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Predictors of outcomes of internet-based cognitive behavioral therapy intervention for individuals with tinnitus

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Abstract

Objectives: The current study examined predictors of outcomes of internet-based cognitive behavioral therapy (ICBT) for individuals with tinnitus.

Design: The study included a secondary analysis of intervention studies.

Setting: Internet-based guided intervention.

Participants: A total of 228 individuals who underwent ICBT in three separate clinical trials.

Interventions: ICBT.

Primary and secondery outcome measures: A significant reduction in tinnitus severity (13-point reduction in Tinnitus Functional Index (TFI) scores) following undertaking the intervention was used as the main outcome variable. Predictor variables included various demographic, tinnitus, hearing-related, and treatment-related variables as well as clinical factors (i.e., anxiety, depression, insomnia, hyperacusis, hearing disability, cognitive function, and life satisfaction).

Results: Of the 228 subjects who were included in the study, 66% had a successful outcome of the treatment. The baseline tinntus severity was found to be a significant variable as per Chi square univariate analysis. Both linear and logistic regression models identified education level, baseline tinnitus severity, and hearing aid use as significant predictor variables contributing to reduction in tinnitus severity post-ICBT intervention after adjusting for the effect of the baseline tinntus severity.

Conclusions: Predictors of intervention outcome can be used as a means of triaging patients to the most suited form of treatment to achieve optimal outcomes and to make healthcare savings. As no strong predictors were identified other than the baseline tinnitus severity, future studies should consider including a heterogeneous group of participants as well as using various

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advanced artificial intelligence and machine learning techniques to identify possible predictive factors.

Key Words

Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive behavioral therapy

Strengths and limitations of the study

- This study examiens the predictors of ICBT on individuals with tinnitus from a pooled sample of several clinical trials.
- Homogenity of participants in the included studies may be the main reason for not having any strong predictors of outcomes.
- The stiudy sample size and also limited number of potential predictors may have also contributed to not finding any strong predictors of ICBT outcome.

Introduction

Tinnitus is the perception of sounds in the absence of external stimulation and is often heard as a ringning or buzzing meaningless sound(s). It is a very common condition with at least 15% of the adult populuation having tinnitus.[1] Tinnitus is highly heterogeneous, both in the way it manifests as well as in the manner those with tinnitus respond to treatment options.[2] Most individuals with tinnitus are not much bothered by the sounds, but a proportion (2/10) find tinnitus much distressing and need help to reduce the negative effects of their tinnitus. Although there are several management strategies described in the literature, most are not evidence based.

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The main exception is Cognitive Behavioral Therapy (CBT), as indicated in various systematic reviews of randomized controlled trials.[3-6] Clinical practice guidelines, based on research evidence and expert consensus, thus recommends CBT as a management option for individuals with tinnitus and is supported by the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS).[7]

Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in their local clinicas. For example, a large-scale epidemiological study in the US showed that medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of the time by health professionals, whereas the CBT was discussed as a management option only 0.2% of the time.[8] This is most likely a consequence of the limited number of trained professionals who provide CBT for tinnitus. One solution to overcome this issue is to use Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over the internet with minimal guidance from a tinnitus expert.[9] A series of controlled studies in Sweden, Germany, the United Kingdom and the United States have demonstrated positive effects of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety, depression, insomnia.[9] In addition to the changes noted in standardized outcome measures, the qualitative analysis of user experiences has highlighted the perceived benefits of this program.[10] In addition, the improvements noted from ICBT have been maintained for 1-year post-intervention. These results suggest that ICBT is a highly promising approach to provide evidence-based tinnitus management.

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Although the previous studies on ICBT have shown favorable results, they have mainly reported group effects. There is limited understanding of who are likely to benefit (or not) from the ICBT intervention. In other words, only a few studies have examined predictors of ICBT outcomes in tinnitus research. For example, the long-term analysis of the previous UK studies suggested that the best predictors of tinnitus improvements at 1-year were the baseline tinnitus severity, engagement with ICBT program (i.e., more modules read), and higher self-reported satisfaction with the intervention.[11] Studies in other health areas have also examined the predictors of outcome for a range of internet-based health interventions.[12-16]These studies have inconsistently identified various demographic as well as disease specific variables that could predict the successful and non-successful participants in internet-interventions.[16] There remains a clear gap in knowledge in terms of predictors of ICBT outcomes for tinnitus.

Predictors of intervention outcomes may help triage patients to the most suitable tinnitus intervention. If interventions are recommended based on their suitability, it can potentially improve the outcomes which would result in healthcare savings. The objective of the current study was to examine the predictors of outcomes of ICBT intervention for individuals with tinnitus based on the secondary analysis of the pooled results from the three-phase clinical trial undertaken in the UK.

Method

Study design and participants

The study was a secondary analysis of data collected three separate ICBT trials. Study participants from the three separate trials with different designs including the single-group

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pretest posttest design,[17] an efficacy RCT design (Clinical Trials.gov: NCT02370810),[18] and an effectiveness RCT design (Clinical Trials.gov: NCT02665975)[19] were combined. These studies were conducted during 2016-18. In the efficacy trial, the experimental group underwent ICBT immediately after allocation whereas the control group underwent the same intervention following an 8-week weekly check-in period. In the effectiveness trial, the experimental group underwent the ICBT interevent whereas the control group underwent treatment as usual consisting of in-person tinnitus counselling and sound therapy, provided by the audiologists at three hospital settings. The data from only those who underwent the ICBT intervention was included in this study. The ethical clearance for these studies was obtained from the Faculty of Science and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference: FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project ID: 195565). The study results are presented using the TRIPOD checklist (see Appendix 1).

Combining the data from three trials resulted in inclusion of 228 participants. Of these, 36 were from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the effectiveness trial.

Intervention

The intervention included a CBT program that was specifically developed for individuals with tinnitus.[20] This intervention was originally developed by psychologists in Sweden,[21] but later adapted by audiologists in the UK[22] and the US.[23] The intervention was administered using a secured ePlatform,[24,25] and presented in a self-help format. The intervention was presented over

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8-weeks period, during which the users were given access to 2-3 modules each week. The CBT program was divided into 21 modules, of which 5 were optional. The modules included content such as applied relaxation, thought analysis, cognitive restructuring, imagery, and exposure techniques. Each module included text, images, and videos to enhance user experience. In addition, they included various exercises that users have to complete to engage them in the intervention. Although the intervention was presented in a self-help format, the users had access to minimal guidance from an audiologist (EB). Generally, this included examining weekly exercises users completed and providing feedback as well as answering any questions they may have in the secured messaging system. An average of 10 minutes per participant was spent on providing guidance and support, although some users required more support.

Outcome measures

The study participants completed an extensive pre-intervention questionnaire that collected data on demographics, tinnitus-related and treatment-related history. In addition, participants also completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at postintervention (T1) and 2-months follow-up (T2). The *primary outcome measure* included the Tinnitus Functional Index (TFI)[26] to assess tinnitus severity/distress. This is a 25-item questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus with no need for intervention, scores ranging between 25 to 50 indicate significant problem with possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly requiring a more intensive intervention. The TFI has good psychometric properties with acceptable internal consistency (0.97) and test-retest reliability (0.8).[26]

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The *secondary outcome measures* included the Insomnia Severity Index (ISI)[27] as a measure of insomnia, the Generalized Anxiety Disorder (GAD-7)[28] as a measure of anxiety, the Patient Health Questionnaire (PHQ-9)[29] as a measure of depression, the Hearing Handicap Inventory for Adults Screening version (HHIA-S)[30] as a measure of self-reported hearing disability, the Hyperacusis Questionnaire (HQ)[31] to assess the presence hyperacusis (i.e., educed tolerance of everyday sounds), the Cognitive Failures Questionnaire (CFQ)[32] was administered to assess cognitive functions, and the Satisfaction with Life Scales (SWLS)[33] to assess the global life satisfaction.

Patient and public involvement

No patient involved.

Variables included in the predictive model

Outcome Variable: The main dependent variable was the pre- and post-intervention change in tinnitus distress based on the TFI score (TFI change). The 13-point change in TFI scores, identified as a clinically meaningful (or significant) change by the original authors[26] was used to define a clinically significant intervention outcome.

Predictor Variables: Thirty-two variables from the pre-intervention questionnaires were selected as potential predictor (independent) variables based on clinical reasoning and findings from previous studies by Beukes et al.[11] (see Appendix 2 for details). These included:

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- Demographic variables (n=7): age (dichotomous), gender (dichotomous), education level (ordinal), employment type (categorical), loud noise exposure (dichotomous), diagnosed with a psychological condition (dichotomous), work less due to tinnitus (categorical).
- Tinnitus and hearing-related variables (n=15): baseline tinntius severity (dichotomous), tinnitus duration (dichotomous), how often tinnitus heard (ordinal), tinnitus location (categorical), tinnitus types (9 different types, dichotomous), multiple tones heard (dichotomous), and hearing loss (categorical).
- Treatment-related to tinnitus (n=4): past treatment sought (dichotomous), sounds can distract from tinnitus (ordinal), hearing aid use (categorical), and medication use (dichotomous).
- Clinical factors (n=7): anxiety (dichotomous), depression (dichotomous), insomnia (dichotomous), hyperacusis (dichotomous), hearing disability (dichotomous), cognitive functions (dichotomous), and life satisfaction (dichotomous).

Data analysis

The data were analyzed using the descriptive statistics as well as univariate and multivariable liner regression and logistic regression models. A careful analysis on missing post TFI scores, with several competeing imputation methods, lead final imputations to be performed based on mean imputation. Therefore, the post-TFI scores of 38 subjects were missing and were imputed using means of their corresponding trials.

The univariate analysis was performed using Chi-square or Fishers exact test to examine the effect of single variables on the ICBT outcome. The multivariate regression model was used to

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identify the effect of the variables on tinnitus reduction post ICBT, while adjusting for the baseline tinnitus severity, as a variable previously identified to related to the success of ICBT.[11] Prior to the multivariate analyses, the full data set was divided into the training (80%, $n = 183$) and testing (20%, $n = 45$). The training data set was used to develop the corresponding (linear/multivariate) regression models while the testing data set was used to evaluate the model predictions. Several competing multivariable models (both linear and logistic) were examined. The best models were selected based on the lowest mean squared error and the lowest Akaike Information Criterion (AIC).[34] Both crude and model-based odds ratios were calculated and used to evaluate the effect of the variable. The Hosmer-Lemeshow goodness-of-fit statistic was calculated to assess the calibration of the final model.[35] The discriminative ability of the model was assessed with the area under the curve (AUC). The predictions were evaluated based on the model accuracy, sensitivity and the specificity on the testing data.

The dependent variable TFI change was used as a continuous variable for a linear regression analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic regression analysis. All statistical analyses were performed with R statistical software (Version: 3.6.3). All tests were two sided and threshold at 10% level of significance due to the exploratory nature of the study to account for the medium sample size and control for both Type I and type II errors effectively.[36,37]

Results

Participant demographics

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The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects (n=130) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on demograhic, tinnitus, hearing-related and treatment related variables are provided in Appendix 3. Table 1 presents details on clinical variables. The mean baseline tinnitus severity and tinnitus severity following the ICBT intervention were 57.93 (SD: 19.17) and 34.22 (SD: 22.78), respectively. Figure 1 presents the pre- and post-intervention tinnitus severity (TFI) score variation, indicating statistically significant differences between these scores (p <0.001). There were 150 participants (66%) with a 13-point or higher reduction after the intervention.

<Table 1 here>

<Figure 1 here>

Univariate Analysis to Examine the Predictors of ICBT Outcome

The details of the univariate analyses are provided in Appendix 3 (see Tables 3.2 to 3.5). With the exception of education level (p = .008), none of the demographic variable were associated with post-intervention tinnitus severity change of 13-point or more. Participants with a master's degree or above had the highest odds of having a larger severity change score, with an odds ratio of 4.50 (95% C.I: 1.59, 18.47), compared to the participants who had education only up to high school or less. In terms of tinnitus and hearing-related variables, the baseline tinnitus severity (p = 0.04) was significantly associated with treatment success. Participants who had a higher baseline tinntus severity (i.e., TFI scores of greater than or equal to 55.2) had a significantly higher odds of treatment success (OR: 1.78) compared to those who had a baseline severity less than 55.2.

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In terms of the treatment-related variables, sounds can distract (p = .027) showed a significant association with treatment success. Those who reported to be distracted by the sound partially (OR: 2.97; 95% C.I: 1.28, 6.88) or not at all (OR: 3.31; 95% CI: 1.02, 10.72) were at higher odds of having a successful treatment outcome when compared to who were fully distracted. However, the odds among the participants who used hearing aid either in one ear or both ears compared to those who did not, was not statistically significantly different (Table 3.4 in Appendix 3). None of the clinical factors were significantly associated with outcome.

Multivariate analyses to examine predictors of ICBT outcome

Multivariate linear regression analysis was used to identify contributing predictors of TFI change. The variables that were included in the final regression model are shown in Table 2. Working less due to tinnitus (p = .004), hearing aid usage (p = .04), maskability of tinnitus (p = .05), baseline tinnitus severity (p < .001), music type of tinnitus (p = .003), education level (p =.018), loud noise exposure (p = .09), and depression (p = .02) showed significant associations with outcome (TFI change). Modified models with the variables gender (p = .10), hearing loss (p = .23), tinnitus type: buzzing (p = .43), tinnitus type: low pitch (p = .10), tinnitus type: pulsing (p = 0.64), tinnitus type: clicking (p = .27), insomnia (p = .26) and satisfaction with life (p = .82) were not statistically significant. Moreover, several two-way interactions were tested. We did not find any gender interactions with regard to the maskability of sounds (p = .42) and) and hearing aid usage variables (p = .44). The overall model fit was evident with R squared = 0.35 and Adj. R squared of 0.30. The final model resulted in a root mean square of 25.38 on the testing data set, indicating a better predictive power. All required regression assumptions were satisfied in the selected model.

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This model helped in identifying the impact on the TFI score with several predictor variables, as a result of the ICBT intervention. Participants with depression had approximately 12 points (SE: 4.79) expected reduction in their TFI score. Moreover, participants who had master's degree or above compared to participants who had college education showed expected reduction of 10-point (SE: 4.20) in their TFI score. Participants who used hearing aid for one ear had an expected TFI reduction of 8.95 (SE: 4.42) compared to those who did not use hearing aids. However, participants who used hearing aid for both ears did not show a significant difference in their TFI reduction (*p*-value: 0.50) compared to those who did not use any. Those who got distracted partially compared to those who were fully distracted showed an expected TFI reduction of 8.42 (SE: 4.42) after the treatment. Nevertheless, participants who were not distract at all did not show a significant TFI reduction compared to those who were fully distracted. Also, participants who described that their tinnitus had a musical quality had the least expected reduction (-51.52, SE:16.87) in their TFI score with the treatment, followed by participants who were working less with disability allowence due to their tinnitus (-21.33, SE:7.21). Participants who had loud noise exposure compared to those who did not also showed an increase in their TFI score (-4.32, SE: 2.58).

<Table 2 here>

Following this, multivariable logistic regressions were performed with 13-point change in TFI following ICBT intervention (i.e., treatment success) as the dependent variable (see Table 3). In this analysis, hearing aid usage ($p = .05$), baseline tinnitus severity ($p < 0.001$), clicking type of

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tinnitus (p = .03), low pitch type of tinnitus (p = .03), education level (p = .001), and the presence of insomnia (p = .05) were identified as significant predictors. This model had an AIC of 220.87. Modified models to the prior model with the variables gender (p = .94), presence of a hearing loss (p = .73), tinnitus being masked by sounds (p = .33), work less due to tinnitus (p = .29), buzzing type of tinnitus (p = 0.15), pulsing type of tinnitus (p = 0.73), musical type of tinnitus (p = .12), loud noise exposure (p = .60), depression (p = .88), and satisfaction with life (p = .70), separately, were not statistically significant. Several two-way interactions were tested but were not statistically significant, including any gender differences regarding sounds masking tinnitus (p = .67) and hearing aid usage variables (p = .82).

