



**COMIT'ID study to agree the tinnitus-related domains comprising a Core Outcome Set for psychology-based clinical trials of chronic subjective tinnitus in adults**



**Consensus meeting report, Wednesday 6<sup>th</sup> September**

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**EXECUTIVE SUMMARY**

***The Core Outcome Set for testing whether sound-based treatments are beneficial for tinnitus considers the domains acceptance, mood, negative thoughts and beliefs, sense of control, and tinnitus intrusiveness.***

Everyone taking part in the COMIT'ID study agreed that one tinnitus-related outcome domain was important to assess no matter which type of tinnitus treatment is being tested. This outcome domain is tinnitus intrusiveness. Tinnitus intrusiveness describes the state of noticing the sound of tinnitus is there and it is invading your life or your personal space. For testing psychology-based therapies for tinnitus acceptance, mood, negative thoughts and beliefs, and sense of control should also be assessed. The final consensus group for psychology-based clinical trials voted in favour of these five outcome domains with over 75% agreement.

The group strongly recommended that the definitions of mood and intrusiveness are revisited to consider what aspects might be considered in their measurement. Opinions from this meeting suggested that intrusiveness encompasses the impact on aspects related to quality of life, including social life. It was unanimously agreed that mood should capture anxiety and depressive symptoms.

The definition of sense of control also warrants further examination since there was some difference in its interpretation according to whether the trial might be evaluating sound-based or psychology-based interventions. For interventions using psychology-based approaches, sense of control appeared to be more about feeling in control over the impact of tinnitus, perhaps as a consequence of more positive coping strategies. The working definition used by this group was: Whether or not you feel you have a choice in how to manage the impact of tinnitus and feelings caused by tinnitus. For interventions using sound-based products, it was felt that the device could give direct sense of personal control

over the tinnitus itself (a feeling that the device can be used to 'switch tinnitus off').

Future efforts will pair these selected outcome domains with suitable outcome instruments.

## **PURPOSE**

Different clinical trials measure and report patient benefit using different methods. As a consequence, the findings of different studies can't be compared and the data can't be pooled together. This hampers progress in finding the best treatments.

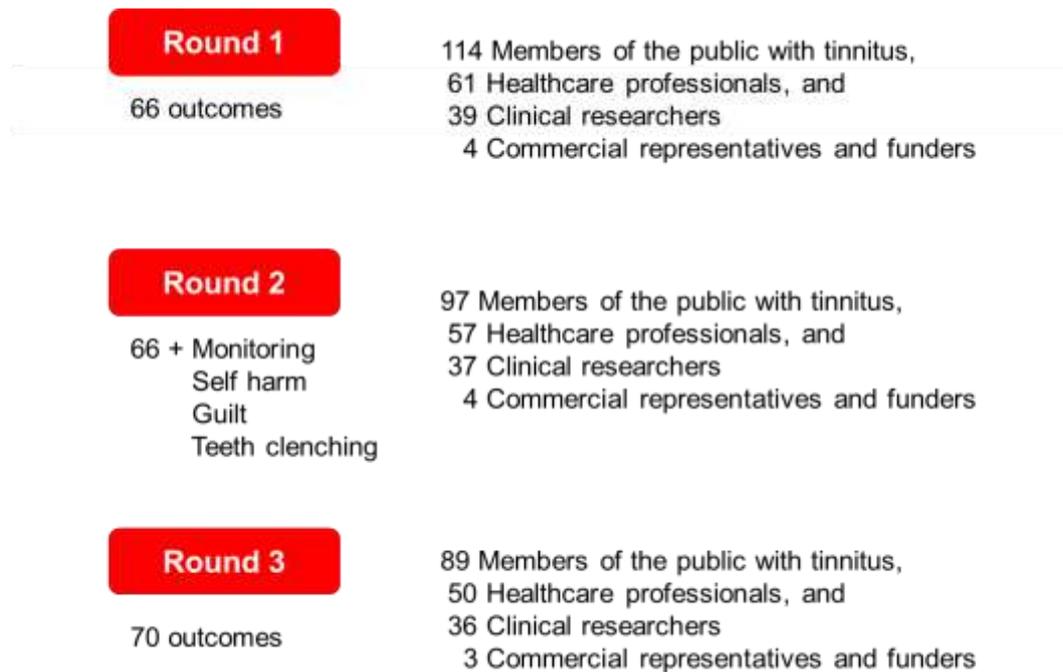
A Core Outcome Set refers to a small number of outcome domains and the corresponding instruments for measuring them that are recommended to be assessed and reported in all clinical trials. If we could agree a Core Outcome Set for tinnitus then that would go a long way to addressing current limitations.

The Core Outcome Set would *always* be measured in *every* clinical trial (at least before and after the intervention), but investigators would be free to add other outcomes as they wish.

