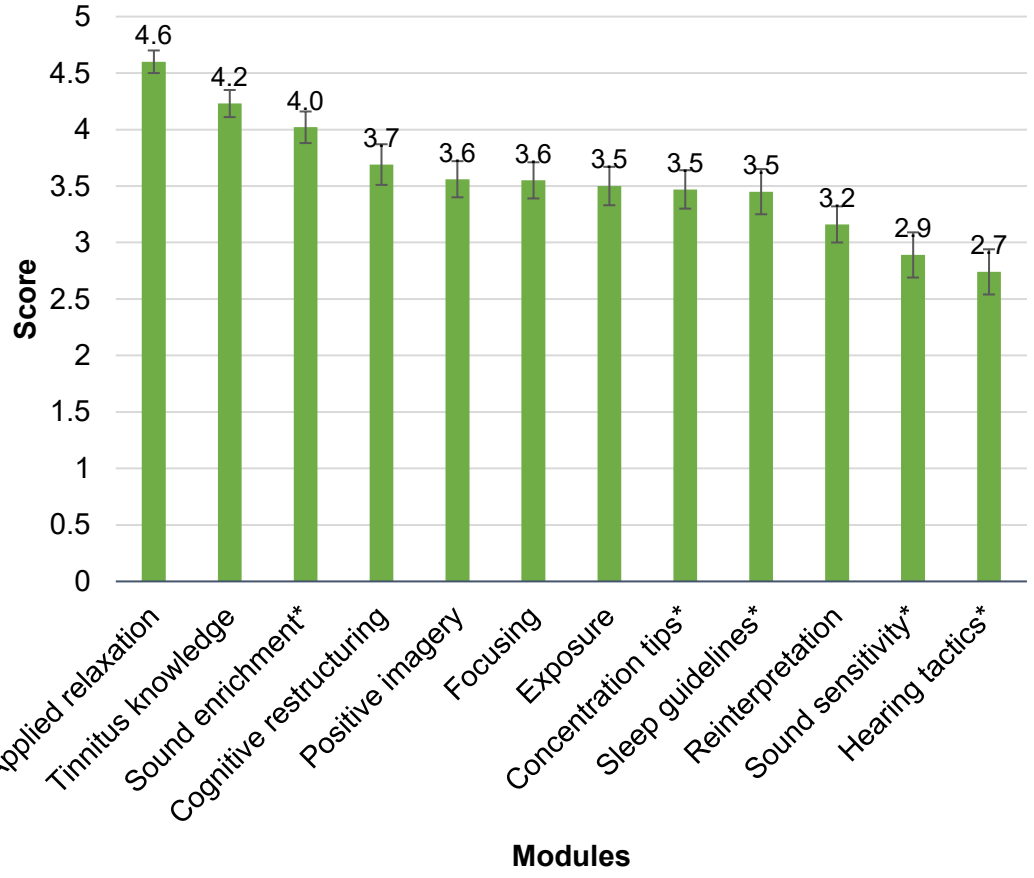


*Figure 6.6 Usefulness of specific modules within the intervention based on pooled results from the control and experimental groups. * Optional modules.*

6.3.8 Intervention adherence

The extent to which participants actively engaged in and interacted with the resources provided by the intervention is shown in Table 6.5. Participants (excluding those who had withdrawn) logged into the programme an average of 24 times during the 8 week intervention period. An average of 74% of the recommended modules and 55% of the optional modules were read. Optional modules and modules occurring later in the intervention were read less than the earlier modules. Overall, 41% of the worksheets were completed. Fewer worksheets were completedfor the later or optional modules than for the initial modules. Weekly comparisons were made(see Figure 6.7) between adherence in terms of modules read, worksheets done, the corresponding module rating and weekly tinnitus distress during the active intervention phase for the experimental group. Bothadherence and tinnitus distress decreased over time. The audiologist sent 1,925 tailored messages (14 on average to each participant). Participants sent fewer messages than the therapist with an average of 4 per participant who had not withdrawn.

Table 6.5 Intervention adherence: Phase II

	Participants n = 138 (those withdrawn exclude)	**Mean per participant**
Logins by participants	3,329	24
Modules read	2,120	15
Worksheets completed	2,532	18
Messages sent by participants	597	4
Reported time spent on the module content on average	22 minutes (SD: 19)	(range 5–60 minutes)

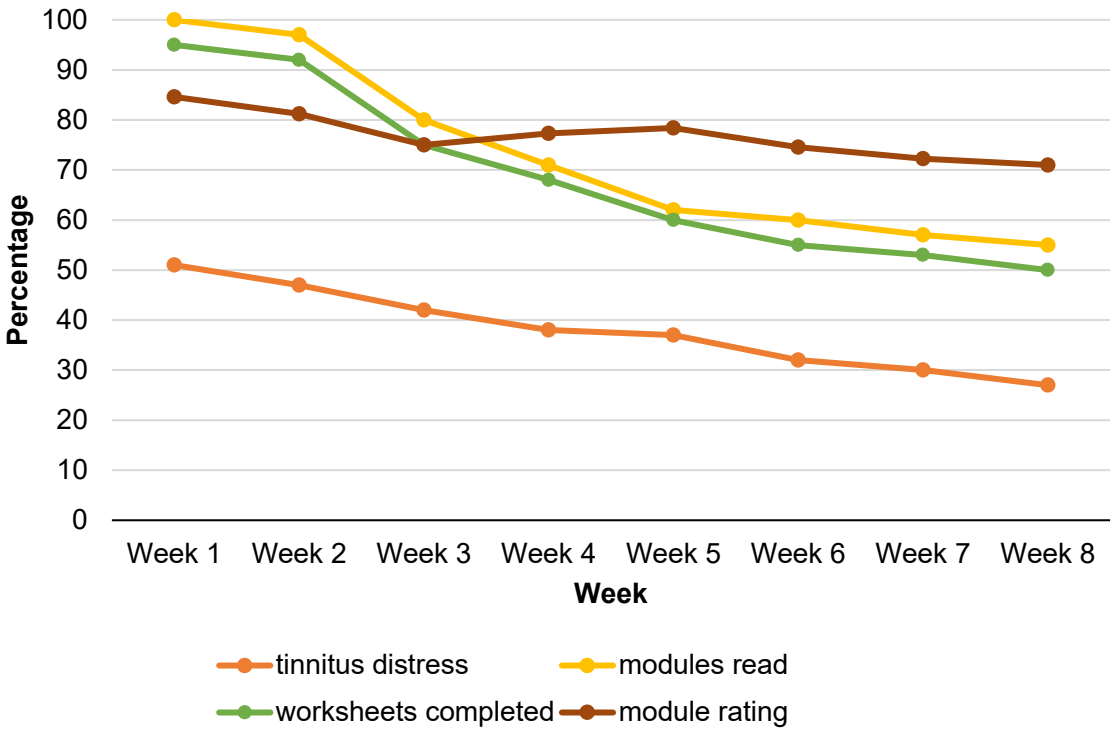


Figure 6.7 Comparison of tinnitus distress, modules read, worksheets completed and and participants ratings of the modules.

6.3.9 Unwanted events

There were 11 (11%) out of the 104 participants who reported unwanted events during the intervention period. There were 12 events in total, as one participant mentioned two unwanted events. These events were rated and classified as related to the intervention 82% of the time and probably related to the intervention 18% of the time, by the author and second independent coder. The events were classified according to the UE-ART checklist (Linden, 2013) in four categories as shown in Table 6.6.

To identify factors that may be associated with the reporting of unwanted events, Spearman rank correlations were calculated for pre-intervention demographical and clinical variables. A weak positive correlation was only found for gender ($r = 0.26$, $p = 0.008$), as significantly more females (n = 9; 82%) reported unwanted events.

Table 6.6 Unwanted events reported

Classification	Example	Number of responses	Severity during the intervention	Severity 1 year post-intervention
Deterioration of symptoms	To begin with the process made me more aware of my tinnitus until I became better at controlling its impact	4	severe	mild
Emergence of new symptoms	I found the exercise where I had to tune into my tinnitus really difficult. It made me extremely anxious and panicky	3	severe	moderate
Negative well-being	I looked at the tinnitus in greater detail and became more aware of the limiting effect it has on me	3	moderate	moderate
Prolongation of treatment	It went on too long	2	moderate	moderate

6.4 DISCUSSION

The objective of this chapter was to evaluate the efficacy of audiologist-guided iCBT for tinnitus distress and some of the comorbidities associated with tinnitus up to 1 year post-intervention. This chapter also investigated unwanted events during the intervention period and processes that contributed to the outcomes obtained. The discussion considers the results obtained for each objective.

6.4.1 Efficacy of audiologist-guided iCBT for tinnitus distress

The main outcome measure for this trial was a change in tinnitus distress as measured by the TFI. Undertaking the iCBT led to significantly greater improvements in tinnitus distress, thanweekly monitoring. The small improvement found in the control group (5.5 points) at T_1 may have been related to the positive effects of being included in an intervention pathway, despite not yet starting the intervention. A systematic review has also shown small but significant improvements in self-reported measures of tinnitus with time in non-intervention

or waiting list control groups in previous tinnitus trials (Hesser et al., 2011; Phillips et al., 2017).

The mean score reduction of 21 between T_0 andT_1 for the experimental group in the present study is comparable to the findings of the initial feasibility study (Chapter 5) which showeda mean difference of 19. The TFI score improvements found for the experimental group were greater than those for the control group.

To relate these findings to clinical significance, the RCI was calculated. Aa T_0–T_1 TFI score change of 23 was regarded as a clinically significant change. This was similar to the change of 24 found in the initial feasibility trial and is a much larger change than the 13-point reduction suggested during the development of the TFI to be an indication of clinical significance (Meikle et al., 2012). At T_1, clinical significance was reached by 51% of the experimental group and 5% of the control group. Although this ratio appears low, previous trials of iCBT for tinnitus trials have reported that clinical significance was only achieved by 29–52% of participants (Andersson et al., 2002; Kaldo et al., 2008; Nyenhuis et al., 2013a; Jasper et al., 2014). The control group reachedsimilar levels of clinical significance to those reported by Andersson et al. (2002),r for a passive control of 4%.A more recent study by Weise and colleagues (2016) reported that a higher proportion (73–81%) reached clinical significance following undertaking iCBT for tinnitus than found in the present trial.

Findings related to clinical significance can becompared with those reported in non-iCBT tinnitus trials. Henry and colleagues (2016), compared tinnitus masking and tinnitus retraining therapy using two control groups. Their criterion for a clinically significant change in THI scores was a difference score of 20 or more points. At the various follow-up points this was achieved by 11–28% of participants in the two intervention groups. In a study comparing the effects of hearing aids in relieving tinnitus (Henry et al., 2017), the criterion for clinical significance was a 13-point reduction in TFI score. With this lower value, clinical significance was achieved by 67–82% of participants. Discrepancies in levels of clinical significance are partially related to ways in which clinical significance is calculated, and some studies have not calculated the RCI. Consistency in calculating clinical significance is required to draw firmer conclusions. Moreover, ways of increasing the level of clinical significance for participants undertaking iCBT for tinnitus need to be considered. This may include identifying the influence of wider contextual factors, intervention modifications or adjustments to the guidance provided.

Andersson (2015) reported that the pooled effect size of previous iCBT controlled studies (Andersson et al., 2002; Abbott et al., 2009; Hesser et al., 2012; Nyenhuis et al., 2013a; Jasper et al., 2014a) was Hedges *g* = 0.58, although a later study by Weise et al. (2016)

was not included. Weise et al. (2016) reported a higher effect size of Hedge's *g* = 0.83 for tinnitus distress, using the THI. The medium effect size found here of Cohen's *d* = 0.69 (Hedge's *g* = 0.68), is, therefore, between the values obtained inprevious iCBT tinnitus trials. This provides encouragement that despite use of audiologist guidance, the results of this trial are consistent with those of previous trials of iCBT for tinnitus using psychological guidance.

Weekly monitoring was used to determine when intervention effectsoccurred. After the experimental group completed 3 weeks of the iCBT intervention, they had significantly lower TFIscores than those not undergoing the intervention. The likely delay in intervention effects is important to convey realistic expectations to future participants..

6.4.2 Efficacy of audiologist-guided iCBT for tinnitus-related comorbidities

Significant improvements in insomnia, depression, hyperacusis, cognitive failures and satisfaction with life were evident post-intervention. No significant improvments were found for anxiety and depression post-intervention. This may be related to the large variability in scores for these measures over time. Low baseline scores were evident for the anxiety assessment measure (7.40 points, SD: 0.26), which may have contributed to the non-significant interaction found. To relate these findings to clinical significance, the RCI was calculated for each secondary assessment measure at T_1. For the ISI, 22% of the experimental group had a clinically significant change, compared with 4% of the control group. The corresponding values for the other secondary assessment measures were 11–18% of the experimental group and 3–5% of the control group. The proportions of those with clinically significant improvements onthe secondary assessment measures werelower than for the TFI.

Previous trials of iCBT for tinnitus have generally used secondary assessment measures for anxiety and depression [using the Hospital Anxiety and Depression scale (HADS); Zigmond and Snaith, 1983], and insomnia (using the ISI; Bastien, Vallières and Morin, 2001). Significant iCBT effects were reported for these tinnitus-related comorbidities (Kaldo-Sandström, Larsen and Andersson, 2004; Kaldo et al., 2008; Jasper et al., 2014; Weise Kleinstauber and Andersson, 2016). These studies did not report whether the changes were clinically significant, as they focused on statistical significance. Effect sizes in the present study for anxiety and depression (*d* = 0.3) were lower than those reported by Jasper et al. (2014) and Weise et al. (2016) of *d* = 0.5. This difference may partly be attributed to the difference in assessment measures used in these trials (HADS) compared with the

present trial (GAD-7, PHQ-9). The effect sizes obtained for insomnia (*d* = 0.55) for the present study was similar to that reported by Jasper et al. (2014) of *d* = 0.6 and lower than reportedby Weise et al. (2016) of *g* = 0.7. These comparisons provide encouragement that audiologist-guided iCBT haspotential to address tinnitus-related comorbidities. Further work is required to improve this potential.

6.4.3 Stability of intervention effects

Maintainance of intervention effects is an important aspect of the efficacy of an intervention. It was found that the intervention effects were stable 2 months post-intervention (T_2) for both tinnitus severity and the secondary assessment measures for the experimental group. Furthermore, the pooled results were stable 1 year post-intervention after both groups had completed the intervention. Stability of iCBT intervention effects hasbeen found in previous trials monitoring these effects over a longer period. Jasper et al. (2014) reported stability 6 months after completing iCBT for tinnitus severity, anxiety, depression, and insomnia. Kaldo et al. (2008) and Hesser et al. (2012) using a Swedish population and Weise et al. (2016) using a German population, found stability (and improvements) of results 1 year after undertaking iCBT for tinnitus severity, anxiety, depression, but not for insomnia. Nyenhuis and colleagues (2013a) reported a deterioration in effect at 6 months follow-up (*d* = 1.04 at T_1 to *d* = 0.66 using ITT analysis). A different programme was selected for that study, in comparison with previous iCBT trials, namely the CBT-oriented tinnitus coping training (Kröner-Herwig et al., 2003).

6.4.4 Unwanted events during the intervention period

As empirical studies on the nature and frequency of unwanted events are scarce in iCBT trials (Boettcher et al., 2014), these were investigated. Unwanted events were reported by 11% of participants. These were coded to be probably related or rated to the intervention. The incidence is similar to the 10% obtained from a meta-analysis of previous studies (Barak et al., 2008). Of these, mostwere female (82%). The most commonly reported unwanted effect was a deterioration of symptoms (n = 4), as participants become more aware of their tinnitus initially due to the focus on tinnitus during the initial parts of the intervention. Three participants also mentioned the emergence of new symptoms, as the exposure techniques caused anxiety. By doing the intervention, three participants realised the impact their tinnitus was having on them and this led to negative wellbeing. Two participant mentioned that the treatment was too prolonged. These events were rated as severe to moderate after the intervention and moderate to mild 1 year following the intervention. These reports have provided further insights regarding unwanted events that need to be addressed or disclosed in future trials of iCBT for tinnitus. It is possible that demographic characteristics not investigated, such as personality type, may be associated

with the experience of unwanted events. Further work is required to fully investigate moderators and mediators of unwanted events.

6.4.5 Processes contributing to the outcomes obtained

Process evaluation was performed to identify factors contributing to outcomes obtained. This was done by exploring processes related to the research context, the intervention delivery and outcomes obtained, which will each be discussed in turn.

6.4.5.1 Processes related to the research context

The recruitment strategies were expanded following the feasibility study. This created more interest in this trial and the required number of participants were recruited. Further strategies may be required to attract more participants for larger-scale studies. Younger adults and females were less inclined to participate. Gender differences may be related to estimates that a slightly higher proportion of men than women experience tinnitus, although a higher percentage of women may find tinnitus bothersome (Seydel et al., 2013; McCormack et al., 2016). It could also be that the flexibility and anonymous nature of this intervention drew more male participants. Identifying factors that deter certain recipients from participating is important.

The intended sample of those with distressing tinnitus who were underserved with evidence-based tinnitus interventions was reached. The majority had not received previous tinnitus treatments and were not attending tinnitus support groups. A large proportion of these (71%) indicated they had seen an ENT specialist. This percentage is higher than the estimated referral rates to specialist services of 37% by GPs (El-Shunnar et al., 2011). Of those who had accessed previous interventions, 14% indicated they had received previoustinnitus therapy from an audiologist or hearing therapist.. This is in line with current estimated referral rates of 12% by GPs (El-Shunnar et al., 2011). Few had undergone psychological treatments, such as CBT. The CBT aspect of the intervention may, therefore, have drawn some participants.

The demographical spread of participants was UK wide, although fewer participants were from regions such as Scotland or Wales. This could partly reflect the effect of the variation of availability of clinical tinnitus provision in the UK (Hoare et al., 2015). Strategies to improve the spread to areas not reached needs consideration. It was encouraging that iCBT appears to be applicable to a range of populations with varying tinnitus characteristics.

6.4.5.2 Processes related to the intervention delivery

A comprehensive audiologist-guided intervention was delivered. The quantity and quality of the guidance differed from that provided by clinical psychologists during previous iCBT studies. The audiologist sent an average of 14 messages per participant. This was more

than the 7.3 sent in the Australian study (Abbott et al., 2009) and 10.7 sent during the study by Hesser and colleagues (2012). Guidance in previous trials was either provided by licensed CBT therapists, clinical psychology (masters degree), or MSc students who had completed their clinical and CBT training. Unlike the present study, these therapists received systematic training and supervision to guide iCBT interventions. These studies also had a lower therapist-participant ratio, as more than one therapist guided the intervention. Hesser et al. (2012), used six therapists, while there were four therapists in the trial by Weise et al. (2016) and Jasper et al. (2014), and three therapists in the trial by Kaldo et al. (2008). Having one therapist in the present trial could have produced a consistent approach for all participants. Although previous therapists had a good understanding of CBT, they had not always had previous experience in treating tinnitus patients. There were, therefore, large differences related to the audiologist in this study compared with the psychologists in previous studies in terms of training and experience. The exact influence of the health professional assigned is not yet known. Outcomes obtained may be related to numerous factors and not only based on the qualifications of the person guiding the intervention. An audiologist may not be as experienced in motivational techniques required to improve engagement and attrition. Direct comparison of audiologist versus psychologist-delivered interventions is required to draw firm conclusions.