The multivariable model adjusted OR (see Table 3) for the participants who were using a hearing aid in one ear had a 5.48 higher odds (95% CI: 1.02, 29.37) of having a successful outcome with ICBT intervention compared to the participants who did not use any hearing aid help while there was no significant difference between the subjects who use hearing aid in both ears compared to those who do not use any (OR: 0.72 95% CI: 0.33, 1.60). Participants who had master's level or above education compared to those who had high school education or less also showed 10.71 higher odds (95% CI: 2.28, 50.22) of having successful outcome. Participants who had either low pitch (OR: 0.16; 95% CI: 0.03, 0.87) or clicking (OR: 0.19; 95% CI: 0.04, 0.82) tinnitus types had significant lower odds of having successful outcome with the ICBT intervention. Participants with insomnia also had a 0.55 lower odds of success (95% CI: 0.20, 0.99) compared to those who did not .

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The Hosmer-Lemeshow goodness-of-fit test confirmed a better fit in the current model with a *p*-value of 0.53 (χ^2=7.10, df=8). This model had an AUC of 0.747 and lead to 77.8% accuracy, 80.0% specificity, and 76.7% sensitivity in the testing data set with a cut-off 0.50.

<Table 3 here>

Fewer variables were statistically significant in the logistic regression model which identified influencing predictors of the ICBT success. Although depression was identified as a key predictor for reducing tinnitus severity in the linear regression model, it was not identified as a key predictor in the multivariate model. Moreover, loud noise exposure was barely significant in the regression model and was not statistically significant in the logistic regression model. This was due to the fact that the logistic regression model evaluated predictors of treatment successes (i.e., 13 point change), while the multivariate regression model identified the predictors of a significant TFI reductions.

Discussion

Accessible and affordable tinnitus interventions are needed to alleviate the tinnitus distress as well as comorbid problems with anxiety, depression and insomnia. The current study examined predictors of outcomes in ICBT. In this exploratory study only a limited number of variables were identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points following undertaking an ICBT intervention and the results varied depending on the model used. Only educational level and using one hearing aid were predictors in both linear and logistic models. Other variables that were significant in either the linear or logistic models included: demographic

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variables (i.e., working less due to tinnitus, loud noise exposure), tinnitus related variables (i.e., tinnitus maskablity, types of tinnitus) and treatment related variables (i.e., hearing aid use) and clinical variables (i.e. higher levels of depression, insomnia) when controlling for baseline tinnitus severity. These key findings are discussed below.

In terms of demographic variables, education level was found to be a significant predictor of ICBT success as those with a master's education or higher had higher odds of having a successful outcome compared with those with high school education in both the linear and logistic models. This was expected as having good literacy skills is essential when understanding the intervention materials. The intervention materials used in these studies were written at an average of 9th reading grade level,[23] suggesting that they were not easily accessible for participants with only a high school education. These results highlight the importance of health literacy considerations when developing text-based self-help interventions such as ICBT. Additionally, those reported to be working less due to tinntius were at a lower odds of having a successful outcome. Those working less because of tinnitus have previously been identified as having higher tinnitus severity.[38] Closely monitoring the effects of tinnitus is important to ensure that tinnitus can be managed so that individuals are still able to work effectively.

When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to be a significant predictor of ICBT success, as seen in previous studies.[11] Tinnitus perceptions vary greatly and in this study those with tinnitus presenting as musical, lower pitched or clicking were less likely to have a positive outcome of ICBT. This finding certainly needs further exploration as the limited number of participants in each group of tinnitus perception. One of the CBT

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intervention aims is to help participants to reinterpret their tinnitus to a less threatening sound. It may be that these sounds are not easily likened to everyday sounds than other types of tinnitus (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation strategies.

Of the four treatment related variables, only those who reported to use of wearing one hearing aid were found to be at better odds of ICBT success. This finding need further exploration as to identify other characteristics that may be associated with outcome such as having tinnitus in only one ear. Although the evidence for use hearing aids alone for tinnitus management is limited,[39,40] hearing aids may for some reduce the tinnitus percept and aid communication difficulties.[41] Ensuring hearing loss is addressed in addition to provision of ICBT may lead to more optimal outcomes for those with co-existing hearing loss.

Regarding studying the clinical factors, those with higher levels of depression were found to have higher rediction in the TFI score. However, the participants with insomnia showed lower odds of success. This may be because those with clinical depression and sleepproblems have higher baseline tinnitus severity.[38] Our previous studies have shown that participants with higher baseline tinnitus are more likely to benefit from ICBT.[11] These observations strengthen the argument that those with more severe tinnitus are more likely to need more intensive interventions.[26] Interestingly, other clinical factors including anxiety, hyperacusis, hearing disability as well as cognitive functioning were not significant predictors of ICBT in the current study.

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Studies in other health areas have also examined the predictors of a range of internet-based health interventions.[12-15] Generally higher baseline symptoms predict an increased treatment response, for example in anxiety and depression,[42] and higher obsessive-compulsive behaviours when treating obsessive-compultive disorder.[43] Variables such as age and gender have been mentioned as significant predictors for some ICBT interventions.[15,42] Most previous ICBT interventions have not identified pre-treatment characteristics to predict or moderate outcomes.[16] Most ICBT studies have indicated that ICBT works irrespective of treatment history.[42] Contrarily, previous treatment has shown worse outcomes in som epevious studies.[44] However, it may be that some participants may have sought alternative therapies which have no evidence for tinnitus. For this reason, it would be useful to examine specific types of previous treatments in future studies to distinguish between those who had evidence-based interventions before enrolling to ICBT than those who did not.

Study limitations and future sesearch

The current study was to our knowledge the first study to combine data from multiple studies to examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study may have included homogeneous group of tinnitus patients due to study inclusion/exclusion criteria and may not have included all the possible variables (e.g., health literacy, acceptability and motivation of users, satisfaction from the intervention, intervention engagement) that may have played a role in ICBT outcome. Second, the sample size remained relatively small when compared to the number of predictive factors included. Third, multivariate analyses may have some limitations in terms of examining the complex relationships. Moreover, due to the high multicollinearity between the predictor variables, there were several competing models which had

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lead to the same prediction accuracies and root mean square errors. Additionally, these linear models lack in identifying any predictor variables that has a non-linear relationship with the response variables. For these reasons, the study results must be viewed as preliminary. Future studies may benefit from using artificial intelligence and machine learning techniques to examine the complex relationship between the variables in predicting the ICBT outcomes. Analyses should be extended with non-linear models like decision trees, support vector machines and neural networks. Future studies could also examine the predictors of adherence and engagement to intervention as well as of dropouts.

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Contributors

HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript. All authors read and approved the final manuscript.

Competing interests

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None to declare.

Patient consent for publication

Not required.

Data availability statement

Data is available for other researchers on request.

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Tables

Table 1: Details of clinical variables of the study participants

Characteristic	Mean (SD)
Pre-intervention tinnitus severity (measured using TFI, scores range 0-11)	57.93 (19.17)
Post-intervention tinnitus severity (measured using TFI, scores range 0-11)	34.22 (22.78)
2-month follow up tinnitus severity (measured using TFI, scores range 0-11)	34.23 (24.19)
Anxiety (measured using GAD-7, scores range 0-21)	7.29 (5.52)
Depression (measured using PHQ-9, scores range 0-27)	7.61 (5.73)
Insomnia (measured using ISI, scores range 0-28)	12.49 (6.67)
Hyperacusis (measured using HQ, scores range 0-40)	18.33 (9.05)
Hearing disability (measured using the HHIA-S, scores range 0-40)	16.18 (11.64)
Cognitive failures (measured using the CFQ, scores range 0-100)	38.54 (15.63)
Life satisfaction (measured using SWLS, scores range 0-40)	20.71 (7.55)

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Table 2: The best multiple linear regression model summary

Predictor Variable	Estimate	SE	P-value
Intercept	-7.97	5.65	0.16
Work less: No	Ref		
Work less: Reduced hours	-4.09	7.68	0.59
Work less: Stopped work	-1.63	3.98	0.68
Work less: Disability allowance	-21.33	7.21	**0.004**
Hearing aids: No	Ref		
Hearing aids: One ear	8.98	4.42	**0.04**
Hearing aids: Both ears	-2.11	3.13	0.5
Sounds mask tinnitus: Fully	Ref		
Sounds mask tinntius: Partially	8.42	4.33	**0.053**
Sounds mask tinnitus: Not at all	0.07	5.93	0.99
Baseline tinntus severity	0.39	0.08	**<0.0001**
Tinnitus type: Music	-52.52	16.87	**0.003**
Education Level: High school or less	Ref		
Education Level: College	-4.61	3.82	0.23
Education Level: Vocational training	0.66	4.2	0.88
Education Level: Batchelor's degree	3.91	3.42	0.25
Education Level: Master's degree or above	10	4.19	**0.018**
Depression: No	Ref		
Depression: Yes	16.86	4.79	**0.014**
Loud noise exposure: No	Ref		

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Loud noise exposure: Yes	-5.28	2.58	**0.097**

Table 3: The multivariable logistic regression model summary and the model adjusted odds ratio (95% confidence interval) for successful ICBT outcome of 13 points of higher.

	Estimate	**SE**	**P-value**	**Model based adjusted OR (95% CI for OR)**
Intercept	-1.43	0.68	0.04	0.24 (0.06, 0.90)
Hearing aid use: No	Ref			
Hearing aid use: One ear	1.7	0.86	**0.047**	**5.48 (1.02, 29.37)**
Hearing aid use: Both ears	-0.32	0.4	0.42	0.72 (0.33,1.60)
Baseline tinntus severity	0.04	0.01	**< 0.001**	**1.04 (1.02, 1.06)**
Tinnitus type; Clicking: No	Ref			
Tinnitus type; Clicking: Yes	-1.66	0.74	**0.03**	**0.19 (0.04, 0.82)**
Tinnitus type; Low pitched: No	Ref			
Tinnitus type; Low pitched: Yes	-1.83	0.86	**0.03**	**0.16 (0.03, 0.87)**
Education level: High school or less	Ref			
Education level: College	-0.5	0.48	0.30	0.61 (0.23, 1.57)
Education level: Vocational training	0.55	0.55	0.32	1.73 (0.59, 5.11)
Education level: Batchelor's degree	0.52	0.46	0.26	1.69 (0.68, 4.2)
Education level: Master's degree or above	2.37	0.79	**0.001**	**10.71 (2.28, 50.22)**
Insomnia: No	Ref			
Insomnia: Yes	-0.81	0.41	**0.047**	**0.45 (0.20, 0.99)**

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Figure Legends

Figure 1: Tinnitus severity (TFI scores) pre- and post-intervention. Boxplot represents the five-number summary (minimum, first quartile, median, third quartile, and maximum). The thick dark line represents the median.

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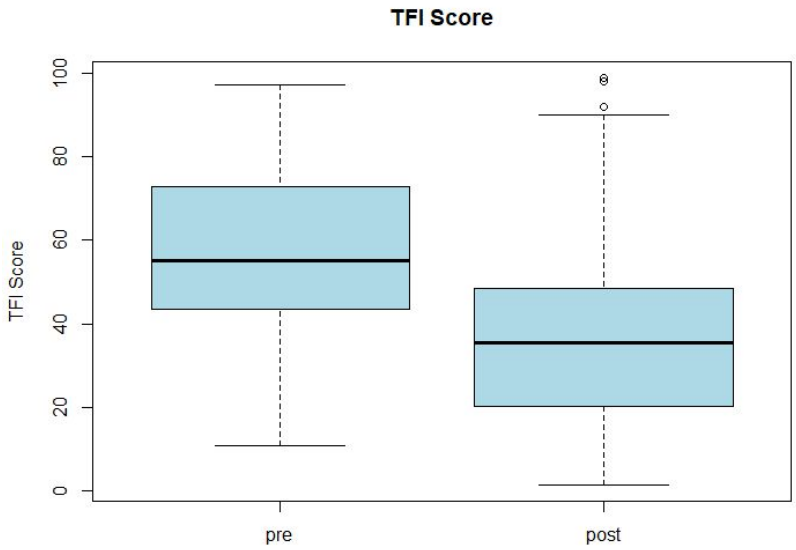
Figures

Figure 1: Tinnitus severity (TFI scores) pre- and post-intervention. Boxplot represents the five-number summary (minimum, first quartile, median, third quartile, and maximum). The thick dark line represents the median.



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TRIPOD

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	6-7
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8-9
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	8-9
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	9
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	10
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	10
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	10
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	10
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	11
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	11
Model development	14a	Specify the number of participants and outcome events in each analysis.	11
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	11-12
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12-15
	15b	Explain how to the use the prediction model.	14-15
Model performance	16	Report performance measures (with CIs) for the prediction model.	14-15
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	18-19
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	15-18
Implications	20	Discuss the potential clinical use of the model and implications for future research.	19
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	9, 11
Funding	22	Give the source of funding and the role of the funders for the present study.	19

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

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Appendix 2: Predictor Variables

Table 2.1: Demographic variables

Variable	Question	Response options
Age	What is your age?	In years Split into dichotomous variables (<=57 years of age and >57 years of age) based on the median
Gender	What is your gender?	Male (1), Female (2)
Education level	What is the highest level of education you have completed?	Highschool or less (1), College (2), Vocational training (3), Bachelor's degree (4), Master's degree or above (5)
Employment type	What best describes your employment?	Manager (1), Professional (2), Technical (3), Administrative (4), Skilled tradesman (5), Service occupation (6), Medical (7), Sales (8), Home maker (9), Student (10), Retired (11), Unemployed (12)
Loud noise exposure	Have you been exposed to loud noise?	Yes (1) , No (0)
Diagnosed with psychological condition	Have you been presently diagnosed with any psychological conditions including anxiety and depression?	Yes (1) , No (0)
Work less due to tinnitus	Do you work less because of your tinnitus?	No (0), Reduced hours (1), Stopped work (2), Disability allowance (3)

Table 2.2: Tinnitus and hearing-related variables

Variable	Question	Response options
Baseline tinnitus severity	Measured using the Tinnitus Functional Index (TFI)	Scores range from 0 to 100. Split into dichotomous variables (<=55.2 and >55.2) based on the median
Tinnitus duration	How long have you had tinnitus for?	In years Split into dichotomous variables (<=10.00 years and >10.00 years) based on the median
How often is tinnitus heard?	How often is tinnitus heard?	Occasionally (1), When taking out my hearing aid(s) (2), At night (3), Most of the time (4), All the time (5)
Tinnitus location	Where do you notice your tinnitus?	One ear (1), Both ears (2), In my head (3), Unsure (4), Other (5)

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Type of tinnitus (9 different types)	▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsing ▪ Clicking ▪ Music ▪ Voices ▪ Humming	For each item: Yes (1) , No (0)
Multiple tones heard	This variable is computed based on responses to types of tinnitus. Answer yes to multiple types of tinnitus was considered as multiple tones heard	Yes (1) , No (0)
Presence of a hearing loss	Do you have a hearing loss?	No (0), Both ears (1), One ear (2), Unsure (3)

Table 2.3: Treatment-related variables

Variable	**Question**	**Response options**
Past treatment sought	Have you received treatment for tinnitus in the past?	Yes (1) , No (0)
Sounds can distract from tinnitus	How well can sounds around you distract you from your tinnitus or make the tinnitus less noticeable?	Fully (1), Partially (2), Not at all (3)
Hearing aid use	Do you wear hearing aid(s) or any other amplification devices?	No (0), One ear (1), Both ears (2)
Medication use	Do you currently take any medications?	Yes (1) , No (0)

Table 2.4: Clinical factors

Variable	**Questionnaire**	**Number of items/ Response options**	**Score**
Anxiety	General Anxiety Disorders (GAD-7)	7-items 4-point scale with "not at all" (score of 0) to "nearly every day" (score of 3)	Higher number indicates more severe anxiety (scores range between 0–21). The total score is interpreted as follows: ▪ 0–4: minimal anxiety ▪ 5–9: mild anxiety ▪ 10–14: moderate anxiety ▪ 15–21: severe anxiety Split into dichotomous variables (<=9 no anxiety and >9 anxiety)
Depression	Patient Health Questionnaire (PHQ-9)	9-items 4-point scale with "not at all" (score of	Higher number indicates more severe depression (scores range between 0–27).