The purpose of this study is to define the tinnitus-related domains comprising a Core Outcome Set for psychology-based interventions of chronic subjective tinnitus in adults.

### **Stage 1. The online Delphi survey**

An online Delphi survey was completed first. Delphi surveys are a tried and tested method for developing consensus in decision making among a panel of experts. Across three survey rounds, we asked tinnitus experts to think about each one of 70 different possible outcomes related to tinnitus: "Is it critically important for deciding if a treatment has worked?"



The above figure illustrates the number of outcomes considered at each round and the number of participants in each stakeholder group. Participants were representing 21 countries across the world. (UK, USA, Germany, Netherlands, Belgium, France, Switzerland, Canada, Portugal, Spain, Australia, Brazil, Italy, Singapore, Austria, Denmark, Greece, Ireland, Poland, Romania, Russia).

In round 1, we also invited participants to suggest any additional outcomes which they felt were missing from our original list of 66. From these suggestions, we identified 4 new outcomes that were not already covered by one of the outcomes already on the list. These were 'Monitoring: Regularly checking up on your tinnitus in different situations', 'Self-harm: To deliberately injure yourself, caused by the distress of your tinnitus', 'Guilt: Feeling responsible or at fault for the tinnitus or for its effects on others close to you', and 'Teeth clenching: Grinding your teeth or clenching your jaw in reaction to your tinnitus'. These were added for consideration by all participants in round 2.

### **Delphi survey findings**

The scores were evaluated for all those participants completing round 3. The study team had pre-defined agreement as when 70% or more participants in each stakeholder group said the outcome was important AND critical for determining if the psychology-based treatment was working (score 7-9) AND 15% or fewer said the outcome was neither important nor critical (score 1-3). The following figure shows the results from this analysis about those outcomes reaching consensus.

**Agreement =**

70% or more people said the outcome was important AND critical for determining if the psychology-based treatment was working (score 7-9)

AND

15% or fewer people said the outcome was neither important nor critical (score 1-3)

**Round 3**

Members of the public with tinnitus, Healthcare professionals, and Clinical researchers <b>all reached agreement to include</b>	24/70 outcomes
Only one or two stakeholder groups reached agreement to include	30/70 outcomes
None of the groups reached agreement to include	16/70 outcomes

All stakeholder groups agreed that these 24 outcome domains are important and critical:

Ability to ignore, Acceptance of tinnitus, Annoyance, Anxiety, Catastrophising, Concentration, Coping, Depressive symptoms, Difficulties getting to sleep, Fear, Helplessness (lack of control), Impact on individual activities, Impact on relationships, Impact on social life, Impact on work, Irritable, Mood, Negative thoughts/beliefs, Quality of sleep, Sense of control, Suicidal thoughts, Tinnitus intrusiveness, Tinnitus related thoughts, Worries/concerns.

**Stage 2. The face-to-face consensus meeting**

19 participants attended this meeting (10 members of the public with tinnitus, 4 healthcare professionals and 5 researchers)

In all voting, agreement was defined as at least 70% or more participants voting for either 'agree' or for 'disagree/unsure'.

The scope of this meeting was constrained by the result of the Delphi survey in which 24 outcomes were considered to be important and critical by all stakeholder groups. If all 24 outcomes were voted into the Core Outcome Set then this could potentially mean that all clinical trials would have to include at least 24 measurement instruments. The Study Team were concerned that this was just not feasible for clinical trial sites, nor ethical. The consensus meeting

therefore started with a discussion and vote on the scope of the agenda (Q1, Table 1). It was agreed that the discussion be constrained to the 24 outcomes, and that the goal should be to reduce these down to a Core Outcome Set of no more than 6. Remember that this Core Outcome Set would *always* be measured in every clinical trial (at least before and after the intervention), but investigators would be free to add other outcomes as they wish.

### **First round: Top and bottom selections proposed by each subgroup**

Participants were first divided into two subgroups (n=10, n=10). Individuals in each subgroup had been asked to choose their top three outcomes from the list of 24, prior to the meeting. The combined total of these votes was then used to lay out cards (each containing one outcome name and description) on a table, ordered from the greatest number of votes at the top downwards.

**Green table** The combined votes for the subgroup facilitated by Deborah gave the following order:

Ability to ignore (n=4), Tinnitus intrusiveness (n=4), Acceptance of tinnitus (n=2), Depressive symptoms (n=2), Difficulties getting to sleep (n=2), Impact on individual activities (n=2), Impact on work (n=2), Sense of control (n=2), Annoyance (n=1), Anxiety (n=1), Catastrophizing (n=1), Fear (n=1), Helplessness (sense of control) (n=1), Suicidal thoughts (n=1), Tinnitus-related thoughts (n=1).

