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

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3 **Predictors of outcomes of internet-based cognitive behavioral therapy**
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6 **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 secondary 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 tinnitus 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 tinnitus 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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3 advanced artificial intelligence and machine learning techniques to identify possible predictive
4 factors.
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10 **Key Words**

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12 Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive
13 behavioral therapy
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20 **Strengths and limitations of the study**

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22 ▪ This study examines the predictors of ICBT on individuals with tinnitus from a pooled
23 sample of several clinical trials.
- 24
25 ▪ Homogeneity of participants in the included studies may be the main reason for not having
26 any strong predictors of outcomes.
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28 ▪ The study sample size and also limited number of potential predictors may have also
29 contributed to not finding any strong predictors of ICBT outcome.
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38 **Introduction**

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41 Tinnitus is the perception of sounds in the absence of external stimulation and is often heard as a
42 ringing or buzzing meaningless sound(s). It is a very common condition with at least 15% of
43 the adult population having tinnitus.¹ Tinnitus is highly heterogeneous, both in the way it
44 manifests as well as in the manner those with tinnitus respond to treatment options.² Most
45 individuals with tinnitus are not much bothered by the sounds, but a proportion (2/10) find
46 tinnitus much distressing and need help to reduce the negative effects of their tinnitus. Although
47 there are several management strategies described in the literature, most are not evidence based.
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3 The main exception is Cognitive Behavioral Therapy (CBT), as indicated in various systematic
4 reviews of randomized controlled trials.³⁻⁶ Clinical practice guidelines, based on research
5 evidence and expert consensus, thus recommends CBT as a management option for individuals
6 with tinnitus and is supported by the American Academy of Otolaryngology – Head and Neck
7 Surgery (AAO-HNS).⁷
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17 Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in
18 their local clinics. For example, a large-scale epidemiological study in the US showed that
19 medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of
20 the time by health professionals, whereas the CBT was discussed as a management option only
21 0.2% of the time.⁸ This is most likely a consequence of the limited number of trained
22 professionals who provide CBT for tinnitus. One solution to overcome this issue is to use
23 Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over
24 the internet with minimal guidance from a tinnitus expert.⁹ A series of controlled studies in
25 Sweden, Germany, the United Kingdom and the United States have demonstrated positive effects
26 of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety,
27 depression, insomnia.⁹ In addition to the changes noted in standardized outcome measures, the
28 qualitative analysis of user experiences has highlighted the perceived benefits of this program.¹⁰
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30 In addition, the improvements noted from ICBT have been maintained for 1-year post-
31 intervention. These results suggest that ICBT is a highly promising approach to provide
32 evidence-based tinnitus management.
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3 Although the previous studies on ICBT have shown favorable results, they have mainly reported
4 group effects. There is limited understanding of who are likely to benefit (or not) from the ICBT
5 intervention. In other words, only a few studies have examined predictors of ICBT outcomes in
6 tinnitus research. For example, the long-term analysis of the previous UK studies suggested that
7 the best predictors of tinnitus improvements at 1-year were the baseline tinnitus severity,
8 engagement with ICBT program (i.e., more modules read), and higher self-reported satisfaction
9 with the intervention.¹¹ Studies in other health areas have also examined the predictors of
10 outcome for a range of internet-based health interventions.¹²⁻¹⁶ These studies have inconsistently
11 identified various demographic as well as disease specific variables that could predict the
12 successful and non-successful participants in internet-interventions.¹⁶ There remains a clear gap
13 in knowledge in terms of predictors of ICBT outcomes for tinnitus.

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

37 38 39 40 41 42 43 44 45 46 47 **Method**

48 49 50 **Study design and participants**

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52 The study was a secondary analysis of data collected three separate ICBT trials. Study
53 participants from the three separate trials with different designs including the single-group
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3 pretest posttest design,¹⁷ an efficacy RCT design (Clinical Trials.gov: NCT02370810),¹⁸ and an
4 effectiveness RCT design (Clinical Trials.gov: NCT02665975)¹⁹ were combined. These studies
5 were conducted during 2016-18. In the efficacy trial, the experimental group underwent ICBT
6 immediately after allocation whereas the control group underwent the same intervention
7 following an 8-week weekly check-in period. In the effectiveness trial, the experimental group
8 underwent the ICBT interevent whereas the control group underwent treatment as usual
9 consisting of in-person tinnitus counselling and sound therapy, provided by the audiologists at
10 three hospital settings. The data from only those who underwent the ICBT intervention was
11 included in this study. The ethical clearance for these studies was obtained from the Faculty of
12 Science and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference:
13 FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research
14 Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project
15 ID: 195565). The study results are presented using the TRIPOD checklist (see Appendix 1).
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35 Combining the data from three trials resulted in inclusion of 228 participants. Of these, 36 were
36 from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the effectiveness
37 trial.
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44 **Intervention**

45 The intervention included a CBT program that was specifically developed for individuals with
46 tinnitus.²⁰ This intervention was originally developed by psychologists in Sweden,²¹ but later
47 adapted by audiologists in the UK²² and the US.²³ The intervention was administered using a
48 secured ePlatform,^{24,25} and presented in a self-help format. The intervention was presented over
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3 8-weeks period, during which the users were given access to 2-3 modules each week. The CBT
4 program was divided into 21 modules, of which 5 were optional. The modules included content
5 such as applied relaxation, thought analysis, cognitive restructuring, imagery, and exposure
6 techniques. Each module included text, images, and videos to enhance user experience. In
7 addition, they included various exercises that users have to complete to engage them in the
8 intervention. Although the intervention was presented in a self-help format, the users had access
9 to minimal guidance from an audiologist (EB). Generally, this included examining weekly
10 exercises users completed and providing feedback as well as answering any questions they may
11 have in the secured messaging system. An average of 10 minutes per participant was spent on
12 providing guidance and support, although some users required more support.
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28 **Outcome measures**

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30 The study participants completed an extensive pre-intervention questionnaire that collected data
31 on demographics, tinnitus-related and treatment-related history. In addition, participants also
32 completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at
33 postintervention (T1) and 2-months follow-up (T2). The *primary outcome measure* included the
34 Tinnitus Functional Index (TFI)²⁶ to assess tinnitus severity/distress. This is a 25-item
35 questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus with
36 no need for intervention, scores ranging between 25 to 50 indicate significant problem with
37 possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly
38 requiring a more intensive intervention. The TFI has good psychometric properties with
39 acceptable internal consistency (0.97) and test-retest reliability (0.8).²⁶
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3 The *secondary outcome measures* included the Insomnia Severity Index (ISI)²⁷ as a measure of
4 insomnia, the Generalized Anxiety Disorder (GAD-7)²⁸ as a measure of anxiety, the Patient
5 Health Questionnaire (PHQ-9)²⁹ as a measure of depression, the Hearing Handicap Inventory for
6 Adults Screening version (HHIA-S)³⁰ as a measure of self-reported hearing disability, the
7 Hyperacusis Questionnaire (HQ)³¹ to assess the presence hyperacusis (i.e., reduced tolerance of
8 everyday sounds), the Cognitive Failures Questionnaire (CFQ)³² was administered to assess
9 cognitive functions, and the Satisfaction with Life Scales (SWLS)³³ to assess the global life
10 satisfaction.
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24 **Patient and public involvement**

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26 No patient involved.
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31 **Variables included in the predictive model**

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33 **Outcome Variable:** The main dependent variable was the pre- and post-intervention change in
34 tinnitus distress based on the TFI score (TFI change). The 13-point change in TFI scores,
35 identified as a clinically meaningful (or significant) change by the original authors²⁶ was used to
36 define a clinically significant intervention outcome.
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44 **Predictor Variables:** Thirty-two variables from the pre-intervention questionnaires were selected
45 as potential predictor (independent) variables based on clinical reasoning and findings from
46 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 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 analyzed using the descriptive statistics as well as univariate and multivariable linear regression and logistic regression models. A careful analysis on missing post TFI scores, with several competing 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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3 identify the effect of the variables on tinnitus reduction post ICBT, while adjusting for the
4
5 baseline tinnitus severity, as a variable previously identified to related to the success of ICBT.¹¹
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7 Prior to the multivariate analyses, the full data set was divided into the training (80%, $n = 183$)
8
9 and testing (20%, $n = 45$). The training data set was used to develop the corresponding
10
11 (linear/multivariate) regression models while the testing data set was used to evaluate the model
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13 predictions. Several competing multivariable models (both linear and logistic) were examined.
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15 The best models were selected based on the lowest mean squared error and the lowest Akaike
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17 Information Criterion (AIC).³⁴ Both crude and model-based odds ratios were calculated and used
18
19 to evaluate the effect of the variable. The Hosmer-Lemeshow goodness-of-fit statistic was
20
21 calculated to assess the calibration of the final model.³⁵ The discriminative ability of the model
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23 was assessed with the area under the curve (AUC). The predictions were evaluated based on the
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25 model accuracy, sensitivity and the specificity on the testing data.
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33 The dependent variable TFI change was used as a continuous variable for a linear regression
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35 analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic
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37 regression analysis. All statistical analyses were performed with R statistical software (Version:
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39 3.6.3). All tests were two sided and threshold at 10% level of significance due to the exploratory
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41 nature of the study to account for the medium sample size and control for both Type I and type II
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43 errors effectively.^{36,37}
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49 **Results**

50 **Participant demographics**

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3 The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects
4 (n=130) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on
5 demographic, tinnitus, hearing-related and treatment related variables are provided in Appendix 3.
6
7 Table 1 presents details on clinical variables. The mean baseline tinnitus severity and tinnitus
8 severity following the ICBT intervention were 57.93 (SD: 19.17) and 34.22 (SD: 22.78),
9
10 respectively. Figure 1 presents the pre- and post-intervention tinnitus severity (TFI) score
11 variation, indicating statistically significant differences between these scores ($p < 0.001$). There
12 were 150 participants (66%) with a 13-point or higher reduction after the intervention.
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24 <Table 1 here>

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26 <Figure 1 here>

27 28 29 30 31 **Univariate Analysis to Examine the Predictors of ICBT Outcome**

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33 The details of the univariate analyses are provided in Appendix 3 (see Tables 3.2 to 3.5). With the
34 exception of education level ($p = .008$), none of the demographic variable were associated with
35 post-intervention tinnitus severity change of 13-point or more. Participants with a master's degree
36 or above had the highest odds of having a larger severity change score, with an odds ratio of 4.50
37 (95% C.I: 1.59, 18.47), compared to the participants who had education only up to high school or
38 less. In terms of tinnitus and hearing-related variables, the baseline tinnitus severity ($p = 0.04$)
39 was significantly associated with treatment success. Participants who had a higher baseline tinntus
40 severity (i.e., TFI scores of greater than or equal to 55.2) had a significantly higher odds of
41 treatment success (OR: 1.78) compared to those who had a baseline severity less than 55.2.
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3 In terms of the treatment-related variables, sounds can distract ($p = .027$) showed a significant
4 association with treatment success. Those who reported to be distracted by the sound partially
5 (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
6 of having a successful treatment outcome when compared to who were fully distracted. However,
7 the odds among the participants who used hearing aid either in one ear or both ears compared to
8 those who did not, was not statistically significantly different (Table 3.4 in Appendix 3). None of
9 the clinical factors were significantly associated with outcome.
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22 **Multivariate analyses to examine predictors of ICBT outcome**