6.4.5.3 Processes related to the outcomes obtained

Engagement was variable, as also found in the initial feasibility trial. This may have affected the outcomes obtained. Self-motivation is an important requirement for such a self-help intervention. Ways of improving motivation are required. Time restrictions and poor health resulted in not all participants being fully engaged with the intervention. The programme is demanding and it was found that over time engagement decreased in terms of reading modules and completion of the worksheets. Tinnitus distress also reduced over time. This may have led to less reliance on the intervention and thus lower engagement. Some participants also mentioned finding the lack of initial results difficult, which decreased motivation. This may have contributed to on average only 4 messages being sent by participants. This issimilar to the 5 messages sent on average in the study by Abbott et al.(2009). Tinnitus distress was significantly lower after completing 4 weeks of the intervention. These findings should be explained to future participants as both encouragement and to help adjust their expectations. Barriers restricting engagement such as time limitations and low motivation levels need addressing to improve iCBT outcomes.

To identify processes contributing to the outcomes obtained, participants rated the modules undertaken. The applied relaxation module was rated as most useful and the hearing tactics

module as the least useful module. These ratings were also reflected in some of the outcomes obtained. There were no significant group differences in hearing disability directly following the experimental group undertaking the intervention. As the hearing tactics module was included as an optional module, many participants chose not to do it. Participants may not have realised the relevance of the module in the context of a tinnitus intervention. The rationale for the hearing tactics module should be describedin future trials. These ratings were different to those given by participants undergoing iCBT for tinnitus in Australia. They rated the sound enrichment, sound sensitivity and cognitive restructuring modules as the least useful (Abbott et al., 2009).

Although the sleep module was not rated as highly as some of the other modules, there was a significant positive between-group difference for insomnia (Cohen's *d* = 0.55) after the experimental group completed the intervention (T_1).

6.4.6 Study limitations

This study is not without limitations, which have implications for the interpretation of the results. Firstly, the participants were recruited from the general public due to interest in undertaking an Internet-intervention and not from a clinical setting. The results may not differe for a clinical sample. The demographic distribution of the participants in the present study showed more male participants, a slightly higher mean age and longer tinnitus duration than those forprevious iCBT trials on tinnitus such as those by Andersson et al. (2002); Kaldo et al. (2008); and Weise et al. (2016). This should be considered when assessing the generalisability of the results. Not all participants completed the assessment measures at the post-intervention time points. Ways of encouraging more participants to complete these questionnaires and minimise attrition are required. A deeper understanding of factors affecting adherence may assist.

6.5 CONCLUSIONS

This chapter has answered three of the research questions investigating the efficacy of iCBT for tinnitus in the UK. The null hypothesis was rejected and the alternative hypothesis accepted for all three questions. Efficacy in audiologist-guided iCBT in reducing tinnitus distress and some associated comorbidities was demonstrated. Moreover, these effects were maintained 1 year post-intervention. The next chapter investigates the effectiveness of iCBT compared with standard clinical care for tinnitus in the UK.

7 CLINICAL TRIAL PHASE III: COMPARISON OF ICBT TO STANDARD CLINICAL CARE

This chapter addresses the final research question by investigating whether clinical outcomes with iCBT are comparable to those obtained when providing individualised face to face (F2F) tinnitus care in the UK.

7.1 INTRODUCTION

Specialised tinnitus clinics can significantly reduce functional and social difficulties related to tinnitus (Cima et al., 2012). In the UK, the usual treatment for tinnitus is attending a tinnitus clinic for individualised F2F management by an audiologist or hearing therapist (Hoare et al., 2015). This management generally includes a mixture of patient education, relaxation therapy, various counselling techniques and sound therapies (Hoare et al., 2015). Not all individuals with distressing tinnitus are able to access these interventions due to service and geographical constraints (Gander et al., 2011; Hoare et al., 2015). To improve access to tinnitus services, an iCBT intervention aimed at a UK population was developed (Chapter 4). Although the feasibility and efficacy of iCBT were found to be high (see Chapters 5 and 6), it is not known how outcomes using iCBT compare with those of established individualised clinical care for tinnitus. Previous comparisons have used psychologist-provided GCBT as the active control (Jasper et al., 2014a; Kaldo et al., 2008; Nyenhuis et al., 2013a) and not individualised audiologist-provided care as is typically provided in the UK. This chapter forms Phase III of the clinical trial regarding the effectiveness of audiologist-guided iCBT in the UK. Specific objectives were as follows:

i) To evaluate the effectiveness of iCBT for tinnitus compared with individualised F2F care in reducing tinnitus severity

ii) To compare the effects of iCBT with individualised F2F care for tinnitus-related comorbidities

iii) To assess stability of results, 2 months post-intervention for iCBT versus F2F care

iv) To investigate treatment adherence and the clinical resources required for each intervention

7.2 METHOD

7.2.1 Study design

An effectiveness trial was needed in which patients were treated in a clinical setting, with regular clinicians without use of advertisements to recruit participants. Selecting the most appropriate effectiveness trial design required much consideration. Effectiveness trials tend to be designed to assess either superiority or non-inferiority of a new intervention (Frampton, 2013). Superiority designs are the design of choice when using a placebo or no-treatment control. As there is an existing standard-of-care regimen available for tinnitus in the UK, a no-treatment design was not regarded as ethical. The objective of non-inferiority trials is to demonstrate that a new intervention is not clinically worse (within the non-inferiority margin) than an active treatment control (Frampton, 2013). The experimental intervention was audiologist-guided iCBT. The most relevant active control in a UK context is individualised F2F audiological care. This is the recommended form of tinnitus treatment in the UK at present (Department of Health, 2009). The design selected was a randomised, two-arm parallel group, non-inferiority trial with a sequential adaptive design. To minimise intervention delays, assigned interventions were sequential rollout out on a continuous basis until the required sample size was reached.

7.2.2 Study centres

To increase chances of achieving the target sample size, a multi-centre study design was incorporated with three UK-based primary care hospitals. To account for some of the variability to be expected at different centres, the investigational sites were selected from the hospitals involved in the East of England professional tinnitus network. This network meets quarterly to share best practice in tinnitus care and provide informational talks about tinnitus. This network therefore promotes consistency of practise across sites. Several centres were approached. After the initial study introduction meeting, three hospitals with reputable clinical tinnitus services were selected. These were Norfolk and Norwich Universities Hospitals Trust, Milton Keynes University Hospital NHS Foundation Trust and Hinchingbrooke Health Care NHS Trust. The study sponsor and central trial management centre was at Anglia Ruskin University, Cambridge, UK. Joint meetings were held quarterly prior to the professional tinnitus network meetings. Further individual centre meeting were arranged during the planning phase and as required during the study. Initial site visits were arranged to provide study files and discuss protocols with both clinicians and the research and development teams for each centre.

Quality control checks were put in place to ensure that the trial protocols were being followed at each site providing the F2F care. These included monitoring the length of time taken to provide the initial appointment and monitoring the content of appointments. The

post-intervention questionnaire and telephone interview were a further means to monitor quality. If anyone was discharged but still experienced distressing tinnitus, a further appointment was requested.

7.2.3 Funding

This phase was funded by the British Society of Audiology applied research grant (Principal investigator, E Beukes, April 2016). As three clinical sites were involved, this study required much coordination and planning to ensure the smooth running of the project.

7.2.4 Recruitment

In addition to the inclusion criteria outlined in Chapter 3, the following criteria were applied for Phase III:

i) Having being examined by an ENT specialist or an audiologist at a participating study centre to exclude any known medical cause for tinnitus. This evaluation would typically include a case history, otoscopy, tympanometry, a hearing test and where indicated, magnetic resonance imaging.
ii) Referral to the participating study centre's tinnitus clinic by an ENT specialist or audiologist due to troublesome tinnitus. Standard site protocols were followed whereby this decision was made on the presenting symptom profile and not the score on a tinnitus assessment measure. To follow these standard referral protocols to minic typical clinical situations, there were no lower or upper limits for tinnitus severity in the inclusion criteria.

As this was an effectiveness trial, the study was not advertised. Recruitment relied on ENT specialists or ENT nurses to pass on the study participant information sheet (Appendix N) to participants meeting the inclusion criteria after their ENT appointment. Travel and parking expenses were reimbursed for those participating to a maximum of £10 per journey. Study registration was on the study website (http://www.tacklingtinnitus.co.uk).

7.2.5 Enrolment and randomisation

Participants meeting the inclusion criteria after completing baseline assessment measures and the telephone screening were sequentially randomly assigned in the ratio of 1:1 to an intervention arm, in a staggered manner, following stratification for tinnitus severity (TFI ≤ 50 or >50). Variable randomly permuted block sizes of four and six were used. Following allocation, participants were informed which group they were randomised to and when their treatment would commence. A blinded design would have been optimal, but was not feasible in this context. Participants allocated to the experimental group undertook the

guided iCBT intervention whereas those in the active control group received care at their local hospital. Both participants and clinicians knew the intervention-arm allocation.

7.2.6 Assessment measures

In addition to the generic assessment methods used in each phase, the full THI (Newman, Jacobson, & Spitzer, 1996) was administered, as this assessment measure was used routinely by the study centres (Appendix D).

The treatment satisfaction questionnaire was shortened to six questions rated on a Likert scale (1–5), posing only questions that were relevant to both treatments. The questions assessed the clinical support, satisfaction with the level of clinician contact, clinician approachability, information provided, the range of topics covered and whether the treatment would be recommended to others.

As this was an initial effectiveness study, no formal cost effectiveness evaluation was done.

7.2.7 Study interventions

The intervention groups, which ran in parallel, were:

- The experimental iCBT group who received the iCBT intervention over an 8 week period
- The F2F active control group who were under the care of their local hospital for an average duration of 8 weeks and received an average of two to three appointments

7.2.7.1 Intervention outline for both groups

- During the initial clinical examination, all participants were assessed regarding their suitability for hearing aids or combination devices. Where indicated, these were provided regardless of group allocation. Existing hearing aid provision was also reassessed regardless of group allocation.
- The estimated duration of the active intervention was an 8 week period for both groups, although some individual variation occurred
- Audiologically trained professionals supported each group. For the F2F group this was a hearing therapist, audiologist or clinical scientist in audiology. Guidance for the iCBT group was by a clinical scientist in audiology as described in chapter 3. Clinicians providing the intervention to both groups, were required to have had training and experience in managing tinnitus patients, to be part of a professional tinnitus network, and to maintain good clinical practice. In this way, the interventions provided were standardised as much as possible despite participants attending different hospitals. Clinicians also agreed to follow a structured protocol in order for similar components to be received by all participants.

- Information about managing tinnitus was provided to both groups. The delivery of this information, however, differed, being online for the iCBT group and explained by an audiologist during an appointment for the active F2F control group.
- A log was kept of the information provided to individuals in both groups. These were the modules actually done by the iCBT group participants and content covered during appointments for individuals in the F2F group.

7.2.7.2 Guided iCBT intervention outline (experimental group)

The experimental group commenced the iCBT intervention, described in Chapter 4, following group allocation.

Table 7.1 Individualised F2F intervention content for the control group

Time-line	**Intervention content (individually tailored) may include**	**Intervention load**	
		Explanation	**Daily Practising**
Initial appointment	In-depth case history	20 minutes	
	Information about tinnitus	20 minutes	
	Sound enrichment advice and equipment demonstration	20 minutes	As required
Follow-up appointment	Recap	5 minutes	
	Relaxation advice	15 minutes	10 minutes
	Sleep management advice	20 minutes	As required
	CBT techniques such as identifying negative automatic thoughts	20 minutes	As required
Second follow-up appointment	Review difficulties and address these	20 minutes	As required
	Advice on further support, including tinnitus support groups, charities, tinnitus apps	20 minutes	As required
	Further options such as mindfulness, hypnosis or concentration management	20 minutes	As required

7.2.7.3 Individualised F2F intervention outline (active control intervention)

The F2F group received individualised therapy for tinnitus using the usual information counselling approach generally followed in the management of tinnitus in the UK. A structured protocol including similar intervention components (see Table 7.1) was developed to standardise the care received across the different hospitals. The content was

tailored to each individual. Initial appointments were generally used to provide explanations about tinnitus and discuss some basic tinnitus management strategies, such as use of sound enrichment. A follow-up was made four to eight weeks later to discuss additional strategies for tinnitus management, such as relaxation techniques. Further follow-up appointment were made as required to address remaining difficulties. Appointments lasted 60 minutes on average.

7.2.8 Statistical analysis

CONSORT guidelines for non-inferiority randomised clinical trials were followed (Piaggio et al., 2012).

7.2.8.1 Establishment of the non-inferiority margin for the primary assessment measure

A fundamental principle in the analysis of non-inferiority trials is establishing the non-inferiority margin for analysis of the main assessment measure (Piaggio et al., 2012). Setting this margin was challenging, as no non-inferiority trials using the TFI as the primary assessment measure were found. As there was no established non-inferiority margin, it was set using both statistical reasoning and clinical judgment. When developing the TFI, the authors reported that a 13 point difference was considered a clinically significant change in scores for an individual (Meikle et al., 2012). Further studies using the TFI have reported larger differences. Fackrell and colleagues (2016) for instance suggested 22.4 points to be a significant change in pre-post intervention TFI scores. They used a research volunteer population rather than a clinical population and concerns have been raised about the applicability of these results for a clinical population (Folmer, 2016; Henry, Thielman, & Zaugg, 2017b). The research and clinical teams were consulted and it was agreed that differences larger than 13 points would not be classed as clinically non-significant. A 13 point non-inferiority margin to compare the results of the TFI was thus selected as the most reasonable, both statistically and clinically.

7.2.8.2 Sample size calculations

The SampSize app for non-inferiority parallel groups was used for sample size calculations (Flight & Julious, 2016). Alpha was set to 0.025, power at 90%, and the non-inferiority margin to 13 points. The standard deviation was estimated to be 17 points, by using the standard deviation optained from the baseline TFI scores obtained during the efficacy randomised control trial (chapter 6). The minimal sample size for each group was 39 participants. An additional seven participants were assigned to each group to allow for possible drop outs, estimated from previous effectiveness trials of a similar nature to be

between 10–20% (Kaldo et al., 2013; Kaldo-Sandström et al., 2004). Each intervention arm was, therefore, assigned 46 participants (n = 92).

7.2.8.3 Missing Data Analysis

Per-protocol results were compared with those using an ITT paradigm. Participants were per-protocol if they completed the post-intervention assessment measures at the time point under investigation (T_1 or T_2). As there were no differences, the per-protocol analysis results are reported in accordance with current guidelines for non-inferiority trials (Piaggio et al., 2012).

7.2.8.4 Baseline group differences (T_o)

Baseline group differences were analysed using independent samples *t*-tests for continuous variables and Chi-square tests for categorical variables.

7.2.8.5 Group comparisons (T_0–T_1 and T_0–T_2)

To determine whether iCBT is not inferior to F2F care, a confidence interval approach was used. Non-inferiority of iCBT in comparison to F2F care for tinnitus distress was established if the lower limit of the two-sided 95% confidence interval of the mean difference between these two interventions was less than the non-inferiority margin of 13 points on the TFI. For the secondary assessment measures non-inferiority was established if the between-group effect size was less than Cohen's d = 0.20, as this margin is considered a marginal change (Cohen, 1988).

7.2.8.6 Clinically significant Change

Clinically significant change was calculated only for the main assessment measure using the standard deviation and means at T_0, the means at T_1, and the test-retest reliability coefficient of 0.8 for the TFI (Meikle et al., 2012). Individual's mean difference scores for those completing their assigned intervention arm between T_0–T_1 and T_0–T_2 were evaluated against the RCI criterion (see Chapter 3).

7.2.8.7 Monitoring intervention effects Between T_0–T_1

A mixed 2x8 ANOVA for repeated measures was used to compare the weekly THI-S scores with the within-subject factor of time (weeks 1–8) and between-subject factor of group (experimental and control). Main effects were followed up by paired-samples *t*-tests to compare within-group differences at individual time points and independent samples *t*-tests to compare results between the two groups at each time point.

7.2.8.8 Stability of results

Paired-samples *t*-tests were used to compare within-group differences between T_1 and T_2 for each assessment measure, to assess the stability of the results.

7.2.8.9 Satisfaction ratings

Independent samples *t*-tests were used to compare evaluations of each group regarding the intervention they undertook. Levene's test for equality of variances was performed to compare the variances for the two groups.

7.3 RESULTS

7.3.1 Participant characteristics

During the recruitment period 374 adults were invited to participate. The baseline assessment measures were completed by 92 participants who all met the eligibility criteria. The spread of geographic location in relation to the study centre is shown in Figure 7.1. Participants were randomly assigned to the experimental (n = 46) and active control groups (n = 46) as shown in the CONSORT diagram (Figure 7.2). Recruitment rates were 38% from Site A, 49% from Site B and 11% from Site C (overall recruitment rate of 24%). As recruitment was not via advertisement, achieving the required sample size was challenging. Recruitment started at sites A and B in August 2016. Due to a delay in capability and capacity approvals from their research and development department, recruitment only started in September 2016 at Site C. Recruitment was planned for a period of 5 months. This had to be extended by a further 3 months before the target sample size was achieved (Table 7.2). Strategies to boost recruitment were implemented during this period. These included the principle investigator providing monthly reports, visits and talks to the hospitals during the recruitment period together with encouraging emails to keep the study in mind. As recruitment was problematic, additional centres were invited to participate, but the invitation was declined due to research trials already being active at these centres.

The average age was 53 years (SD: 12) with more male participants overall (60%). There were 41% (19 from each group) wearing hearing aids, either fitted before starting or during the trial. The groups were well matched, as there were no significant demographic (Table 7.3) or clinically meaningful differences (Table 7.4) at baseline. The ranges of baseline TFI scores were similar at 21–95 for the experimental group and 21–93 for the control group.

7.3.2 Attrition

No participants withdrew during the study. Assessment measures were completed by 96% of participants at T_1 and 80% at T_2, with no group differences. No significant baseline differences in terms of age, gender, employment status, level of education, tinnitus severity, insomnia, anxiety or depression were found between those who completed the assessment measures and those who chose not to complete them.