		0) to "nearly every day" (score of 3)	The total score is interpreted as follows: ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression Split into dichotomous variables (<=14 no depression and >14 depression)
Insomnia	Insomnia Severity Index (ISA)	7-item 5-point scale with "no problem" (score of 0) to "very severe problem" (score of 4)	Higher number indicates more severe insomnia (scores range between 0–28). The total score is interpreted as follows: ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) Split into dichotomous variables (<=14 no insomnia and >15 insomnia)
Hyperacusis	Hyperacusis Questionnaire (HQ)	14-items 4-point scale with "no" (score of 0) to "yes, a lot" (score of 3)	Higher number more severe hyperacusis (scores range between 0–42). The total score is interpreted as follows: ▪ >28: strong hypersensitivity Split into dichotomous variables (<=28 no hyperacusis and >28 hyperacusis)
Hearing disability	Hearing Handicap Inventory for Adults – Screening (HHIA-S)	10-items 3-point scale with "yes" (score of 4) to "no" day (0)	Higher number more severe hearing disability (scores range between 0–40). The total score is interpreted as follows: ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability Split into dichotomous variables (<=8 no hearing disability and >=10 hearing disability)

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Cognitive failures	Cognitive Failures Questionnaire (CFQ)	25-items 5-point scale with "never" (score of 0) to "very often" (score of 4)	Higher scores indicate more difficulties (cognitive failures) in perception, memory, and motor function (score range 0–100). The total score is interpreted as follows: The scores range 0–100 with higher scores indicating more cognitive failures/problems (or reduced cognitive functioning). Split into dichotomous variables (<=32 no cognitive problems and >32 cognitive problems)
Life satisfaction	Satisfaction with Life Scale (SWLS)	5-items 7-point scale with "strongly disagree" (score of 1) to "strongly agree" (7)	Higher number indicated more satisfaction with life (scores range between 5–35). The total score is interpreted as follows: ▪ 0–9: extremely dissatisfied ▪ 10–14: dissatisfied ▪ 15–19: below average satisfaction ▪ 20–24: average satisfaction ▪ 25–29: high satisfaction ▪ 30–35: highly satisfied Split into dichotomous variables (<=19 life satisfaction and >19 high satisfaction)

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Appendix 3: Univariate analysis to examine association between predictor variables and outcome variable

Table 3.1: Participant demographic characteristics (n=228)

Characteristic	N (%)	Mean (SD)
Demographic characteristics		
Age (in years)		55.14 (12.92)
Gender ▪ Female ▪ Male	 98 (43%) 130 (57%)	
Highest level of education ▪ High school or below ▪ College ▪ Vocational training ▪ Bachelor's degree ▪ Masters degree or above	 59 (26%) 47 (21%) 31 (13%) 61 (26%) 30 (13%)	
Employment ▪ Manager ▪ Professional ▪ Technical ▪ Administrative ▪ Skilled tradesman ▪ Service occupation ▪ Medical ▪ Sales ▪ Homemaker ▪ Student ▪ Retired ▪ Unemployed	 27 (12%) 46 (20%) 16 (6%) 17 (7%) 11 (5%) 11 (5%) 6 (3%) 8 (3%) 4 (2%) 1 (0%) 73 (32%) 11 (5%)	
Loud noise exposure ▪ Yes ▪ No	 103 (45%) 125 (55%)	
Diagnosed with a psychological condition ▪ Yes ▪ No	 50 (22%) 178 (78%)	
Working less due to tinnitus ▪ Reduced hours ▪ Stopped work ▪ Disability allowance ▪ No	 8 (4%) 32 (14%) 7 (3%) 181 (79%)	
Tinnitus and hearing-related characteristics		
Baseline tinnitus severity (measured using Tinnitus Functional Index)		57.93 (19.17)
Tinnitus duration (in years)		17.68 (19.42)
How often tinnitus is heard		

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▪ Occasionally	4 (2%)	
▪ When taking out my hearing aid(s)	3 (1%)	
▪ At night	4 (2%)	
▪ Most of the time	63 (27%)	
▪ All the time	154 (68%)	
Tinnitus location		
▪ One ear	61 (27%)	
▪ Both ears	109 (48%)	
▪ In my head	34 (15%)	
▪ Other location	3 (1%)	
▪ Unsure	21 (9%)	
Type of tinnitus sound (answering Yes)		
▪ Ringing	71 (31%)	
▪ Buzzing	75 (33%)	
▪ High pitched sound	130 (57%)	
▪ Low pitched sound	16 (7%)	
▪ Pulsating	28 (12%)	
▪ Clicking	14 (6%)	
▪ Music	4 (2%)	
▪ Voices	3 (1%)	
▪ Humming	21 (9%)	
Multiple sounds heard		
▪ Yes	73 (32%)	
▪ No	155 (68%)	
Presence of a hearing loss		
▪ No	49 (21%)	
▪ Both ears	104 (46%)	
▪ One ear	46 (20%)	
▪ Unsure	29 (13%)	
Treatment-related characteristics		
Past tinnitus treatment sought		
▪ Yes	58 (25%)	
▪ No	170 (75%)	
Sounds can distract from tinnitus		
▪ Fully	26 (11%)	
▪ Partially	178 (78%)	
▪ Not at all	24 (10%)	
Hearing aid use		
▪ No	159 (70%)	
▪ Unilateral	19 (8%)	
▪ Bilateral	50 (22%)	
Medication use		
▪ Yes	130 (57%)	
▪ No	98 (43%)	

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Table 3.2: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the demographic predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% C.I)**	**P-Value**
Age	>57 years	1.00 (0.58, 1.73)	0.99
	<=57 years	Ref	
Gender	Female	1.04 (0.60, 1.81)	0.88
	Male	Ref	
Education level	College	0.72 (0.36, 1.68)	**0.0085***
	Vocational training	1.47 (0.65, 4.09)	
	Bachelor's degree	1.30 (0.68, 2.92)	
	Master's degree or above	**4.50 (1.59, 18.47)**	
	High school or less	Ref	
Employment type	Professional	0.70 (0.30, 2.10)	0.95*
	Technical	0.47 (0.16, 2.20)	
	Administrative	0.74 (0.26, 3.14)	
	Skilled tradesman	0.95 (0.29, 5.43)	
	Service occupation	0.95 (0.29, 5.43)	
	Medical	1.18 (0.26, 13.47)	
	Sales	0.38 (0.11, 2.35)	
	Home maker	0.32 (0.08, 3.50)	
	Student	0.47 (0.06, 41.55)	
	Retired	0.99 (0.44, 2.78)	
	Unemployed	0.95 (0.29, 5.43)	
	Manager	Ref	
Loud noise exposure	Yes	0.69 (0.40, 1.19)	0.18
	No	Ref	
Presence of a psychological condition	Yes	1.64 (0.81, 3.30)	0.17
	No	Ref	
Work less due to tinnitus	Reduced hours	1.81 (0.44, 15.50)	0.37*
	Stopped work	0.90 (0.45, 2.13)	
	Disability allowance	0.31 (0.10, 1.70)	
	No	Ref	

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Table 3.3: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the tinnitus and hearing-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% C.I)**	**P-Value**
Baseline tinnitus severity	>55.2	**1.78 (1.02, 3.10)**	**0.04**
	<=55.2	Ref	
Tinnitus duration	>10.00 years	1.16 (0.66, 2.02)	0.6
	<=10.00 years	Ref	
How often tinnitus is heard	When taking out my hearing aid(s)	0.25 (0.04, 11.57)	0.12*
	At night	0.06 (0.01, 2.75)	
	Most of the time	0.32 (0.08, 4.10)	
	All the time	0.57 (0.14, 6.98)	
	Occasionally	Ref	
Tinnitus location	Both ears	1.12 (0.62, 2.25)	0.95*
	In my head	1.13 (0.52, 2.98)	
	Unsure	0.59 (0.13, 8.21)	
	Other	1.26 (0.51, 4.16)	
	One ear	Ref	
Tinnitus type: Ringing	Yes	1.23 (0.68, 2.25)	0.49
	No	Ref	
Tinnitus type: Buzzing	Yes	1.39 (0.77, 2.52)	0.28
	No	Ref	
Tinnitus type: High pitch	Yes	0.75 (0.43, 1.32)	0.32
	No	Ref	
Tinnitus type: Low pitch	Yes	0.65 (0.23, 1.81)	0.40
	No	Ref	
Tinnitus type: Pulsing	Yes	0.66 (0.29, 1.47)	0.30
	No	Ref	
Tinnitus type: Clicking	Yes	0.36 (0.12, 1.09)	0.12
	No	Ref	
Tinnitus type: Music	Yes	1.57 (0.12, 83.52)	1.0*
	No	Ref	
Tinnitus type: Voices	Yes	0.00 (0.00, 1.24)	0.04
	No	Ref	
Tinnitus type: Humming	Yes	0.67 (0.27, 1.66)	0.53
	No	Ref	
Multiple tones heard	Yes	0.84 (0.47, 1.49)	0.54
	No	Ref	
Presence of a hearing loss	Both ears	0.92 (0.45, 1.88)	0.99
	One ear	0.91 (0.39, 2.13)	
	Unsure	0.92 (0.35, 2.43)	

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	No	Ref	

Table 3.4: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the treatment-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% C.I)**	**P-Value**
Past treatment sought	Yes	0.89 (0.48, 1.66)	0.71
	No	Ref	
Sounds can distract	Partially	**2.97 (1.28, 6.88)**	**0.027**
	Not at all	**3.31 (1.02, 10.72)**	
	Fully	Ref	
Hearing aid use	One ear	**1.98 (0.71, 7.86)**	**0.089**
	Both ear	0.60 (0.33, 1.21)	
	No	Ref	
Medication use	Yes	1.22 (0.70, 2.11)	0.49
	No	Ref	

Table 3.5: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the clinical factors predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Odds Ratio (95% C.I)**	**P-Value**
Anxiety	Yes	1.09 (0.60, 1.98)	0.77
	No	Ref	
Depression	Yes	1.19 (0.49, 2.88)	0.69
	No	Ref	
Insomnia	Yes	0.86 (0.49, 1.50)	0.59
	No	Ref	
Hyperacusis	Yes	1.16 (0.54, 2.51)	0.71
	No	Ref	
Hearing disability	Yes	1.23 (0.69, 2.19)	0.49
	No	Ref	
Cognitive functions	Yes	1.05 (0.60, 1.86)	0.86
	No	Ref	
Life satisfaction	Yes	0.69 (0.40, 1.22)	0.20
	No	Ref	

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Internet-based cognitive-behavioral therapy for tinnitus: Secondary analysis to examine predictors of outcomes

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Abstract

Objectives: The current study examined predictors of outcomes of internet-based cognitive behavioural therapy (ICBT) for individuals with tinnitus.

Design: Secondary analysis of intervention studies.

Setting: Internet-based guided tinnitus intervention provided in the UK.

Participants: 228 individuals who underwent ICBT.

Interventions: ICBT.

Primary and secondary outcome measures: The key predictor variables included demographic, tinnitus, hearing-related, and treatment-related variables as well as clinical factors (i.e., anxiety, depression, insomnia, hyperacusis, hearing disability, cognitive function, and life satisfaction) which can have an impact on the treatment outcome. A 13-point reduction in Tinnitus Functional Index (TFI) scores has been defined as a successful outcome.

Results: Of the 228 subjects who were included in the study, 65% had a successful ICBT outcome. As per the univariate analysis, participants with a master's degree or above had the highest odds of having a larger reduction in tinnitus severity (OR: 3.47), compared to the participants who had education only up to high school or less. Additionally, the baseline tinnitus severity was found to be a significant variable (OR: 1.05) contributing to a successful outcome with the intervention. Both linear and logistic regression models have identified education level and baseline tinnitus severity, to be significant predictor variables contributing to reduction in tinnitus severity post-ICBT. As per linear regression model, participants who had received disability allowance had shown 25.3-point lower TFI reduction compared to those who didn't have to work less due to tinnitus after adjusting for baseline tinnitus severity and their education level.

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Conclusions: Predictors of intervention outcome can be used as a means of triaging patients to the most suited form of treatment to achieve optimal outcomes and to make healthcare savings. Future studies should consider including a heterogeneous group of participants as well as other predictor variables that might have not included in the current study.

Key Words

Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive behavioural therapy

Strengths and limitations of the study

- This study investigated if there are predictors of outcomes for ICBT for tinnitus.
- Analysis included univariate, multivariable and logistic regression models.
- The results were hampered by homogeneity of the participants undertaking ICBT.
- Results may be biased by the sample size and number of predictors included in the model.

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Introduction

Tinnitus is the perception of sounds in the absence of external stimulation and is often heard as a ringing or buzzing meaningless sound(s). It is a very common condition, with at least 15% of the adult population having tinnitus.[1] Tinnitus is highly heterogeneous, both in the way it manifests as well as in the manner those with tinnitus respond to treatment options.[2] The National Study of Hearing in England found that of the general population surveyed ($N = 48, 313$), 10.1% reported any tinnitus, 2.8% reported moderately annoying tinnitus, 1.6% reported severely annoying tinnitus, and 0.5% were unable to lead a normal life due to the severity of the tinnitus.[1]

Although there are several management strategies described in the literature, most are not evidence based. The main exception is Cognitive Behavioural Therapy (CBT), as indicated in various systematic reviews of randomized controlled trials.[3-6] Clinical practice guidelines, based on research evidence and expert consensus, thus recommends CBT as a management option for individuals with tinnitus and is supported by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS).[7]

Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in their local clinics. For example, a large-scale epidemiological study in the US showed that medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of the time by health professionals, whereas the CBT was discussed as a management option only 0.2% of the time.[8] This is most likely a consequence of the limited number of trained professionals who provide CBT for tinnitus. One solution to overcome this issue is to use Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over the internet with minimal guidance from a tinnitus expert.[9] A series of controlled studies in

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Sweden, Germany, the United Kingdom, and the United States have demonstrated positive effects of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety, depression, insomnia.[9] In addition to the changes noted in standardized outcome measures, the qualitative analysis of user experiences has highlighted the perceived benefits of this program.[10] In addition, the improvements noted from ICBT have been maintained for 1-year post-intervention.[11] . These results suggest that ICBT is a highly promising approach to provide evidence-based tinnitus management.

Although the previous studies on ICBT have shown favourable results, they have mainly reported group effects. There is limited understanding of who is likely to benefit (or not) from the ICBT intervention. In other words, only a few studies have examined predictors of ICBT outcomes in tinnitus research. For example, the long-term analysis of the previous UK studies suggested that the best predictors of tinnitus improvements at 1-year were the baseline tinnitus severity, engagement with ICBT program (i.e., more modules read), and higher self-reported satisfaction with the intervention.[11] Studies in other health areas have also examined the predictors of outcome for a range of internet-based health interventions.[12-16] These studies have inconsistently identified various demographic as well as disease-specific variables that could predict the successful and non-successful participants on internet interventions.[16] There remains a clear gap in knowledge in terms of predictors of ICBT outcomes for tinnitus.