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24 Multivariate linear regression analysis was used to identify contributing predictors of TFI change.
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26 The variables that were included in the final regression model are shown in Table 2. Working less
27 due to tinnitus ($p = .004$), hearing aid usage ($p = .04$), maskability of tinnitus ($p = .05$), baseline
28 tinnitus severity ($p < .001$), music type of tinnitus ($p = .003$), education level ($p = .018$), loud noise
29 exposure ($p = .09$), and depression ($p = .02$) showed significant associations with outcome (TFI
30 change). Modified models with the variables gender ($p = .10$), hearing loss ($p = .23$), tinnitus type:
31 buzzing ($p = .43$), tinnitus type: low pitch ($p = .10$), tinnitus type: pulsing ($p = 0.64$), tinnitus type:
32 clicking ($p = .27$), insomnia ($p = .26$) and satisfaction with life ($p = .82$) were not statistically
33 significant. Moreover, several two-way interactions were tested. We did not find any gender
34 interactions with regard to the maskability of sounds ($p = .42$) and) and hearing aid usage
35 variables ($p = .44$). The overall model fit was evident with R squared = 0.35 and Adj. R squared
36 of 0.30. The final model resulted in a root mean square of 25.38 on the testing data set, indicating
37 a better predictive power. All required regression assumptions were satisfied in the selected
38 model.
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5 This model helped in identifying the impact on the TFI score with several predictor variables, as a
6 result of the ICBT intervention. Participants with depression had approximately 12 points (SE:
7 4.79) expected reduction in their TFI score. Moreover, participants who had master's degree or
8 above compared to participants who had college education showed expected reduction of 10-point
9 (SE: 4.20) in their TFI score. Participants who used hearing aid for one ear had an expected TFI
10 reduction of 8.95 (SE: 4.42) compared to those who did not use hearing aids. However,
11 participants who used hearing aid for both ears did not show a significant difference in their TFI
12 reduction (p -value: 0.50) compared to those who did not use any. Those who got distracted
13 partially compared to those who were fully distracted showed an expected TFI reduction of 8.42
14 (SE: 4.42) after the treatment. Nevertheless, participants who were not distract at all did not show
15 a significant TFI reduction compared to those who were fully distracted. Also, participants who
16 described that their tinnitus had a musical quality had the least expected reduction (-51.52,
17 SE:16.87) in their TFI score with the treatment, followed by participants who were working less
18 with disability allowance due to their tinnitus (-21.33, SE:7.21). Participants who had loud noise
19 exposure compared to those who did not also showed an increase in their TFI score (-4.32, SE:
20 2.58).

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49 Following this, multivariable logistic regressions were performed with 13-point change in TFI
50 following ICBT intervention (i.e., treatment success) as the dependent variable (see Table 3). In
51 this analysis, hearing aid usage ($p = .05$), baseline tinnitus severity ($p < 0.001$), clicking type of
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3 tinnitus ($p = .03$), low pitch type of tinnitus ($p = .03$), education level ($p = .001$), and the presence
4 of insomnia ($p = .05$) were identified as significant predictors. This model had an AIC of 220.87.
5
6 Modified models to the prior model with the variables gender ($p = .94$), presence of a hearing
7 loss ($p = .73$), tinnitus being masked by sounds ($p = .33$), work less due to tinnitus ($p = .29$),
8 buzzing type of tinnitus ($p = 0.15$), pulsing type of tinnitus ($p = 0.73$), musical type of tinnitus (p
9 = .12), loud noise exposure ($p = .60$), depression ($p = .88$), and satisfaction with life ($p = .70$),
10 separately, were not statistically significant. Several two-way interactions were tested but were
11 not statistically significant, including any gender differences regarding sounds masking tinnitus
12 ($p = .67$) and hearing aid usage variables ($p = .82$).
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26 The multivariable model adjusted OR (see Table 3) for the participants who were using a hearing
27 aid in one ear had a 5.48 higher odds (95% CI: 1.02, 29.37) of having a successful outcome with
28 ICBT intervention compared to the participants who did not use any hearing aid help while there
29 was no significant difference between the subjects who use hearing aid in both ears compared to
30 those who do not use any (OR: 0.72 95% CI: 0.33, 1.60). Participants who had master's level or
31 above education compared to those who had high school education or less also showed 10.71
32 higher odds (95% CI: 2.28, 50.22) of having successful outcome. Participants who had either low
33 pitch (OR: 0.16; 95% CI: 0.03, 0.87) or clicking (OR: 0.19; 95% CI: 0.04, 0.82) tinnitus types
34 had significant lower odds of having successful outcome with the ICBT intervention.
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46 Participants with insomnia also had a 0.55 lower odds of success (95% CI: 0.20, 0.99) compared
47 to those who did not .
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3 The Hosmer-Lemeshow goodness-of-fit test confirmed a better fit in the current model with a p -
4 value of 0.53 ($\chi^2=7.10$, $df=8$). This model had an AUC of 0.747 and lead to 77.8% accuracy,
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8 80.0% specificity, and 76.7% sensitivity in the testing data set with a cut-off 0.50.
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17 Fewer variables were statistically significant in the logistic regression model which identified
18 influencing predictors of the ICBT success. Although depression was identified as a key predictor
19 for reducing tinnitus severity in the linear regression model, it was not identified as a key
20 predictor in the multivariate model. Moreover, loud noise exposure was barely significant in the
21 regression model and was not statistically significant in the logistic regression model. This was
22 due to the fact that the logistic regression model evaluated predictors of treatment successes (i.e.,
23 13 point change), while the multivariate regression model identified the predictors of a
24 significant TFI reductions.
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38 Discussion

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40 Accessible and affordable tinnitus interventions are needed to alleviate the tinnitus distress as well
41 as comorbid problems with anxiety, depression and insomnia. The current study examined
42 predictors of outcomes in ICBT. In this exploratory study only a limited number of variables were
43 identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points following
44 undertaking an ICBT intervention and the results varied depending on the model used. Only
45 educational level and using one hearing aid were predictors in both linear and logistic models.
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54 Other variables that were significant in either the linear or logistic models included: demographic
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3 variables (i.e., working less due to tinnitus, loud noise exposure), tinnitus related variables (i.e.,
4 tinnitus maskability, types of tinnitus) and treatment related variables (i.e., hearing aid use) and
5 clinical variables (i.e. higher levels of depression, insomnia) when controlling for baseline tinnitus
6 severity. These key findings are discussed below.
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15 In terms of demographic variables, education level was found to be a significant predictor of
16 ICBT success as those with a master's education or higher had higher odds of having a successful
17 outcome compared with those with high school education in both the linear and logistic models.
18 This was expected as having good literacy skills is essential when understanding the intervention
19 materials. The intervention materials used in these studies were written at an average of 9th
20 reading grade level,²³ suggesting that they were not easily accessible for participants with only a
21 high school education. These results highlight the importance of health literacy considerations
22 when developing text-based self-help interventions such as ICBT. Additionally, those reported to
23 be working less due to tinnitus were at a lower odds of having a successful outcome. Those
24 working less because of tinnitus have previously been identified as having higher tinnitus
25 severity.³⁸ Closely monitoring the effects of tinnitus is important to ensure that tinnitus can be
26 managed so that individuals are still able to work effectively.
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45 When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to
46 be a significant predictor of ICBT success, as seen in previous studies.¹¹ Tinnitus perceptions vary
47 greatly and in this study those with tinnitus presenting as musical, lower pitched or clicking were
48 less likely to have a positive outcome of ICBT. This finding certainly needs further exploration as
49 the limited number of participants in each group of tinnitus perception. One of the CBT
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3 intervention aims is to help participants to reinterpret their tinnitus to a less threatening sound. It
4 may be that these sounds are not easily likened to everyday sounds than other types of tinnitus
5 (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation strategies.
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12 Of the four treatment related variables, only those who reported to use of wearing one hearing aid
13 were found to be at better odds of ICBT success. This finding need further exploration as to
14 identify other characteristics that may be associated with outcome such as having tinnitus in only
15 one ear. Although the evidence for use hearing aids alone for tinnitus management is limited,^{39,40}
16 hearing aids may for some reduce the tinnitus percept and aid communication difficulties.⁴¹
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18 Ensuring hearing loss is addressed in addition to provision of ICBT may lead to more optimal
19 outcomes for those with co-existing hearing loss.
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31 Regarding studying the clinical factors, those with higher levels of depression were found to have
32 higher reduction in the TFI score. However, the participants with insomnia showed lower odds of
33 success. This may be because those with clinical depression and sleepproblems have higher
34 baseline tinnitus severity.³⁸ Our previous studies have shown that participants with higher
35 baseline tinnitus are more likely to benefit from ICBT.¹¹ These observations strengthen the
36 argument that those with more severe tinnitus are more likely to need more intensive
37 interventions.²⁶ Interestingly, other clinical factors including anxiety, hyperacusis, hearing
38 disability as well as cognitive functioning were not significant predictors of ICBT in the current
39 study.
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3 Studies in other health areas have also examined the predictors of a range of internet-based health
4 interventions.¹²⁻¹⁵ Generally higher baseline symptoms predict an increased treatment response,
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6 for example in anxiety and depression,⁴² and higher obsessive-compulsive behaviours when
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8 treating obsessive-compulsive disorder.⁴³ Variables such as age and gender have been mentioned
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10 as significant predictors for some ICBT interventions.^{15,42} Most previous ICBT interventions have
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12 not identified pre-treatment characteristics to predict or moderate outcomes.¹⁶ Most ICBT studies
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14 have indicated that ICBT works irrespective of treatment history.⁴² Contrarily, previous treatment
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16 has shown worse outcomes in some previous studies.⁴⁴ However, it may be that some participants
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18 may have sought alternative therapies which have no evidence for tinnitus. For this reason, it
19
20 would be useful to examine specific types of previous treatments in future studies to distinguish
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22 between those who had evidence-based interventions before enrolling to ICBT than those who did
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33 **Study limitations and future research**