Table 7.2 Number of participants recruited per month

Month	Number recruited	Cumulative number recruited
2016		
August	5	5
September	5	10
October	18	28
November	15	43
December	14	57
2017		
January	9	66
February	16	82
March	10	92

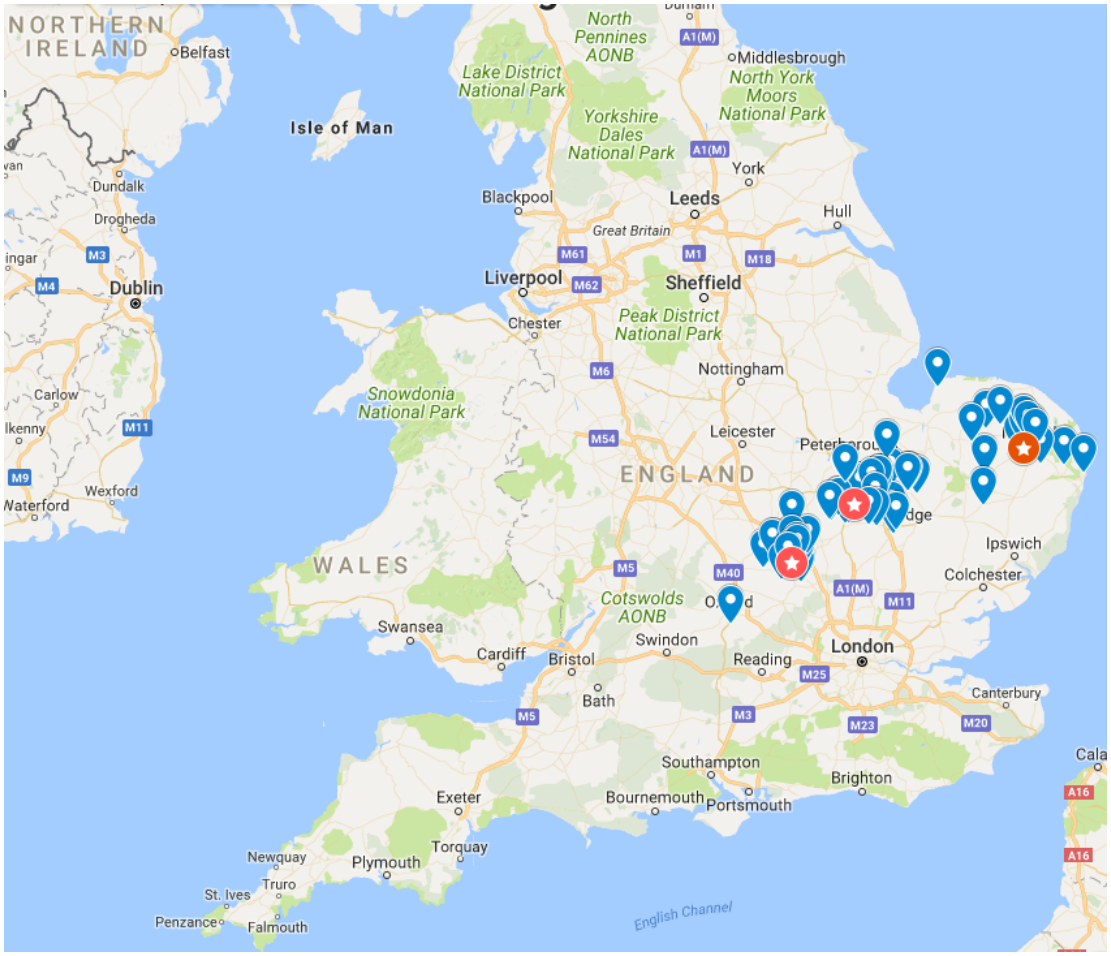
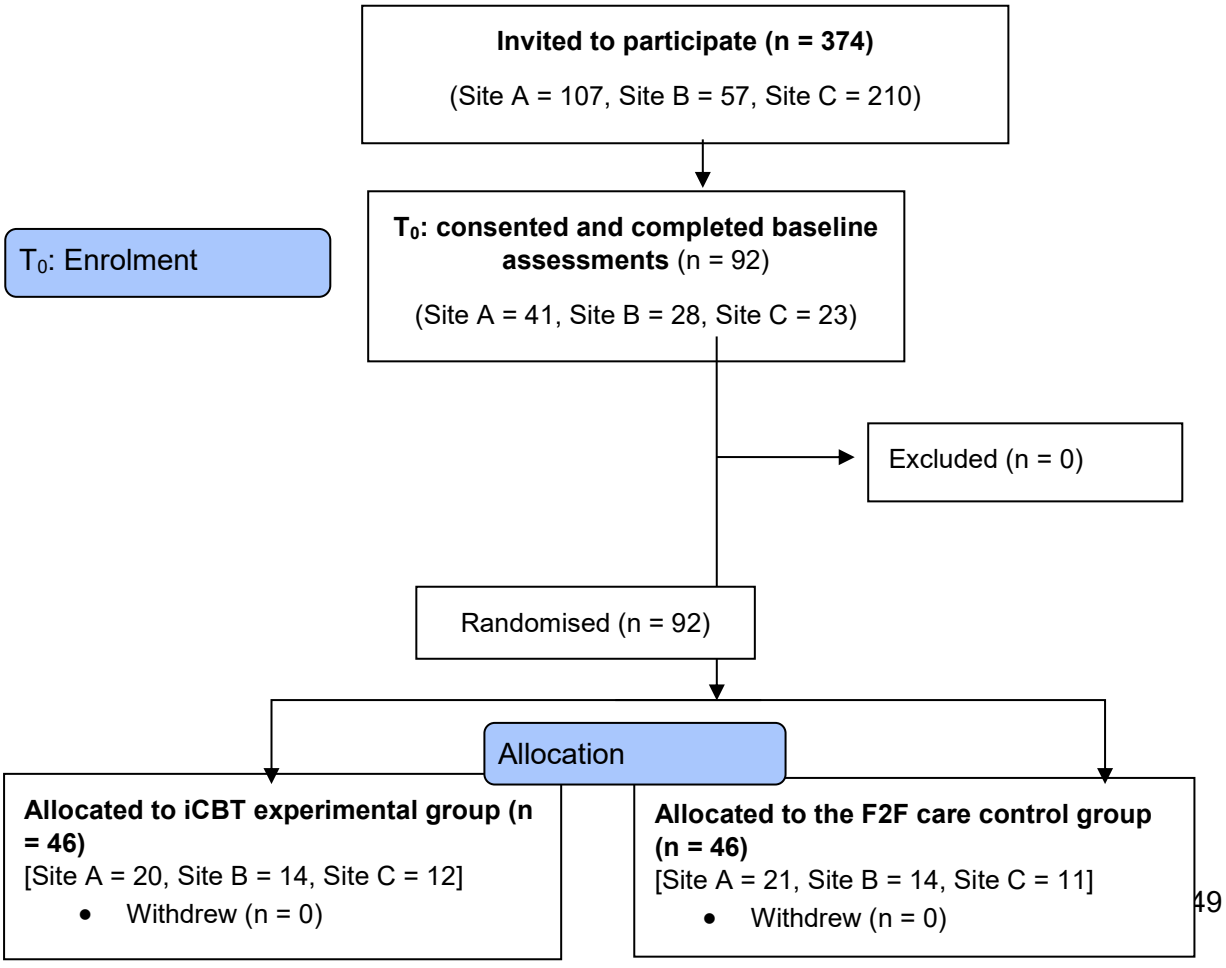


Figure 7.1 Spread of participants *(blue markers) in the East of England associated with the three study centres (red stars) for Phase III.*



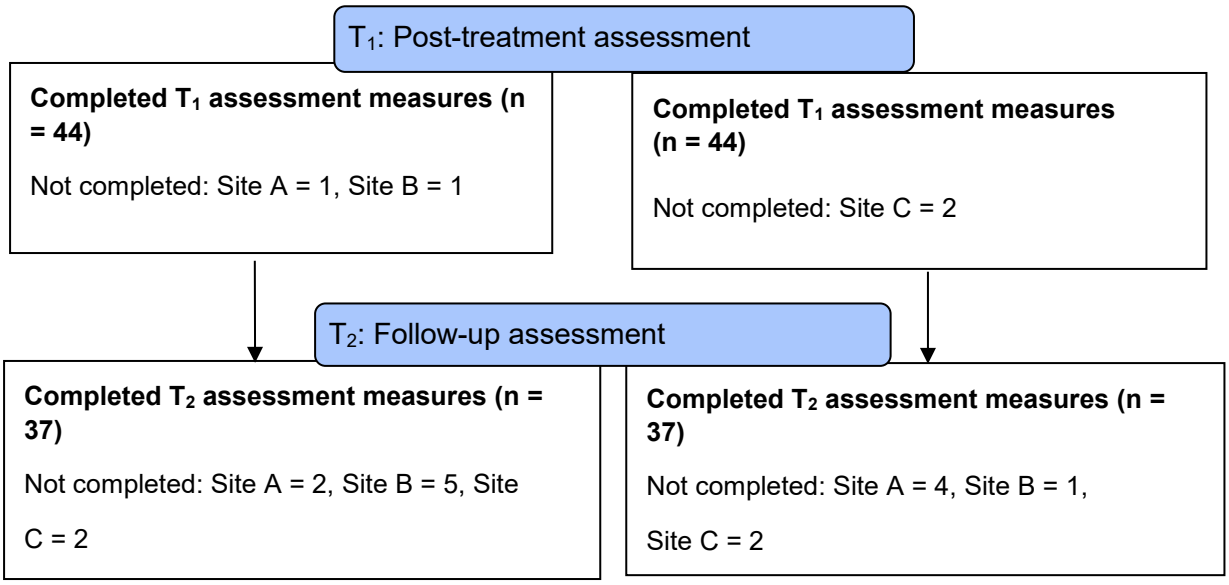


Figure 7.2 The CONSORT study profile for Phase III.

Table 7.3 Demographical characteristics of the participants: Phase III

Category	Description	Experimental group (n = 46)	Control group (n = 46)	Overall (n = 92)	Group difference
Gender	Male	29 (63%)	26 (57%)	55 (60%)	χ^2 (1) = 0.41, p = 0.52
	Female	17 (37%)	20 (44%)	37 (40%)	
Age	Mean years (SD)	51 (12)	55 (12)	53 (12)	t(90) = -1.86, p = 0.07
	Range	26–79 years	29–76 years	26–79 years	
Tinnitus duration	Mean years (SD)	5 years	8	6.54 (9.25)	t(90) = -1.36, p = 0.18
	Range	3 months to 40 years	3 months to 50 years	3 months to 50 years	
Using hearing aids	No	27 (59%)	27 (59%)	54 (59%)	χ^2 (1) = 0.28, p = 0.79
	Yes	19 (41%)	19 (41%)	38 (41%)	
Working less due to tinnitus	Reduced hours	1 (2%)	2 (4%)	3 (7%)	χ^2 (2) = 0.69, p = 0.16
	Stopped work	0 (0%)	4 (9%)	4 (9%)	
	Disability allowance	1 (2%)	2 (4%)	3 (7%)	

7.3.3 Efficacy of iCBT versus standard care for tinnitus distress

The within-group effect sizes for both tinnitus assessment measures (the TFI and THI) were large for both groups at both T_1 and T_2 (Table 7.4). At T_2 the means had further reduced for both groups, indicating further improvements. At T_1 and T_2 the mean TFI scores were 26 (SD: 18) and 27 (SD: 21) points lower, respectively, compared with baseline for the experimental group. For the control group, the mean TFI scores at T_1 and T_2 were 22 (SD: 19) and 24 (SD: 22) points lower than at baseline.

The between-group difference was 5 points [95% CI: -4 to 15] at T_1 and 6 points at T_2 [95% CI: -5 to 16], favouring the experimental group, as seen in Figure 7.3. The results for the TFI fell within the non-inferiority margin of 13 points for the lower 95% CI for both per-protocol and ITT analysis at T_1 and T_2. There were no statistically significant between-group interactions [$F(1, 72) = 1.03$, $p = 0.35$] although significant time differences were found [$F(1, 72) = 95.19$, $p = 0.001$] . Pairwise comparisons found significant time effects between T_1-T_2 and T_1-T_3 but not T_2-T_3.

Similar results were obtained for the THI, as shown in Table 7.4. At T_1 and T_2 the mean THI scores were 16 (SD: 22) and 20 (SD: 18) points lower, respectively, compared with baseline among those in the experimental group. For the control group, the mean THI scores at T_1 and T_2 were 11 (SD: 27) and 17 (SD: 18) points lower than at baseline

Clinical significance using per-protocol analysis was achieved by 25 (57%) of the experimental group and 18 (41%) of the control group at T_1, using the RCI criterion of a 21 point change in TFI score (i.e. 1.96 times the standard error of 7.6). At T_2 a clinically significant change was found for 20 participants (54%) of the experimental group and 17 (46%) of the control group. There were 23 (52%) from the experimental group and 15 (34%) from the control group at T_1 with TFI scores below the level requiring intervention (less than a score of 25) who also had a reliable change of 21 points.

Table 7.4 Group comparisons over time: Phase III

Measure	Group	Means (Standard deviation)			Between-group analysis				Within-group analysis	
		T_0	T_1	T_2	T_0–T_1 M (95%CI)	T_0–T_2 M (95%CI)	T_1 Cohen's *d* (95% CI)	T_2 Cohen's *d* (95% CI)	T_0–T_1 Cohen's *d* (95% CI)	T_0–T_2 Cohen's *d* (95% CI)
TFI	**iCBT**	55 (22)	28 (21)	23 (19)	5.18 (-4.17–14.53)	5.51 (-4.60–15.61)	0.30 (-0.12– 0.72)	0.45 (-0.01–0.91)	1.28 (0.81–1.72)	1.56 (1.06–2.04)
	F2F	56 (21)	35 (25)	33 (23)					0.95 (0.51–1.38)	1.10 (0.63–1.56)
THI	**iCBT**	45 (23)	23 (20)	18 (15)	4.91 (-5.51–15.33)	3.67 (-4.81–12.14)	0.32 (-0.11–0.73)	0.33 (-0.13–0.79)	1.08 (0.63–1.51)	1.28 (0.80–1.74)
	F2F	47 (20)	29 (20)	27 (22)					0.96 (0.55–1.38)	1.05 (0.58–1.50)
ISI	**iCBT**	11.4 (6.4)	6.7 (6.2)	5.7 (4.6)	0.38 (-1.99–2.75)	1.45 (-1.10–4.00)	0.46 (0.03– 0.88)	0.74 (0.26–1.20)	0.75 (0.32–1.17)	1.01 (0.55–1.46)
	F2F	13.7 (6.6)	9.6 (6.2)	10.0 (6.9)					0.65 (0.21–1.06)	0.54 (0.09–0.97)
GAD-7	**iCBT**	6.4 (5.6)	3.5 (3.7)	3.3 (3.2)	-1.19 (-3.40–1.02)	-0.78 (-2.72–1.17)	0.06 (-0.36–0.48)	-0.03 (-0.49–0.42)	0.62 (0.20–1.04)	0.66 (0.21–1.09)
	F2F	6.8 (5.5)	3.3 (3.8)	3.4 (3.6)					0.72 (0.29–1.14)	0.70 (0.25–1.14)
PHQ-9	**iCBT**	6.5 (5.5)	3.7 (3.6)	2.8 (3.0)	-1.40	0.53	0.03 (-0.42–0.49)	0.57 (0.10–1.03)	0.61 (0.18–1.02)	0.82 (0.36–1.26)

	F2F	8.0 (6.1)	4.2 (4.1)	5.0 (4.5)	(-3.66–0.85)	(-1.79–2.84)			0.73 (0.30–1.15)		0.55 (0.11–0.99)
HHIA-S	**iCBT**	11.7 (10.7)	10.1 (10.8)	9.1 (11.6)	-1.29 (-4.84–2.27)	0.22 (-3.68–4.13)	0.19 (-0.23–0.61)	0.27 (-0.19–0.73)	0.15	(-0.26–0.57)	0.24 (-0.20–0.67)
	F2F	14.3 (11.6)	12.1 (10.7)	12.0 (9.6)					0.19	(-0.22–0.61)	0.21 (-0.22–0.65)
HQ	**iCBT**	15.6 (9.1)	12.2 (7.6)	12.5 (9.0)	-0.43 (-3.63–2.77)	-0.28 (-3.90–3.34)	0.16 (-0.26–0.57)	0.05 (-0.40–0.51)	0.41	(-0.01–0.82)	0.35 (-0.09–0.78)
	F2F	16.5 (7.4)	13.4 (7.3)	13.0 (7.5)					0.43 (0.01–0.84)		0.48 (0.04–0.92)
CFQ	**iCBT**	35 (14.4)	30.8 (12.1)	30.1 (12.9)	0.12 (-4.7–5.12)	-0.05 (-6.21–6.10)	0.29 (-0.23–0.61)	0.18 (-0.28–0.64)	0.31	(-0.11–0.72)	0.35 (-0.08–0.79)
	F2F	39.7 (19.3)	35.6 (19.2)	33.1 (19.2)					0.21	(-0.20–0.62)	0.34 (-0.10–0.77)
SWLS	**iCBT**	18.7 (5.7)	20.1 (5.0)	21.0 (5.1)	0.14 (-1.83–2.12)	0.60 (-1.57–2.77)	0.01 (-0.41–0.43)	0.10 (-0.36–0.56)	0.26	(-0.16–0.67)	0.43 (0.00–0.84)
	F2F	19.5 (5.5)	20.1 (5.6)	20.5 (5.0)					0.10	(-0.31–0.51)	0.19 (-0.24–0.62)

Acronyms: M: means, CI: confidence interval, SD: Standard Deviation, T_0: pre-intervention, T_1: post-intervention, T_2: follow-up, TFI: Tinnitus Functional Index, ISI: Insomnia Severity Index, GAD: Generalised Anxiety Disorder, PHQ: Patient Health Questionnaire, HHIA-S: Hearing Handicap Inventory for Adults-screening version, HQ: Hyperacusis Questionnaire, CFQ: Cognitive Failures Questionnaire, SWLS= Satisfaction with Life Scale

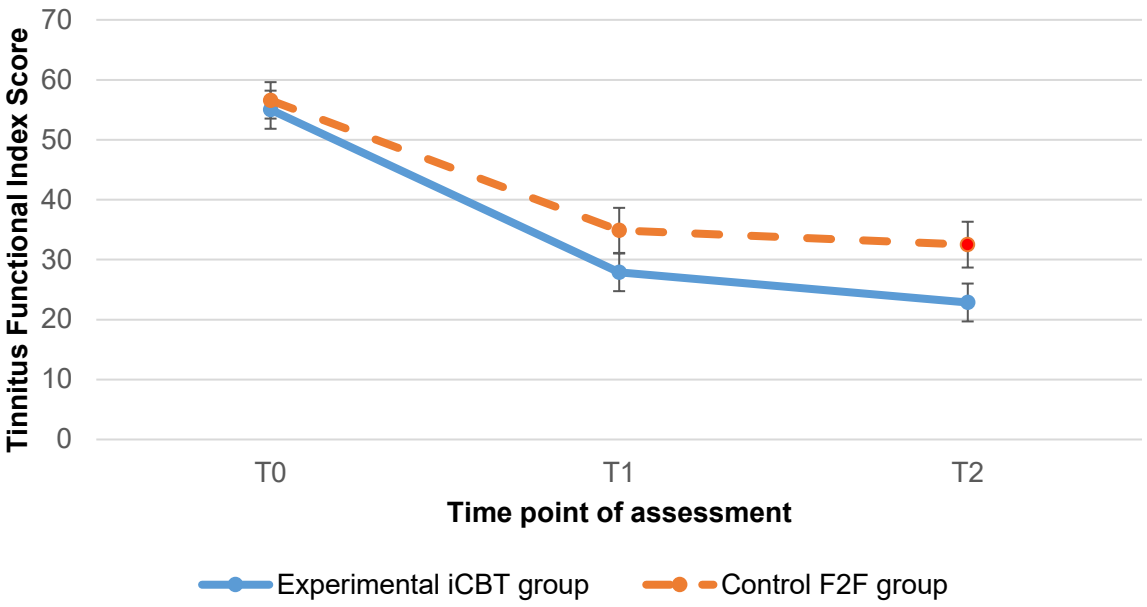


Figure 7.3 Tinnitus distress over time as measured by the Tinnitus Functional Index: Phase III. Error bars represent the ±1 standard error of the mean.

The majority of the experimental group had a T_o–T_1 difference score falling between 10 and 50 points, with a maximum difference of 70 points (Figure 7.4). In comparison, the control group had more participants not improving and had more with larger improvements of 50–69 points (maximum improvement of 69 points). These differences were not significantly different [$F(1,9) = 0{\cdot}008$, $p = 0{\cdot}93$].