Predictors of intervention outcomes may help triage patients to the most suitable tinnitus intervention. If interventions are recommended based on their suitability, it can potentially improve the outcomes, which would result in healthcare savings. The objective of the current

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study was to examine the predictors of outcomes of ICBT intervention for individuals with tinnitus based on the secondary analysis of the pooled results from the three-phase clinical trial undertaken in the UK.

Method

Study design and participants

A large data set was sought to identify predictors of outcome. Trials with similar methodologies were hence sought to merge to form a larger data set. Although a few previous studies regarding ICBT were conducted in Europe, these did not use extensive outcome measures. Following these trials, three trials were conducted in the UK, all using the same outcome measures. These trials were used due to a lack of other controlled trials available to pool data from. This present study thus formed a secondary analysis of data collected from three separate ICBT trials. Study participants from the three separate trials with different designs, including the single-group pre-post-test design,[17] an efficacy RCT design (Clinical Trials.gov: NCT02370810),[18] and an effectiveness RCT design (Clinical Trials.gov: NCT02665975)[19] were combined. These studies were conducted during 2016-18. In the efficacy trial, the experimental group underwent ICBT immediately after allocation whereas the control group underwent the same intervention following an 8-week weekly check-in period. In the effectiveness trial, the experimental group underwent the ICBT interevent whereas the control group underwent treatment as usual consisting of in-person tinnitus counselling and sound therapy, provided by the audiologists at three hospital settings. The data were collected from only those who underwent the ICBT intervention and were included in this study. The study team was granted access to the de-identified datasets, not containing any personally identifiable information, as part of a data

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sharing policy. The ethical clearance for these studies was obtained from the Faculty of Science and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference: FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project ID: 195565). The study results are presented using the TRIPOD checklist (see Supplementary file 1).

Combining the data from three trials resulted in the inclusion of 228 participants. Of these, 36 were from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the effectiveness trial.

Intervention

The intervention included a CBT program that was specifically developed for individuals with tinnitus.[20] This intervention was originally developed by psychologists in Sweden,[21] but later adapted by audiologists in the UK[22] and the US.[23] The intervention was administered using a secured ePlatform,[24,25] and presented in a self-help format. The intervention was presented over an 8-weeks period, during which the users were given access to 2-3 modules each week. The CBT program was divided into 21 modules, of which 5 were optional. The modules included content such as applied relaxation, thought analysis, cognitive restructuring, imagery, and exposure techniques. Each module included text, images, and videos to enhance the user experience. In addition, they included various exercises that users have to complete to engage them in the intervention. Although the intervention was presented in a self-help format, the users had access to minimal guidance from an audiologist (EB). Generally, this included examining

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weekly exercises users completed and providing feedback as well as answering any questions they may have in the secured messaging system. An average of 10 minutes per participant was spent on providing guidance and support, although some users required more support.

Outcome measures

The study participants completed an extensive pre-intervention questionnaire that collected data on demographics, tinnitus-related and treatment-related history. In addition, participants also completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at post-intervention (T1) and 2-months follow-up (T2). The *primary outcome measure* included the Tinnitus Functional Index (TFI)[26] to assess tinnitus severity/distress. This is a 25-item questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus with no need for intervention, scores ranging between 25 to 50 indicate a significant problem with possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly requiring a more intensive intervention. The TFI has good psychometric properties with acceptable internal consistency (0.97) and test-retest reliability (0.8).[26]

The *secondary outcome measures* included the Insomnia Severity Index (ISI)[27] as a measure of insomnia, the Generalized Anxiety Disorder (GAD-7)[28] as a measure of anxiety, the Patient Health Questionnaire (PHQ-9)[29] as a measure of depression, the Hearing Handicap Inventory for Adults Screening version (HHIA-S)[30] as a measure of self-reported hearing disability, the Hyperacusis Questionnaire (HQ)[31] to assess the presence hyperacusis (i.e., educed tolerance of everyday sounds), the Cognitive Failures Questionnaire (CFQ)[32] was administered to assess

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cognitive functions, and the Satisfaction with Life Scales (SWLS)[33] to assess the global life satisfaction.

Patient and public involvement

As a secondary analysis, no patients were involved in these studies. The data originates for individuals with tinnitus who had previously received CBT delivered via the internet (i.e., ICBT). As the same protocol was followed for all study participants and the all received the same intervention, merging this data was possible.

Variables included in the predictive model

Outcome Variable: The main dependent variable was the pre-and post-intervention change in tinnitus distress based on the TFI score (TFI change). The 13-point change in TFI scores, identified as a clinically meaningful (or significant) change by the original authors[26] was used to define a clinically significant intervention outcome.

Predictor Variables:

Predictor variables were selected, based on clinical reasoning and findings from previous studies by Beukes et al.[11] (see Supplementary file 2 for details). Thirty-two variables were selected as potential predictor (independent) variables and included demographic, tinnitus and hearing-related variables, tinnitus treatment related variables, clinical factors as follows:

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- Demographic variables (*n*=7): age (dichotomous), gender (dichotomous), education level (ordinal), employment type (categorical), loud noise exposure (dichotomous), diagnosed with a psychological condition (dichotomous), work less due to tinnitus (categorical).
- Tinnitus and hearing-related variables (*n*=15): baseline tinnitus severity (dichotomous), tinnitus duration (dichotomous), how often tinnitus heard (ordinal), tinnitus location (categorical), tinnitus types (9 different types, dichotomous), multiple tones heard (dichotomous), and hearing loss (categorical).
- Treatment-related to tinnitus (*n*=4): past treatment sought (dichotomous), sounds can distract from tinnitus (ordinal), hearing aid use (categorical), and medication use (dichotomous).
- Clinical factors (*n*=7): anxiety (dichotomous), depression (dichotomous), insomnia (dichotomous), hyperacusis (dichotomous), hearing disability (dichotomous), cognitive functions (dichotomous), and life satisfaction (dichotomous).

Data analysis

The data were analysed using descriptive statistics as well as univariate and multivariable linear regression and logistic regression models. Linear models were used to identify the factors affecting a significant TFI score change, while the logistic model was used to evaluate the factors which specifically effects outcomes and was thus selected. There were 98 subjects who had all their predictive variables except their post TFI scores. With the intention of preserving the power of the analysis, we have retained those subjects in the analysis after applying the predictive mean matching (PMM) data imputation.[34] Data imputation with PMM has been identified to be less

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vulnerable to model misspecification as, there is no need to define an explicit model for the distribution of the missing values[35] with that.

The univariate analysis was performed using Chi-square or Fisher's exact test to examine the effect of single variables on the ICBT outcome using all the variables. The multivariable regression model was used to identify the effect of the variables on tinnitus reduction post ICBT, while adjusting for the baseline tinnitus severity, as a variable previously identified to related to the success of ICBT.[11] Prior to the multivariable analyses, the full data set was divided into the training (80%, $n = 183$) and testing (20%, $n = 45$) to make a fair comparison among all the predictive models. The training data set was used to develop the corresponding multivariable regression models while the testing data set was used to evaluate the model predictions. Several competing multivariable models (both linear and logistic) were examined. The best models were selected based on the lowest mean squared error and the lowest Akaike Information Criterion (AIC).[36] During multivariable analysis, we started off with the full model, including all the predictor variables and used backward elimination based on AIC to select the final model. R squared and Adj. R squared values has been reported as they are statistical measures of fit that indicates how much variation of the outcome is explained by the predictor variable(s) in a linear regression model.[37] We also reported the mean squared error as it is a better measure of prediction accuracy. Both crude and model-based odds ratios were calculated and used to evaluate the effect of the variable. The Hosmer-Lemeshow goodness-of-fit statistic was calculated to assess the calibration of the final model.[38]

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The dependent variable TFI change was used as a continuous variable for a linear regression analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic regression analysis. All statistical analyses were performed with R statistical software (Version: 3.6.3). All tests were two-sided and threshold at 5% level of significance.

Results

Participant demographics

The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects (*n*=130) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on demographic, tinnitus, hearing-related and treatment-related variables are provided in Table 1 of the Supplementary file 3. Table 1 presents details on clinical variables. The mean baseline tinnitus severity and tinnitus severity following the ICBT intervention were 57.93 (SD: 19.17) and 34.22 (SD: 22.76), respectively. Figure 1 presents the pre-and post-intervention tinnitus severity (TFI) score variation, indicating statistically significant differences between these scores (p <0.001) with the paired t-test. There were 148 participants (65%) with a 13-point or higher reduction after the intervention.

<Table 1 here>

<Figure 1 here>

Univariate analysis to examine the predictors of ICBT outcome

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With the exception of education level (p = .01), none of the demographic variables were associated with post-intervention tinnitus severity change of 13-point or more. Participants with a master's degree or above had the highest odds of having a larger severity change score, with an odds ratio of 3.47 (95% CIs: 1.32, 12.51), compared to the participants who had education only up to high school or less. In terms of tinnitus and hearing-related variables, the baseline tinnitus severity (p = 0.001) was significantly associated with treatment success. Participants who had a higher baseline tinnitus severity (i.e., TFI scores of greater than or equal to 55.2) had significantly higher odds of treatment success (OR: 2.65; 95% CIs: 1.50, 4.67) compared to those who had a baseline severity less than 55.2. The details of the univariate analyses are provided in Tables 2-5 of the Supplementary file 3.

In terms of the treatment-related variables, sounds can distract (p = .001) showed a significant association with treatment success. Those who reported being distracted by the sound partially (OR: 4.34; 95% CIs: 1.82, 10.34) or not at all (OR: 3.15; 95% CIs: 0.99, 10.00) were at higher odds of having a successful treatment outcome when compared to who was fully distracted. However, the odds among the participants who used hearing aid either in one ear or both ears compared to those who did not, was not statistically significantly different with a p-value 0.26 (see Table 4 of the Supplementary file 3). Tinnitus described as voice-like had a 91% lower odds of success with the treatment. None of the clinical factors were significantly associated with the outcome.

Multivariable analyses to examine predictors of ICBT outcome

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Working less due to tinnitus (p = .046), baseline tinnitus severity (p < .001), and education level (p =.014), showed significant associations with outcome (i.e., TFI reduction). Modified models with the remaining variables were not statistically significant. Moreover, several two-way interactions were tested. We did not find any gender interactions with regard to the maskability of sounds (p = .87) and) and hearing aid usage (p = .68) variables. The overall model resulted with an R squared = 0.35 and Adj. R squared of 0.20. The final model resulted in a root mean square of 22.81on the testing data set. All required regression assumptions were satisfied with the selected model. The final regression model (see Table 2) was selected with backward elimination based on AIC.

This model indicated that those who received disability allowance due to having severe tinnitus and being unable to work, had shown a reduction of 25.30-point (95% CIs: -46.35,-4.24) inTFI compared to those who did not have to work less due to tinnitus. Moreover, for every 10 unit increase in the baseline tinnitus severity, there was 8.3 (95% CIs: 0.65,1.00) reduction in their TFI score after adjusting for other variables. Participants who had master's degree or above compared to participants who had a college education showed an expected reduction of 17-point (95% CIs: 5.78, 27.84) in their TFI score.

<Table 2 here>

Multivariable logistic regressions were performed next and indicated that baseline tinnitus severity (p < 0.001), and education level (p = .001), and were identified as significant predictors (see Table 3). This model had an AIC of 212.21. Modified models to the prior model indicated that other variables were not statistically significant (see Table 4).

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The multivariable model adjusted OR (see Table 3) for the participants who had master's level or above education compared to those who had high school education or less also showed 9.65 higher odds (95% CIs: 2.32, 40.15) of having a successful outcome. Similar to the linear regression model, baseline tinnitus severity had also shown a significant association (OR: 1.04; 95% CIs: 1.02, 1.06) with the treatment outcome. The Hosmer-Lemeshow goodness-of-fit test confirmed a better fit in the current model with a *p*-value of 0.50 (χ^2=7.36, df=8).

<Table 3 here>

<Table 4 here>

Fewer variables were statistically significant in the logistic regression model, which identified influencing predictors of the ICBT success. This was due to the fact that the logistic regression model evaluated predictors of treatment successes (i.e., 13 point change), while the multivariable regression model identified the predictors of a significant TFI reduction.

Discussion

Accessible and affordable tinnitus interventions are needed to alleviate tinnitus distress as well as comorbid problems with anxiety, depression, and insomnia. The current study examined predictors of outcomes for ICBT. In this exploratory study, only a limited number of variables were identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points following undertaking an ICBT intervention and the results vary depending on the model used. Only educational level and baseline tinnitus severity were predictors in both linear and logistic

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models. Other variable that were significant in the linear regression models included the demographic variable working less due to tinnitus, when controlling for baseline tinnitus severity and education level. These key findings are discussed below.

In terms of demographic variables, education level was found to be a significant predictor of ICBT success as those with a master's education or higher had higher odds of having a successful outcome compared with those with high school education in both the linear and logistic models. This was expected as having good literacy skills is essential when understanding the intervention materials. The intervention materials used in these studies were written at an average of 9th reading grade level,[23] suggesting that they were not easily accessible for participants with only a high school education. These results highlight the importance of health literacy considerations when developing text-based self-help interventions such as ICBT. Additionally, those reported to be working less due to tinnitus were at a lower odds of having a successful outcome. This finding needs further exploration in future studies. Working, may for instance provide some distraction from tinnitus as supported by reports during the 2020 COVID-19 pandemic that tinnitus was more bothersome for some individuals as they did not have the distractions from commuting and sounds at work.[39] Closely monitoring the effects of tinnitus is important to ensure that tinnitus can be managed so that individuals are still able to work effectively.

When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to be a significant predictor of ICBT success, as seen in previous studies.[11] Tinnitus perceptions vary greatly and in this study those with tinnitus presenting as musical, lower-pitched or clicking were less likely to have a positive outcome of ICBT. This finding certainly needs further exploration as

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the limited number of participants in each group of tinnitus perception. One of the CBT intervention aims is to help participants to reinterpret their tinnitus to a less threatening sound. It may be that these sounds are not easily likened to everyday sounds than other types of tinnitus (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation strategies.

Of the four treatment-related variables, only those who reported to use of wearing one hearing aid were found to be at better odds of ICBT success. This finding needs further exploration to identify other characteristics that may be associated with an outcome such as having tinnitus in only one ear. Although the evidence for the use of hearing aids alone for tinnitus management is limited,[40,41] hearing aids may for some reduce the tinnitus percept and aid communication difficulties.[42] Ensuring hearing loss is addressed in addition to the provision of ICBT may lead to more optimal outcomes for those with co-existing hearing loss.

Regarding studying the clinical factors, those with higher levels of depression were found to have higher reduction in the TFI score. However, the participants with insomnia showed lower odds of success. Interestingly, other clinical factors including anxiety, hyperacusis, hearing disability as well as cognitive functioning were not significant predictors of ICBT in the current study. Further studies and models are required to verify these results.

Studies in other health areas have also examined the predictors of a range of internet-based health interventions.[12-15] Generally higher baseline symptoms predict increased treatment response, for example, in anxiety and depression,[43] and higher obsessive-compulsive behaviours when treating the obsessive-compulsive disorder.[44] Variables such as age and gender have been mentioned as

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significant predictors for some ICBT interventions.[15,43] Most previous ICBT interventions have not identified pre-treatment characteristics to predict or moderate outcomes.[16] Most ICBT studies have indicated that ICBT works irrespective of treatment history.[43] Contrarily, previous treatment has shown worse outcomes in some previous studies.[45] However, it may be that some participants may have sought alternative therapies which have no evidence for tinnitus. For this reason, it would be useful to examine specific types of previous treatments in future studies to distinguish between those who had evidence-based interventions before enrolling to ICBT than those who did not.