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35 The current study was to our knowledge the first study to combine data from multiple studies to
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37 examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study
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39 may have included homogeneous group of tinnitus patients due to study inclusion/exclusion
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41 criteria and may not have included all the possible variables (e.g., health literacy, acceptability
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43 and motivation of users, satisfaction from the intervention, intervention engagement) that may
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45 have played a role in ICBT outcome. Second, the sample size remained relatively small when
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47 compared to the number of predictive factors included. Third, multivariate analyses may have
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49 some limitations in terms of examining the complex relationships. Moreover, due to the high
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51 multicollinearity between the predictor variables, there were several competing models which had
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3 lead to the same prediction accuracies and root mean square errors. Additionally, these linear
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5 models lack in identifying any predictor variables that has a non-linear relationship with the
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7 response variables. For these reasons, the study results must be viewed as preliminary. Future
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9 studies may benefit from using artificial intelligence and machine learning techniques to examine
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11 the complex relationship between the variables in predicting the ICBT outcomes. Analyses should
12
13 be extended with non-linear models like decision trees, support vector machines and neural
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15 networks. Future studies could also examine the predictors of adherence and engagement to
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17 intervention as well as of dropouts.
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36 **Twitter**

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38 @VManchaiah, @Eldre7, @profGergardA
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43 **Contributors**

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45 HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected
46
47 the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript.
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49 All authors read and approved the final manuscript.
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54 **Competing interests**

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3 None to declare.
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8 **Patient consent for publication**

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10 Not required.
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14 **Data availability statement**

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16 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) |

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 tinnitus: Partially | 8.42 | 4.33 | 0.053 |
| Sounds mask tinnitus: Not at all | 0.07 | 5.93 | 0.99 |
| Baseline tinnitus 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: Bachelor'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 | | |

| | | | |
|--------------------------|-------|------|--------------|
| 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 tinnitus 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: Bachelor'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) |

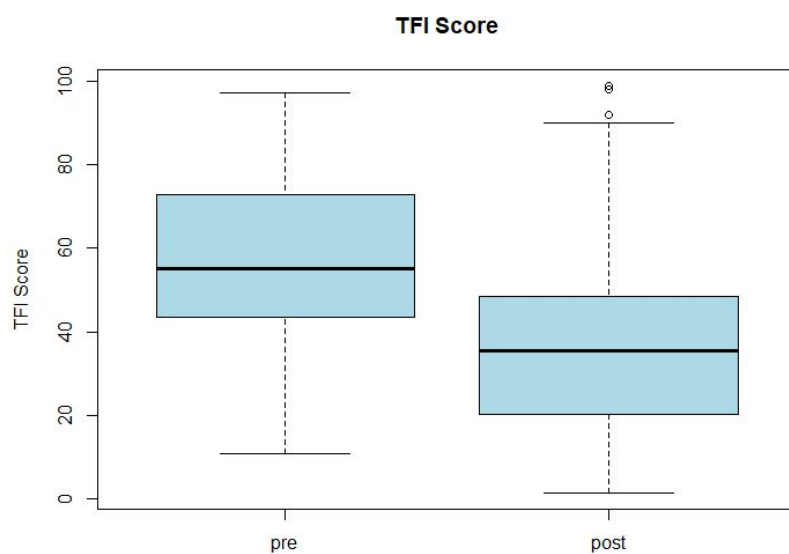
Figure Legends

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.



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 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.

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) |

| | | |
|--------------------------------------|--|--|
| Type of tinnitus (9 different types) | <ul style="list-style-type: none"> ▪ 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: <ul style="list-style-type: none"> ▪ 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) | <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression <p>Split into dichotomous variables (≤ 14 no depression and > 14 depression)</p> |
| Insomnia | Insomnia Severity Index (ISA) | <p>7-item</p> <p>5-point scale with “no problem” (score of 0) to “very severe problem” (score of 4)</p> | <p>Higher number indicates more severe insomnia (scores range between 0–28).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) <p>Split into dichotomous variables (≤ 14 no insomnia and > 15 insomnia)</p> |
| Hyperacusis | Hyperacusis Questionnaire (HQ) | <p>14-items</p> <p>4-point scale with “no” (score of 0) to “yes, a lot” (score of 3)</p> | <p>Higher number more severe hyperacusis (scores range between 0–42).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ > 28: strong hypersensitivity <p>Split into dichotomous variables (≤ 28 no hyperacusis and > 28 hyperacusis)</p> |
| Hearing disability | Hearing Handicap Inventory for Adults – Screening (HHIA-S) | <p>10-items</p> <p>3-point scale with “yes” (score of 4) to “no” day (0)</p> | <p>Higher number more severe hearing disability (scores range between 0–40).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability <p>Split into dichotomous variables (≤ 8 no hearing disability and ≥ 10 hearing disability)</p> |

| | | | |
|--------------------|--|--|--|
| 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: <ul style="list-style-type: none"> ▪ 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) |

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 | 98 (43%) | |
| ▪ Male | 130 (57%) | |
| Highest level of education | | |
| ▪ High school or below | 59 (26%) | |
| ▪ College | 47 (21%) | |
| ▪ Vocational training | 31 (13%) | |
| ▪ Bachelor's degree | 61 (26%) | |
| ▪ Masters degree or above | 30 (13%) | |
| Employment | | |
| ▪ Manager | 27 (12%) | |
| ▪ Professional | 46 (20%) | |
| ▪ Technical | 16 (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 | | |

| | | |
|---|--|--|
| <ul style="list-style-type: none"> ▪ Occasionally ▪ When taking out my hearing aid(s) ▪ At night ▪ Most of the time ▪ All the time | 4 (2%) 3 (1%) 4 (2%) 63 (27%) 154 (68%) | |
| Tinnitus location <ul style="list-style-type: none"> ▪ One ear ▪ Both ears ▪ In my head ▪ Other location ▪ Unsure | 61 (27%) 109 (48%) 34 (15%) 3 (1%) 21 (9%) | |
| Type of tinnitus sound (answering Yes) <ul style="list-style-type: none"> ▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsating ▪ Clicking ▪ Music ▪ Voices ▪ Humming | 71 (31%) 75 (33%) 130 (57%) 16 (7%) 28 (12%) 14 (6%) 4 (2%) 3 (1%) 21 (9%) | |
| Multiple sounds heard <ul style="list-style-type: none"> ▪ Yes ▪ No | 73 (32%) 155 (68%) | |
| Presence of a hearing loss <ul style="list-style-type: none"> ▪ No ▪ Both ears ▪ One ear ▪ Unsure | 49 (21%) 104 (46%) 46 (20%) 29 (13%) | |
| Treatment-related characteristics | | |
| Past tinnitus treatment sought <ul style="list-style-type: none"> ▪ Yes ▪ No | 58 (25%) 170 (75%) | |
| Sounds can distract from tinnitus <ul style="list-style-type: none"> ▪ Fully ▪ Partially ▪ Not at all | 26 (11%) 178 (78%) 24 (10%) | |
| Hearing aid use <ul style="list-style-type: none"> ▪ No ▪ Unilateral ▪ Bilateral | 159 (70%) 19 (8%) 50 (22%) | |
| Medication use <ul style="list-style-type: none"> ▪ Yes ▪ No | 130 (57%) 98 (43%) | |

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) |
| 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 | |

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) | |
| Tinnitus location | Occasionally | Ref | |
| | 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) | |
| Tinnitus type: Ringing | 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) | |

| | | | |
|--|----|-----|--|
| | 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 | |

BMJ Open

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

| | |
|---------------------------------|--|
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| Secondary Subject Heading: | Ear, nose and throat/otolaryngology, Communication, Mental health, Patient-centred medicine, Research methods |
| Keywords: | Audiology < OTOLARYNGOLOGY, Adult otolaryngology < OTOLARYNGOLOGY, Depression & mood disorders < PSYCHIATRY |
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3 1 **Internet-based cognitive-behavioral therapy for tinnitus: Secondary analysis**
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6 2 **to examine predictors of outcomes**
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11 4 **Hansapani Rodrigo,¹ Eldré W. Beukes,^{2,3} Gerhard Andersson,^{4,5} & Vinaya Manchaiah,^{2,6}**
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24 **Abstract**

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

27 **Design:** Secondary analysis of intervention studies.

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

29 **Participants:** 228 individuals who underwent ICBT.

30 **Interventions:** ICBT.

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

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

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3 47 **Conclusions:** Predictors of intervention outcome can be used as a means of triaging patients to
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5 48 the most suited form of treatment to achieve optimal outcomes and to make healthcare savings.
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7 49 Future studies should consider including a heterogeneous group of participants as well as other
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9 50 predictor variables that might have not included in the current study.
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15 52 **Key Words**

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17 53 Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive
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19 54 behavioural therapy
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24 56 **Strengths and limitations of the study**

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27 57
 - This study investigated if there are predictors of outcomes for ICBT for tinnitus.
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 - Analysis included univariate, multivariable and logistic regression models.
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 - The results were hampered by homogeneity of the participants undertaking ICBT.
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 - Results may be biased by the sample size and number of predictors included in the
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35 61 model.
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66 Introduction

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

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

80
81 Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in
82 their local clinics. For example, a large-scale epidemiological study in the US showed that
83 medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of
84 the time by health professionals, whereas the CBT was discussed as a management option only
85 0.2% of the time.⁸ This is most likely a consequence of the limited number of trained
86 professionals who provide CBT for tinnitus. One solution to overcome this issue is to use
87 Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over
88 the internet with minimal guidance from a tinnitus expert.⁹ A series of controlled studies in

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3 89 Sweden, Germany, the United Kingdom, and the United States have demonstrated positive
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5 90 effects of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety,
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7 91 depression, insomnia.⁹ In addition to the changes noted in standardized outcome measures, the
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9 92 qualitative analysis of user experiences has highlighted the perceived benefits of this program.¹⁰
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12 93 In addition, the improvements noted from ICBT have been maintained for 1-year post-
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14 94 intervention.¹¹ . These results suggest that ICBT is a highly promising approach to provide
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16 95 evidence-based tinnitus management.
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21 97 Although the previous studies on ICBT have shown favourable results, they have mainly
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23 98 reported group effects. There is limited understanding of who is likely to benefit (or not) from
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25 99 the ICBT intervention. In other words, only a few studies have examined predictors of ICBT
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27 100 outcomes in tinnitus research. For example, the long-term analysis of the previous UK studies
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29 101 suggested that the best predictors of tinnitus improvements at 1-year were the baseline tinnitus
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31 102 severity, engagement with ICBT program (i.e., more modules read), and higher self-reported
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33 103 satisfaction with the intervention.¹¹ Studies in other health areas have also examined the
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35 104 predictors of outcome for a range of internet-based health interventions.¹²⁻¹⁶ These studies have
36
37 105 inconsistently identified various demographic as well as disease-specific variables that could
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39 106 predict the successful and non-successful participants on internet interventions.¹⁶ There remains
40
41 107 a clear gap in knowledge in terms of predictors of ICBT outcomes for tinnitus.
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49 109 Predictors of intervention outcomes may help triage patients to the most suitable tinnitus
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51 110 intervention. If interventions are recommended based on their suitability, it can potentially
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53 111 improve the outcomes, which would result in healthcare savings. The objective of the current
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3 112 study was to examine the predictors of outcomes of ICBT intervention for individuals with
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5 113 tinnitus based on the secondary analysis of the pooled results from the three-phase clinical trial
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8 114 undertaken in the UK.
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116 **Method**

117 **Study design and participants**

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

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3 135 sharing policy. The ethical clearance for these studies was obtained from the Faculty of Science
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5 136 and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference:
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7 137 FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research
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9 138 Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project
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11 139 ID: 195565). The study results are presented using the TRIPOD checklist (see Supplementary
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14 140 file 1).