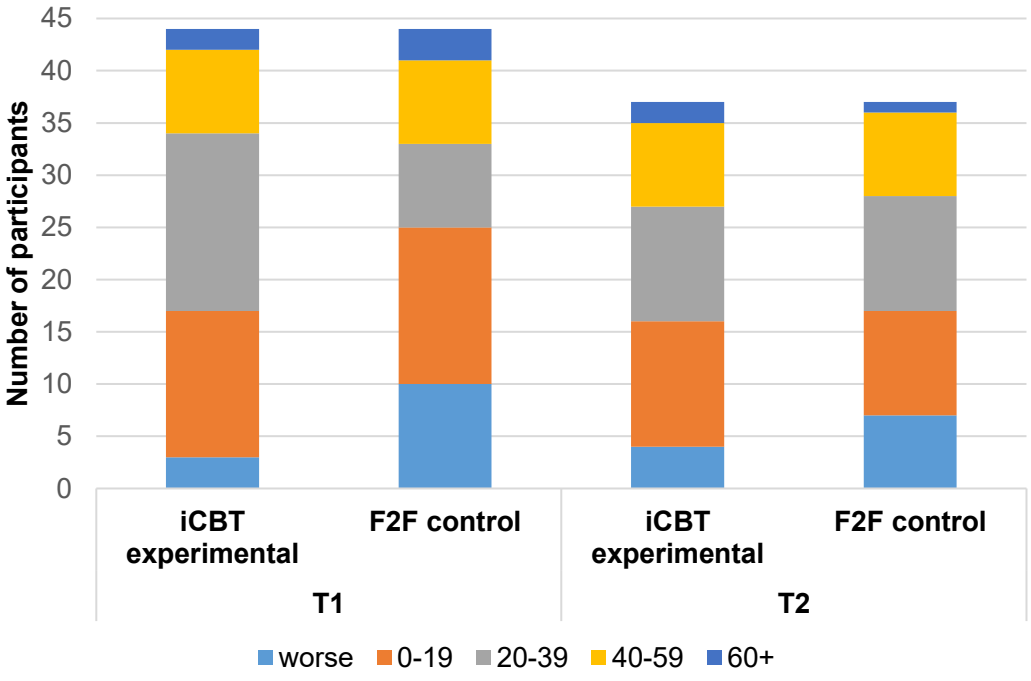


Figure 7.4 Distribution of the Tinnitus Functional Index score change. Change between T_0–T_1 (n = 44) and T_0–T_2 (n = 37).

7.3.4 Monitoring intervention effects between T_0 and T_1

Differences between the two groups tended to increase across the 8 time points between T_0 and T_1 as shown in Figure 7.5. The experimental group had greater reductions in tinnitus distress, as evidenced by the significant between-group effect [$F(7, 524) = 2.80$, $p = 0.037$; Cohen's $d = 0.57$]. Follow-up analysis indicated no group differences in weeks 1 to 3 of this period. From weeks 4 to 8, tinnitus distress was significantly lower for the experimental group than for the control group.

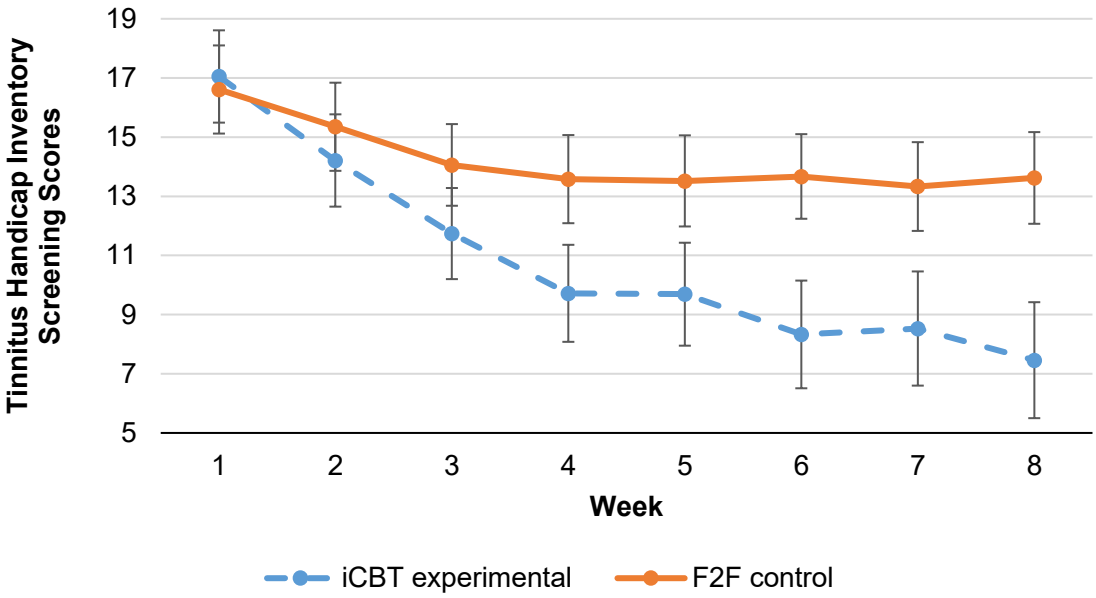


Figure 7.5 Phase III weekly Tinnitus Handicap Inventory-screening scores for each group across the first 8 week period between T_0 and T_1. Error bars represent the ±1 standard error of the mean.

7.3.5 Effectiveness of iCBT versus standard care for tinnitus-related comorbidities

The within-group effect sizes for the ISI were medium to large for both groups. They were medium for the GAD and PHQ (except at T_2 for the experimental group where a large difference occurred) and small for the other assessment measures. The T_1 between-group effect sizes for the secondary assessment measures were within the non-inferiority margin (Cohen's $d < 0.20$) for anxiety, depression, hearing disability, hyperacusis and life satisfaction. They were outside this margin, favouring the iCBT group for insomnia and cognitive failures. At T_2 they were outside this margin for insomnia, hearing handicap and depression, again favouring the iCBT group.

7.3.6 Stability of intervention effects

AT T_2 the means for tinnitus distress had further reduced for both groups (Figure 7.3). These reductions were not statistically significant for either the TFI or THI, indicating stability of the results for tinnitus distress over time.

There were no statistically significant changes between T_1 and T_2 for any of the secondary assessment measures, again indicating stability of results over time for both groups. For the experimental group, improvements in means were found for all secondary assessment measures except for hyperacusis. For the control group improvements in means were found for hearing disability, hyperacusis, cognitive failures, and life satisfaction, but not for anxiety, depression and insomnia. This resulted in a medium between-group effect size for insomnia (d = 0.74) and depression (d = 0.57) at T_2 and small effect size for the T_1–T_2 difference for other assessment measures.

7.3.7 Treatment satisfaction

Participants were asked to rate satisfaction with six aspects of the intervention using a five point Likert scale. The ratings for each aspect is shown in Figure 7.6. Overall the ratings were high with a mean of 4.3 (SD: 0.2). Independent samples *t*-tests indicated no statistical differences between the ratings of the two groups.

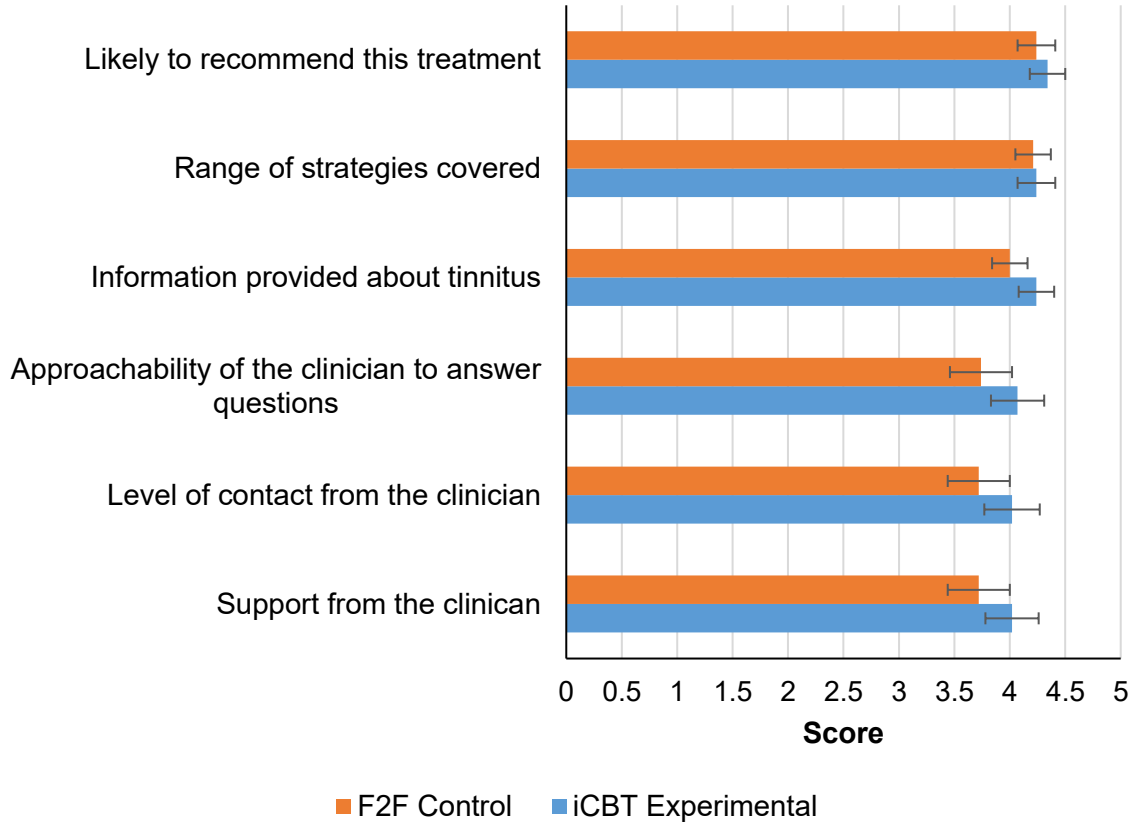


Figure 7.6 Intervention satisfaction ratings.

7.3.8 Treatment adherence and clinician resources

On average, those in the F2F group received 2.3 (SD: 1.1) appointments with a maximum of five appointments. This corresponded to 137 minutes of contact time per participant during the intervention period. Seven appointments were arranged that were not attended.

On average those in the iCBT group read 12.7 (SD: 7.7) of the 21 modules (16 recommended, five optional). There were 15 (36%) who completed all the modules. Users sent an average of 7.5 messages (SD: 9.7) and the therapist sent an average of 20.6 messages per iCBT participant, i.e. 2.6 weekly per participant. This corresponded to 64 minutes of contact time per participant during the intervention period.

7.4 DISCUSSION

This chapter evaluated the effectiveness of audiologist-guided iCBT compared with standard F2F clinical care for tinnitus. This discussion considers the results obtained for each research objective.

7.4.1 Effectiveness of iCBT versus F2F clinical care for tinnitus distress

The results indicated that the two interventions were equally effective within the boundaries of non-inferiority for reducing tinnitus distress. A reduction in tinnitus distress was found for each group for both tinnitus assessment measures (the TFI and THI) with large within-group effect sizes at T_1 and T_2.

Closer analysis indicated some between-group variations, although not significantly different. Of interest was the difference in magnitude of the TFI score changes from T_0 to T_1 between the groups. For the experimental group the majority had a 40–59 point difference. Slightly more participants from the control group had a maximum score difference exceeding 60 points in comparison with the experimental group. Pinpointing the intervention elements that may lead to these differences is important.

Intervention effects differed between the two groups during weeks 4-8 between T_0–T_1. Tinnitus distress in the experimental group was rated significantly lower than that of the control group from weeks 4 onwards. This was possibly related to the differences in the structure followed for each intervention arm. The experimental group received weekly input whereas the control group received an intervention session with a follow-up session scheduled 4–8 weeks later. For the control group, the improvements in tinnitus distress were only found towards the end of the intervention period. Further investigations are

required regarding the effects of more intensive weekly interventions as opposed to those with longer follow-up periods.

There have been two previous effectivenss studies of iCBT for tinnitus. Both were run at the Uppsala Clinic in Sweden. There were 77 participants receiving iCBT in the first study by Kaldo-Sandström and colleagues (2004). The within-group effect size was *d* = 0.56 for tinnitus distress using the (TRQ; Wilson et al., 1991). In the subsequent effectiveness trial 293 participants were sequentially provided with iCBT (Kaldo et al., 2013). Those not meeting the inclusion criteria due to mild tinnitus distress received low intensity iCBT (n = 81). This consisted of the same text, no homework assignments and less therapist contact. The within-group effect size was *d* = 0.58 for the iCBT group and *d* = 0.26 for the low intensity group. Differences between these trials at Uppsala and the present trial include the assessment measures used (TRQ versus TFI), the type of clinician providing the guidance (psychologist versus audiologist), use of randomisation (absent and present), and the format of the intervention (text-based versus a more interactive version). This may account for the differences in clinical significance found between studies. For the present study clinical significance was achieved by 54–57% of the experimental group and 41–46% of the control group at T_1 and T_2. In addition to achieving clinical significance, 52% from the experimental group and 34% from the control group had post-intervention TFI scores below the level requiring intervention (< 25) at T_1. This is higher than the 27% (Kaldo-Sandström et al., 2004) and 38% (Kaldo et al., 2013) reaching clinical significance in the previous studies. Although similar clinical populations were studied, differences in ways of calculating clinical significance (50% reduction in TRQ scores versus using a RCI criterion), probably contributed to these discrepancies.

Weekly assessments were not completed during previous effectiveness trials. Measurements were taken after completing each treatment step in the trial by Kaldo et al. (2013). Participants rated tinnitus loudness and distress on a Likert scale after each treatment step was completed. For those completing the first treatment step, the mean rating was 6.5 (SD: 1.5) for tinnitus loudness and 6.2 (SD: 1.6) for tinnitus distress. After completing the last treatment step, the mean rating was 5.6 (SD: 1.8) for tinnitus loudness and 5.3 (SD: 1.9) for tinnitus distress. These differences were not as great as in the present study. Direct comparison between the studies is difficult, as a weekly assessment measure was not used by Kaldo et al. (2013) and the assessment measures used differed between these studies (Likert scale versus THI-S).

The present trial was unique as it compared iCBT with individualised F2F clinical care, as opposed to GCBT used in previous efficacy studies. Kaldo et al. (2008) compared 6 weeks of iCBT (n = 26) with seven sessions of GCBT (n = 25). With regard to tinnitus distress, no significant group differences were found. Smaller effect sizes were reported than for the

present study at *d* = 0.73 for iCBT and *d* = 0.64 for GCBT. Nyenhuis and colleagues (2013a), compared four groups, namely iCBT (n = 79), CBT bibliotherapy [CBT self-help book] (n = 77), GCBT (n = 71) and an information only control (n = 77). Between-group effect sizes relative to the control condition were *d* = 1.04 for iCBT, *d* = 0.89 for GCBT and *d* = 0.24 for the bibliotherapy group. In a further efficacy study by Jasper and colleagues (2014a), three groups were compared, iCBT (n = 41), GCBT (n = 43) and an Internet-based discussion forum control (n = 44). The results favoured the CBT interventions compared with the discussion forum ($0.56 \leq g \leq 0.93$; all $p \leq 0.001$).

7.4.2 Effectiveness of iCBT versus F2F clinical care for tinnitus-related comorbidities

Secondary intervention effects were largest for insomnia followed by anxiety and depression for both groups. The combined results across T_1 and T_2 indicated that the two interventions were equally effective within the boundaries of non-inferiority for tinnitus-related comorbidities, except for the results for insomnia, which favoured the iCBT group. For phase II, intervention effects were also greatest for insomnia. Identifying the mediators of this effect may be of value in identifying aspects of iCBT that lead to positive effects, particularly for insomnia.

Previous efficacy trials comparing iCBT to GCBT found varying effects on secondary assessment measures (see Appendix A). Kaldo and colleagues (2008) reported that insomnia and anxiety improved in both the iCBT and GCBT groups but depression only improved in the iCBT group. Nyenhuis and colleagues (2013a), found small effect sizes for depression and psychosomatic discomfort for all three active groups (iCBT, GCBT, bibliotherapy) compared with the information-only control group (when using per-protocol analysis). When comparing iCBT and GCBT to a discussion forum control group, Jasper et al. (2014a), reported medium effect sizes for insomnia and anxiety and small effect sizes for depression.

In the effectiveness trial by Kaldo-Sandström and colleagues (2004), significant pre-post intervention within-group differences for insomnia, anxiety and depression were found. Kaldo et al. (2013) reported medium within-iCBT group effect sizes for depression, anxiety and insomnia. There was a small effect size for a question on hyperacusis. These results indicate that iCBT for tinnitus can improve tinnitus-related comorbidities. Effects have generally been shown for insomnia, anxiety and depression and little emphasis has been placed on other comorbidities. Further work is required to identify how tinnitus interventions can further target the comorbidities associated with tinnitus.

7.4.3 Effectiveness of iCBT versus F2F clinical care at maintaining intervention effects

Results for both groups indicated the stability of results at 2 month follow up for both tinnitus distress and the secondary assessment measures. At the 2 month follow-up period, medium between-group effect sizes were found for insomnia (*d* = 0.74) and depression (*d* = 0.57), favouring the experimental group. Small between-group effect sizes were found for other assessment measures.

Mixed results have been reported regarding the longer term effects of iCBT compared with GCBT in previous trials. Kaldo and colleagues (2008), reported that tinnitus distress and insomnia remained stable at 1 year post intervention for both groups, whereas depression remained reduced for the iCBT group only and anxiety remained reduced for the GCBT group only. Nyenhuis and colleagues (2013a) found that tinnitus distress and depression scores were maintained at 6 months follow up for GCBT but not iCBT. Psychosomatic discomfort was maintained at the 6-month period for both groups. On the other hand, Jasper and colleagues (2014a) reported that tinnitus distress, depression and insomnia remained stable for both the iCBT and GCBT groups at 6 months post-intervention.

In the previous effectiveness trial by Kaldo-Sandström and colleagues (2004), tinnitus distress, anxiety, depression and insomnia remained stable 3 months post-intervention. In contrast, scores deteriorated slightly for tinnitus distress, anxiety, depression, insomnia and hyperacusis in the next effectiveness trial by Kaldo et al. (2013). These discrepancies could partially be attributed to differences in assessment measures used, varying time periods of assessing post-intervention effects and sample size differences, as shown in Appendix A. Further well-controlled studies with sufficient power using the same measuring period and identical assessment measures are required to draw firm conclusions regarding the stability of intervention effects for iCBT versus F2F.

7.4.4 Intervention attrition, adherence and clinician resources

Comparing attrition and adherence rates for interventions provides useful information. Attrition rates were equal for the two groups. At T_1 and T_2, 96% and 78% of participants, respectively, completed post-intervention assessment measures. These rates were higher than those reported for previous effectiveness trials. Kaldo-Sandström et al. (2004) reported 70% completion rate at T_1 and 72% at 3 month follow up. Kaldo and colleagues (2013), reported 63% completion immediately post-intervention and 54% completion at 3 months follow-up for those undertaking the full iCBT intervention. No demographic or clinical differences were identified between those completing and those dropping out in the present study. In contrast, Kaldo and colleagues (2013) found that younger participants were more likely to drop out. In addition, those with higher ratings of loudness and tinnitus distress (on

a scale of 1–9) after finishing the first treatment step took longer to complete the whole intervention.

The F2F group had an average of 137 minutes audiologist contact time per participant. Seven F2F appointments were not attended in total. The iCBT group required less audiologist time at 64 minutes contact time per participant during the intervention period. Kaldo and colleagues (2008), reported that in comparison with iCBT, the therapist time was twice as long for GCBT. GCBT sessions involved seven participants per group attending 120-minute sessions. Therefore, iCBT was 1.7 times as cost-effective as GCBT in terms of staff time (assuming equality of grading of the therapists involved). In contrast, Jasper et al. (2014a) found no difference in therapist time, largely due to more participants being included in each GCBT group (10 participants) with shorter 90-minute sessions. The iCBT group had an average of 14 minutes therapist time per week. The standard individualised F2F tinnitus care provision in the UK is likely to consume more therapist time than iCBT. The cost-effectiveness of these different intervention routes in the UK should be determined.