Study limitations and future research

The current study was to our knowledge the first study to combine data from multiple studies to examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study may have included a homogeneous group of tinnitus patients due to study inclusion/exclusion criteria and may not have included all the possible variables (e.g., health literacy, acceptability and motivation of users, satisfaction from the intervention, intervention engagement) that may have played a role in ICBT outcome. These factors were not investigated for this study. As they have been found to contribute to outcomes,[46] they should be included in future studies. Second, the sample size remained relatively small when compared to the number of predictive factors included. Third, multivariable analyses may have some limitations in terms of examining complex relationships. Moreover, due to the high multicollinearity between the predictor variables, there were several competing models which had led to the same prediction accuracies and root mean square errors. Additionally, these linear models lack in identifying any predictor variables that have a non-linear relationship with the response variables. For these reasons, the study results

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must be viewed as preliminary. Future studies may benefit from examining more relevant predictor variables and also using artificial intelligence and machine learning techniques to examine the non-linear relationship between the variables in predicting the ICBT outcomes. Brier scores should also be used to compare models. Analyses should be extended with non-linear models like decision trees, support vector machines and neural networks. Future studies could also examine the predictors of adherence and engagement to intervention as well as of dropouts.

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Contributors

HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript. All authors read and approved the final manuscript.

Competing interests

None to declare.

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Patient consent for publication

Not required.

Data availability statement

Data is available for other researchers on request.

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Tables

Table 1: Details of clinical variables of the study participants

Characteristic	Mean (SD)
Pre-intervention tinnitus severity (measured using TFI, scores range 0-11)	57.93 (19.17)
Post-intervention tinnitus severity (measured using TFI, scores range 0-11)	34.22 (22.76)
2-month follow up tinnitus severity (measured using TFI, scores range 0-11)	34.23 (24.19)
Anxiety (measured using GAD-7, scores range 0-21)	7.29 (5.52)
Depression (measured using PHQ-9, scores range 0-27)	7. 61 (5.73)
Insomnia (measured using ISI, scores range 0-28)	12.49 (6.67)
Hyperacusis (measured using HQ, scores range 0-40)	18.33 (9.05)
Hearing disability (measured using the HHIA-S, scores range 0-40)	16.18 (11.64)
Cognitive failures (measured using the CFQ, scores range 0-100)	38.54 (15.63)
Life satisfaction (measured using SWLS, scores range 0-40)	20.71 (7.55)

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589 **Table 2: The best multiple linear regression model summary**

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Predictor Variable	Estimate	95% CI	P-value
Intercept	-28.94	-41.70, -16.18	<0.0000
Work less: No	Ref		
Work less: Reduced hours	-6.25	-23.90, 11.39	0.48
Work less: Stopped work	-0.58	-10.52, 9.36	0.91
Work less: Disability allowance	-25.30	-46.35, -4.24	**0.02**
Baseline tinnitus severity	0.83	0.65, 1.00	**<0.0001**
Education Level: High school or less	Ref		
Education Level: College	-2.25	-12.61, 8.11	0.67
Education Level: Vocational training	0.98	-10.29, 12.25	0.86
Education Level: Batchelor's degree	5.14	-4.13, 14.42	0.28
Education Level: Master's degree or above	16.81	5.78, 27.84	**0.003**

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Table 3: The multivariable logistic regression model summary and the model adjusted odds ratio (95% confidence interval) for successful ICBT outcome of 13 points of higher.

	Estimate	P-value	Model based adjusted OR (95% CI for OR)
Intercept	-2.32	0.0005	0.10 (0.03, 0.37)
Baseline tinnitus severity	0.04	**< 0.001**	**1.04 (1.02, 1.06)**
Education level: High school or less	Ref		
Education level: College	-0.4	0.41	0.67 (0.26, 1.74)
Education level: Vocational training	0.41	0.47	1.49 (0.50, 4.48
Education level: Batchelor's degree	0.68	0.14	1.98 (0.79, 4.98)
Education level: Master's degree or above	2.27	**0.001**	**9.65 (2.32, 40.15)**

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598 **Table 4: Predictor variables which were insignificant in multivariable regression models**

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		P-value	
	Predictor Variable	**Multivariable Linear Regression Model**	**Multivariable Logistic Regression Model**
1	Gender	0.47	0.83
2	Hearing Loss	0.89	0.72
3	Tinnitus type: Ringing	0.38	0.91
4	Tinnitus type: Buzzing	0.43	0.53
5	Tinnitus type: High pitch	0.56	0.48
6	Tinnitus type: Low pitch	0.33	0.46
7	Tinnitus type: Pulsing	0.99	0.34
8	Tinnitus type: Clicking	0.09	0.01
9	Tinnitus type: Music	0.37	0.69
10	Tinnitus type: Voices	0.34	0.09
11	Tinnitus type: Humming	0.96	0.06
12	Anxiety	0.07	0.48
13	Depression	0.76	0.86
14	Insomnia	0.94	0.53
15	Hyperacusis	0.75	0.53
16	Hearing disability	0.84	0.57
17	Cognitive functions	0.71	0.72
18	Life satisfaction	0.75	0.84

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19	Multiple tones heard	0.26	0.81
20	Loud noise exposure	0.32	0.76
21	Work less due to tinnitus	Refer Table 2	0.46
22	Presence of a psychological condition	0.88	0.72
23	Past treatment sought	0.60	0.83
24	Hearing aid use	0.21	0.20
25	Sounds can distract	0.51	0.11
26	Medication use	0.73	0.87
27	Tinnitus location	0.50	0.27
28	Employment type	0.63	0.90
29	Age	0.88	0.70
30	Tinnitus Duration	0.17	0.93
31	How often tinnitus is heard	0.23	0.57

Figure Legends

Figure 1: Tinnitus severity (TFI scores) pre- and post-intervention. Boxplot represents the five-number summary (minimum, first quartile, median, third quartile, and maximum). The thick dark line represents the median.

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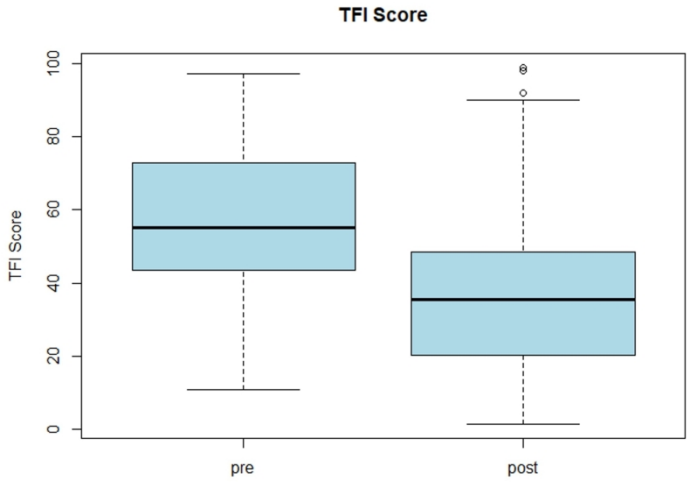

Figure 1

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Supplementary File 1

Table 1: TRIPOD Checklist – Prediction model development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	6-7
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8-9
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	8-9
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	9
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	10
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	10
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	10
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	10
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	11
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	11
Model development	14a	Specify the number of participants and outcome events in each analysis.	11
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	11-12
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12-15
	15b	Explain how to the use the prediction model.	14-15
Model performance	16	Report performance measures (with CIs) for the prediction model.	14-15
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	18-19
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	15-18
Implications	20	Discuss the potential clinical use of the model and implications for future research.	19
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	9, 11
Funding	22	Give the source of funding and the role of the funders for the present study.	19

Supplementary File 2: Predictor Variables

Table 1: Demographic variables

Variable	Question	Response options
Age	What is your age?	In years Split into dichotomous variables (<=57 years of age and >57 years of age) based on the median
Gender	What is your gender?	Male (1), Female (2)
Education level	What is the highest level of education you have completed?	Highschool or less (1), College (2), Vocational training (3), Bachelor's degree (4), Master's degree or above (5)
Employment type	What best describes your employment?	Manager (1), Professional (2), Technical (3), Administrative (4), Skilled tradesman (5), Service occupation (6), Medical (7), Sales (8), Home maker (9), Student (10), Retired (11), Unemployed (12)
Loud noise exposure	Have you been exposed to loud noise?	Yes (1) , No (0)
Diagnosed with psychological condition	Have you been presently diagnosed with any psychological conditions including anxiety and depression?	Yes (1) , No (0)
Work less due to tinnitus	Do you work less because of your tinnitus?	No (0), Reduced hours (1), Stopped work (2), Disability allowance (3)

Table 2: Tinnitus and hearing-related variables

Variable	Question	Response options
Baseline tinnitus severity	Measured using the Tinnitus Functional Index (TFI)	Scores range from 0 to 100. Split into dichotomous variables (<=55.2 and >55.2) based on the median
Tinnitus duration	How long have you had tinnitus for?	In years Split into dichotomous variables (<=10.00 years and >10.00 years) based on the median
How often is tinnitus heard?	How often is tinnitus heard?	Occasionally (1), When taking out my hearing aid(s) (2), At night (3), Most of the time (4), All the time (5)
Tinnitus location	Where do you notice your tinnitus?	One ear (1), Both ears (2), In my head (3), Unsure (4), Other (5)

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Type of tinnitus (9 different types)	▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsing ▪ Clicking ▪ Music ▪ Voices ▪ Humming	For each item: Yes (1) , No (0)
Multiple tones heard	This variable is computed based on responses to types of tinnitus. Answer yes to multiple types of tinnitus was considered as multiple tones heard	Yes (1) , No (0)
Presence of a hearing loss	Do you have a hearing loss?	No (0), Both ears (1), One ear (2), Unsure (3)

Table 3: Treatment-related variables

Variable	**Question**	**Response options**
Past treatment sought	Have you received treatment for tinnitus in the past?	Yes (1) , No (0)
Sounds can distract from tinnitus	How well can sounds around you distract you from your tinnitus or make the tinnitus less noticeable?	Fully (1), Partially (2), Not at all (3)
Hearing aid use	Do you wear hearing aid(s) or any other amplification devices?	No (0), One ear (1), Both ears (2)
Medication use	Do you currently take any medications?	Yes (1) , No (0)

Table 4: Clinical factors

Variable	**Questionnaire**	**Number of items/ Response options**	**Score**
Anxiety	General Anxiety Disorders (GAD-7)	7-items 4-point scale with "not at all" (score of 0) to "nearly every day" (score of 3)	Higher number indicates more severe anxiety (scores range between 0–21). The total score is interpreted as follows: ▪ 0–4: minimal anxiety ▪ 5–9: mild anxiety ▪ 10–14: moderate anxiety ▪ 15–21: severe anxiety Split into dichotomous variables (<=9 no anxiety and >9 anxiety)
Depression	Patient Health Questionnaire (PHQ-9)	9-items 4-point scale with "not at all" (score of	Higher number indicates more severe depression (scores range between 0–27).

		0) to "nearly every day" (score of 3)	The total score is interpreted as follows: ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression Split into dichotomous variables (<=14 no depression and >14 depression)
Insomnia	Insomnia Severity Index (ISA)	7-item 5-point scale with "no problem" (score of 0) to "very severe problem" (score of 4)	Higher number indicates more severe insomnia (scores range between 0–28). The total score is interpreted as follows: ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) Split into dichotomous variables (<=14 no insomnia and >15 insomnia)
Hyperacusis	Hyperacusis Questionnaire (HQ)	14-items 4-point scale with "no" (score of 0) to "yes, a lot" (score of 3)	Higher number more severe hyperacusis (scores range between 0–42). The total score is interpreted as follows: ▪ >28: strong hypersensitivity Split into dichotomous variables (<=28 no hyperacusis and >28 hyperacusis)
Hearing disability	Hearing Handicap Inventory for Adults – Screening (HHIA-S)	10-items 3-point scale with "yes" (score of 4) to "no" day (0)	Higher number more severe hearing disability (scores range between 0–40). The total score is interpreted as follows: ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability Split into dichotomous variables (<=8 no hearing disability and >=10 hearing disability)

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Cognitive failures	Cognitive Failures Questionnaire (CFQ)	25-items 5-point scale with "never" (score of 0) to "very often" (score of 4)	Higher scores indicate more difficulties (cognitive failures) in perception, memory, and motor function (score range 0–100). The total score is interpreted as follows: The scores range 0–100 with higher scores indicating more cognitive failures/problems (or reduced cognitive functioning). Split into dichotomous variables (<=32 no cognitive problems and >32 cognitive problems)
Life satisfaction	Satisfaction with Life Scale (SWLS)	5-items 7-point scale with "strongly disagree" (score of 1) to "strongly agree" (7)	Higher number indicated more satisfaction with life (scores range between 5–35). The total score is interpreted as follows: ▪ 0–9: extremely dissatisfied ▪ 10–14: dissatisfied ▪ 15–19: below average satisfaction ▪ 20–24: average satisfaction ▪ 25–29: high satisfaction ▪ 30–35: highly satisfied Split into dichotomous variables (<=19 life satisfaction and >19 high satisfaction)

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Supplementary File 3: Univariate analysis to examine association between predictor variables and outcome variable

Table 1: Participant demographic characteristics (n=228)

Characteristic	N (%)	Mean (SD)
Demographic characteristics		
Age (in years)		55.14 (12.92)
Gender		
▪ Female	98 (43%)	
▪ Male	130 (57%)	
Highest level of education		
▪ High school or below	59 (26%)	
▪ College	47 (21%)	
▪ Vocational training	31 (14%)	
▪ Bachelor's degree	61 (27%)	
▪ Masters degree or above	30 (13%)	
Employment		
▪ Manager	27 (12%)	
▪ Professional	46 (20%)	
▪ Technical	13 (6%)	
▪ Administrative	17 (7%)	
▪ Skilled tradesman	11 (5%)	
▪ Service occupation	11 (5%)	
▪ Medical	6 (3%)	
▪ Sales	8 (3%)	
▪ Homemaker	4 (2%)	
▪ Student	1 (0%)	
▪ Retired	73 (32%)	
▪ Unemployed	11 (5%)	
Loud noise exposure		
▪ Yes	103 (45%)	
▪ No	125 (55%)	
Diagnosed with a psychological condition		
▪ Yes	50 (22%)	
▪ No	178 (78%)	
Working less due to tinnitus		
▪ Reduced hours	8 (4%)	
▪ Stopped work	32 (14%)	
▪ Disability allowance	7 (3%)	
▪ No	181 (79%)	
Tinnitus and hearing-related characteristics		
Baseline tinnitus severity (measured using Tinnitus Functional Index)		57.93 (19.17)
Tinnitus duration (in years)		17.68 (19.42)
How often tinnitus is heard		

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▪ Occasionally	4 (2%)	
▪ When taking out my hearing aid(s)	3 (1%)	
▪ At night	4 (2%)	
▪ Most of the time	63 (27%)	
▪ All the time	154 (68%)	
Tinnitus location		
▪ One ear	61 (27%)	
▪ Both ears	109 (48%)	
▪ In my head	34 (15%)	
▪ Other location	3 (1%)	
▪ Unsure	21 (9%)	
Type of tinnitus sound (answering Yes)		
▪ Ringing	71 (31%)	
▪ Buzzing	75 (33%)	
▪ High pitched sound	130 (57%)	
▪ Low pitched sound	16 (7%)	
▪ Pulsating	28 (12%)	
▪ Clicking	14 (6%)	
▪ Music	4 (2%)	
▪ Voices	3 (1%)	
▪ Humming	21 (9%)	
Multiple sounds heard		
▪ Yes	73 (32%)	
▪ No	155 (68%)	
Presence of a hearing loss		
▪ No	49 (21%)	
▪ Both ears	104 (46%)	
▪ One ear	46 (20%)	
▪ Unsure	29 (13%)	
Treatment-related characteristics		
Past tinnitus treatment sought		
▪ Yes	58 (25%)	
▪ No	170 (75%)	
Sounds can distract from tinnitus		
▪ Fully	26 (11%)	
▪ Partially	178 (78%)	
▪ Not at all	24 (10%)	
Hearing aid use		
▪ No	159 (70%)	
▪ Unilateral	19 (8%)	
▪ Bilateral	50 (22%)	
Medication use		
▪ Yes	130 (57%)	
▪ No	98 (43%)	