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19 142 Combining the data from three trials resulted in the inclusion of 228 participants. Of these, 36
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21 143 were from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the
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23 144 effectiveness trial.

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27 28 146 **Intervention**

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31 147 The intervention included a CBT program that was specifically developed for individuals with
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33 148 tinnitus.²⁰ This intervention was originally developed by psychologists in Sweden,²¹ but later
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35 149 adapted by audiologists in the UK²² and the US.²³ The intervention was administered using a
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37 150 secured ePlatform,^{24,25} and presented in a self-help format. The intervention was presented over
38
39 151 an 8-weeks period, during which the users were given access to 2-3 modules each week. The
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41 152 CBT program was divided into 21 modules, of which 5 were optional. The modules included
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43 153 content such as applied relaxation, thought analysis, cognitive restructuring, imagery, and
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45 154 exposure techniques. Each module included text, images, and videos to enhance the user
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47 155 experience. In addition, they included various exercises that users have to complete to engage
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49 156 them in the intervention. Although the intervention was presented in a self-help format, the users
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53 157 had access to minimal guidance from an audiologist (EB). Generally, this included examining

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3 158 weekly exercises users completed and providing feedback as well as answering any questions
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5 159 they may have in the secured messaging system. An average of 10 minutes per participant was
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7 160 spent on providing guidance and support, although some users required more support.
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12 162 **Outcome measures**

14 163 The study participants completed an extensive pre-intervention questionnaire that collected data
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16 164 on demographics, tinnitus-related and treatment-related history. In addition, participants also
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18 165 completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at
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20 166 post-intervention (T1) and 2-months follow-up (T2). The *primary outcome measure* included the
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22 167 Tinnitus Functional Index (TFI)²⁶ to assess tinnitus severity/distress. This is a 25-item
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24 168 questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus with
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26 169 no need for intervention, scores ranging between 25 to 50 indicate a significant problem with
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28 170 possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly
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30 171 requiring a more intensive intervention. The TFI has good psychometric properties with
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32 172 acceptable internal consistency (0.97) and test-retest reliability (0.8).²⁶
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40 174 The *secondary outcome measures* included the Insomnia Severity Index (ISI)²⁷ as a measure of
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42 175 insomnia, the Generalized Anxiety Disorder (GAD-7)²⁸ as a measure of anxiety, the Patient
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44 176 Health Questionnaire (PHQ-9)²⁹ as a measure of depression, the Hearing Handicap Inventory for
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46 177 Adults Screening version (HHIA-S)³⁰ as a measure of self-reported hearing disability, the
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48 178 Hyperacusis Questionnaire (HQ)³¹ to assess the presence hyperacusis (i.e., reduced tolerance of
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50 179 everyday sounds), the Cognitive Failures Questionnaire (CFQ)³² was administered to assess
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180 cognitive functions, and the Satisfaction with Life Scales (SWLS)³³ to assess the global life
181 satisfaction.

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183 **Patient and public involvement**

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

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189 **Variables included in the predictive model**

190 **Outcome Variable:** The main dependent variable was the pre-and post-intervention change in
191 tinnitus distress based on the TFI score (TFI change). The 13-point change in TFI scores,
192 identified as a clinically meaningful (or significant) change by the original authors²⁶ was used to
193 define a clinically significant intervention outcome.

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195 **Predictor Variables:**

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

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3 201 ▪ Demographic variables (n=7): age (dichotomous), gender (dichotomous), education level
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5 202 (ordinal), employment type (categorical), loud noise exposure (dichotomous), diagnosed
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7 203 with a psychological condition (dichotomous), work less due to tinnitus (categorical).
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10 204 ▪ Tinnitus and hearing-related variables (n=15): baseline tinnitus severity (dichotomous),
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12 205 tinnitus duration (dichotomous), how often tinnitus heard (ordinal), tinnitus location
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14 206 (categorical), tinnitus types (9 different types, dichotomous), multiple tones heard
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16 207 (dichotomous), and hearing loss (categorical).
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19 208 ▪ Treatment-related to tinnitus (n=4): past treatment sought (dichotomous), sounds can
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21 209 distract from tinnitus (ordinal), hearing aid use (categorical), and medication use
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23 210 (dichotomous).
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26 211 ▪ Clinical factors (n=7): anxiety (dichotomous), depression (dichotomous), insomnia
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28 212 (dichotomous), hyperacusis (dichotomous), hearing disability (dichotomous), cognitive
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30 213 functions (dichotomous), and life satisfaction (dichotomous).
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33 214 34 35 215 **Data analysis**

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37 216 The data were analysed using descriptive statistics as well as univariate and multivariable linear
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39 217 regression and logistic regression models. Linear models were used to identify the factors
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41 218 affecting a significant TFI score change, while the logistic model was used to evaluate the factors
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43 219 which specifically effects outcomes and was thus selected. There were 98 subjects who had all
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45 220 their predictive variables except their post TFI scores. With the intention of preserving the power
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47 221 of the analysis, we have retained those subjects in the analysis after applying the predictive mean
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49 222 matching (PMM) data imputation.³⁴ Data imputation with PMM has been identified to be less
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3 223 vulnerable to model misspecification as, there is no need to define an explicit model for the
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5 224 distribution of the missing values³⁵ with that.
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10 226 The univariate analysis was performed using Chi-square or Fisher's exact test to examine the
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12 227 effect of single variables on the ICBT outcome using all the variables. The multivariable
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14 228 regression model was used to identify the effect of the variables on tinnitus reduction post ICBT,
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16 229 while adjusting for the baseline tinnitus severity, as a variable previously identified to related to
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18 230 the success of ICBT.¹¹ Prior to the multivariable analyses, the full data set was divided into the
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20 231 training (80%, $n = 183$) and testing (20%, $n = 45$) to make a fair comparison among all the
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22 232 predictive models. The training data set was used to develop the corresponding multivariable
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24 233 regression models while the testing data set was used to evaluate the model predictions. Several
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26 234 competing multivariable models (both linear and logistic) were examined. The best models were
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28 235 selected based on the lowest mean squared error and the lowest Akaike Information Criterion
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30 236 (AIC).³⁶ During multivariable analysis, we started off with the full model, including all the
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32 237 predictor variables and used backward elimination based on AIC to select the final model. R
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34 238 squared and Adj. R squared values has been reported as they are statistical measures of fit that
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36 239 indicates how much variation of the outcome is explained by the predictor variable(s) in a linear
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38 240 regression model.³⁷ We also reported the mean squared error as it is a better measure of
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40 241 prediction accuracy. Both crude and model-based odds ratios were calculated and used to
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42 242 evaluate the effect of the variable. The Hosmer-Lemeshow goodness-of-fit statistic was
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44 243 calculated to assess the calibration of the final model.³⁸
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3 245 The dependent variable TFI change was used as a continuous variable for a linear regression
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5 246 analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic
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8 247 regression analysis. All statistical analyses were performed with R statistical software (Version:
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10 248 3.6.3). All tests were two-sided and threshold at 5% level of significance.
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16 17 18 19 252 **Results**

20 21 22 253 **Participant demographics**

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24 254 The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects
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26 255 ($n=130$) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on
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29 256 demographic, tinnitus, hearing-related and treatment-related variables are provided in Table 1 of
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31 257 the Supplementary file 3. Table 1 presents details on clinical variables. The mean baseline
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33 258 tinnitus severity and tinnitus severity following the ICBT intervention were 57.93 (SD: 19.17)
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36 259 and 34.22 (SD: 22.76), respectively. Figure 1 presents the pre-and post-intervention tinnitus
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38 260 severity (TFI) score variation, indicating statistically significant differences between these scores
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40 261 ($p < 0.001$) with the paired t-test. There were 148 participants (65%) with a 13-point or higher
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42 262 reduction after the intervention.
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47 264 <Table 1 here>48
49 265 <Figure 1 here>50
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53 54 267 **Univariate analysis to examine the predictors of ICBT outcome**

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3 268 With the exception of education level ($p = .01$), none of the demographic variables were
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5 269 associated with post-intervention tinnitus severity change of 13-point or more. Participants with a
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7 270 master's degree or above had the highest odds of having a larger severity change score, with an
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9 271 odds ratio of 3.47 (95% CIs: 1.32, 12.51), compared to the participants who had education only
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11 272 up to high school or less. In terms of tinnitus and hearing-related variables, the baseline tinnitus
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13 273 severity ($p = 0.001$) was significantly associated with treatment success. Participants who had a
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15 274 higher baseline tinnitus severity (i.e., TFI scores of greater than or equal to 55.2) had significantly
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17 275 higher odds of treatment success (OR: 2.65; 95% CIs: 1.50, 4.67) compared to those who had a
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19 276 baseline severity less than 55.2. The details of the univariate analyses are provided in Tables 2-5
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21 277 of the Supplementary file 3.
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28 279 In terms of the treatment-related variables, sounds can distract ($p = .001$) showed a significant
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30 280 association with treatment success. Those who reported being distracted by the sound partially
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32 281 (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
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34 282 odds of having a successful treatment outcome when compared to who was fully distracted.
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36 283 However, the odds among the participants who used hearing aid either in one ear or both ears
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38 284 compared to those who did not, was not statistically significantly different with a p -value 0.26
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40 285 (see Table 4 of the Supplementary file 3). Tinnitus described as voice-like had a 91% lower odds
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42 286 of success with the treatment. None of the clinical factors were significantly associated with the
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44 287 outcome.
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51 289 **Multivariable analyses to examine predictors of ICBT outcome**
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3 290 Working less due to tinnitus ($p = .046$), baseline tinnitus severity ($p < .001$), and education level
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5 291 ($p = .014$), showed significant associations (p with outcome (i.e., TFI reduction). Modified models
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7 292 with the remaining variables were not statistically significant. Moreover, several two-way
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9 293 interactions were tested. We did not find any gender interactions with regard to the maskability of
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11 294 sounds ($p = .87$) and) and hearing aid usage ($p = .68$) variables. The overall model resulted with
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13 295 an R squared = 0.35 and Adj. R squared of 0.20. The final model resulted in a root mean square of
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15 296 22.81 on the testing data set. All required regression assumptions were satisfied with the selected
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17 297 model. The final regression model (see Table 2) was selected with backward elimination based on
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19 298 AIC.