For the present trial, post-intervention satisfaction was high for both group. Jasper et al. (2014a) asked participants to provide treatment credibility ratings and indicate their preferred treatment. Credibility was rated significantly higher for GCBT (46%) than for iCBT (21%). There were 33% of participants with no preference. Post-intervention GCBT participants were more satisfied than iCBT participants. Measurement of pre- and post-intervention credibility, unwanted effects and process evaluations should be incorporated into future effectiveness trials to further evaluate these aspects.

More information about the therapeutic relationship (working alliance) between Audiologists and patients when recieving Internet-based or F2F interventions is required. A higher working alliance for GCBT when compared with iCBT for tinnitus when provided by clinical psychologists has previously been reported (Jasper, Weise, Conrad, Andersson, Hiller, & Kleinstäuber, 2014b). The working alliance of audiologist-provided iCBT guidance compared with individualised F2F clinical care for tinnitus still requires investigation. Comparing these outcomes with those using audiologist guidance and different treatment formats will be of interest.

Further cost reductions may be achieved in provision of low-intensity intervention formats, as described by Kaldo and colleagues (2013). Participants in the low-intensity group required less therapist time and did not contact the therapist as much, but effect-sizes were smaller. Further work is required to determine if certain patients are best suited for iCBT or F2F interventions. This may include identifying moderators and mediators of outcome or factors related to individuals.

7.4.5 Study limitations

Running this trial had many challenges. The main difficulty was recruiting sufficient numbers of participants. This could partly be attributed to the way the trial was set up. Participants were invited following their ENT appointment. Invitations may not always have reached participants when clinics were busy. Understandably, after following a long pathway to reach ENT and audiology services, many wanted to continue on this pathway and not take part in a research study. The main reasons provided for why people did not want to participate were that they wanted to see a clinician F2F or did not have a good Internet connection. At one of the hospitals, the ENT department was running another tinnitus trial in parallel. Potential participants may have been allocated to this trial instead. Implementation of more effective recruitment strategies will be required for future effectiveness trials. The low ratio of those participating to those invited was a potential source of bias. To address the research question, no waiting list control group was included. The benefits found in this study may thus be partly due to spontaneous improvements (or placebo effects) rather than the interventions. In addition, the non-uniform nature of the clinical care received from the different study centres may have contributed to the variability found.

7.5 CONCLUSIONS

This chapter has addressed the final research question, comparing clinical outcomes of iCBT with those from individualised tinnitus care, as typically provided in the UK. Results indicated that the null hypothesis can be rejected and the alternative hypothesis accepted, namely outcomes using iCBT for tinnitus are comparable to those for the usual tinnitus care in the UK. The next chapter provides a general discussion regarding the research findings from these experimental chapters.

8 GENERAL DISCUSSION

This thesis has outlined the development and evaluation of an iCBT intervention for tinnitus in the UK. This discussion will focus on the relevance of the research findings from a broader perspective by summarising the findings, the study limitations and suggestions for further research.

8.1 OVERVIEW

The literature review indicated that experiencing tinnitus can be distressing and affect many aspects of life. The purpose of this research was to identify a clinically- and cost-effective means of reducing the impact of tinnitus for participants based in the UK. The literature review furthermore indicated current knowledge gaps, leading to six research questions on which this thesis was based. The findng are summarised in the sections that follow.

8.1.1 An iCBT intervention for a UK population

Appropriate clinical care pathways are crucial, due to the distress associated with tinnitus. Unfortunately, these are not always available, due to obstacles preventing delivery of suitable interventions. Three main restrictions to tinnitus care in the UK were identified in Chapter 2, namely access to specialised tinnitus services, provision of evidence-based care and the cost associated with provision of tinnitus services. This research has considered these constraints and how they can be addressed. One significant barrier was lack of access to tinnitus interventions. Using the Internet as the delivery model was considered a means of increasing access by overcoming geographical, personal and service constraints (Andersson & Titov, 2014). A further identified limitation was that existing tinnitus interventions are not always evidence based (Hoare et al., 2011). To date CBT for tinnitus has the most evidence of efficacy in reducing tinnitus distress (Andersson & Lyttkens, 1999; Hesser et al., 2011a; Martinez-Devesa et al., 2010) but is rarely provided in clinical practice, particularly in the UK (Hall et al., 2011; McFerran & Baguley, 2009). CBT principles were incorporated into an Internet-based intervention so that all individuals received the same level of evidence-based care.

The high cost of provision of tinnitus services (Stockdale et al., 2017) was found to be a further barrier. These costs can potentially be reduced using an Internet intervention as less time on average per patient is required (see Chapter 7). For this particular intervention, costs were further lowered as an audiologist as opposed to a clinical psychologist (with a lower hourly rate for the former as seen in Chapter 2) guided participants.

This led to a conceptual framework that incorporated creating an accessible delivery pathway using the Internet to provide evidence-based CBT strategies with audiologist guidance (Figure 3.2). Combing these three principles led to the creation of an audiologist-guided iCBT intervention, proposed to reduce tinnitus-related distress using fewer resources than current service delivery models.

The first research question was how to develop an intervention that would improve the potential of such an intervention for the intended population. Principles known to enhance outcomes were incorporated during the development (Chapter 4). These included minimising technological barriers, presenting the content in an easily readable format and simplifying navigational aspects (Andersson et al., 2009). Ease of access was ensured by availability of the intervention on various devices (PC, smartphone, tablets). Identified functionality barriers (such as the login process) were addressed in four subsequent revisions. A tailored intervention was offered by including personalised guidance and allowing participants to self-select optional modules. Ways of improving information retention and addressing differences in learning styles were sought, as information was provided in various text, visual and auditory formats. Interactive elements were incorporated to promote engagement.

Establishing the acceptability of the intervention, by both tinnitus professionals and adults with tinnitus, was important. Satisfaction ratings from both groups were high. The intervention's potential was improved by inclusion of multidimensional features. An original aspect of this research was the development of an Internet-based tinnitus intervention complying with UK legislation for electronic communications. An acceptable, accessible, and evidence-based intervention adapted for a UK population was developed.

8.1.2 Feasibility and acceptance of iCBT for a UK population

This intervention was evaluated systematically in a controlled and powered manner. A wide range of assessment measures was used to fully evaluate intervention effects on both tinnitus severity and associated comorbidities. The clinical trial was designed to increase participant retention by use of regular contact and use of online assessments.

As standard UK tinnitus care is delivered in a clinical setting, the feasibility of an Internet-intervention was unknown. The second research question investigated the feasibility of audiologist-guided iCBT for tinnitus in the UK (see Chapter 5). Feasibility in terms of recruitment potential, attrition, and intervention adherence was established. Although the second research question was answered affirmatively, factors hampering feasibility were identified. These included a sub-optimal recruitment strategy, the need to adapt the demographic questionnaire and the way information was presented. A wider recruitment

strategy was utilised to target individuals distressed by tinnitus who were underserved with tinnitus interventions. The demographic questionnaire was adapted and the intervention was modified with the aim of improving attrition and adherence.

The feasibility of a new intervention is linked to professional and public perceptions of its potential. Introducing the intervention at tinnitus support groups, writing articles in tinnitus magazines, presenting at ENT/audiology departments and audiology network events, providing webinars, discussion videos, provision of articles for professional magazines and presentations at conferences was prioritised. Concerns were evident within the audiology community that such an intervention may result in audiologists losing their role in providing tinnitus interventions. Although iCBT has potential in increasing access to care, it is not intended to replace individualised clinical care. More contact with the tinnitus community will be required prior to such an intervention being fully accepted within the tinnitus community.

8.1.3 Efficacy of audiologist-guided iCBT for tinnitus distress

One of the pillars of the conceptual framework was selection of audiologist to provide CBT. This selection was controversial, but was based on considering that tinnitus management is generally provided by audiologists in a UK context. This profession has the expertise to manage tinnitus, but they are not generally trained to provide CBT. Previous iCBT trials have been developed and supported by experienced clinical psychologists (see Jasper et al., 2014a; Kaldo et al., 2008; Weise et al., 2016). Delivery of iCBT for tinnitus by a non-psychological professional has not previously been investigated. The third research question addressed the efficacy of audiologist-guided iCBT in reducing tinnitus distress in the UK (see Chapter 6). The efficacy of iCBT (d = 0.69) compared with a weekly check-in group was established for tinnitus distress. Results indicated comparable outcomes to previous iCBT tinnitus trials, despite using audiologist guidance. Although efficacy was demonstrated, large effect sizes were small. In addition, only half of the participants obtained improvements that were considered clinically significant. Ways of improving these outcomes are required. This task is not straightforward, as not enough is known regarding the mediators and moderators of outcome. The outtomes may be partially related to the nature of the guidance, assessment measures selected, intervention features or a combination of these. Protocol and intervention refinements are needed to further improve outcomes. Further systematic investigations are required to identify factors associated with obtaining a high proportion of clinically significant results.

8.1.4 Efficacy of iCBT for reducing tinnitus-related comorbidities

For some, the experience of tinnitus is devastating, leading to significant clinical problems (Belli et al., 2008) and indirect psychosocial effects (Langguth, 2011). Establishing intervention effects on a wide range of these associated comorbidities was required. This led to the fourth research question, determining whether iCBT for tinnitus could reduce the impact of tinnitus-related comorbidities (insomnia, anxiety, depression, hearing handicap, hyperacusis, cognitive functioning, and life satisfaction). When investigating the efficacy of iCBT for tinnitus-related comorbidities (Chapter 6), a medium effect size was found for insomnia and small effect sizes for depression, hyperacusis, cognitive failures and life satisfaction when compared with weekly monitoring. During the effectiveness trial (Chapter 7) pre-post within-group iCBT intervention effect sizes were large for insomnia, medium for anxiety and depression and small for the other outcome measures. These results are in line with previous trials of iCBT for tinnitus (Jasper et al., 2014a; Kaldo et al., 2008; Kaldo-Sandström et al., 2004; Weise et al., 2016). It is of interest that previous meta-analyses (Andersson & Lyttkens, 1999; Hesser et al., 2011a) and a Cochrane review (Martinez-Devesa, Perera, Theodoulou, & Waddell, 2010), largely based on F2F interventions, failed to show the effectiveness of CBT used with a tinnitus population for sleep problems. An updated meta-analysis of iCBT for tinnitus and tinnitus-related comorbidities is required. Identifying the moderators and mediators that result in differences between Internet-based and F2F CBT interventions would be of value.

The fourth research question was answered by identifying the potential for iCBT in reducing tinnitus-related comorbidities, such as insomnia and depression. For many of the secondary assessment measures (e.g. anxiety and depression) low baseline results were evident. This finding requires further exploration and may reflect the populations selected or the assessment measures used.

8.1.5 Longer term intervention effects

Maintainance of intervention effects is an important aspect of the efficacy of an intervention and formed the fifth research question. The stability of iCBT intervention effects was evident up to 1 year post-intervention for this research population (Chapter 6). The nature and frequency of unwanted treatment effects were also investigated 1 year post-intervention. Previous trials of iCBT for tinnitus have not investigated unwanted treatment effects. These finding have been of value regarding the frequency and types of unwanted effects to be expected from such an intervention. This knowledge can be used to implement strategies to minimise such effects in subsequent trials.

8.1.6 Effectiveness of iCBT compared with standard clinical care for tinnitus

The final research question investigated whether clinical outcomes with iCBT were comparable to those for the standard tinnitus care provided in the UK. This was the first randomised controlled trial evaluating the effectiveness of iCBT for tinnitus in a multicentre study. It was also the first to compare iCBT to individualised F2F tinnitus care, as previous comparisons have been group-based interventions. Intervention effects fell within the non-inferiority margin, favouring iCBT (Chapter 7). Comparable results were obtained regardless of the intervention format. The effectiveness of iCBT was comparable to that of the standard provision of F2F clinical care for tinnitus in the UK. Although more research is required, this finding opens up the possibility of future implementation of this intervention.

8.1.7 Framework provision

A final contribution of this thesis is provision of a comprehensive and systematic framework that can be used as a model for development and evaluation of new interventions. This framework outlines the importance of each research phase, as summarised in the Medical Research Council guidelines (Craig et al. 2008). These include sequentially evaluating functionality, acceptability, feasibility, efficacy and effectiveness. The importance of performing process evaluations in parallel to obtaining outcome data is indicated. It has highlighted the value of obtaining cross-sectional information, and determining unwanted effects, long-term outcomes and intervention effects on a range of secondary measures. Transparency has been promoted by sharing this knowledge. The publication of each stage of this process (see list of publications) to improve the quality of research for purposes of replication was prioritised. Future research in similar fields may be speeded up through access to this framework and research process.

8.2 GENERAL LIMITATIONS

Various limitations of the research were identified. Those need to be considered during interpretation of the results and future trial designs.

8.2.1 Reliability of the assessment measures selected

Unreliable assessment measures may increase the potential for Type II errors. The TFI was used as the main assessment measure. Substantial floor effects have recently been identified on many of the items on the TFI (Fackrell et al., 2016). These authors suggest the TFI may not be suitable for detecting treatment-related benefits in a research population. A modified seven-factor structure has been recommended for use of the TFI in a UK clinical

population (Fackrell, Hall, Barry, & Hoare, 2017). Furthermore, concerns have been raised regarding the three-factor solution proposed for the HQ and caution needs to be applied when interpreting results using this assessment measure (Fackrell et al., 2015). Aazh and Moore (2017b) indicated that scores of ≥ 22 may be a more accurate reflection of the presence of hyperacusis when using the HQ.

The weekly measure that was used, namely the THI-S, only had three options (yes, sometimes, no). This limited range may have introduced bias. Moreover, the satisfaction questionnaire used here was not validated. Using a validated measure would have been preferable. Many of the secondary assessment measures used, have not been validated on a tinnitus population. Furthermore, test-retest reliability has not been determined for many of the assessment measures. An investigation into the applicability of psychological assessment for those with tinnitus indicated that questionnaires relating to anxiety, social phobia, obsessive compulsive behaviour, depression and worry were rated as relevant, whereas a questionnaire related to panic disorder was not rated as applicable by those with tinnitus (Aazh & Moore, 2017a). Further work is required to establish the most appropriate and psychometrically robust measures for a tinnitus population. In view of these limitations, work is currently underway to identify a core set of outcome measures for tinnitus (Fackrell et al., 2017; Hall, 2017; Hall et al., 2015). More careful selection of assessment measures is required for future trials.

8.2.2 Generalisability of the results

Multiple biases not accounted for at various stages of the setup, conduct and analysis of this research may reduce the validity of inferences drawn from the results. Internal validity was affected by selection, performance, detection, and attrition bias. Selection bias may have been introduced in the way that recruitment strategies were implemented. Bias was reduced by allocating participants using computerised block randomisation and stratifying for tinnitus severity. Performance bias was introduced since iCBT guidance was not provided equally to all participants. Participants who sent regular messages and those completing more worksheets received more guidance than those who were not so engaged. The F2F treatment participants were seen at different centres by different clinicians, resulting in performance bias. Detection bias could have occurred, as self-report measures were used as assessment measures. It was evident that some participants were more guarded when completing baseline assessment measures compared with responses at follow-up.

Attrition bias was present for Phase II post-intervention results, since significantly fewer participants from the experimental group completed assessment measures at this time

point. In Phase III, loss to follow up was balanced, minimising attrition bias. The extent to which the present results may be extrapolated to other age groups and populations is not clear. The results found are limited to participants with similar demographical and clinical profiles based in the UK. Generalisation of the results to other populations is not possible without further systematic replication in other settings.

8.2.3 Data analysis

The statistical procedures selected may have affected the validity of the statistical results. The initial statistical methods selected were altered following peer review. The final statistical methods could, however, still be questioned. As a consequence of multiple testing of the various outcomes, there is an increased likelihood of falsely concluding that a statistical relationship exists when it does not. Although a main outcome was selected and emphasis was on effect size reporting, Type I errors cannot be excluded.

Most of the outcome data were analysed quantitatively. Additional qualitative data analysis would be of value. Opportunities to collect such data were lost in many instances, including failure to record telephone conversations during Phase II. Determination of the occurrence of post-intervention positive experiences related to tinnitus, and how difficult tinnitus situations were addressed post-intervention, would have been of value, but such data were not collected.

8.2.4 Treatment credibility

Pre- and post-intervention treatment credibility ratings for the interventions were not obtained. Participant's views regarding the credibility of the assessment measures may have affected engagement and indirectly influenced the results. Previous trials have reported conflicting findings regarding credibility ratings. Kaldo and colleagues (2008) found that participants rated group CBT sessions as more credible than iCBT whereas Kaldo-Sandström and colleagues (2004) did not find this difference. Credibility ratings should be included in further trials.

8.2.5 Involving stakeholders

A key strategy for dissemination of new interventions is to involve stakeholders from inception in the choice of research design in order, to identify elements relevant to decision-making, such as benefits, harms, and costs. Although service user groups were involved, more could have been done to include stakeholders. Ensuring that health professionals are positive about implementing these services is important. Strategies to involve health professionals were introduced, However, more will be required to build credibility and positivity surrounding an Intervention such as this prior to implementation.

8.2.6 Public-patient led research

Perhaps the greatest limitation of this research was that this research was not patient led from the onset. Including patients' views on what they would like incorporated into the intervention prior to developing the intervention, would have been of great value. Patients' views on outcome domains for this research would have further enhanced this research. Research emerging from this thesis should place more emphasis on incorporting patient-led research.

8.3 FUTURE RESEARCH RECOMMENDATIONS

This research has demonstrated the potential of iCBT for tinnitus. Such an intervention deserves further exploration, as many further research questions remain. Suggested future research themes are discussed below.

8.3.1 Improving outcomes

The goal would be to increase the percentage of participants reaching clinically significant changes post-intervention and to maximise the intervention effects for secondary assessment methods. The first task would be to re-evaluate the intervention content and incorporate feedback received from participants after closely investigating their experiences (see section 8.3.3). Synthesis of information regarding unwanted intervention effects, the most suitable modules and the outcomes obtained is required to identify what needs improving and which elements may be adding to beneficial outcomes. Populations with higher mean age may, for instance, need a different intervention emphasis (Aazh, Lammaing, & Moore, 2017).

8.3.2 Establishing cost-effectiveness

The research questions focused on clinical effectiveness. More work is required to determine cost effectiveness, as this information is required by stakeholders (Cima et al., 2009; Maes et al., 2014; Stockdale et al., 2017). A lexicon of assessment and outcome measures for tele-mental health has been developed as a resource for the evaluation of these services (Shore et al., 2014). Evaluation metrics include treatment utilisation, travel costs, stigma, anxiety, waiting times, training, and motivational readiness. Future research can use these domains to standardise approaches, to determine cost effectiveness and provide a more comprehensive comparison of services. The only iCBT tinnitus trial to date reporting cost effectiveness was carried out by Kaldo and colleagues (2008). Comparison of the cost effectiveness of iCBT vs individualised therapy in a UK-based clinical setting is required, together with determination of the cost effectiveness when different professionals provide guidance (psychologist versus an audiologist).

8.3.3 Moderators and mediators of outcome

To date, there are no established predictors of outcomes for guided iCBT interventions (Andersson, 2016). Moreover, moderators and mediators of outcome and which specific aspects of iCBT result in positive outcomes need further exploration (Hesser, Westin, & Andersson, 2014). The effectiveness of CBT in reducing tinnitus-related fear has been suggested to be one possible factor that contributes to reducing tinnitus severity (Cima, van Breukelen, & Vlaeyen, 2017). There may also be specific moderators associated with the reporting of unwanted events while undertaking such an intervention. Further work is required to identify these moderators and mediators. This knowledge will aid identifying for whom these Internet interventions are most suited. Wider demographic and clinical variables, such as personality type, self-motivation and perseverance, should be investigated in the search for moderators and mediators of outcome. It is of interest that overall more males than females participated in these studies. The reasons for this may be related to either a higher tinnitus prevalence or that this intervention format may attractpeople who find attending hospitals difficult. This may be related to practical reasons for example being in full-time employment or self-employment or the association with some stigma regarding attending specialised clinics. Further investigations into moderators and mediators of outcome may help to triage participants to the most appropriate intervention route.