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Table 2: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the demographic predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Age	>57 years	0.85 (0.50, 1.47)	0.57
	<=57 years	Ref	
Gender	Female	1.12 (0.64, 1.94)	0.70
	Male	Ref	
Education level	College	0.61 (0.31, 1.42)	**0.01***
	Vocational training	1.70 (0.75, 4.88)	
	Bachelor's degree	1.30 (0.67, 2.92)	
	Master's degree or above	**3.47 (1.32, 12.51)**	
	High school or less	Ref	
Employment type	Professional	0.59 (0.25, 1.82)	0.95*
	Technical	0.40 (0.13, 1.89)	
	Administrative	0.40 (0.14, 1.66)	
	Skilled tradesman	0.56 (0.18, 3.00)	
	Service occupation	0.80 (0.24, 4.66)	
	Medical	1.00 (0.22, 11.54)	
	Sales	0.80 (0.21, 6.00)	
	Home maker	0.27 (0.06, 3.00)	
	Student	0.40 (0.05, 35.47)	
	Retired	0.74 (0.32, 2.12)	
	Unemployed	0.80 (0.24, 4.66)	
	Manager	Ref	
Loud noise exposure	Yes	0.80 (0.46, 1.38)	0.43
	No	Ref	
Presence of a psychological condition	Yes	1.72 (0.85, 3.46)	0.13
	No	Ref	
Work less due to tinnitus	Reduced hours	1.05 (0.31, 6.18)	0.89*
	Stopped work	0.81 (0.41, 1.89)	
	Disability allowance	0.53 (0.16, 2.88)	
	No	Ref	

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Table 3: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the tinnitus and hearing-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Baseline tinnitus severity	>55.2	**2.65 (1.50, 4.67)**	**0.001**
	<=55.2	Ref	
Tinnitus duration	>10.00 years	1.16 (0.66, 2.02)	0.60
	<=10.00 years	Ref	
How often tinnitus is heard	When taking out my hearing aid(s)	0.67 (0.02, 18.06)	0.19*
	At night	0.33 (0.02, 6.65)	
	Most of the time	0.39 (0.04, 3.96)	
	All the time	0.76 (0.08, 7.49)	
	Occasionally	Ref	
Tinnitus location	Both ears	1.41(0.48, 4.16)	0.90*
	In my head	0.94 (0.48, 1.80)	
	Unsure	1.35 (0.55, 3.34)	
	Other	1.13 (0.10,13.16)	
	One ear	Ref	
Tinnitus type: Ringing	Yes	1.30 (0.72, 2.37)	0.38
	No	Ref	
Tinnitus type: Buzzing	Yes	1.34 (0.74, 2.42)	0.32
	No	Ref	
Tinnitus type: High pitch	Yes	0.76 (0.44, 1.33)	0.34
	No	Ref	
Tinnitus type: Low pitch	Yes	0.89 (0.31, 2.56)	0.83
	No	Ref	
Tinnitus type: Pulsing	Yes	0.97 (0.42, 2.21)	0.94
	No	Ref	
Tinnitus type: Clicking	Yes	0.52 (0.17, 1.53)	0.23
	No	Ref	
Tinnitus type: Music	Yes	1.63 (0.17, 15.98)	1.00*
	No	Ref	
Tinnitus type: Voices	Yes	0.09 (0.00, 1.75)	0.04*
	No	Ref	
Tinnitus type: Humming	Yes	0.56 (0.23, 1.39)	0.21
	No	Ref	
Multiple tones heard	Yes	1.15 (0.64, 2.08)	0.63
	No	Ref	
Presence of a hearing loss	Both ears	1.20 (0.59, 2.41)	0.92
	One ear	1.19 (0.51, 2.74)	
	Unsure	1.41 (0.53, 3.73)	
	No	Ref	

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Table 4: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the treatment-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Past treatment sought	Yes	0.94 (0.50, 1.74)	0.83
	No	Ref	
Sounds can distract	Partially	**4.34 (1.82, 10.34)**	**0.001**
	Not at all	**3.15 (0.99, 10.00)**	
	Fully	Ref	
Hearing aid use	One ear	**1.57 (0.61, 5.49)**	**0.26**
	Both ear	0.69 (0.38, 1.39)	
	No	Ref	
Medication use	Yes	1.22 (0.71, 2.12)	0.46
	No	Ref	

Table 5: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the clinical factors predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Odds Ratio (95% CIs)**	**P-Value**
Anxiety	Yes	1.53 (0.83, 2.82)	0.17
	No	Ref	
Depression	Yes	1.54 (0.62, 3.83)	0.35
	No	Ref	
Insomnia	Yes	1.27 (0.72, 2.23)	0.41
	No	Ref	
Hyperacusis	Yes	1.21 (0.56, 2.63)	0.62
	No	Ref	
Hearing disability	Yes	1.37 (0.77, 2.43)	0.28
	No	Ref	
Cognitive functions	Yes	0.99 (0.56, 1.74)	0.97
	No	Ref	
Life satisfaction	Yes	0.76 (0.44, 1.33)	0.34
	No	Ref	

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Internet-based cognitive-behavioral therapy for tinnitus: Secondary analysis to examine predictors of outcomes

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Abstract

Objectives: The current study examined predictors of outcomes of internet-based cognitive behavioural therapy (ICBT) for individuals with tinnitus.

Design: Secondary analysis of intervention studies.

Setting: Internet-based guided tinnitus intervention provided in the UK.

Participants: 228 individuals who underwent ICBT.

Interventions: ICBT.

Primary and secondary outcome measures: The key predictor variables included demographic, tinnitus, hearing-related, and treatment-related variables as well as clinical factors (e.g., anxiety, depression, insomnia) which can have an impact on the treatment outcome. A 13-point reduction in Tinnitus Functional Index (TFI) scores has been defined as a successful outcome.

Results: Of the 228 subjects who were included in the study, 65% had a successful ICBT outcome. As per the univariate analysis, participants with a master's degree or above had the highest odds of having a larger reduction in tinnitus severity (OR 3.47; 95% CI 1.32-12.51), compared to the participants who had education only up to high school or less. Additionally, the baseline tinnitus severity was found to be a significant variable (OR 2.65; 95% CI 1.50-4.67) contributing to a successful outcome with the intervention. Both linear and logistic regression models have identified education level and baseline tinnitus severity to be significant predictor variables contributing to reduction in tinnitus severity post-ICBT. As per the linear regression model, participants who had received disability allowance had shown a 25.3-point lower TFI reduction compared to those who did not experience a decrease in their workload due to tinnitus after adjusting for baseline tinnitus severity and their education level.

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Conclusions: Predictors of intervention outcome can be used as a means of triaging patients to the most suited form of treatment to achieve optimal outcomes and to make healthcare savings. Future studies should consider including a heterogeneous group of participants as well as other predictor variables not included in the current study.

Key Words

Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive behavioural therapy

Strengths and limitations of the study

- The current study, to our knowledge is the first study to use combined data from multiple studies to examine the predictors of ICBT outcome for tinnitus.
- The study included a homogeneous group of tinnitus patients due to the strict inclusion/exclusion criteria and may not have included all the possible variables (e.g., health literacy, acceptability and motivation of users, satisfaction from the intervention, intervention engagement) that may have played a role in ICBT outcome.
- The sample size remained relatively small when compared to the number of predictive factors included which may have hampered the study results.
- The multivariable analyses may have some limitations in terms of examining complex relationships. Other statistical models including artificial intelligence and machine learning techniques may have more value in examining the non-linear relationship.

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Introduction

Tinnitus is the perception of sounds in the absence of external stimulation and is often heard as a ringing or buzzing meaningless sound(s). It is a very common condition with at least 15% of the adult population having tinnitus.[1] Tinnitus is highly heterogeneous, both in the way it manifests as well as in the manner those with tinnitus respond to treatment options.[2] The National Study of Hearing in England found that of the general population surveyed ($N = 48, 313$), 10.1% reported any tinnitus, 2.8% reported moderately annoying tinnitus, 1.6% reported severely annoying tinnitus, and 0.5% were unable to lead a normal life due to the severity of the tinnitus.[1]

Although there are several management strategies described in the literature, most are not evidence based. The main exception is Cognitive Behavioural Therapy (CBT), as indicated in various systematic reviews of randomized controlled trials.[3-6] Clinical practice guidelines based on research evidence and expert consensus recommend CBT as a management option for individuals with tinnitus and is supported by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS).[7]

Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in their local clinics. For example, a large-scale epidemiological study in the US showed that medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of the time by health professionals, whereas the CBT was discussed as a management option only 0.2% of the time.[8] This is most likely a consequence of the limited number of trained professionals who provide CBT for tinnitus. One solution to overcome this issue is to use Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over the internet with minimal guidance from a tinnitus expert.[9] A series of controlled studies in

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Sweden, Germany, the United Kingdom, and the United States have demonstrated positive effects of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety, depression, and insomnia.[9] In addition to the changes noted in standardized outcome measures, the qualitative analysis of user experiences has highlighted the perceived benefits of this program.[10] In addition, the improvements noted from ICBT have been maintained for 1-year post-intervention.[11] These results suggest that ICBT is a highly promising approach to provide evidence-based tinnitus management.

Although the previous studies on ICBT have shown favourable results, group effects were mainly reported. There is limited understanding of who is likely to benefit (or not) from the ICBT intervention. In other words, only a few studies have examined predictors of ICBT outcomes in tinnitus research. For example, the long-term analysis of the previous UK studies suggested that the best predictors of tinnitus improvements at 1-year were the baseline tinnitus severity, engagement with ICBT program (i.e., more modules read), and higher self-reported satisfaction with the intervention.[11] Studies in other health areas have also examined the predictors of outcome for a range of internet-based health interventions.[12-16] These studies have inconsistently identified various demographic as well as disease-specific variables that could predict the successful and non-successful participants on internet interventions.[16] There remains a clear gap in knowledge in terms of predictors of ICBT outcomes for tinnitus.

Predictors of intervention outcomes may help triage patients to the most suitable tinnitus intervention. If interventions are recommended based on their suitability, it can potentially improve the outcomes resulting in healthcare savings. The objective of the current study was to

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examine the predictors of outcomes of ICBT intervention for individuals with tinnitus based on the secondary analysis of the pooled results from the three-phase clinical trial undertaken in the UK.

Method

Study design and participants

A large data set was sought to identify predictors of outcome. Trials with similar methodologies were hence sought to merge to form a larger data set. Although a few previous studies regarding ICBT were conducted in Europe, extensive outcome measures were not used. Following these trials, three trials were conducted in the UK using the same outcome measures. These trials were used due to a lack of other controlled trials available to pool data from. This present study thus formed a secondary analysis of data collected from three separate ICBT trials. Study participants from the three separate trials with different designs including the single-group pre-post-test design,[17] an efficacy RCT design (Clinical Trials.gov: NCT02370810),[18] and an effectiveness RCT design (Clinical Trials.gov: NCT02665975)[19] were combined. These studies were conducted during 2016-18. In the efficacy trial, the experimental group underwent ICBT immediately after allocation whereas the control group underwent the same intervention following an 8-week weekly check-in period. In the effectiveness trial, the experimental group underwent the ICBT intervention whereas the control group underwent treatment as usual, consisting of in-person tinnitus counselling and sound therapy, provided by the audiologists at three hospital settings. The data were collected from only those who underwent the ICBT intervention and were included in this study. The study team was granted access to the de-identified datasets, not containing any personally identifiable information, as part of a data

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sharing policy. The ethical clearance for these studies was obtained from the Faculty of Science and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference: FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project ID: 195565). The study results are presented using the TRIPOD checklist (see Supplementary file 1).

Combining the data from three trials resulted in the inclusion of 228 participants. Of these, 36 were from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the effectiveness trial.

Intervention

The intervention included a CBT program that was specifically developed for individuals with tinnitus.[20] This intervention was originally developed by psychologists in Sweden,[21] but later adapted by audiologists in the UK[22] and the US.[23] The intervention was administered using a secured ePlatform[24,25] and presented in a self-help format. The intervention was presented over an 8-weeks period, during which the users were given access to 2-3 modules each week. The CBT program was divided into 21 modules, of which 5 were optional. The modules included content such as applied relaxation, thought analysis, cognitive restructuring, imagery, and exposure techniques. Each module included text, images, and videos to enhance the user experience. In addition, users were required to complete various exercises to engage them in the intervention. Although the intervention was presented in a self-help format, the users had access to minimal guidance from an audiologist (EB). Generally, this included examining weekly

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exercises users completed and providing feedback as well as answering any questions they may have in the secured messaging system. An average of 10 minutes per participant was spent on providing guidance and support, although some users required more support.

Outcome measures

The study participants completed an extensive pre-intervention questionnaire that collected data on demographics, tinnitus-related and treatment-related history. In addition, participants also completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at post-intervention (T1) and at the 2-month follow-up (T2). The *primary outcome measure* included the Tinnitus Functional Index (TFI)[26] to assess tinnitus severity/distress. This is a 25-item questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus with no need for intervention, scores ranging between 25 to 50 indicate a significant problem with possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly requiring a more intensive intervention. The TFI has good psychometric properties with acceptable internal consistency (0.97) and test-retest reliability (0.8).[26]

The *secondary outcome measures* included the Insomnia Severity Index (ISI)[27] as a measure of insomnia, the Generalized Anxiety Disorder (GAD-7)[28] as a measure of anxiety, the Patient Health Questionnaire (PHQ-9)[29] as a measure of depression, the Hearing Handicap Inventory for Adults Screening version (HHIA-S)[30] as a measure of self-reported hearing disability, the Hyperacusis Questionnaire (HQ)[31] to assess the presence hyperacusis (i.e., educed tolerance of everyday sounds), the Cognitive Failures Questionnaire (CFQ)[32] was administered to assess

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cognitive functions, and the Satisfaction with Life Scales (SWLS)[33] to assess the global life satisfaction.

Patient and public involvement

As a secondary analysis, no patients were involved in these studies. The data originates for individuals with tinnitus who had previously received CBT delivered via the internet (i.e., ICBT). As the same protocol was followed for all study participants and all received the same intervention, merging this data was possible.

Variables included in the predictive model

Outcome Variable: The dependent variable was the pre-and post-intervention change in tinnitus distress based on the TFI score (TFI change). The 13-point change in TFI scores identified as a clinically meaningful (or significant) change by the original authors[26] was used to define a clinically significant intervention outcome.

Predictor Variables:

Predictor variables were selected based on clinical reasoning and findings from previous studies by Beukes et al.[11] (see Supplementary file 2 for details). Thirty-two variables were selected as potential predictor (independent) variables and included demographic, tinnitus and hearing-related variables, tinnitus treatment related variables. Clinical factors are as follows:

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- Demographic variables (*n*=7): age (dichotomous), gender (dichotomous), education level (ordinal), employment type (categorical), loud noise exposure (dichotomous), diagnosed with a psychological condition (dichotomous), work less due to tinnitus (categorical).
- Tinnitus and hearing-related variables (*n*=15): baseline tinnitus severity (dichotomous), tinnitus duration (dichotomous), how often tinnitus heard (ordinal), tinnitus location (categorical), tinnitus types (9 different types, dichotomous), multiple tones heard (dichotomous), and hearing loss (categorical).
- Treatment-related to tinnitus (*n*=4): past treatment sought (dichotomous), sounds can distract from tinnitus (ordinal), hearing aid use (categorical), and medication use (dichotomous).
- Clinical factors (*n*=7): anxiety (dichotomous), depression (dichotomous), insomnia (dichotomous), hyperacusis (dichotomous), hearing disability (dichotomous), cognitive functions (dichotomous), and life satisfaction (dichotomous).