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23 299 This model indicated that those who received disability allowance due to having severe tinnitus
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25 300 and being unable to work, had shown a reduction of 25.30-point (95% CIs: -46.35,-4.24) in TFI
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27 301 compared to those who did not have to work less due to tinnitus. Moreover, for every 10 unit
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29 302 increase in the baseline tinnitus severity, there was 8.3 (95% CIs: 0.65,1.00) reduction in their
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31 303 TFI score after adjusting for other variables. Participants who had master's degree or above
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33 304 compared to participants who had a college education showed an expected reduction of 17-point
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35 305 (95% CIs: 5.78, 27.84) in their TFI score.
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42 307 <Table 2 here>
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46 309 Multivariable logistic regressions were performed next and indicated that baseline tinnitus
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48 310 severity ($p < 0.001$), and education level ($p = .001$), and were identified as significant predictors
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50 311 (see Table 3). This model had an AIC of 212.21. Modified models to the prior model indicated
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52 312 that other variables were not statistically significant (see Table 4).
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5 314 The multivariable model adjusted OR (see Table 3) for the participants who had master's level
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8 315 or above education compared to those who had high school education or less also showed 9.65
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10 316 higher odds (95% CIs: 2.32, 40.15) of having a successful outcome. Similar to the linear
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12 317 regression model, baseline tinnitus severity had also shown a significant association (OR: 1.04;
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14 318 95% CIs: 1.02, 1.06) with the treatment outcome. The Hosmer-Lemeshow goodness-of-fit test
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16 319 confirmed a better fit in the current model with a p -value of 0.50 ($\chi^2=7.36$, $df=8$).
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28 324 Fewer variables were statistically significant in the logistic regression model, which identified
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30 325 influencing predictors of the ICBT success. This was due to the fact that the logistic regression
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32 326 model evaluated predictors of treatment successes (i.e., 13 point change), while the multivariable
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34 327 regression model identified the predictors of a significant TFI reduction.
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39 329 **Discussion**

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42 330 Accessible and affordable tinnitus interventions are needed to alleviate tinnitus distress as well as
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44 331 comorbid problems with anxiety, depression, and insomnia. The current study examined
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46 332 predictors of outcomes for ICBT. In this exploratory study, only a limited number of variables
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48 333 were identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points
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50 334 following undertaking an ICBT intervention and the results vary depending on the model used.
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53 335 Only educational level and baseline tinnitus severity were predictors in both linear and logistic
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3 336 models. Other variable that were significant in the linear regression models included the
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5 337 demographic variable working less due to tinnitus, when controlling for baseline tinnitus severity
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7 338 and education level. These key findings are discussed below.
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12 340 In terms of demographic variables, education level was found to be a significant predictor of
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14 341 ICBT success as those with a master's education or higher had higher odds of having a successful
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16 342 outcome compared with those with high school education in both the linear and logistic models.
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18 343 This was expected as having good literacy skills is essential when understanding the intervention
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20 344 materials. The intervention materials used in these studies were written at an average of 9th
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22 345 reading grade level,²³ suggesting that they were not easily accessible for participants with only a
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24 346 high school education. These results highlight the importance of health literacy considerations
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26 347 when developing text-based self-help interventions such as ICBT. Additionally, those reported to
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28 348 be working less due to tinnitus were at a lower odds of having a successful outcome. This finding
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30 349 needs further exploration in future studies. Working, may for instance provide some distraction
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32 350 from tinnitus as supported by reports during the 2020 COVID-19 pandemic that tinnitus was more
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34 351 bothersome for some individuals as they did not have the distractions from commuting and
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36 352 sounds at work.³⁹ Closely monitoring the effects of tinnitus is important to ensure that tinnitus can
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38 353 be managed so that individuals are still able to work effectively.
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47 355 When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to
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49 356 be a significant predictor of ICBT success, as seen in previous studies.¹¹ Tinnitus perceptions vary
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51 357 greatly and in this study those with tinnitus presenting as musical, lower-pitched or clicking were
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53 358 less likely to have a positive outcome of ICBT. This finding certainly needs further exploration as
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3 359 the limited number of participants in each group of tinnitus perception. One of the CBT
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5 360 intervention aims is to help participants to reinterpret their tinnitus to a less threatening sound. It
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7 361 may be that these sounds are not easily likened to everyday sounds than other types of tinnitus
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10 362 (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation strategies.
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14 364 Of the four treatment-related variables, only those who reported to use of wearing one hearing aid
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16 365 were found to be at better odds of ICBT success. This finding needs further exploration to identify
17
18 366 other characteristics that may be associated with an outcome such as having tinnitus in only one
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20 367 ear. Although the evidence for the use of hearing aids alone for tinnitus management is
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22 368 limited,^{40,41} hearing aids may for some reduce the tinnitus percept and aid communication
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24 369 difficulties.⁴² Ensuring hearing loss is addressed in addition to the provision of ICBT may lead to
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26 370 more optimal outcomes for those with co-existing hearing loss.
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33 372 Regarding studying the clinical factors, those with higher levels of depression were found to have
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35 373 higher reduction in the TFI score. However, the participants with insomnia showed lower odds of
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37 374 success. Interestingly, other clinical factors including anxiety, hyperacusis, hearing disability as
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39 375 well as cognitive functioning were not significant predictors of ICBT in the current study. Further
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41 376 studies and models are required to verify these results.
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47 378 Studies in other health areas have also examined the predictors of a range of internet-based health
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49 379 interventions.¹²⁻¹⁵ Generally higher baseline symptoms predict increased treatment response, for
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51 380 example, in anxiety and depression,⁴³ and higher obsessive-compulsive behaviours when treating
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53 381 the obsessive-compulsive disorder.⁴⁴ Variables such as age and gender have been mentioned as
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3 382 significant predictors for some ICBT interventions.^{15,43} Most previous ICBT interventions have
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5 383 not identified pre-treatment characteristics to predict or moderate outcomes.¹⁶ Most ICBT studies
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7 384 have indicated that ICBT works irrespective of treatment history.⁴³ Contrarily, previous treatment
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9 385 has shown worse outcomes in some previous studies.⁴⁵ However, it may be that some participants
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11 386 may have sought alternative therapies which have no evidence for tinnitus. For this reason, it
12
13 387 would be useful to examine specific types of previous treatments in future studies to distinguish
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15 388 between those who had evidence-based interventions before enrolling to ICBT than those who did
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17 389 not.
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391 **Study limitations and future research**

26 392 The current study was to our knowledge the first study to combine data from multiple studies to
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28 393 examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study
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30 394 may have included a homogeneous group of tinnitus patients due to study inclusion/exclusion
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32 395 criteria and may not have included all the possible variables (e.g., health literacy, acceptability
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34 396 and motivation of users, satisfaction from the intervention, intervention engagement) that may
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36 397 have played a role in ICBT outcome. These factors were not investigated for this study. As they
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38 398 have been found to contribute to outcomes,⁴⁶ they should be included in future studies. Second,
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40 399 the sample size remained relatively small when compared to the number of predictive factors
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42 400 included. Third, multivariable analyses may have some limitations in terms of examining complex
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44 401 relationships. Moreover, due to the high multicollinearity between the predictor variables, there
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46 402 were several competing models which had led to the same prediction accuracies and root mean
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48 403 square errors. Additionally, these linear models lack in identifying any predictor variables that
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50 404 have a non-linear relationship with the response variables. For these reasons, the study results
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3 405 must be viewed as preliminary. Future studies may benefit from examining more relevant
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5 406 predictor variables and also using artificial intelligence and machine learning techniques to
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7 407 examine the non-linear relationship between the variables in predicting the ICBT outcomes. Brier
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9 408 scores should also be used to compare models. Analyses should be extended with non-linear
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11 409 models like decision trees, support vector machines and neural networks. Future studies could
12
13 410 also examine the predictors of adherence and engagement to intervention as well as of dropouts.
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29 416 30 417 **Twitter**

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38 420 **Contributors**

39
40 421 HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected
41
42 422 the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript.
43
44 423 All authors read and approved the final manuscript.
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48 424 49 425 **Competing interests**

50
51 426 None to declare.
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3 428 **Patient consent for publication**
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6 429 Not required.
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10 431 **Data availability statement**
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12
13 432 Data is available for other researchers on request.
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18 434 **References**
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584 **Tables**585 **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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587

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

590

| 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: Bachelor'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 |

591

593 **Table 3: The multivariable logistic regression model summary and the model adjusted**
 594 **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: Bachelor'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) |

596

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 |

| | | | |
|----|---------------------------------------|---------------|------|
| 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 |

600

601 Figure Legends

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

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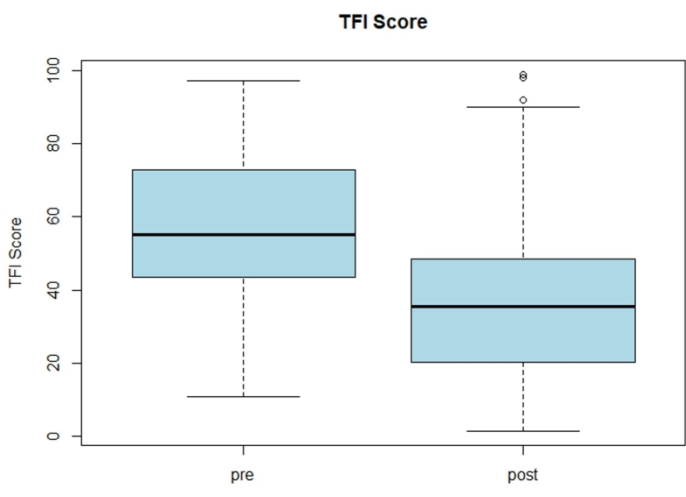


Figure 1

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 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) |

| | | |
|--------------------------------------|--|--|
| Type of tinnitus (9 different types) | <ul style="list-style-type: none"> ▪ 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: <ul style="list-style-type: none"> ▪ 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) | <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression <p>Split into dichotomous variables (≤ 14 no depression and > 14 depression)</p> |
| Insomnia | Insomnia Severity Index (ISA) | <p>7-item</p> <p>5-point scale with “no problem” (score of 0) to “very severe problem” (score of 4)</p> | <p>Higher number indicates more severe insomnia (scores range between 0–28).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) <p>Split into dichotomous variables (≤ 14 no insomnia and > 15 insomnia)</p> |
| Hyperacusis | Hyperacusis Questionnaire (HQ) | <p>14-items</p> <p>4-point scale with “no” (score of 0) to “yes, a lot” (score of 3)</p> | <p>Higher number more severe hyperacusis (scores range between 0–42).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ > 28: strong hypersensitivity <p>Split into dichotomous variables (≤ 28 no hyperacusis and > 28 hyperacusis)</p> |
| Hearing disability | Hearing Handicap Inventory for Adults – Screening (HHIA-S) | <p>10-items</p> <p>3-point scale with “yes” (score of 4) to “no” day (0)</p> | <p>Higher number more severe hearing disability (scores range between 0–40).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability <p>Split into dichotomous variables (≤ 8 no hearing disability and ≥ 10 hearing disability)</p> |

| | | | |
|--------------------|--|--|--|
| 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: <ul style="list-style-type: none"> ▪ 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) |