8.3.4 Participant experiences

Determination of participants' perceptions and experiences of both iCBT and F2F tinnitus interventions, as well as factors influencing these views,is needed.. Additional longitudinal analysis of participant's experiences would be of value. Qualitative analysis of participants' expectations and experiences (both positive and negative) is required. This could provide valuable insights into factors that mightdeter participants from undertaking the intervention. Evaluation of participants' tinnitus-related behaviours longitudinally during the intervention from the perspective of their significant others, would add further insight into the application of iCBT. Identification of factors deterring some people from participating is also important. This information may alsobe beneficial in providing a deeper understanding of factors affecting attrition and adherence.

8.3.5 Therapeutic alliance

As described in Chapter 3, much is still unknown regarding therapeutic alliance with regards to Internet interventions (Berger, 2017). Although common therapist behaviours such as conveying understanding, empathy and care for participants is required (Andersson et al., 2012), different aspects of therapeutic alliance may be important for treatment success in

iCBT versus GCBT (Jasper et al., 2014a). For iCBT, explanation and configuration of the therapeutic tasks may be more important than the therapeutic bond (Jasper et al., 2014a). Identification of the key aspects for therapeutic success for iCBT for tinnitus is needed. Establishing pre- and post-intervention perceptions of therapeutic alliance is important from both the participants and the clinician's perspectives. The indications from this thesis that iCBT for tinnitus can be guided by a non-psychological professional opens further questions regarding the nature of iCBT guidance. Audiologist-guided iCBT may have potential for other audiology problems. Systematic investigations of the dose-response relationship, communication mode used and quantity and quality of guidance are needed. . Direct comparison of intervention effects and participant experiences when guidance is provided by an audiologist versus a psychologist is needed. Comparison of therapeutic alliance (clinical psychologist) for individualised tinnitus care versus online interventions is required.

The support offered by peers within these interventions should be further explored. In this clinical trial, a closedforum was used, where participants could not communicate with each other directly.Various other formats for providing peer support are possible and should be further explored.

8.3.6 Internet-based delivery of other therapeutic approaches

Combining iCBT with other therapies is another possibility. The focus was on CBT due to the efficacy of this intervention for tinnitus (Hesser et al., 2011). Other psychological therapies such as acceptance and commitment therapy and mindfulness may be incorporated into Internet-based interventions as the knowledge base for these therapies increases.

8.3.7 Contrasting and comparing iCBT and F2F CBT for tinnitus

Further research and meta-analysis is required to investigate whether effects using iCBT for tinnitus may differ from those for F2F . Information regarding the effects of these interventions on tinnitus distress and tinnitus-related comorbidities is required. This may provide further insights into the effects of these interventions, moderators and mediators of outcome and for which populations these interventions may be most suited.

8.3.8 Adaptations for different cultures and age groups

The lack of access to tinnitus services is evident worldwide and not isolated to the UK (Andersson, 2016). The present research shows that an intervention originating and hosted in Sweden can be transferred to a different population (UK population). It has also been

transferred successfully to a German population (Weise et al., 2016). Transferring this intervention to other cultures and settings may help alleviate tinnitus, particularly where these services do not exist. Adapting this intervention for parents of young children and for older children with distressing tinnitus may also be of value. The best way of assessing adapted interventions in the least amount of time needs considering. One strategy would be to simultaneously investigate the effects of adapted and translated versions across various cultures in an International trial.

8.4 GOING FORWARD

This thesis has shownthe potential of iCBT for tinnitus. The ultimate aim would be to improve outcomes iva wider implementation of such an intervention in the UK.. Numerous research themes require exploration before Internet-interventions for tinnitus can be integrated into clinical care. The present findings support the potential use of iCBT in other auditory-related conditions, such as hyperacusis and imbalance. The next and final chapter summarises the main conclusions drawn from this research.

9 CONCLUSIONS

The objective of this research was to address restrictions in the provision of tinnitus care in the UK. The literature review identified an Internet-based intervention as a possible solution. Evidence of efficacy for such an intervention in the UK was lacking. This led to the formation of six research questions regarding the development, feasibility, efficacy (for both tinnitus distress and tinnitus-related comorbidities), longer-term outcomes and the effectiveness of such an intervention. The intervention was developed for a UK population. Initially the intervention was developed by incorporating three key features, namely: providing evidence-based content (CBT), usingan accessible intervention tool (the Internet), and using a suitable healthcare professional to guide individuals in a UK context (audiologist guided). The audiologist-guided iCBT intervention was adapted to be appropriate for a UK population in terms of security requirements, linguistic content and engaging features.

The developed intervention was sequentially evaluated using an established clinical trial methodology to increase the quality of evidence obtained. Original research designs were incorporated to address knowledge gaps. This was the first tiral of iCBT for tinnitus using a main outcome measure designed to be responsive to change (the TFI). It extended previous iCBT for tinnitus research by investigating intervention effects on seven commonly co-occurring comorbidities.

Phase I of the clinical trial established feasibility in terms of recruitment potential, attrition rates and compliance. Phase II of the trial was the first research to indicate the efficacy of iCBT for tinnitus distress and some associated comorbidities in a UK population (insomnia, depression, hyperacusis, cognitive failures, life satisfaction). Intervention effects were maintained up to one year post-intervention, adding to the credibility of the intervention.

The final research phase entailed the first randomised effectiveness trial of iCBT for tinnitus. This research compared the outcomes of iCBT with those of individualised tinnitus care as typically provided in the UK. Such a comparison has not previously beendone. The outcomes were comparable.This was the first research to empirically investigate unwanted effects of iCBT for tinnitus. Information regarding the type, frequency and probability of these unwanted effects is important to address in subsequent research. In addition, it is the only example of a full clinical trial run together with a process evaluation.

iCBT for tinnitus has proven potential as an accessible tinnitus management option that can reduce the burden on current healthcare and costs of tinnitus-related services. It may be recommended for certain tinnitus sufferers following their clinical examination. Having an additional intervention may free up clinical appointments for those with the greatest need and provide care for those who have limited access to clinical care due to geographical or healthrelated reasons. Although the potential of iCBT for tinnitus has been demonstrated, various challenges surrounding many aspects of this intervention need to be addressed. These include keeping up with the dynamic nature of the field by continually updating the intervention in line with these advances. Perhaps the greatest research challenge is to identify factors that aid acceptability and credibility of this intervention by individuals with tinnitus, health professionals, and stakeholders.

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APPENDICES

APPENDIX A SUMMARY OF PREVIOUS ICBT FOR TINNITUS TRIALS (2002-2016)

Study and location	Groups & intervention duration	Attrition	Clinical significance	Effect size for tinnitus distress post-intervention at T_1 and T_2	T_1 Results for secondary effects	Follow-up results for secondary effects
Efficacy Trials: passive control						
Andersson, Strömgren, Ström, & Lyttkens, 2002 *Sweden*	1. iCBT: n = 26 2. WLC: n = 64 who later undertook the intervention	*iCBT: 51%* *WLC: 0%* *1 year post: 18% both groups*	*iCBT: 29% WLC: 4%* *1 year: 31% both groups* *(50% of TRQ)*	*TRQ* *T_1: g* = 0.26 1 year FUP: significant difference *p* = 0.001	• Anxiety (HADS-A) *p* = 0.004 • Depression (HADS-D) *p* = 0.002	1 year FUP *p* = 0.002 1 year FUP *p* = 0.006

	6 weeks				• Fear of anxiety-related somatic sensations (ASI) *p* = 0.015	1 year FUP *p* = 0.06
					• Tinnitus loudness (VAS 1-10) *p* = 0.04 • Tinnitus annoyance (VAS 1-10) *p* = 0.001	
Abbott et al. (2009) *Australia*	1. iCBT: n = 32 2. Information only control (IOC): n = 24 6 weeks (cluster randomisation)	iCBT:72%, IOC: 21% Overall: 50%		*ITT analysis* *TRQ: g* = 0.24 (no difference between the groups *p* = 0.20) T_2: none	• Depression, anxiety, stress (DASS) *p* = 0.80 • Quality of Life Questionnaire (WHOQOL-BREF) 0.68 • Occupational stress (OSI-R) *p* = 0.14-0.68	none

Weise et al. (2016) Germany	1. iCBT (n = 62) 2. Online discussion forum group (n = 62) 10 weeks	10.3% at baseline and follow-up	THI: 72.6% Mini TQ: 80.6% (RCI and THI < 36 = 56.5%)	*ITI: MI* *6 month FUP* *THI: g* = 0.83 Mini-TQ: *g* = 1.08 1 year FUP: THI: *d* = 1.38 Mini TQ: *d* =1.88	6 month FUP: • Tinnitus Acceptance (TAQ) *g* = 0.76	1 year FUP: *d* = 1.00
					• Anxiety (HADS-A) *g* = 0.35	1 year FUP *d* = 1.04
					• Depression (HADS-D) *g* = 0.36	1 year FUP *d* = 0.64
					• Insomnia (ISI) *g* = 0.66	1 year FUP *d*= 0.39
Efficacy trials: active control						
Kaldo et al. (2008) *Uppsala, Sweden*	1. iCBT (n = 25) 2.GCBT (n = 26) 6 weeks	T1: 4% at 1 yr FUP: 13%	iCBT T1: 38% 1 yr FUP: 35% GCBT: 44% at post and FUP	ITT: LOCF TRQ 1. *d* = 0.73 2. *d* = 0.64	*IMPROVED* • Anxiety (HAD-A) • Depression (HAD-D) (not for GCBT) • Insomnia (ISI) improved	1 year F-UP *IMPROVED* • HAD-D (for the GCBT) • ISI • VAS tinnitus distress

					• VAS tinnitus distress • VAS tinnitus loudness	• VAS tinnitus loudness • VAS perceived stress
					NOT IMPROVED • VAS perceived stress (both groups)	*NOT IMPROVED* • HAD-A (for iCBT)
Hesser et al. (2012) *Sweden*	1. iCBT: n = 32 [shorter text of 157 pages divided into 8 modules] 2. Internet based acceptance and commitment therapy (iACT): n = 35 [104 pages]	T1: 4% 1 yr FUP: 6%	iCBT: 44% iACT: 60% DFC: 15%	*THI* *iCBT: d* = 0.70 for iCBT vs DFC iACT:*d* = 0.68 for iACT vs DFC	For iCBT improved more than DFC for • Anxiety (HADS-A) *d* = 0.68 • Quality of life Inventory (QoLI) *d* = 0.45 No difference compared with DFC • Depression (HADS-D) • Perceived stress Scale (PSS)	1 year FUP Effects maintained irrespective of treatment assignment (although ACT group scores increase tended to increase again at 1 year FUP)

	3. A discussion forum group control (DFC): n = 32 8 weeks				• Insomnia (ISI)	
Nyenhuis et al. (2013a) Two centres in the southern region of the Lower Saxony, Germany	1. iCBT self-management (n = 79) 2. CBT bibliotherapy (n = 77) 3. GCBT (n = 71) 4. IOC (n = 77)	*Total: 39%* *iCBT: 44.3%* *GCBT: 33.8%*	*iCBT: 45.6%* *Bibliotherapy: 33.8%* *GCBT: 46.7%* *IOC: 24.7%* *(14 points on the TQ Scale)*	TQ, ITI-MI. Group vs control: iCBT: *d*= 1.04 *Bibliotherapy: d* = 0.24 *GCBT:* *d* = 0.89 *6 months FUP:* *iCBT: d = 0.66* *Bibilotherapy: d = 0.39*	iCBT vs control: • von Zerssen's complaint list (von Zerssen, 1971) *d* = 0.29 • Depression (PHQ-D) *d*= 0.38	6 months *d* = 0.31 *d* = 0.04

	Intervention based on 67 page manual from CBT-oriented Tinnitus Coping Training			*GCBT: d = 0.74*	• Treatment satisfaction (11 point rating scale): M = 7.4 (SD: 2.3)	
Jasper et al. (2014a) *Mainz, Germany*	1. iCBT (n = 41) 2. Group- CBT (n = 43) 3. Internet-based	*6 month follow up*	*g = 0.55 against control*	*THI* *iCBT: d* = 0.71 *GCBT: d* = 0.81 *DFC d* = 0.14 *TAQ*	• Depression (HADS-D) *d* = 0.39	*6 month FUP* *d* = 0.46

	discussion forum control (DFC) (n = 44) 10 weeks			*iCBT: d = 0.52* *Mini-TQ* *iCBT: d = 0.96* 6 month follow up iCBT Mini-TQ *d* = 1.03 THI: *d* = 0.71 TAQ *d* = 0.52	• Insomnia (ISI) *d* = 0.68	*d* = 0.63
Effectiveness trials: non-randomised						
Kaldo-Sandström et al. (2004) Regular clinical setting University Hospital Uppsala	Non-RCT (n = 77) in clinical setting (from CBT waiting list) 6-10 weeks	*Did not complete-* *29.87%* *T_2 3 months:* *28.57%*	*50% or TRQ score* *27.3%* *23.4% at T_2 (3 mo)*	*LOCF* *TRQ: d* = 0.66 *within-group* 3 month FUP: *d* = 0.68	• Anxiety (HADS-A) *p*< 0.001	3 month FUP: stable results *p* < 0.001
					• Depression (HADS-D) *p* < 0.001	*p* < 0.001
					• Insomnia (ISI) *p* < 0.001	*p* < 0.001

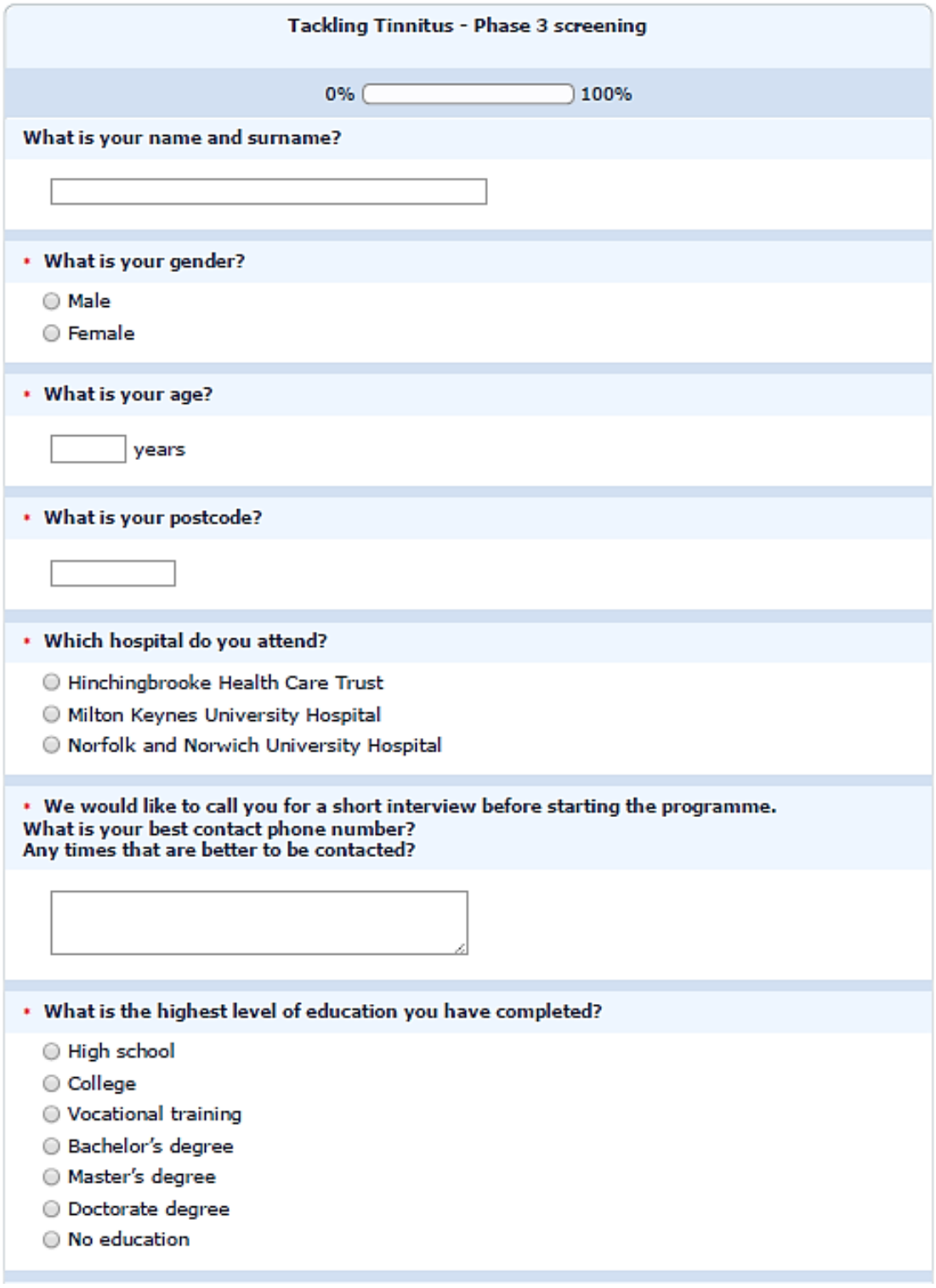
Kaldo et al. (2013) Non-RCT, group according to severity regular clinical setting University Hospital Uppsala	1.iCBT (n = 293) 2. Low intensity iCBT (n = 81) (all text, without homework and active therapist contact) No set time: average was 94.4 days (SD: 75.5)	iCBT group Completion T_1: 63% (37% attrition) T_2: 54% Dropouts significantly younger Low-intensity 63%	*Those completing, Defined as 50% of TRQ score 37.5% (23.5% of LOCF).* *T_2 at 3 month FUP 40.1% (21.5% ITT)*	*TRQ: iCBT:* *d = 0.58 for within-group per-protocol* *Low intensity group:* *d = 0.26* 3 month FUP *d* = 0.55 for iCBT	*Per-protocol results (lower for LOCF)* • Depression (HADS-D) *d* = 0.53	3 month FUP *d* = 0.46
					• Anxiety • (HADS-A) • *d* = 0.53	*d* = 0.47
					• Insomnia (ISI) *d* = 0.63	*d* = 0.53
					• Hyperacusis (are you sensitive to sound- rate 1–5) *d* = 0.26	*d* = 0.25

***Acronyms**: ASI: Anxiety Sensitivity Index (Peterson & Heilbronner, 1987), DASS: Depression, Anxiety and Stress Scales (Lovibond & Lovibond, 1995), FUP: follow up, HADS-A/D: Hospital anxiety and depression scale (A: anxiety section, D: depression section) (Zigmond & Snaith, 1983), ISI: Insomnia Severity Index (Bastien et al., 2001), IOC: Information only control, ITI: Intention-to- treat analysis, LOCF: last observation carried forward analysis, iACT: Internet based acceptance and commitment therapy, Mini-TQ: Mini-Tinnitus Questionnaire (Hiller & Goebel, 2004), MI: multiple Imputations, Occupational stress (OSI-R) (Osipow & Spokane, 1998), PSS: Perceived stress Scale (S. Cohen et al., 1983), QoLI: Quality of life Inventory (Frisch et al., 1992), Quality of Life Questionnaire- Brief Version [WHOQOL-BREF] (Whoqol Group, 1998), TAQ: Tinnitus Acceptance Questionnaire (Weise et al., 2013), T1: post-intervention,*

THI: Tinnitus Handicap Inventory (Newman et al., 1996), TRQ: Tinnitus Reaction Questionnaire (Wilson et al., 1991), VAS: Visual Analogue Scale (Adamchic et al., 2012), WLC: Waiting list control

APPENDIX B DEMOGRAPHIC QUESTIONNAIRE

PHASE III questionnaire provided as an example. Phase II questionnaire was similar



Tackling Tinnitus - Phase 3 screening

0% 100%

What is your name and surname?