Data analysis

The data were analysed using descriptive statistics as well as univariate and multivariable linear regression and logistic regression models. Linear models were used to identify the factors affecting a significant TFI score change while the logistic model was used to evaluate the factors which specifically effects outcomes and was thus selected. There were 98 subjects who had all their predictive variables except their post TFI scores. With the intention of preserving the power of the analysis, we have retained those subjects in the analysis after applying the predictive mean matching (PMM) data imputation.[34] Data imputation with PMM has been identified to be less

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vulnerable to model misspecification as there is no need to define an explicit model for the distribution of the missing values.[35]

The univariate analysis was performed using Chi-square or Fisher's exact test to examine the effect of single variables on the ICBT outcome using all the variables. The multivariable regression model was used to identify the effect of the variables on tinnitus reduction post ICBT while adjusting for the baseline tinnitus severity as a variable previously identified to relate to the success of ICBT.[11] Prior to the multivariable analyses, the full data set was divided into training (80%, $n = 183$) and testing (20%, $n = 45$) to make a fair comparison among all the predictive models. The training data set was used to develop the corresponding multivariable regression models while the testing data set was used to evaluate the model predictions. Several competing multivariable models (both linear and logistic) were examined. The best models were selected based on the lowest mean squared error and the lowest Akaike Information Criterion (AIC).[36] During multivariable analysis, we began with the full model, including all the predictor variables, and used backward elimination based on AIC to select the final model. R squared and Adj. R squared values have been reported, as they are statistical measures of fit that indicate how much variation of the outcome is explained by the predictor variable(s) in a linear regression model.[37] We also reported the mean squared error as it is a better measure of prediction accuracy. Both crude and model-based odds ratios were calculated and used to evaluate the effect of the variable. The Hosmer-Lemeshow goodness-of-fit statistic was calculated to assess the calibration of the final model.[38]

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The dependent variable TFI change was used as a continuous variable for a linear regression analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic regression analysis. All statistical analyses were performed with R statistical software (Version: 3.6.3). All tests were two-sided and threshold at 5% level of significance.

Results

Participant demographics

The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects (n=130) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on demographic, tinnitus, hearing-related and treatment-related variables are provided in Table 1 of the Supplementary file 3. Table 1 presents details on clinical variables. The mean baseline tinnitus severity and tinnitus severity following the ICBT intervention were 57.93 (SD: 19.17) and 34.22 (SD: 22.76) respectively. Figure 1 presents the pre-and post-intervention tinnitus severity (TFI) score variation, indicating statistically significant differences between these scores (p <0.001) with the paired t-test. There were 148 participants (65%) with a 13-point or higher reduction after the intervention.

<Table 1 here>

<Figure 1 here>

Univariate analysis to examine the predictors of ICBT outcome

With the exception of education level (p = .01), none of the demographic variables were associated with post-intervention tinnitus severity change of 13-point or more. Participants with a

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master's degree or above had the highest odds of having a larger severity change score, with an odds ratio of 3.47 (95% CIs: 1.32, 12.51), compared to the participants who had education only up to high school or less. In terms of tinnitus and hearing-related variables, the baseline tinnitus severity ($p = 0.001$) was significantly associated with treatment success. Participants who had a higher baseline tinnitus severity (i.e., TFI scores of greater than or equal to 55.2) had significantly higher odds of treatment success (OR: 2.65; 95% CIs: 1.50, 4.67) compared to those who had a baseline severity less than 55.2. The details of the univariate analyses are provided in Tables 2-5 of the Supplementary file 3.

In terms of the treatment-related variables, sounds can distract ($p = .001$) showed a significant association with treatment success. Those who reported being distracted by the sound partially (OR: 4.34; 95% CIs: 1.82, 10.34) or not at all (OR: 3.15; 95% CIs: 0.99, 10.00) were at higher odds of having a successful treatment outcome when compared to those who were fully distracted. However, the odds among the participants who used hearing aids either in one ear or both ears compared to those who did not were not statistically significantly different with a *p*-value 0.26 (see Table 4 of the Supplementary file 3). Tinnitus described as voice-like had a 91% lower odds of success with the treatment. None of the clinical factors were significantly associated with the outcome.

Multivariable analyses to examine predictors of ICBT outcome

Working less due to tinnitus ($p = .046$), baseline tinnitus severity ($p < .001$), and education level ($p = .014$), showed significant associations with outcome (i.e., TFI reduction). Modified models with the remaining variables were not statistically significant. Moreover, several two-way

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interactions were tested. We did not find any gender interactions with regard to the maskability of sounds (p = .87) and) and hearing aid usage (p = .68) variables. The overall model resulted with an R squared = 0.35 and Adj. R squared of 0.20. The final model resulted in a root mean square of 22.81on the testing data set. All required regression assumptions were satisfied with the selected model. The final regression model (see Table 2) was selected with backward elimination based on AIC.

This model indicated that those who received disability allowance due to having severe tinnitus and being unable to work had shown a reduction of 25.30-points (95% CIs: -46.35, -4.24) inTFI compared to those who did not have to work less due to tinnitus. Moreover, for every 10 unit increase in the baseline tinnitus severity, there was a 8.3-point (95% CIs: 0.65,1.00) reduction in their TFI score after adjusting for other variables. Participants who had master's degree or above compared to participants who had a college education showed an expected reduction of 17-points (95% CIs: 5.78, 27.84) in their TFI score.

<Table 2 here>

Multivariable logistic regressions were performed next and indicated that baseline tinnitus severity (p < 0.001) and education level (p = .001) were identified as significant predictors (see Table 3). This model had an AIC of 212.21. Modified models to the prior model indicated that other variables were not statistically significant (see Table 4).

The multivariable model adjusted OR (see Table 3) for the participants who had master's level or above education compared to those who had high school education or less also showed 9.65

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higher odds (95% CIs: 2.32, 40.15) of having a successful outcome. Similar to the linear regression model, baseline tinnitus severity had also shown a significant association (OR: 1.04; 95% CIs: 1.02, 1.06) with the treatment outcome. The Hosmer-Lemeshow goodness-of-fit test confirmed a better fit in the current model with a *p*-value of 0.50 (χ^2=7.36, df=8).

<Table 3 here>

<Table 4 here>

Fewer variables were statistically significant in the logistic regression model, which identified influencing predictors of the ICBT success. This was due to the fact that the logistic regression model evaluated predictors of treatment successes (i.e., 13-point change), while the multivariable regression model identified the predictors of a significant TFI reduction.

Discussion

Accessible and affordable tinnitus interventions are needed to alleviate tinnitus distress as well as comorbid problems with anxiety, depression, and insomnia. The current study examined predictors of outcomes for ICBT. In this exploratory study, only a limited number of variables were identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points following ICBT intervention, and the results vary depending on the model used. Only educational level and baseline tinnitus severity were predictors in both linear and logistic models. The other significant variable in the linear regression models included the demographic variable, work restrictions due to tinnitus when controlling for baseline tinnitus severity and education level. These key findings are discussed below.

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In terms of demographic variables, education level was found to be a significant predictor of ICBT success as those with a master's education or higher had higher odds of having a successful outcome compared with those with high school education in both the linear and logistic models. This was expected as having good literacy skills is essential when understanding the intervention materials. The intervention materials used in these studies were written at an average of 9th grade readinglevel[23] suggesting that they were not easily accessible for participants with only a high school education. These results highlight the importance of health literacy considerations when developing text-based self-help interventions such as ICBT. Additionally, those who reported work restrictions due to tinnitus were at a lower odds of having a successful outcome. This finding needs further exploration in future studies. Working may, for instance, provide some distraction from tinnitus as supported by reports during the 2020 COVID-19 pandemic that tinnitus was more bothersome for some individuals due to the lack of distractions from commuting and sounds at work.[39] Closely monitoring the effects of tinnitus is important to ensure that tinnitus can be managed so that individuals are still able to work effectively.

When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to be a significant predictor of ICBT success, as seen in previous studies.[11] Tinnitus perceptions vary greatly, and in this study, those with tinnitus presenting as musical, lower-pitched or clicking were less likely to have a positive outcome of ICBT. This finding certainly needs further exploration as the limited number of participants in each group of tinnitus perception. One of the CBT intervention aims is to help participants to reinterpret their tinnitus to a less threatening sound. It may be that these sounds are not easily likened to everyday sounds than other types of

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tinnitus (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation strategies.

Of the four treatment-related variables, only those who reported to use of wearing one hearing aid were found to be at better odds of ICBT success. This finding needs further exploration to identify other characteristics that may be associated with an outcome such as having tinnitus in only one ear. Although the evidence for the use of hearing aids alone for tinnitus management is limited,[40,41] hearing aids may for some reduce the tinnitus percept and aid communication difficulties.[42] Ensuring hearing loss is addressed in addition to the provision of ICBT may lead to more optimal outcomes for those with co-existing hearing loss.

Regarding studying the clinical factors, those with higher levels of depression were found to have higher reduction in the TFI score. However, the participants with insomnia showed lower odds of success. Interestingly, other clinical factors including anxiety, hyperacusis, hearing disability as well as cognitive functioning were not significant predictors of ICBT in the current study. Further studies and models are required to verify these results.

Studies in other health areas have also examined the predictors of a range of internet-based health interventions.[12-15] Generally, higher baseline symptoms predict increased treatment response, as in anxiety and depression,[43] and higher obsessive-compulsive behaviours when treating the obsessive-compulsive disorder.[44] Variables such as age and gender have been mentioned as significant predictors for some ICBT interventions.[15,43] Most previous ICBT interventions have not identified pre-treatment characteristics to predict or moderate outcomes.[16] Most ICBT studies

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have indicated that ICBT works irrespective of treatment history.[43] Contrarily, previous treatment has shown worse outcomes in some previous studies.[45] However, it may be that some participants may have sought alternative therapies which have no evidence for tinnitus. For this reason, it would be useful to examine specific types of previous treatments in future studies to distinguish between those who had evidence-based interventions before enrolling to ICBT than those who did not.

Study limitations and future research

The current study was to our knowledge the first study to combine data from multiple studies to examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study may have included a homogeneous group of tinnitus patients due to study inclusion/exclusion criteria and may not have included all the possible variables (e.g., health literacy, acceptability and motivation of users, satisfaction from the intervention, intervention engagement) that may have played a role in ICBT outcome. These factors were not investigated for this study. As they have been found to contribute to outcomes,[46] they should be included in future studies. Second, the sample size remained relatively small when compared to the number of predictive factors included. Third, multivariable analyses may have some limitations in terms of examining complex relationships. Moreover, due to the high multicollinearity between the predictor variables, there were several competing models which had led to the same prediction accuracies and root mean square errors. Additionally, these linear models lack in identifying any predictor variables that have a non-linear relationship with the response variables. For these reasons, the study results must be viewed as preliminary. Future studies may benefit from utilizing non-linear statistical models such as Generalized Additive Models (GAMs), and also artificial intelligence and

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machine learning models like neural networks, random forest and support vector machines, as some variables like tinnitus duration and depression had shown lower correlation with the response (with correlations: -0.10 and 0.29, respectively). In addition, including more relevant predictive factors (e.g., health literacy, motivation, engagement, adherence) in future studies may help improve predictive accuracy. Currently, we have used AIC value to compare the competing models. For future studies, we are planning to use average AUC and Brier scores to compare models.

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Contributors

HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript. All authors read and approved the final manuscript.

Competing interests

None to declare.

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Patient consent for publication

Not required.

Data availability statement

De-identified data are available upon reasonable request.

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Tables

Table 1: Details of clinical variables of the study participants

Characteristic	Mean (SD)
Pre-intervention tinnitus severity (measured using TFI, scores range 0-11)	57.93 (19.17)
Post-intervention tinnitus severity (measured using TFI, scores range 0-11)	34.22 (22.76)
2-month follow up tinnitus severity (measured using TFI, scores range 0-11)	34.23 (24.19)
Anxiety (measured using GAD-7, scores range 0-21)	7.29 (5.52)
Depression (measured using PHQ-9, scores range 0-27)	7. 61 (5.73)
Insomnia (measured using ISI, scores range 0-28)	12.49 (6.67)
Hyperacusis (measured using HQ, scores range 0-40)	18.33 (9.05)
Hearing disability (measured using the HHIA-S, scores range 0-40)	16.18 (11.64)
Cognitive failures (measured using the CFQ, scores range 0-100)	38.54 (15.63)
Life satisfaction (measured using SWLS, scores range 0-40)	20.71 (7.55)

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Table 2: The best multiple linear regression model summary

Predictor Variable	Estimate	95% CI	P-value
Intercept	-28.94	-41.70, -16.18	<0.0000
Work less: No	Ref		
Work less: Reduced hours	-6.25	-23.90, 11.39	0.48
Work less: Stopped work	-0.58	-10.52, 9.36	0.91
Work less: Disability allowance	-25.30	-46.35, -4.24	**0.02**
Baseline tinnitus severity	0.83	0.65, 1.00	**<0.0001**
Education Level: High school or less	Ref		
Education Level: College	-2.25	-12.61, 8.11	0.67
Education Level: Vocational training	0.98	-10.29, 12.25	0.86
Education Level: Batchelor's degree	5.14	-4.13, 14.42	0.28
Education Level: Master's degree or above	16.81	5.78, 27.84	**0.003**

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Table 3: The multivariable logistic regression model summary and the model adjusted odds ratio (95% confidence interval) for successful ICBT outcome of 13 points of higher.

	Estimate	P-value	Model based adjusted OR (95% CI for OR)
Intercept	-2.32	0.0005	0.10 (0.03, 0.37)
Baseline tinnitus severity	0.04	**< 0.001**	**1.04 (1.02, 1.06)**
Education level: High school or less	Ref		
Education level: College	-0.4	0.41	0.67 (0.26, 1.74)
Education level: Vocational training	0.41	0.47	1.49 (0.50, 4.48
Education level: Batchelor's degree	0.68	0.14	1.98 (0.79, 4.98)
Education level: Master's degree or above	2.27	**0.001**	**9.65 (2.32, 40.15)**

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Table 4: Predictor variables which were insignificant in multivariable regression models

		P-value	
	Predictor Variable	**Multivariable Linear Regression Model**	**Multivariable Logistic Regression Model**
1	Gender	0.47	0.83
2	Hearing Loss	0.89	0.72
3	Tinnitus type: Ringing	0.38	0.91
4	Tinnitus type: Buzzing	0.43	0.53
5	Tinnitus type: High pitch	0.56	0.48
6	Tinnitus type: Low pitch	0.33	0.46
7	Tinnitus type: Pulsing	0.99	0.34
8	Tinnitus type: Clicking	0.09	0.01
9	Tinnitus type: Music	0.37	0.69
10	Tinnitus type: Voices	0.34	0.09
11	Tinnitus type: Humming	0.96	0.06
12	Anxiety	0.07	0.48
13	Depression	0.76	0.86
14	Insomnia	0.94	0.53
15	Hyperacusis	0.75	0.53
16	Hearing disability	0.84	0.57
17	Cognitive functions	0.71	0.72
18	Life satisfaction	0.75	0.84

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19	Multiple tones heard	0.26	0.81
20	Loud noise exposure	0.32	0.76
21	Work less due to tinnitus	Refer Table 2	0.46
22	Presence of a psychological condition	0.88	0.72
23	Past treatment sought	0.60	0.83
24	Hearing aid use	0.21	0.20
25	Sounds can distract	0.51	0.11
26	Medication use	0.73	0.87
27	Tinnitus location	0.50	0.27
28	Employment type	0.63	0.90
29	Age	0.88	0.70
30	Tinnitus Duration	0.17	0.93
31	How often tinnitus is heard	0.23	0.57

Figure Legends

Figure 1: Tinnitus severity (TFI scores) pre- and post-intervention. Boxplot represents the five-number summary (minimum, first quartile, median, third quartile, and maximum). The thick dark line represents the median.