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 | | |

| | | |
|--|---|--|
| <ul style="list-style-type: none"> ▪ Occasionally ▪ When taking out my hearing aid(s) ▪ At night ▪ Most of the time ▪ All the time | <p>4 (2%)</p> <p>3 (1%)</p> <p>4 (2%)</p> <p>63 (27%)</p> <p>154 (68%)</p> | |
| <p>Tinnitus location</p> <ul style="list-style-type: none"> ▪ One ear ▪ Both ears ▪ In my head ▪ Other location ▪ Unsure | <p>61 (27%)</p> <p>109 (48%)</p> <p>34 (15%)</p> <p>3 (1%)</p> <p>21 (9%)</p> | |
| <p>Type of tinnitus sound (answering Yes)</p> <ul style="list-style-type: none"> ▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsating ▪ Clicking ▪ Music ▪ Voices ▪ Humming | <p>71 (31%)</p> <p>75 (33%)</p> <p>130 (57%)</p> <p>16 (7%)</p> <p>28 (12%)</p> <p>14 (6%)</p> <p>4 (2%)</p> <p>3 (1%)</p> <p>21 (9%)</p> | |
| <p>Multiple sounds heard</p> <ul style="list-style-type: none"> ▪ Yes ▪ No | <p>73 (32%)</p> <p>155 (68%)</p> | |
| <p>Presence of a hearing loss</p> <ul style="list-style-type: none"> ▪ No ▪ Both ears ▪ One ear ▪ Unsure | <p>49 (21%)</p> <p>104 (46%)</p> <p>46 (20%)</p> <p>29 (13%)</p> | |
| Treatment-related characteristics | | |
| <p>Past tinnitus treatment sought</p> <ul style="list-style-type: none"> ▪ Yes ▪ No | <p>58 (25%)</p> <p>170 (75%)</p> | |
| <p>Sounds can distract from tinnitus</p> <ul style="list-style-type: none"> ▪ Fully ▪ Partially ▪ Not at all | <p>26 (11%)</p> <p>178 (78%)</p> <p>24 (10%)</p> | |
| <p>Hearing aid use</p> <ul style="list-style-type: none"> ▪ No ▪ Unilateral ▪ Bilateral | <p>159 (70%)</p> <p>19 (8%)</p> <p>50 (22%)</p> | |
| <p>Medication use</p> <ul style="list-style-type: none"> ▪ Yes ▪ No | <p>130 (57%)</p> <p>98 (43%)</p> | |

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 | |

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 | |

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 | |

BMJ Open

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

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| Keywords: | Audiology < OTOLARYNGOLOGY, Adult otolaryngology < OTOLARYNGOLOGY, Depression & mood disorders < PSYCHIATRY |
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3 1 **Internet-based cognitive-behavioral therapy for tinnitus: Secondary analysis**
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24 **Abstract**

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

27 **Design:** Secondary analysis of intervention studies.

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

29 **Participants:** 228 individuals who underwent ICBT.

30 **Interventions:** ICBT.

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

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

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3 47 **Conclusions:** Predictors of intervention outcome can be used as a means of triaging patients to
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5 48 the most suited form of treatment to achieve optimal outcomes and to make healthcare savings.
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7 49 Future studies should consider including a heterogeneous group of participants as well as other
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9 50 predictor variables not included in the current study.
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15 52 **Key Words**

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17 53 Tinnitus, Internet interventions, Digital therapeutics, Predictors of outcomes, Cognitive
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19 54 behavioural therapy
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24 56 **Strengths and limitations of the study**

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27 57 ▪ The current study, to our knowledge is the first study to use combined data from multiple
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29 58 studies to examine the predictors of ICBT outcome for tinnitus.
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31 59 ▪ The study included a homogeneous group of tinnitus patients due to the strict
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33 60 inclusion/exclusion criteria and may not have included all the possible variables (e.g.,
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35 61 health literacy, acceptability and motivation of users, satisfaction from the intervention,
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37 62 intervention engagement) that may have played a role in ICBT outcome.
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39 63 ▪ The sample size remained relatively small when compared to the number of predictive
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41 64 factors included which may have hampered the study results.
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43 65 ▪ The multivariable analyses may have some limitations in terms of examining complex
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45 66 relationships. Other statistical models including artificial intelligence and machine
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47 67 learning techniques may have more value in examining the non-linear relationship.
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70 **Introduction**

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

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

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85 Despite positive and strong evidence for CBT, individuals with tinnitus are rarely offered CBT in
86 their local clinics. For example, a large-scale epidemiological study in the US showed that
87 medication (which is not recommended for tinnitus in clinical guidelines) was discussed 50% of
88 the time by health professionals, whereas the CBT was discussed as a management option only
89 0.2% of the time.⁸ This is most likely a consequence of the limited number of trained
90 professionals who provide CBT for tinnitus. One solution to overcome this issue is to use
91 Internet-based CBT (ICBT), in which patients are provided with CBT in a self-help format over
92 the internet with minimal guidance from a tinnitus expert.⁹ A series of controlled studies in

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3 93 Sweden, Germany, the United Kingdom, and the United States have demonstrated positive
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5 94 effects of ICBT in reducing tinnitus distress as well as reducing its comorbidities such as anxiety,
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8 95 depression, and insomnia.⁹ In addition to the changes noted in standardized outcome measures,
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10 96 the qualitative analysis of user experiences has highlighted the perceived benefits of this
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12 97 program.¹⁰ In addition, the improvements noted from ICBT have been maintained for 1-year
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15 98 post-intervention.¹¹ These results suggest that ICBT is a highly promising approach to provide
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17 99 evidence-based tinnitus management.
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21 101 Although the previous studies on ICBT have shown favourable results, group effects were
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23 102 mainly reported. There is limited understanding of who is likely to benefit (or not) from the
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26 103 ICBT intervention. In other words, only a few studies have examined predictors of ICBT
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28 104 outcomes in tinnitus research. For example, the long-term analysis of the previous UK studies
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30 105 suggested that the best predictors of tinnitus improvements at 1-year were the baseline tinnitus
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32 106 severity, engagement with ICBT program (i.e., more modules read), and higher self-reported
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34 107 satisfaction with the intervention.¹¹ Studies in other health areas have also examined the
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36 108 predictors of outcome for a range of internet-based health interventions.¹²⁻¹⁶ These studies have
37
38 109 inconsistently identified various demographic as well as disease-specific variables that could
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40 110 predict the successful and non-successful participants on internet interventions.¹⁶ There remains
41
42 111 a clear gap in knowledge in terms of predictors of ICBT outcomes for tinnitus.
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49 113 Predictors of intervention outcomes may help triage patients to the most suitable tinnitus
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51 114 intervention. If interventions are recommended based on their suitability, it can potentially
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53 115 improve the outcomes resulting in healthcare savings. The objective of the current study was to
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3 116 examine the predictors of outcomes of ICBT intervention for individuals with tinnitus based on
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5 117 the secondary analysis of the pooled results from the three-phase clinical trial undertaken in the
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120 **Method**

121 **Study design and participants**

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

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3 139 sharing policy. The ethical clearance for these studies was obtained from the Faculty of Science
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5 140 and Technology Research Ethics Panel of Anglia Ruskin University (ARU reference:
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7 141 FST/FREP/14/478 and FST/FREP/14/478) and the East of England–Cambridge South Research
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9 142 Ethics Committee (REC reference: 16/EE/0148) and Health Research Authority (IRAS project
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11 143 ID: 195565). The study results are presented using the TRIPOD checklist (see Supplementary
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13 144 file 1).
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19 146 Combining the data from three trials resulted in the inclusion of 228 participants. Of these, 36
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21 147 were from the pilot trial, 146 from the efficacy trial, and the remaining 46 were from the
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23 148 effectiveness trial.
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27 28 150 **Intervention**

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30 151 The intervention included a CBT program that was specifically developed for individuals with
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32 152 tinnitus.²⁰ This intervention was originally developed by psychologists in Sweden,²¹ but later
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34 153 adapted by audiologists in the UK²² and the US.²³ The intervention was administered using a
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36 154 secured ePlatform^{24,25} and presented in a self-help format. The intervention was presented over
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38 155 an 8-weeks period, during which the users were given access to 2-3 modules each week. The
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40 156 CBT program was divided into 21 modules, of which 5 were optional. The modules included
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42 157 content such as applied relaxation, thought analysis, cognitive restructuring, imagery, and
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44 158 exposure techniques. Each module included text, images, and videos to enhance the user
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46 159 experience. In addition, users were required to complete various exercises to engage them in the
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48 160 intervention. Although the intervention was presented in a self-help format, the users had access
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50 161 to minimal guidance from an audiologist (EB). Generally, this included examining weekly
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3 162 exercises users completed and providing feedback as well as answering any questions they may
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5 163 have in the secured messaging system. An average of 10 minutes per participant was spent on
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7 164 providing guidance and support, although some users required more support.
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11 166 **Outcome measures**

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14 167 The study participants completed an extensive pre-intervention questionnaire that collected data
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16 168 on demographics, tinnitus-related and treatment-related history. In addition, participants also
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18 169 completed various standardized patient-reported outcome measures (PROMs) at baseline (T0), at
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20 170 post-intervention (T1) and at the 2-month follow-up (T2). The *primary outcome measure*
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22 171 included the Tinnitus Functional Index (TFI)²⁶ to assess tinnitus severity/distress. This is a 25-
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24 172 item questionnaire with scores ranging between 0 to 100. Scores below 25 indicate mild tinnitus
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26 173 with no need for intervention, scores ranging between 25 to 50 indicate a significant problem
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28 174 with possible need for intervention, and scores above 50 indicate severe enough tinnitus possibly
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30 175 requiring a more intensive intervention. The TFI has good psychometric properties with
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32 176 acceptable internal consistency (0.97) and test-retest reliability (0.8).²⁶
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40 178 The *secondary outcome measures* included the Insomnia Severity Index (ISI)²⁷ as a measure of
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42 179 insomnia, the Generalized Anxiety Disorder (GAD-7)²⁸ as a measure of anxiety, the Patient
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44 180 Health Questionnaire (PHQ-9)²⁹ as a measure of depression, the Hearing Handicap Inventory for
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46 181 Adults Screening version (HHIA-S)³⁰ as a measure of self-reported hearing disability, the
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48 182 Hyperacusis Questionnaire (HQ)³¹ to assess the presence hyperacusis (i.e., reduced tolerance of
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50 183 everyday sounds), the Cognitive Failures Questionnaire (CFQ)³² was administered to assess
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184 cognitive functions, and the Satisfaction with Life Scales (SWLS)³³ to assess the global life
185 satisfaction.