What is your gender?

- Male
- Female

What is your age?

years

What is your postcode?

Which hospital do you attend?

- Hinchingbrooke Health Care Trust
- Milton Keynes University Hospital
- Norfolk and Norwich University Hospital

We would like to call you for a short interview before starting the programme.
What is your best contact phone number?
Any times that are better to be contacted?

What is the highest level of education you have completed?

- High school
- College
- Vocational training
- Bachelor's degree
- Master's degree
- Doctorate degree
- No education

- **Do you work less because of your tinnitus?**
  - ○ No
  - ○ Reduced hours
  - ○ Stopped work
  - ○ Disability allowance
- **Do you have a hearing loss?**
  - ○ No
  - ○ Both ears
  - ○ Left ear
  - ○ Right ear
  - ○ Unsure
- **How much difficulty do you have to hear?**
  - ○ None
  - ○ Slight difficulty
  - ○ Moderate difficulty
  - ○ Great difficulty
- **Do you wear hearing aid/s or any other amplification devices?**
  - ○ No
  - ○ Right ear
  - ○ Left ear
  - ◉ Both ears
  - ○ Not applicable
- **What amplification do you use?**
  - ○ Hearing aid/s
  - ○ Cochlear implant/s

  - ○ Bone anchored hearing aid/s
  - ○ Other (please specify): [ ]

- **Do the hearing aid/s or amplification devices help reduce your tinnitus in any way?**

  - ○ Yes, very effectively
  - ○ At times
  - ○ Only a little
  - ○ It makes no difference
  - ○ No, it makes the tinnitus worse

- **Please explain how and when the tinnitus is better or worse when using hearing aid/s or other amplification devices:**

- **Have you been exposed to loud noise?**

  - ◉ Yes
  - ○ No

- **If so please describe the noise, length of exposure and how often this was?**

- **How long have you had tinnitus for?**

- **What do you think lead to you having tinnitus?**

- **Where do you notice your tinnitus?**

  - ○ Right ear
  - ○ Left ear
  - ○ Both ears

- ○ In my head
- ○ Unsure
- ○ Other:

* **Have you seen your GP about your tinnitus?**

- ○ Yes
- ○ No

* **Have you seen an ENT consultant about your tinnitus?**

- ○ Yes
- ○ No

What investigations have been done due to you having tinnitus?

What diagnosis or reasons for the tinnitus was given?

* **Which best describes your tinnitus?**

- ☐ Ringing
- ☐ Buzzing
- ☐ High pitched sound
- ☐ Low pitched sound
- ☐ Pulsing
- ☐ Clicking
- ☐ Music
- ☐ Voices
- ☐ Humming
- ☐ Other:

* **Do you hear the sounds in time with your pulse or heart beat?**

- ○ Yes
- ○ No

• **How often do you hear the tinnitus?**

- ○ All the time
- ○ Most of the time
- ○ At night
- ○ When taking out my hearing aid/s
- ○ Occasionally
- ○ Not very often

• **How well can sounds around you distract you from your tinnitus or make the tinnitus less noticeable?**

- ○ Fully
- ○ Partially
- ○ Not at all

• **Make a list of problems / difficulties which you have as a result of your tinnitus. Write down as many as you can think of.**

• **Make a list of the effects your tinnitus has on your life. Write down as many as you can think of.**

• **Make a list of any positive experiences you have encountered due to tinnitus. Write down as many as you can think of.**

- Describe a specific situation in the last week when you experienced tinnitus as a problem. Describe how you responded and what you did in the situation.

- Are you currently receiving any treatment for tinnitus?

  - (•) Yes
  - ( ) No

- ...If so, what?

- Have you received treatment for tinnitus in the past?

  - (•) Yes
  - ( ) No

- ...If so, what and how long for?

- Have you read anything about tinnitus?

  - (•) Yes
  - ( ) No

- ...If so, what and where (e.g. on the internet, in books)?

* Have you been presently diagnosed with any psychological conditions including anxiety and depression?

- (•) Yes
- ( ) No

* ...If so, please list them:

* Do you currently take any medications?

- (•) Yes
- ( ) No

* ...If so, please list them:

* What effects do these medications have on your tinnitus?

- ( ) No effect
- ( ) Improves tinnitus
- ( ) Worsens tinnitus

* Do you attend a tinnitus support group?

- ( ) Regularly
- ( ) Occasionally
- ( ) No

APPENDIX C TINNITUS FUNCTIONAL INDEX

TINNITUS FUNCTIONAL INDEX

Today's Date _____ (Month / Day / Year) Your Name _____ (Please Print)

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

I — Over the PAST WEEK...

1. What percentage of your time awake were you consciously **AWARE OF** your tinnitus?

Never aware ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *Always aware*

2. How **STRONG** or **LOUD** was your tinnitus?

Not at all strong or loud ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely strong or loud*

3. What percentage of your time awake were you **ANNOYED** by your tinnitus?

None of the time ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *All of the time*

SC — Over the PAST WEEK...

4. Did you feel **IN CONTROL** in regard to your tinnitus?

Very much in control ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Never in control*

5. How easy was it for you to **COPE** with your tinnitus?

Very easy to cope ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to cope*

6. How easy was it for you to **IGNORE** your tinnitus?

Very easy to ignore ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to ignore*

C — Over the PAST WEEK...

7. Your ability to **CONCENTRATE**?

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

8. Your ability to **THINK CLEARLY**?

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

9. Your ability to **FOCUS ATTENTION** on other things besides your tinnitus?

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

SL — Over the PAST WEEK...

10. How often did your tinnitus make it difficult to **FALL ASLEEP** or **STAY ASLEEP**?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

11. How often did your tinnitus cause you difficulty in getting **AS MUCH SLEEP** as you needed?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

12. How much of the time did your tinnitus keep you from **SLEEPING** as **DEEPLY** or as **PEACEFULLY** as you would have liked?

None of the time ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *All of the time*

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

A	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	13. Your ability to **HEAR CLEARLY?**	0	1	2	3	4	5	6	7	8	9	10
	14. Your ability to **UNDERSTAND PEOPLE** who are talking?	0	1	2	3	4	5	6	7	8	9	10
	15. Your ability to **FOLLOW CONVERSATIONS** in a group or at meetings?	0	1	2	3	4	5	6	7	8	9	10

R	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	16. Your **QUIET RESTING ACTIVITIES?**	0	1	2	3	4	5	6	7	8	9	10
	17. Your ability to **RELAX?**	0	1	2	3	4	5	6	7	8	9	10
	18. Your ability to enjoy **"PEACE AND QUIET"?**	0	1	2	3	4	5	6	7	8	9	10

Q	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*										*Completely interfered*
	19. Your enjoyment of **SOCIAL ACTIVITIES?**	0	1	2	3	4	5	6	7	8	9	10
	20. Your **ENJOYMENT OF LIFE?**	0	1	2	3	4	5	6	7	8	9	10
	21. Your **RELATIONSHIPS** with family, friends and other people?	0	1	2	3	4	5	6	7	8	9	10

22. How often did your tinnitus cause you to have difficulty performing your **WORK OR OTHER TASKS**, such as home maintenance, school work, or caring for children or others?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

E	**Over the PAST WEEK...**

23. How **ANXIOUS** or **WORRIED** has your tinnitus made you feel?

Not at all anxious or worried ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely anxious or worried*

24. How **BOTHERED** or **UPSET** have you been because of your tinnitus?

Not at all bothered or upset ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely bothered or upset*

25. How **DEPRESSED** were you because of your tinnitus?

Not at all depressed ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely depressed*

APPENDIX D TINNITUS HANDICAP INVENTORY (PHASE III ONLY)

TINNITUS HANDICAP INVENTORY

Patient Name: _____ Date: _____

INSTRUCTIONS: The purpose of this questionnaire is to identify difficulties that you may be experiencing because of your tinnitus. Please answer every question. Please do not skip any questions.

1. Because of your tinnitus, is it difficult for you to concentrate?	Yes	Sometimes	No
2. Does the loudness of your tinnitus make it difficult for you to hear people?	Yes	Sometimes	No
3. Does your tinnitus make you angry?	Yes	Sometimes	No
4. Does your tinnitus make you feel confused?	Yes	Sometimes	No
5. Because of your tinnitus, do you feel desperate?	Yes	Sometimes	No
6. Do you complain a great deal about your tinnitus?	Yes	Sometimes	No
7. Because of your tinnitus, do you have trouble falling to sleep at night?	Yes	Sometimes	No
8. Do you feel as though you cannot escape your tinnitus?	Yes	Sometimes	No
9. Does your tinnitus interfere with your ability to enjoy your social activities (such as going out to dinner, to the movies)?	Yes	Sometimes	No
10. Because of your tinnitus, do you feel frustrated?	Yes	Sometimes	No
11. Because of your tinnitus, do you feel that you have a terrible disease?	Yes	Sometimes	No
12. Does your tinnitus make it difficult for you to enjoy life?	Yes	Sometimes	No
13. Does your tinnitus interfere with your job or household responsibilities?	Yes	Sometimes	No
14. Because of your tinnitus, do you find that you are often irritable?	Yes	Sometimes	No
15. Because of your tinnitus, is it difficult for you to read?	Yes	Sometimes	No
16. Does your tinnitus make you upset?	Yes	Sometimes	No
17. Do you feel that your tinnitus problem has placed stress on your relationships with members of your family and friends?	Yes	Sometimes	No
18. Do you find it difficult to focus your attention away from your tinnitus and on other things?	Yes	Sometimes	No
19. Do you feel that you have no control over your tinnitus?	Yes	Sometimes	No
20. Because of your tinnitus, do you often feel tired?	Yes	Sometimes	No
21. Because of your tinnitus, do you feel depressed?	Yes	Sometimes	No
22. Does your tinnitus make you feel anxious?	Yes	Sometimes	No
23. Do you feel that you can no longer cope with your tinnitus?	Yes	Sometimes	No
24. Does your tinnitus get worse when you are under stress?	Yes	Sometimes	No
25. Does your tinnitus make you feel insecure?	Yes	Sometimes	No

APPENDIX E HEARING HANDICAP INVENTORY SCREENING VERSION

HEARING HANDICAP INVENTORY - ADULT

Name/ID: _____ Age: _____ Date: _____

INSTRUCTIONS: The purpose of this questionnaire is to identify the problems your hearing loss may be causing you. Circle ***Yes***, ***Sometimes***, or ***No***, for each question. **DO NOT SKIP A QUESTION IF YOU AVOID A SITUATION BECAUSE OF A HEARING PROBLEM**. If you currently use hearing aids, please answer as to how you do **WITHOUT** your hearing aids.

E-1	Does your hearing problem cause you to feel embarrassed when meeting new people?	Yes	Sometimes	No
E-2	Does a hearing problem cause you to feel frustrated when talking to members of your family?	Yes	Sometimes	No
S-3	Does a hearing problem cause you difficulty understanding co-workers, clients, or customers?	Yes	Sometimes	No
E-4	Do you feel handicapped by a hearing problem?	Yes	Sometimes	No
S-5	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?	Yes	Sometimes	No
S-6	Does a hearing problem cause you difficulty in the movie or theater?	Yes	Sometimes	No
S-7	Does a hearing problem cause you to have arguments with family members?	Yes	Sometimes	No
S-8	Does a hearing problem cause you difficulty when listening to the TV or radio?	Yes	Sometimes	No
E-9	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?	Yes	Sometimes	No
S-10	Does a hearing problem cause you difficulty when in a restaurant with relatives or friends?	Yes	Sometimes	No

APPENDIX F INSOMNIA SEVERITY INDEX

Insomnia Severity Index

The Insomnia Severity Index has seven questions. The seven answers are added up to get a total score. When you have your total score, look at the 'Guidelines for Scoring/Interpretation' below to see where your sleep difficulty fits.

For each question, please CIRCLE the number that best describes your answer.

Please rate the CURRENT (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

APPENDIX G GENERAL ANXIETY DISORDER

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

APPENDIX H PATIENT HEALTH QUESTIONNAIRE

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)				
Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

APPENDIX I HYPERACUSIS QUESTIONNAIRE

In the following questionnaire, put a cross in the box corresponding to the answer which best applies to you:

		No	Yes, a little	Yes, quite a lot	Yes, a lot
1	Do you ever use earplugs or earmuffs to reduce your noise perception (Do not consider the use of hearing protection during abnormally high noise exposure situations)?	☐	☐	☐	☐
2	Do you find it harder to ignore sounds around you in everyday situations?	☐	☐	☐	☐
3	Do you have trouble reading in a noisy or loud environment?	☐	☐	☐	☐
4	Do you have trouble concentrating in noisy surroundings?	☐	☐	☐	☐
5	Do you have difficulty listening to conversations in noisy places?	☐	☐	☐	☐
6	Has anyone you know ever told you that you tolerate noise or certain kinds of sound badly?	☐	☐	☐	☐
7	Are you particularly sensitive to or bothered by street noise?	☐	☐	☐	☐
8	Do you find the noise unpleasant in certain social situations (e.g. night clubs, pubs or bars, concerts, firework displays, cocktail receptions)?	☐	☐	☐	☐
9	When someone suggests doing something (going out, to the cinema, to a concert, etc.), do you immediately think about the noise you are going to have to put up with?	☐	☐	☐	☐
10	Do you ever turn down an invitation or not go out because of the noise you would have to face?	☐	☐	☐	☐
11	Do noises or particular sounds bother you more in a quiet place than in a slightly noisy room?	☐	☐	☐	☐
12	Do stress and tiredness reduce your ability to concentrate in noise?	☐	☐	☐	☐
13	Are you less able to concentrate in noise towards the end of the day?	☐	☐	☐	☐
14	Do noise and certain sounds cause you stress and irritation?	☐	☐	☐	☐

APPENDIX J COGNITIVE FAILURES QUESTIONNAIRE

The Cognitive Failures Questionnaire (Broadbent, Cooper, FitzGerald & Parkes, 1982)

The following questions are about minor mistakes which everyone makes from time to time, but some of which happen more often than others. We want to know how often these things have happened to your in the past 6 months. Please circle the appropriate number.

		Very often	Quite often	Occasion-ally	Very rarely	Never
1.	Do you read something and find you haven't been thinking about it and must read it again?	4	3	2	1	0
2.	Do you find you forget why you went from one part of the house to the other?	4	3	2	1	0
3.	Do you fail to notice signposts on the road?	4	3	2	1	0
4.	Do you find you confuse right and left when giving directions?	4	3	2	1	0
5.	Do you bump into people?	4	3	2	1	0
6.	Do you find you forget whether you've turned off a light or a fire or locked the door?	4	3	2	1	0
7.	Do you fail to listen to people's names when you are meeting them?	4	3	2	1	0
8.	Do you say something and realize afterwards that it might be taken as insulting?	4	3	2	1	0
9.	Do you fail to hear people speaking to you when you are doing something else?	4	3	2	1	0
10.	Do you lose your temper and regret it?	4	3	2	1	0
11.	Do you leave important letters unanswered for days?	4	3	2	1	0
12.	Do you find you forget which way to turn on a road you know well but rarely use?	4	3	2	1	0
13.	Do you fail to see what you want in a supermarket (although it's there)?	4	3	2	1	0
14.	Do you find yourself suddenly wondering whether you've used a word correctly?	4	3	2	1	0

		Very often	Quite often	Occasion-ally	Very rarely	Never
15.	Do you have trouble making up your mind?	4	3	2	1	0
16.	Do you find you forget appointments?	4	3	2	1	0
17.	Do you forget where you put something like a newspaper or a book?	4	3	2	1	0
18.	Do you find you accidentally throw away the thing you want and keep what you meant to throw away – as in the example of throwing away the matchbox and putting the used match in your pocket?	4	3	2	1	0
19.	Do you daydream when you ought to be listening to something?	4	3	2	1	0
20.	Do you find you forget people's names?	4	3	2	1	0
21.	Do you start doing one thing at home and get distracted into doing something else (unintentionally)?	4	3	2	1	0
22.	Do you find you can't quite remember something although it's "on the tip of your tongue"?	4	3	2	1	0
23.	Do you find you forget what you came to the shops to buy?	4	3	2	1	0
24.	Do you drop things?	4	3	2	1	0
25.	Do you find you can't think of anything to say?	4	3	2	1	0

The Satisfaction with Life Scale

By Ed Diener, Ph.D.

DIRECTIONS: Below are five statements with which you may agree or disagree. Using the 1-7 scale below, indicate your agreement with each item by placing the appropriate number in the line preceding that item. Please be open and honest in your responding.

1 = Strongly Disagree
2 = Disagree
3 = Slightly Disagree
4 = Neither Agree or Disagree
5 = Slightly Agree
6 = Agree
7 = Strongly Agree

_____1. In most ways my life is close to my ideal.

_____2. The conditions of my life are excellent.

_____3. I am satisfied with life.

_____4. So far I have gotten the important things I want in life.

_____5. If I could live my life over, I would change almost nothing.

APPENDIX L TINNITUS HANDICAP INVENTORY SCREENING VERSION

TINNITUS HANDICAP INVENTORY-SCREENING VERSION

Instructions: The purpose of this questionnaire is to identify problems your tinnitus may be causing you. Check Yes, Sometimes or No for each question. Do not skip a question.

Scores on tinnitus questionnaires have absolutely no bearing on a claim for tinnitus service connection.

1: Because of your tinnitus is it difficult for you to concentrate?	Yes	Sometimes	No
2: Do you complain a great deal regarding your tinnitus?	Yes	Sometimes	No
3: Do you feel as though you cannot escape your tinnitus?	Yes	Sometimes	No
4: Does your tinnitus make you feel confused?	Yes	Sometimes	No
5: Because of your tinnitus, do you feel frustrated?	Yes	Sometimes	No
6: Do you feel that you can no longer cope with your tinnitus?	Yes	Sometimes	No
7: Does your tinnitus make it difficult for you to enjoy life?	Yes	Sometimes	No
8: Does your tinnitus make you upset?	Yes	Sometimes	No
9: Because of your tinnitus do you have trouble falling asleep at night?	Yes	Sometimes	No
10: Because of your tinnitus, do you feel depressed?	Yes	Sometimes	No

APPENDIX M INTERVENTION SATISFACTION EVALUATION

Please state the extent to which you agree or disagree with the following statements, where 1 is Strongly Disagree and 5 is Strongly Agree (choose one per statement).

- ABOUT THE USABILITY
    - It was straightforward to use the internet platform
    - It was easy to navigate through the materials
    - The length of the modules was appropriate
- ABOUT THE CONTENT
    - The level of information was at a suitable level
    - The materials were informative
    - The subject matter was interesting
- ABOUT THE PRESENTATION
    - The content was presented in a well-structured manner
    - The use of presentation of materials was suitable i.e. the use of diagrams, text, pictures, videos
    - The text was easy to read
- ABOUT THE SUITABILITY
    - The intervention is suitable for those suffering with tinnitus
    - The range of modules were appropriate
    - The topics covered were beneficial
- ABOUT THE EXCERSISES GIVEN
    - The worksheets and quizzes asked appropriate questions
    - I clearly understood how to practice the various techniques
    - I was motivated to do the exercises
- Open-ended questions:
- ABOUT THE INTERVENTION AS A WHOLE
- How long did it take you take to read each module's information on average?
- What was the best aspect of the intervention?
- What needs improving?
- Any further suggestions?