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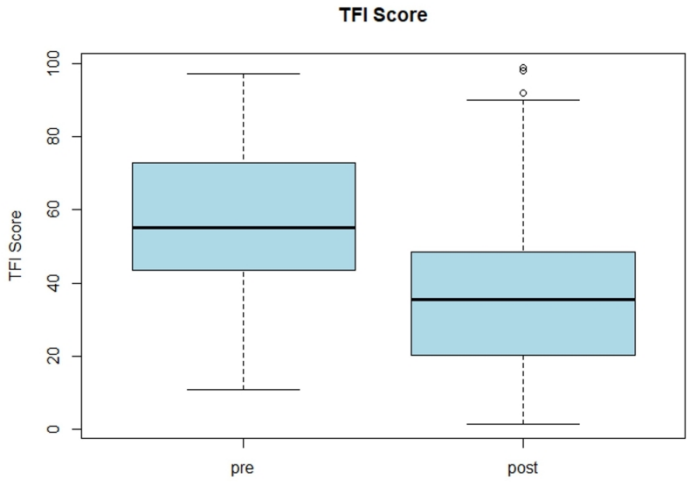

Figure 1

338x190mm (225 x 225 DPI)

Supplementary File 1

Table 1: TRIPOD Checklist – Prediction model development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	6-7
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8-9
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	8-9
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	9
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	10
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	10
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	10
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	10
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	11
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	11
Model development	14a	Specify the number of participants and outcome events in each analysis.	11
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	11-12
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12-15
	15b	Explain how to the use the prediction model.	14-15
Model performance	16	Report performance measures (with CIs) for the prediction model.	14-15
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	18-19
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	15-18
Implications	20	Discuss the potential clinical use of the model and implications for future research.	19
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	9, 11
Funding	22	Give the source of funding and the role of the funders for the present study.	19

Supplementary File 2: Predictor Variables

Table 1: Demographic variables

Variable	Question	Response options
Age	What is your age?	In years Split into dichotomous variables (<=57 years of age and >57 years of age) based on the median
Gender	What is your gender?	Male (1), Female (2)
Education level	What is the highest level of education you have completed?	Highschool or less (1), College (2), Vocational training (3), Bachelor's degree (4), Master's degree or above (5)
Employment type	What best describes your employment?	Manager (1), Professional (2), Technical (3), Administrative (4), Skilled tradesman (5), Service occupation (6), Medical (7), Sales (8), Home maker (9), Student (10), Retired (11), Unemployed (12)
Loud noise exposure	Have you been exposed to loud noise?	Yes (1) , No (0)
Diagnosed with psychological condition	Have you been presently diagnosed with any psychological conditions including anxiety and depression?	Yes (1) , No (0)
Work less due to tinnitus	Do you work less because of your tinnitus?	No (0), Reduced hours (1), Stopped work (2), Disability allowance (3)

Table 2: Tinnitus and hearing-related variables

Variable	Question	Response options
Baseline tinnitus severity	Measured using the Tinnitus Functional Index (TFI)	Scores range from 0 to 100. Split into dichotomous variables (<=55.2 and >55.2) based on the median
Tinnitus duration	How long have you had tinnitus for?	In years Split into dichotomous variables (<=10.00 years and >10.00 years) based on the median
How often is tinnitus heard?	How often is tinnitus heard?	Occasionally (1), When taking out my hearing aid(s) (2), At night (3), Most of the time (4), All the time (5)
Tinnitus location	Where do you notice your tinnitus?	One ear (1), Both ears (2), In my head (3), Unsure (4), Other (5)

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Type of tinnitus (9 different types)	▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsing ▪ Clicking ▪ Music ▪ Voices ▪ Humming	For each item: Yes (1) , No (0)
Multiple tones heard	This variable is computed based on responses to types of tinnitus. Answer yes to multiple types of tinnitus was considered as multiple tones heard	Yes (1) , No (0)
Presence of a hearing loss	Do you have a hearing loss?	No (0), Both ears (1), One ear (2), Unsure (3)

Table 3: Treatment-related variables

Variable	**Question**	**Response options**
Past treatment sought	Have you received treatment for tinnitus in the past?	Yes (1) , No (0)
Sounds can distract from tinnitus	How well can sounds around you distract you from your tinnitus or make the tinnitus less noticeable?	Fully (1), Partially (2), Not at all (3)
Hearing aid use	Do you wear hearing aid(s) or any other amplification devices?	No (0), One ear (1), Both ears (2)
Medication use	Do you currently take any medications?	Yes (1) , No (0)

Table 4: Clinical factors

Variable	**Questionnaire**	**Number of items/ Response options**	**Score**
Anxiety	General Anxiety Disorders (GAD-7)	7-items 4-point scale with "not at all" (score of 0) to "nearly every day" (score of 3)	Higher number indicates more severe anxiety (scores range between 0–21). The total score is interpreted as follows: ▪ 0–4: minimal anxiety ▪ 5–9: mild anxiety ▪ 10–14: moderate anxiety ▪ 15–21: severe anxiety Split into dichotomous variables (<=9 no anxiety and >9 anxiety)
Depression	Patient Health Questionnaire (PHQ-9)	9-items 4-point scale with "not at all" (score of	Higher number indicates more severe depression (scores range between 0–27).

		0) to "nearly every day" (score of 3)	The total score is interpreted as follows: ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression Split into dichotomous variables (<=14 no depression and >14 depression)
Insomnia	Insomnia Severity Index (ISA)	7-item 5-point scale with "no problem" (score of 0) to "very severe problem" (score of 4)	Higher number indicates more severe insomnia (scores range between 0–28). The total score is interpreted as follows: ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) Split into dichotomous variables (<=14 no insomnia and >15 insomnia)
Hyperacusis	Hyperacusis Questionnaire (HQ)	14-items 4-point scale with "no" (score of 0) to "yes, a lot" (score of 3)	Higher number more severe hyperacusis (scores range between 0–42). The total score is interpreted as follows: ▪ >28: strong hypersensitivity Split into dichotomous variables (<=28 no hyperacusis and >28 hyperacusis)
Hearing disability	Hearing Handicap Inventory for Adults – Screening (HHIA-S)	10-items 3-point scale with "yes" (score of 4) to "no" day (0)	Higher number more severe hearing disability (scores range between 0–40). The total score is interpreted as follows: ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability Split into dichotomous variables (<=8 no hearing disability and >=10 hearing disability)

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Cognitive failures	Cognitive Failures Questionnaire (CFQ)	25-items 5-point scale with "never" (score of 0) to "very often" (score of 4)	Higher scores indicate more difficulties (cognitive failures) in perception, memory, and motor function (score range 0–100). The total score is interpreted as follows: The scores range 0–100 with higher scores indicating more cognitive failures/problems (or reduced cognitive functioning). Split into dichotomous variables (<=32 no cognitive problems and >32 cognitive problems)
Life satisfaction	Satisfaction with Life Scale (SWLS)	5-items 7-point scale with "strongly disagree" (score of 1) to "strongly agree" (7)	Higher number indicated more satisfaction with life (scores range between 5–35). The total score is interpreted as follows: ▪ 0–9: extremely dissatisfied ▪ 10–14: dissatisfied ▪ 15–19: below average satisfaction ▪ 20–24: average satisfaction ▪ 25–29: high satisfaction ▪ 30–35: highly satisfied Split into dichotomous variables (<=19 life satisfaction and >19 high satisfaction)

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Supplementary File 3: Univariate analysis to examine association between predictor variables and outcome variable

Table 1: Participant demographic characteristics (n=228)

Characteristic	N (%)	Mean (SD)
Demographic characteristics		
Age (in years)		55.14 (12.92)
Gender		
▪ Female	98 (43%)	
▪ Male	130 (57%)	
Highest level of education		
▪ High school or below	59 (26%)	
▪ College	47 (21%)	
▪ Vocational training	31 (14%)	
▪ Bachelor's degree	61 (27%)	
▪ Masters degree or above	30 (13%)	
Employment		
▪ Manager	27 (12%)	
▪ Professional	46 (20%)	
▪ Technical	13 (6%)	
▪ Administrative	17 (7%)	
▪ Skilled tradesman	11 (5%)	
▪ Service occupation	11 (5%)	
▪ Medical	6 (3%)	
▪ Sales	8 (3%)	
▪ Homemaker	4 (2%)	
▪ Student	1 (0%)	
▪ Retired	73 (32%)	
▪ Unemployed	11 (5%)	
Loud noise exposure		
▪ Yes	103 (45%)	
▪ No	125 (55%)	
Diagnosed with a psychological condition		
▪ Yes	50 (22%)	
▪ No	178 (78%)	
Working less due to tinnitus		
▪ Reduced hours	8 (4%)	
▪ Stopped work	32 (14%)	
▪ Disability allowance	7 (3%)	
▪ No	181 (79%)	
Tinnitus and hearing-related characteristics		
Baseline tinnitus severity (measured using Tinnitus Functional Index)		57.93 (19.17)
Tinnitus duration (in years)		17.68 (19.42)
How often tinnitus is heard		

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▪ Occasionally	4 (2%)	
▪ When taking out my hearing aid(s)	3 (1%)	
▪ At night	4 (2%)	
▪ Most of the time	63 (27%)	
▪ All the time	154 (68%)	
Tinnitus location		
▪ One ear	61 (27%)	
▪ Both ears	109 (48%)	
▪ In my head	34 (15%)	
▪ Other location	3 (1%)	
▪ Unsure	21 (9%)	
Type of tinnitus sound (answering Yes)		
▪ Ringing	71 (31%)	
▪ Buzzing	75 (33%)	
▪ High pitched sound	130 (57%)	
▪ Low pitched sound	16 (7%)	
▪ Pulsating	28 (12%)	
▪ Clicking	14 (6%)	
▪ Music	4 (2%)	
▪ Voices	3 (1%)	
▪ Humming	21 (9%)	
Multiple sounds heard		
▪ Yes	73 (32%)	
▪ No	155 (68%)	
Presence of a hearing loss		
▪ No	49 (21%)	
▪ Both ears	104 (46%)	
▪ One ear	46 (20%)	
▪ Unsure	29 (13%)	
Treatment-related characteristics		
Past tinnitus treatment sought		
▪ Yes	58 (25%)	
▪ No	170 (75%)	
Sounds can distract from tinnitus		
▪ Fully	26 (11%)	
▪ Partially	178 (78%)	
▪ Not at all	24 (10%)	
Hearing aid use		
▪ No	159 (70%)	
▪ Unilateral	19 (8%)	
▪ Bilateral	50 (22%)	
Medication use		
▪ Yes	130 (57%)	
▪ No	98 (43%)	

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Table 2: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the demographic predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Age	>57 years	0.85 (0.50, 1.47)	0.57
	<=57 years	Ref	
Gender	Female	1.12 (0.64, 1.94)	0.70
	Male	Ref	
Education level	College	0.61 (0.31, 1.42)	**0.01***
	Vocational training	1.70 (0.75, 4.88)	
	Bachelor's degree	1.30 (0.67, 2.92)	
	Master's degree or above	**3.47 (1.32, 12.51)**	
	High school or less	Ref	
Employment type	Professional	0.59 (0.25, 1.82)	0.95*
	Technical	0.40 (0.13, 1.89)	
	Administrative	0.40 (0.14, 1.66)	
	Skilled tradesman	0.56 (0.18, 3.00)	
	Service occupation	0.80 (0.24, 4.66)	
	Medical	1.00 (0.22, 11.54)	
	Sales	0.80 (0.21, 6.00)	
	Home maker	0.27 (0.06, 3.00)	
	Student	0.40 (0.05, 35.47)	
	Retired	0.74 (0.32, 2.12)	
	Unemployed	0.80 (0.24, 4.66)	
	Manager	Ref	
Loud noise exposure	Yes	0.80 (0.46, 1.38)	0.43
	No	Ref	
Presence of a psychological condition	Yes	1.72 (0.85, 3.46)	0.13
	No	Ref	
Work less due to tinnitus	Reduced hours	1.05 (0.31, 6.18)	0.89*
	Stopped work	0.81 (0.41, 1.89)	
	Disability allowance	0.53 (0.16, 2.88)	
	No	Ref	

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Table 3: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the tinnitus and hearing-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Baseline tinnitus severity	>55.2	**2.65 (1.50, 4.67)**	**0.001**
	<=55.2	Ref	
Tinnitus duration	>10.00 years	1.16 (0.66, 2.02)	0.60
	<=10.00 years	Ref	
How often tinnitus is heard	When taking out my hearing aid(s)	0.67 (0.02, 18.06)	0.19*
	At night	0.33 (0.02, 6.65)	
	Most of the time	0.39 (0.04, 3.96)	
	All the time	0.76 (0.08, 7.49)	
	Occasionally	Ref	
Tinnitus location	Both ears	1.41(0.48, 4.16)	0.90*
	In my head	0.94 (0.48, 1.80)	
	Unsure	1.35 (0.55, 3.34)	
	Other	1.13 (0.10,13.16)	
	One ear	Ref	
Tinnitus type: Ringing	Yes	1.30 (0.72, 2.37)	0.38
	No	Ref	
Tinnitus type: Buzzing	Yes	1.34 (0.74, 2.42)	0.32
	No	Ref	
Tinnitus type: High pitch	Yes	0.76 (0.44, 1.33)	0.34
	No	Ref	
Tinnitus type: Low pitch	Yes	0.89 (0.31, 2.56)	0.83
	No	Ref	
Tinnitus type: Pulsing	Yes	0.97 (0.42, 2.21)	0.94
	No	Ref	
Tinnitus type: Clicking	Yes	0.52 (0.17, 1.53)	0.23
	No	Ref	
Tinnitus type: Music	Yes	1.63 (0.17, 15.98)	1.00*
	No	Ref	
Tinnitus type: Voices	Yes	0.09 (0.00, 1.75)	0.04*
	No	Ref	
Tinnitus type: Humming	Yes	0.56 (0.23, 1.39)	0.21
	No	Ref	
Multiple tones heard	Yes	1.15 (0.64, 2.08)	0.63
	No	Ref	
Presence of a hearing loss	Both ears	1.20 (0.59, 2.41)	0.92
	One ear	1.19 (0.51, 2.74)	
	Unsure	1.41 (0.53, 3.73)	
	No	Ref	

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Table 4: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the treatment-related predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Crude Odds Ratio (95% CIs)**	**P-Value**
Past treatment sought	Yes	0.94 (0.50, 1.74)	0.83
	No	Ref	
Sounds can distract	Partially	**4.34 (1.82, 10.34)**	**0.001**
	Not at all	**3.15 (0.99, 10.00)**	
	Fully	Ref	
Hearing aid use	One ear	**1.57 (0.61, 5.49)**	**0.26**
	Both ear	0.69 (0.38, 1.39)	
	No	Ref	
Medication use	Yes	1.22 (0.71, 2.12)	0.46
	No	Ref	

Table 5: Univariate analysis with the Chi-square/ Fishers exact test results on the association between the clinical factors predictor categories and outcome variable (success as defined by a TFI-score changes >=13 points or a failure). *Indicates use of Fisher's exact test results due to less than 5 cases in subcategories.

Predictor variable	**Sub-Categories**	**Odds Ratio (95% CIs)**	**P-Value**
Anxiety	Yes	1.53 (0.83, 2.82)	0.17
	No	Ref	
Depression	Yes	1.54 (0.62, 3.83)	0.35
	No	Ref	
Insomnia	Yes	1.27 (0.72, 2.23)	0.41
	No	Ref	
Hyperacusis	Yes	1.21 (0.56, 2.63)	0.62
	No	Ref	
Hearing disability	Yes	1.37 (0.77, 2.43)	0.28
	No	Ref	
Cognitive functions	Yes	0.99 (0.56, 1.74)	0.97
	No	Ref	
Life satisfaction	Yes	0.76 (0.44, 1.33)	0.34
	No	Ref	

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