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187 **Patient and public involvement**

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

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193 **Variables included in the predictive model**

194 **Outcome Variable:** The dependent variable was the pre-and post-intervention change in tinnitus
195 distress based on the TFI score (TFI change). The 13-point change in TFI scores identified as a
196 clinically meaningful (or significant) change by the original authors²⁶ was used to define a
197 clinically significant intervention outcome.

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199 **Predictor Variables:**

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

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3 205 ▪ Demographic variables (n=7): age (dichotomous), gender (dichotomous), education level
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5 206 (ordinal), employment type (categorical), loud noise exposure (dichotomous), diagnosed
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7 207 with a psychological condition (dichotomous), work less due to tinnitus (categorical).
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10 208 ▪ Tinnitus and hearing-related variables (n=15): baseline tinnitus severity (dichotomous),
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12 209 tinnitus duration (dichotomous), how often tinnitus heard (ordinal), tinnitus location
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14 210 (categorical), tinnitus types (9 different types, dichotomous), multiple tones heard
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16 211 (dichotomous), and hearing loss (categorical).
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19 212 ▪ Treatment-related to tinnitus (n=4): past treatment sought (dichotomous), sounds can
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21 213 distract from tinnitus (ordinal), hearing aid use (categorical), and medication use
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23 214 (dichotomous).
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26 215 ▪ Clinical factors (n=7): anxiety (dichotomous), depression (dichotomous), insomnia
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28 216 (dichotomous), hyperacusis (dichotomous), hearing disability (dichotomous), cognitive
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30 217 functions (dichotomous), and life satisfaction (dichotomous).
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35 219 **Data analysis**

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37 220 The data were analysed using descriptive statistics as well as univariate and multivariable linear
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39 221 regression and logistic regression models. Linear models were used to identify the factors
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41 222 affecting a significant TFI score change while the logistic model was used to evaluate the factors
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43 223 which specifically effects outcomes and was thus selected. There were 98 subjects who had all
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45 224 their predictive variables except their post TFI scores. With the intention of preserving the power
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47 225 of the analysis, we have retained those subjects in the analysis after applying the predictive mean
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49 226 matching (PMM) data imputation.³⁴ Data imputation with PMM has been identified to be less
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3 227 vulnerable to model misspecification as there is no need to define an explicit model for the
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5 228 distribution of the missing values.³⁵
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10 230 The univariate analysis was performed using Chi-square or Fisher's exact test to examine the
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12 231 effect of single variables on the ICBT outcome using all the variables. The multivariable
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14 232 regression model was used to identify the effect of the variables on tinnitus reduction post ICBT
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16 233 while adjusting for the baseline tinnitus severity as a variable previously identified to relate to
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18 234 the success of ICBT.¹¹ Prior to the multivariable analyses, the full data set was divided into
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20 235 training (80%, $n = 183$) and testing (20%, $n = 45$) to make a fair comparison among all the
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22 236 predictive models. The training data set was used to develop the corresponding multivariable
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24 237 regression models while the testing data set was used to evaluate the model predictions. Several
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26 238 competing multivariable models (both linear and logistic) were examined. The best models were
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28 239 selected based on the lowest mean squared error and the lowest Akaike Information Criterion
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30 240 (AIC).³⁶ During multivariable analysis, we began with the full model, including all the predictor
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32 241 variables, and used backward elimination based on AIC to select the final model. R squared and
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34 242 Adj. R squared values have been reported, as they are statistical measures of fit that indicate how
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36 243 much variation of the outcome is explained by the predictor variable(s) in a linear regression
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38 244 model.³⁷ We also reported the mean squared error as it is a better measure of prediction accuracy.
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40 245 Both crude and model-based odds ratios were calculated and used to evaluate the effect of the
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42 246 variable. The Hosmer-Lemeshow goodness-of-fit statistic was calculated to assess the calibration
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44 247 of the final model.³⁸
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3 249 The dependent variable TFI change was used as a continuous variable for a linear regression
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5 250 analysis whereas the dichotomous variable (i.e., 13-point change yes or no) was used for logistic
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8 251 regression analysis. All statistical analyses were performed with R statistical software (Version:
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10 252 3.6.3). All tests were two-sided and threshold at 5% level of significance.
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14 254 **Results**

15 255 **Participant demographics**

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17 256 The mean age of study participants was 55.14 (SD: 12.92) years, and 57% of the subjects
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19 257 ($n=130$) were males. The mean tinnitus duration was 17.68 (SD: 19.42) years. Further details on
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22 258 demographic, tinnitus, hearing-related and treatment-related variables are provided in Table 1 of
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25 259 the Supplementary file 3. Table 1 presents details on clinical variables. The mean baseline
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27 260 tinnitus severity and tinnitus severity following the ICBT intervention were 57.93 (SD: 19.17)
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29 261 and 34.22 (SD: 22.76) respectively. Figure 1 presents the pre-and post-intervention tinnitus
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32 262 severity (TFI) score variation, indicating statistically significant differences between these scores
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35 263 ($p < 0.001$) with the paired t-test. There were 148 participants (65%) with a 13-point or higher
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37 264 reduction after the intervention.
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42 266 <Table 1 here>

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46 269 **Univariate analysis to examine the predictors of ICBT outcome**

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49 270 With the exception of education level ($p = .01$), none of the demographic variables were
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52 271 associated with post-intervention tinnitus severity change of 13-point or more. Participants with a
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3 272 master's degree or above had the highest odds of having a larger severity change score, with an
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5 273 odds ratio of 3.47 (95% CIs: 1.32, 12.51), compared to the participants who had education only
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8 274 up to high school or less. In terms of tinnitus and hearing-related variables, the baseline tinnitus
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10 275 severity ($p = 0.001$) was significantly associated with treatment success. Participants who had a
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12 276 higher baseline tinnitus severity (i.e., TFI scores of greater than or equal to 55.2) had significantly
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14 277 higher odds of treatment success (OR: 2.65; 95% CIs: 1.50, 4.67) compared to those who had a
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16 278 baseline severity less than 55.2. The details of the univariate analyses are provided in Tables 2-5
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19 279 of the Supplementary file 3.
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24 281 In terms of the treatment-related variables, sounds can distract ($p = .001$) showed a significant
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26 282 association with treatment success. Those who reported being distracted by the sound partially
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28 283 (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
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30 284 odds of having a successful treatment outcome when compared to those who were fully
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32 285 distracted. However, the odds among the participants who used hearing aids either in one ear or
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34 286 both ears compared to those who did not were not statistically significantly different with a p -
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36 287 value 0.26 (see Table 4 of the Supplementary file 3). Tinnitus described as voice-like had a 91%
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38 288 lower odds of success with the treatment. None of the clinical factors were significantly
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40 289 associated with the outcome.
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47 291 **Multivariable analyses to examine predictors of ICBT outcome**

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49 292 Working less due to tinnitus ($p = .046$), baseline tinnitus severity ($p < .001$), and education level
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51 293 ($p = .014$), showed significant associations with outcome (i.e., TFI reduction). Modified models
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53 294 with the remaining variables were not statistically significant. Moreover, several two-way
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3 295 interactions were tested. We did not find any gender interactions with regard to the maskability of
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5 296 sounds ($p = .87$) and) and hearing aid usage ($p = .68$) variables. The overall model resulted with
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7 297 an R squared = 0.35 and Adj. R squared of 0.20. The final model resulted in a root mean square of
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9 298 22.81 on the testing data set. All required regression assumptions were satisfied with the selected
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11 299 model. The final regression model (see Table 2) was selected with backward elimination based on
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13 300 AIC.
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17 301 This model indicated that those who received disability allowance due to having severe tinnitus
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19 302 and being unable to work had shown a reduction of 25.30-points (95% CIs: -46.35, -4.24) in TFI
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21 303 compared to those who did not have to work less due to tinnitus. Moreover, for every 10 unit
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23 304 increase in the baseline tinnitus severity, there was a 8.3-point (95% CIs: 0.65, 1.00) reduction in
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25 305 their TFI score after adjusting for other variables. Participants who had master's degree or above
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27 306 compared to participants who had a college education showed an expected reduction of 17-points
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29 307 (95% CIs: 5.78, 27.84) in their TFI score.
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35 309 <Table 2 here>
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40 311 Multivariable logistic regressions were performed next and indicated that baseline tinnitus
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42 312 severity ($p < 0.001$) and education level ($p = .001$) were identified as significant predictors (see
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44 313 Table 3). This model had an AIC of 212.21. Modified models to the prior model indicated that
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46 314 other variables were not statistically significant (see Table 4).
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51 316 The multivariable model adjusted OR (see Table 3) for the participants who had master's level or
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53 317 above education compared to those who had high school education or less also showed 9.65
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3 318 higher odds (95% CIs: 2.32, 40.15) of having a successful outcome. Similar to the linear
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5 319 regression model, baseline tinnitus severity had also shown a significant association (OR: 1.04;
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7 320 95% CIs: 1.02, 1.06) with the treatment outcome. The Hosmer-Lemeshow goodness-of-fit test
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9 321 confirmed a better fit in the current model with a p -value of 0.50 ($\chi^2=7.36$, $df=8$).
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21 326 Fewer variables were statistically significant in the logistic regression model, which identified
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23 327 influencing predictors of the ICBT success. This was due to the fact that the logistic regression
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25 328 model evaluated predictors of treatment successes (i.e., 13-point change), while the multivariable
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27 329 regression model identified the predictors of a significant TFI reduction.
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32 331 **Discussion**

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34 332 Accessible and affordable tinnitus interventions are needed to alleviate tinnitus distress as well as
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36 333 comorbid problems with anxiety, depression, and insomnia. The current study examined
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38 334 predictors of outcomes for ICBT. In this exploratory study, only a limited number of variables
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40 335 were identified as possibly reducing tinnitus severity scores on the TFI by at least 13 points
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42 336 following ICBT intervention, and the results vary depending on the model used. Only
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44 337 educational level and baseline tinnitus severity were predictors in both linear and logistic models.
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46 338 The other significant variable in the linear regression models included the demographic variable,
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48 339 work restrictions due to tinnitus when controlling for baseline tinnitus severity and education
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52 340 level. These key findings are discussed below.
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5 342 In terms of demographic variables, education level was found to be a significant predictor of
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7 343 ICBT success as those with a master's education or higher had higher odds of having a successful
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9 344 outcome compared with those with high school education in both the linear and logistic models.
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11 345 This was expected as having good literacy skills is essential when understanding the intervention
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13 346 materials. The intervention materials used in these studies were written at an average of 9th grade
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15 347 readinglevel²³ suggesting that they were not easily accessible for participants with only a high
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17 348 school education. These results highlight the importance of health literacy considerations when
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19 349 developing text-based self-help interventions such as ICBT. Additionally, those who reported
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21 350 work restrictions due to tinnitus were at a lower odds of having a successful outcome. This
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23 351 finding needs further exploration in future studies. Working may, for instance, provide some
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25 352 distraction from tinnitus as supported by reports during the 2020 COVID-19 pandemic that
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27 353 tinnitus was more bothersome for some individuals due to the lack of distractions from
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29 354 commuting and sounds at work.³⁹ Closely monitoring the effects of tinnitus is important to ensure
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31 355 that tinnitus can be managed so that individuals are still able to work effectively.
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35 357 When examining the tinnitus and hearing-related variables, baseline tinnitus severity was found to
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37 358 be a significant predictor of ICBT success, as seen in previous studies.¹¹ Tinnitus perceptions vary
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39 359 greatly, and in this study, those with tinnitus presenting as musical, lower-pitched or clicking
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41 360 were less likely to have a positive outcome of ICBT. This finding certainly needs further
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43 361 exploration as the limited number of participants in each group of tinnitus perception. One of the
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45 362 CBT intervention aims is to help participants to reinterpret their tinnitus to a less threatening
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47 363 sound. It may be that these sounds are not easily likened to everyday sounds than other types of
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3 364 tinnitus (i.e., buzzing, high pitch, pulsing, humming) making it difficult to develop adaptation
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5 365 strategies.