APPENDIX N PARTICIPANT INFORMATION SHEET

An example from one site for Phase III

INVITATION TO PARTAKE IN RESEARCH

Tackling tinnitus: An internet-based intervention for tinnitus

To whom it may concern **August 2016**

As you have tinnitus, you are invited to partake in this study, designed to help you learn how to better manage your tinnitus.

Please read through the information enclosed, to give you more information about the study.

Please do not hesitate to contact us for any further enquiries. If you are interested in partaking. Please register for the study at: **http://www.tacklingtinnitus.co.uk/register**

Best wishes,

Eldré Beukes

Principle investigator

Website: http://www.tacklingtinnitus.co.uk

Email: tinnitusuk@anglia.ac.uk

Telephone: 01223-698847

WHAT IS THIS RESEARCH ABOUT?

Experiencing tinnitus can be very bothersome and interfere with many aspects of daily life. Although there is no cure for tinnitus, research has identified strategies that can help people better manage their tinnitus. To provide additional support to individuals with tinnitus, the Tackling Tinnitus programme was developed. This is an Internet-based intervention for tinnitus, which can be compared with an e-learning programme. The information provided is similar to that received at a tinnitus clinic, but the delivery of the

information is different. Instead of going to a clinic to receive information about tinnitus, you receive it online. This research is designed to evaluate the effectiveness of this programme, by comparing it to services offered within three NHS Audiology departments, namely Norfolk and Norwich Universities Hospitals, Milton Keynes University Hospital, and Hinchingbrooke Health Care NHS Trust.

WHO IS ELIGIBLE TO TAKE PART?

To partake, you need to be 18 years or over and attend one of the hospitals involved in this study. You will require access to a computer and the internet and be able to read and type in English. You should not be undergoing any other tinnitus therapy or have any major medical or psychiatric conditions which may hamper your ability to partake in the programme.

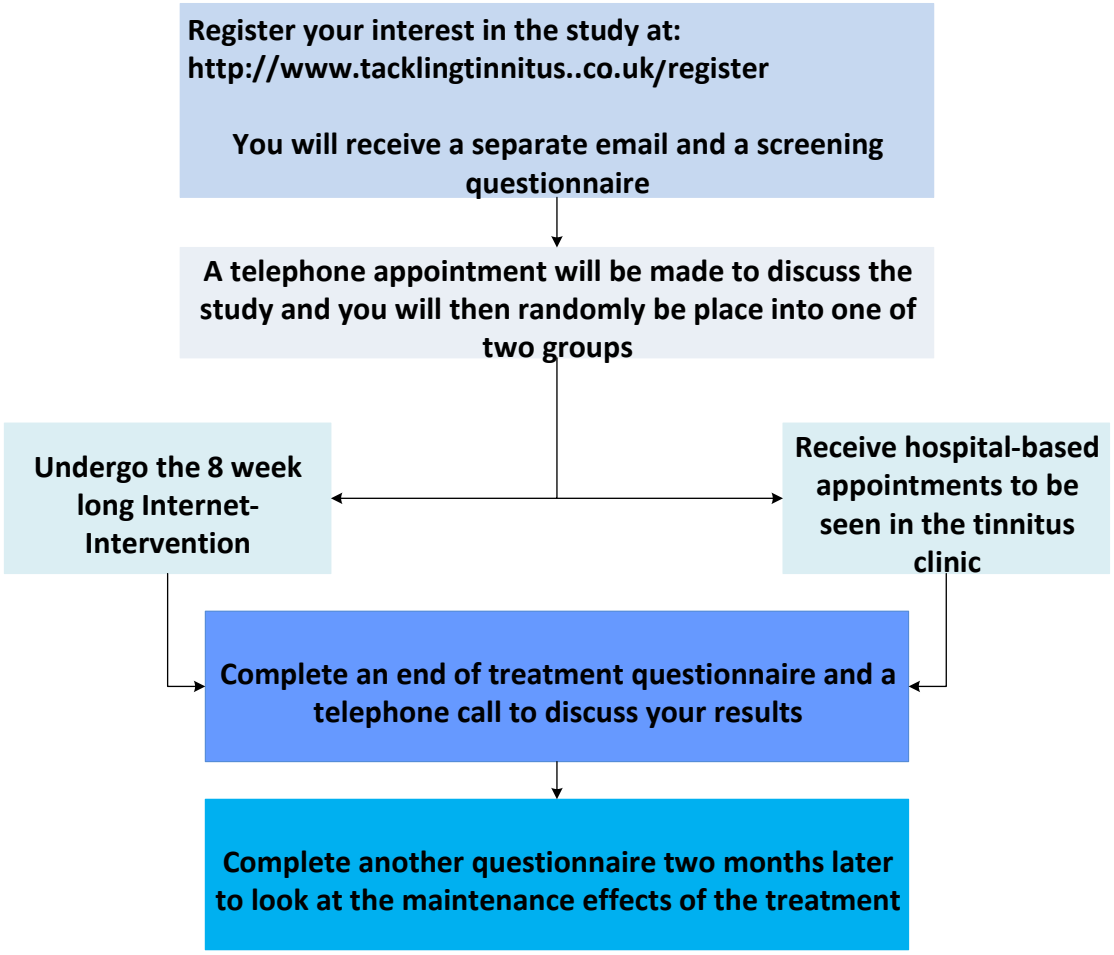
WHAT ARE THE POSSIBLE BENEFITS OF PARTAKING?

You will receive a wealth of information about tinnitus and how to manage it. You will be given strategies regarding how to reduce the impact of tinnitus by a qualified Audiologist. Following the study, you will also have access to the treatment stream you were not allocated to.

WHAT WILL HAPPEN IF I TAKE PART?

If you are interested in participating, you need to register for the study online, by logging onto http://www.tacklingtinnitus.co.uk/register and provide consent to partake.

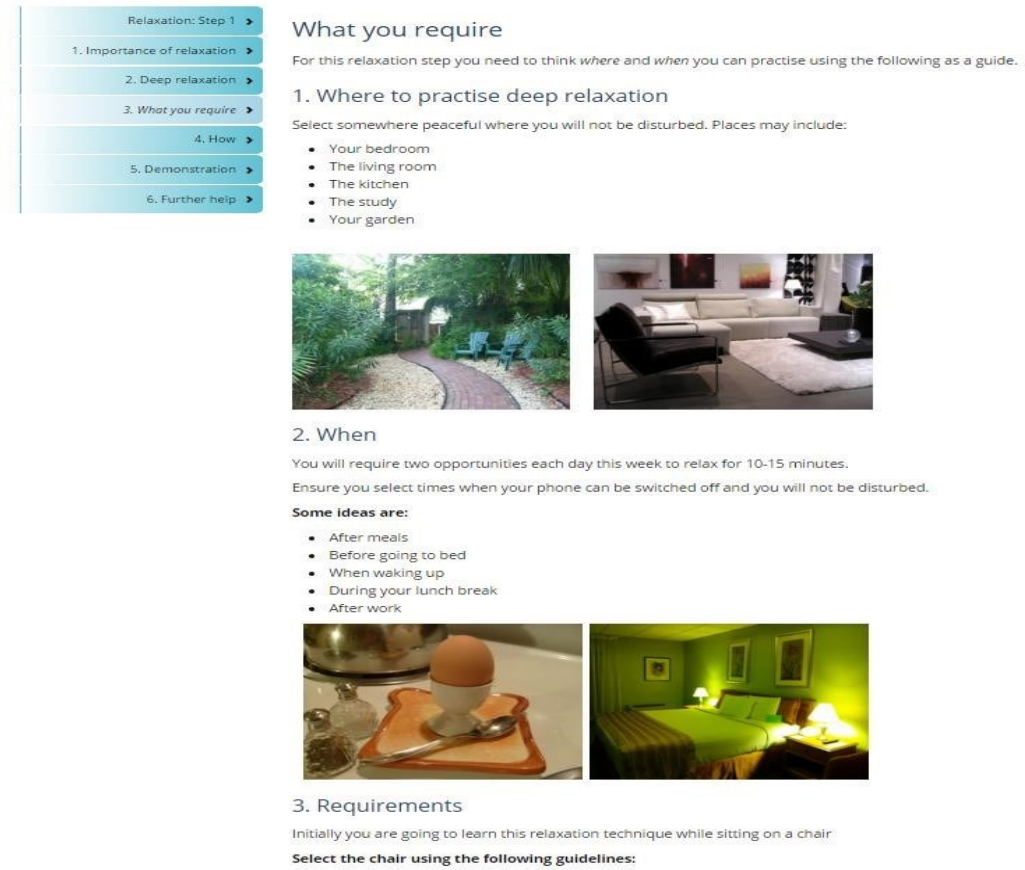
A summary of what the research involves is shown and discussed on the next few pages.



- To find out more about your tinnitus and the effects your tinnitus may have, you will be asked to complete an online screening questionnaire. An example of this is shown on the next page and should take no more than 30 minutes to do.

- A 10 minute telephone appointment will be made to ensure you are clear on what the research involves and provide the opportunity for you to ask any questions.
- You will be placed by chance (randomly) into one of two groups and be told which group you have been allocated to.
- If you are allocated to receive hospital-based treatment, an appointment will be arranged, during which you will be provided with information about tinnitus and management strategies. These may include sound enrichment advice, sleep management advice, and relaxation advice. A follow-up appointment may be booked.

- If you are allocated to receive internet-based treatment, you will be sent details to login to the website, where you will read about suggested strategies to try. An Audiologist will support you through a messaging system and by telephone as required. The internet programme lasts 8 weeks and includes videos, worksheets, and easily readable information. An example is shown below.



HOW WILL MY PROGRESS BE MONITORED

- You will be sent 10 questions on a weekly basis, which should take less than three minutes to complete
- After receiving your treatment, your progress will be evaluated by an online questionnaire, which should take less than 20 minutes to complete

WHAT ARE THE POSSIBLE RISKS INVOLVED IN TAKING PART?

Are there risks to my confidentiality?

No, as all the information collected for the research will be kept confidential. Your personal information will only be available to a few members of the research team and the NHS Hospital you attend.

Will my data be safely stored?

All information provided by participants will be saved safely at Linköping University, Sweden at the address https://www.iterapi.se/sites/tinnitusuk as they are the world

leaders in internet interventions. The servers are located in a locked room and all data will be stored encrypted and require passwords to access.

WHAT IF I WANT TO FILE A COMPLAINT?

If you have any enquiries or concerns, please feel free to contact any of the researchers on the team, so that these concerns can be addressed. If your concerns are not dealt with, contact details to raise concerns are found in the table below.

Organisation	**Contact email address**	**Telephone**
Milton Keynes, University NHS Hospital Foundation Trust, PALS services	PALS@mkhospital.nhs.uk	01908243633
Anglia Ruskin University Complaints services	xx@anglia.ac.uk	01245 683730

WILL MY EXPENSES BE PAID?

If you are allocated to be in the hospital treatment group, your travel expenses to and from the hospital during the treatment phase will be covered. Please retain your parking receipts so that you can be reimbursed.

WHO IS INVOLVED IN THE RESEARCH?

The research is being carried out by Anglia Ruskin University and Linköping University in Sweden and is supported by a multidisciplinary team as shown below:

ROLE	**NAME**
Principle researcher	Eldré Beukes (registered Clinical Scientist)
Advisory Team	Dr David Baguley (Tinnitus Specialist) and Prof Gerhard Andersson (Clinical Psychologist), Dr Vinaya Manchaiah and Prof Peter Allen (Researchers)
Audiologist Milton Keynes, University Hospital NHS Foundation Trust	xxx (Specialist audiologist)

HOW DO I GET FURTHER INFORMATION ABOUT THIS STUDY?

WHERE	**HOW**
Study website	See http://www.tacklingtinnitus.co.uk
To register	http://www.tacklingtinnitus.co.uk/register
Contacting the research team email	email: tinnitusuk@anglia.ac.uk Telephone: 01223-698847
Independent advice	Contact the research team and they will put you in touch with a member of the public-patient involvement group for this study

Thank you for reading this leaflet and considering taking part in the Tackling Tinnitus Study

APPENDIX O: PHASE III ONLINE CONSENT FORM

Title of Project: Internet-based Versus Face-to-face Clinical Care for Tinnitus
IRAS identification: 195565

Thank you for your interest in taking part in this research.
Before you agree to take part, please read all the information provided about the study first from the study website: http://www.tacklingtinnitus.co.uk
If you have any questions arising, please do not hesitate to contact the researcher at email address: tinnitusuk@anglia.ac.uk

Please read the following statement and provide consent below by ticking each box. You must agree with all the statements to be eligible to take part in the study.

I confirm that I have read and understood the participant information sheet for this study. I understand what the research involves, and all my questions have been answered to my satisfaction.	
I understand that my participation is voluntary and that I am free to withdraw from the research at any time, for any reason and without prejudice. To do so I can send a message to tinnitusuk@anglia.ac.uk or a message to the therapist using the encrypted conversations facility within the treatment	
I understand that I am free to ask any questions at any time before and during the study.	
I agree to the processing of data to be presented and shared. I understand that no personal information will be shared as confidentiality and anonymity will be maintained and the information I provide will be safeguarded.	
I am 18 year or older and am a resident within the UK	
I agree to provide an email address for members of the study team to communicate with me during the study. I understand that my personal details will not be used for any other purposes.	
email address:	
I agree to take part in the above study	

APPENDIX P GP NOTIFICATION OF PARTICIPATION

(Name) has kindly volunteered to participate in a research study run by Anglia Ruskin University. The research is investigating and internet intervention for tinnitus. This intervention follows an e-learning approach and aims to reduce the impact of the tinnitus.

(If required) As people experiencing tinnitus may also experience (condition: anxiety/ depression/hearing loss), the (questionnaire name) self-reported questionnaire was administered during the initial stage of this research. Results of this questionnaire indicated that (name) may have high levels of (condition anxiety/ depression). Although (name) is still able to participate in this research, we wanted to draw this finding to your attention. This finding has been discussed with (name).

If you feel this warrants further investigation would you please see (name) and manage as you find appropriate?

Please do not hesitate to contact ourselves if you require any further information.

Kind regards,

APPENDIX Q GP NOTIFICATION OF END OF PARTICIPATION

(Name) has participate in a research study run by Anglia Ruskin University. The research is investigating a guided Internet intervention for tinnitus, Tackling Tinnitus, which aims to empower those experiencing tinnitus to be able to better control their tinnitus, with the flexibility of carrying out the treatment programme online, whenever and wherever it suits them. The techniques shared are largely based on Cognitive Behavioural Therapy, which is very effective, but not readily accessible to those experiencing tinnitus.

This clinical trial is designed to compare the outcomes of patients undergoing this Internet-based intervention to that of standard clinical care given in the tinnitus clinics as part of a multi-centre study.

(Name) was randomised to receive (standard clinical care at the hospital) (Internet-based treatment) and has now completed their treatment. Post-treatment assessments have indicated that their tinnitus severity and associated problems have decreased they have therefore been discharged from the Tinnitus Clinic.

If they, however, require any help in future, please do not hesitate to get in touch.

Kind regards,

APPENDIX R FACULTY RESEARCH ETHICS PANEL APPROVAL PHASE I AND II

29th April 2015

Dear Eldré

Project Number: *FST/FREP/14/478*
Project Title: *Internet interventions for tinnitus.*
Principal Investigator: Eldré Beukes

Thank you for supplying revisions to your application for ethical approval, as requested by the Faculty Research Ethics Panel (FREP) following its meeting on 22nd April 2015.

I am pleased to inform you that your application has been approved by the Chair of the Faculty Research Ethics Panel under the terms of Anglia Ruskin University's *Research Ethics Policy*. Approval is for a period of three years from 29th April 2015.

It is your responsibility to ensure that you comply with *the Code of Practice for Ethical Approval at Anglia Ruskin University*, and specifically:

- The Participant Information Sheet and Participant Consent Form should be on Anglia Ruskin University headed paper.
- For online surveys it is recommended that the researcher turns off the IP logging software to ensure secure communication between the survey taker and server.
- The procedure for submitting substantial amendments to the committee, should there be any changes to your research. You cannot implement these changes until you have received approval from FREP for them.
- The procedure for reporting adverse events and incidents.
- The Data Protection Act (1998) and any other legislation relevant to your research. You must also ensure that you are aware of any emerging legislation relating to your research and make any changes to your study (which you will need to obtain ethical approval for) to comply with this.
- Obtaining any further ethical approval required from the organisation or country (if not carrying out research in the UK) where you will be carrying the research out. Please ensure that you send the FREP Secretary copies of this documentation.
- Any laws of the country where you are carrying the research out (if these conflict with any aspects of the ethical approval given, please notify FREP prior to starting the research).
- Any professional codes of conduct relating to research or research or requirements from your funding body (please note that for externally funded research, a project risk assessment must have been carried out prior to starting the research).
- Notifying the FREP Secretary when your study has ended.

Information about the above can be obtained on our website at:

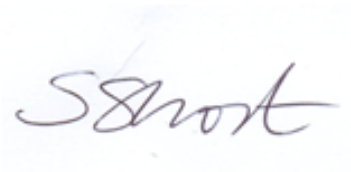
http://web.anglia.ac.uk/anet/rdcs/ethics/index.phtml/ and or
http://www.anglia.ac.uk/ruskin/en/home/faculties/fst/research0/ethics.html

Please also note that your research may be subject to random monitoring by the Committee.

Please be advised that, if your research has not been completed within three years, you will need to apply to our Faculty Research Ethics Panel for an extension of ethics approval prior to the date your approval expires. The procedure for this can also be found on the above website.

Should you have any queries, please do not hesitate to contact me. I wish you the best of luck with your research.

Yours sincerely,



Sue Short

Secretary to the Faculty Research Ethics Panel (FREP)
Faculty of Science and Technology
MAR325
Tel: 01245 683927 or 0845 196 3927
Email: FST-Ethics@anglia.ac.uk

cc. Prof Peter Allen

APPENDIX S RESEARCH ETHICS COMMITTEE APPROVAL FOR PHASE III

East of England - Cambridge South Research Ethics Committee

The Old Chapel

Royal Standard Place

Nottingham

NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

06 June 2016

Mrs Eldre Beukes

The Eastings 201

East Road, Anglia Ruskin University

Cambridge

CB1 1PT

Dear Mrs Beukes

Study title:	**Internet-based intervention versus face-to-face clinical care for tinnitus: A randomised control trial**
REC reference:	**16/EE/0148**
Protocol number:	**Clinical trial**
IRAS project ID:	**195565**

Thank you for your letter of 2 June 2016, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair and Mr John Kirkpatrick.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Ellen Swainston, nrescommittee.eastofengland-cambridgesouth@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

16/EE/0148	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Frank Wells
Vice Chair

Email: nrescommittee.eastofengland-cambridgesouth@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Professor Michael Cole*
Mr Michael Sherida

APPENDIX T HEALTH RESEARCH AUTHORITY APPROVAL FOR PHASE III

22 June 2016

Dear Mrs Beukes

Study title:	**Internet-based intervention versus face-to-face clinical care for tinnitus: A randomised control trial**
IRAS project ID:	**195565**
Protocol number:	**Clinical trial**
REC reference:	**16/EE/0148**
Sponsor	**Anglia Ruskin University**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study,

on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations

in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also

provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.

- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from http://www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

A – List of documents reviewed during HRA assessment

B – Summary of HRA assessment

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators",* issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial

amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.

- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Your IRAS project ID is **195565**. Please quote this on all correspondence.

Yours sincerely

Thomas Fairman
HRA Assessor