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10 367 Of the four treatment-related variables, only those who reported to use of wearing one hearing aid
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12 368 were found to be at better odds of ICBT success. This finding needs further exploration to identify
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14 369 other characteristics that may be associated with an outcome such as having tinnitus in only one
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16 370 ear. Although the evidence for the use of hearing aids alone for tinnitus management is
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18 371 limited,^{40,41} hearing aids may for some reduce the tinnitus percept and aid communication
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20 372 difficulties.⁴² Ensuring hearing loss is addressed in addition to the provision of ICBT may lead to
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22 373 more optimal outcomes for those with co-existing hearing loss.
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28 375 Regarding studying the clinical factors, those with higher levels of depression were found to have
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30 376 higher reduction in the TFI score. However, the participants with insomnia showed lower odds of
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32 377 success. Interestingly, other clinical factors including anxiety, hyperacusis, hearing disability as
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34 378 well as cognitive functioning were not significant predictors of ICBT in the current study. Further
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36 379 studies and models are required to verify these results.
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42 381 Studies in other health areas have also examined the predictors of a range of internet-based health
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44 382 interventions.¹²⁻¹⁵ Generally, higher baseline symptoms predict increased treatment response, as
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46 383 in anxiety and depression,⁴³ and higher obsessive-compulsive behaviours when treating the
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48 384 obsessive-compulsive disorder.⁴⁴ Variables such as age and gender have been mentioned as
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50 385 significant predictors for some ICBT interventions.^{15,43} Most previous ICBT interventions have
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52 386 not identified pre-treatment characteristics to predict or moderate outcomes.¹⁶ Most ICBT studies
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3 387 have indicated that ICBT works irrespective of treatment history.⁴³ Contrarily, previous treatment
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5 388 has shown worse outcomes in some previous studies.⁴⁵ However, it may be that some participants
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7 389 may have sought alternative therapies which have no evidence for tinnitus. For this reason, it
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10 390 would be useful to examine specific types of previous treatments in future studies to distinguish
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12 391 between those who had evidence-based interventions before enrolling to ICBT than those who did
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14 392 not.
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19 394 **Study limitations and future research**

21 395 The current study was to our knowledge the first study to combine data from multiple studies to
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23 396 examine the predictors of ICBT outcome for tinnitus. However, it has limitations. First, the study
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25 397 may have included a homogeneous group of tinnitus patients due to study inclusion/exclusion
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27 398 criteria and may not have included all the possible variables (e.g., health literacy, acceptability
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29 399 and motivation of users, satisfaction from the intervention, intervention engagement) that may
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31 400 have played a role in ICBT outcome. These factors were not investigated for this study. As they
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33 401 have been found to contribute to outcomes,⁴⁶ they should be included in future studies. Second,
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35 402 the sample size remained relatively small when compared to the number of predictive factors
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37 403 included. Third, multivariable analyses may have some limitations in terms of examining complex
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39 404 relationships. Moreover, due to the high multicollinearity between the predictor variables, there
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41 405 were several competing models which had led to the same prediction accuracies and root mean
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43 406 square errors. Additionally, these linear models lack in identifying any predictor variables that
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45 407 have a non-linear relationship with the response variables. For these reasons, the study results
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47 408 must be viewed as preliminary. Future studies may benefit from utilizing non-linear statistical
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49 409 models such as Generalized Additive Models (GAMs), and also artificial intelligence and
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3 410 machine learning models like neural networks, random forest and support vector machines, as
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5 411 some variables like tinnitus duration and depression had shown lower correlation with the
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7 412 response (with correlations: -0.10 and 0.29, respectively). In addition, including more relevant
8
9 413 predictive factors (e.g., health literacy, motivation, engagement, adherence) in future studies may
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11 414 help improve predictive accuracy. Currently, we have used AIC value to compare the competing
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13 415 models. For future studies, we are planning to use average AUC and Brier scores to compare
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15 416 models.
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21

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31 422 32 33 **Twitter**

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41 426 **Contributors**

42
43 427 HR, VM, EB and GA conceptualized the study. EB administered the intervention and collected
44
45 428 the data. HR performed the data analysis. VM and HR prepared the first draft of the manuscript.
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47 429 All authors read and approved the final manuscript.
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51 431 **Competing interests**

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55 432 None to declare.
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5 434 **Patient consent for publication**

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8 435 Not required.
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13 437 **Data availability statement**

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15 438 De-identified data are available upon reasonable request.
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20 440 **References**

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590 **Tables**591 **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) |

592

593

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

596

| 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: Bachelor'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 |

597

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

601

| | 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: Bachelor'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) |

602

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

605

| | | 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 |

| | | | |
|----|---------------------------------------|---------------|------|
| 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 |

606

607 Figure Legends

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

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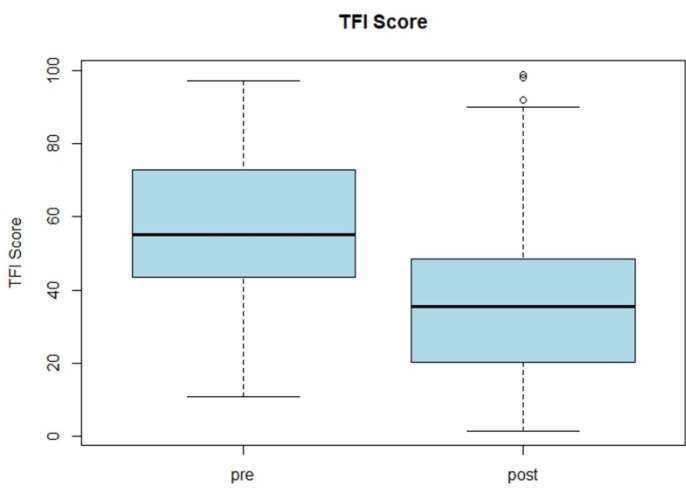


Figure 1

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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 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) |

| | | |
|--------------------------------------|--|--|
| Type of tinnitus (9 different types) | <ul style="list-style-type: none"> ▪ 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: <ul style="list-style-type: none"> ▪ 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) | <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 5–9: mild depression ▪ 10–14: moderate ▪ 15–19: moderately severe ▪ 20–18: severe depression <p>Split into dichotomous variables (≤ 14 no depression and > 14 depression)</p> |
| Insomnia | Insomnia Severity Index (ISA) | <p>7-item</p> <p>5-point scale with “no problem” (score of 0) to “very severe problem” (score of 4)</p> | <p>Higher number indicates more severe insomnia (scores range between 0–28).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–7: not clinically significant ▪ 8–14: subthreshold insomnia ▪ 15–21: clinical insomnia (moderate severity) ▪ 22–28: clinical insomnia (severe degree) <p>Split into dichotomous variables (≤ 14 no insomnia and > 15 insomnia)</p> |
| Hyperacusis | Hyperacusis Questionnaire (HQ) | <p>14-items</p> <p>4-point scale with “no” (score of 0) to “yes, a lot” (score of 3)</p> | <p>Higher number more severe hyperacusis (scores range between 0–42).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ > 28: strong hypersensitivity <p>Split into dichotomous variables (≤ 28 no hyperacusis and > 28 hyperacusis)</p> |
| Hearing disability | Hearing Handicap Inventory for Adults – Screening (HHIA-S) | <p>10-items</p> <p>3-point scale with “yes” (score of 4) to “no” day (0)</p> | <p>Higher number more severe hearing disability (scores range between 0–40).</p> <p>The total score is interpreted as follows:</p> <ul style="list-style-type: none"> ▪ 0–8: no hearing disability ▪ 10–24: mild to moderate hearing disability ▪ 26–40: severe hearing disability <p>Split into dichotomous variables (≤ 8 no hearing disability and ≥ 10 hearing disability)</p> |

| | | | |
|--------------------|--|--|--|
| 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: <ul style="list-style-type: none"> ▪ 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) |

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 | | |

| | | |
|---|--|--|
| <ul style="list-style-type: none"> ▪ Occasionally ▪ When taking out my hearing aid(s) ▪ At night ▪ Most of the time ▪ All the time | 4 (2%) 3 (1%) 4 (2%) 63 (27%) 154 (68%) | |
| Tinnitus location <ul style="list-style-type: none"> ▪ One ear ▪ Both ears ▪ In my head ▪ Other location ▪ Unsure | 61 (27%) 109 (48%) 34 (15%) 3 (1%) 21 (9%) | |
| Type of tinnitus sound (answering Yes) <ul style="list-style-type: none"> ▪ Ringing ▪ Buzzing ▪ High pitched sound ▪ Low pitched sound ▪ Pulsating ▪ Clicking ▪ Music ▪ Voices ▪ Humming | 71 (31%) 75 (33%) 130 (57%) 16 (7%) 28 (12%) 14 (6%) 4 (2%) 3 (1%) 21 (9%) | |
| Multiple sounds heard <ul style="list-style-type: none"> ▪ Yes ▪ No | 73 (32%) 155 (68%) | |
| Presence of a hearing loss <ul style="list-style-type: none"> ▪ No ▪ Both ears ▪ One ear ▪ Unsure | 49 (21%) 104 (46%) 46 (20%) 29 (13%) | |
| Treatment-related characteristics | | |
| Past tinnitus treatment sought <ul style="list-style-type: none"> ▪ Yes ▪ No | 58 (25%) 170 (75%) | |
| Sounds can distract from tinnitus <ul style="list-style-type: none"> ▪ Fully ▪ Partially ▪ Not at all | 26 (11%) 178 (78%) 24 (10%) | |
| Hearing aid use <ul style="list-style-type: none"> ▪ No ▪ Unilateral ▪ Bilateral | 159 (70%) 19 (8%) 50 (22%) | |
| Medication use <ul style="list-style-type: none"> ▪ Yes ▪ No | 130 (57%) 98 (43%) | |

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 | |

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 | |

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 | |