**Orange table** The combined votes for the subgroup facilitated by Sarah gave the following order:

Tinnitus intrusiveness (n=5), Ability to ignore (n=4), Acceptance of tinnitus (n=4), Sense of control (n=3), Concentration (n=2), Coping (n=2), Impact on individual activities (n=2), Mood (n=2), Negative thoughts/beliefs (n=2), Anxiety (n=1), Catastrophizing (n=1), Depressive symptoms (n=1), Fear (n=1).

The goal for each subgroup was to initially discuss and jointly agree which domains are sufficiently critical and important to make it into the Core Outcome Set (maximum = 6) and which are **not** sufficiently critical to include in every clinical trial. To facilitate discussion, the cards could be moved around the table and reordered according to the majority views of the subgroup. Two pieces of string marked the cut-offs for the top and bottom selections proposed by each subgroup.

The green table discussions lead to the following interim top 4:

- Ability to ignore
- Sense of control
- Difficulties getting to sleep
- Tinnitus intrusiveness

There were 4 other outcomes which were highlighted, but there was no agreement about these in the timescale of the discussion.

- Depressive symptoms
- Acceptance of tinnitus
- Impact on work

- Impact on activities

Anxiety and fear were recognised as being of specific personal importance for some people with tinnitus, but not all.

The orange table discussions lead to the following interim top 8:

- Tinnitus intrusiveness
- Ability to ignore
- Acceptance of tinnitus
- Impact on activities
- Concentration
- Negative thoughts/beliefs
- Coping
- Mood

Sense of control was discussed extensively, because this was of specific personal importance for some people with tinnitus, where others mentioned one can never really “control” tinnitus in the sense of “being able to switch it on and off”. Sense of control was eventually set aside, because the subgroup felt that some psychological approaches are focused on acceptance rather than control. So sense of control may not be relevant to all therapies.

Results from the two subgroups were first pooled to cluster outcomes into three categories according to those selections:

Outcomes that were included in the top ‘set’ by both subgroups were : Ability to ignore, Acceptance of tinnitus, Impact on activities, and Tinnitus intrusiveness.

Outcomes included in the top set by one subgroup but not the other were : Concentration, Coping, Depressive symptoms, Difficulties getting to sleep, Impact on work, Mood, Negative thoughts/beliefs, and Sense of control.

Outcomes that both subgroups selected as **not** critical and important for every clinical trial of a psychology-based intervention were: Annoyance, Anxiety, Catastrophizing, Fear, Helplessness, Irritable, Impact on relationships, Impact on social life, Quality of sleep, Suicidal thoughts, Tinnitus-related thoughts, and Worries/concerns.

This selection led to full group discussion and then voting on Q2-4 (Table 1). 74% of the group agreed to set aside 10 outcomes (Annoyance, Catastrophising, Fear, Helplessness, Irritable, Impact on relationships, Quality of sleep, Suicidal thoughts, Tinnitus-related thoughts, and Worries/concerns). Reasons given can be found in Table 2. This gave 14 outcomes for further discussion and voting.

### **Second round: Top and bottom selections proposed by each subgroup**

The next goal for each subgroup was to discuss and jointly agree on no more than 6 outcomes for further consideration. To facilitate discussion, the cards could be moved around the table. This time only one piece of string marked the cut-off for the top and bottom selections proposed by each subgroup. The results from both groups were pooled to cluster the outcomes into three categories.

Outcomes that were included in the top 'set' by both subgroups were: Mood, Sense of control, and Tinnitus intrusiveness.

Outcomes in the top 6 of one subgroup but not the other: Acceptance of tinnitus, Coping, Difficulties getting to sleep, Negative thoughts/beliefs

Outcomes not in the top 6 of either subgroup lists : Ability to ignore, Concentration, Depressive symptoms, Impact on activities, and Impact on work.

This selection led to a full group discussion and voting on several matters arising (Q5-6, Table 1). One concerned the overlap in constructs between the various facets of mental health. The group agreed unanimously (100%) that it was acceptable to set aside the two outcomes Anxiety and Depressive symptoms, if these feelings were captured by Mood. Another concerned the scope of Tinnitus intrusiveness. Again, the group agreed unanimously (100%) that it was acceptable to set aside Impact on relationships and Impact on work, if these specific ways in which tinnitus can intrude in your everyday life were captured by Tinnitus intrusiveness. Furthermore, an important facet of Intrusiveness was also considered to be the impact on Concentration. The group agreed that a lot further discussion is needed about how Intrusiveness should be measured, because it impacts on so many situations/scenarios as well as at different times of the day.

Voting then decided to set aside 6 more outcomes from the Core Domain Set: Ability to ignore, Anxiety, Depressive symptoms, Impact on work, Impact on activities, Impact on social life (Q7, Table 1). Reasons given can be found in Table 2. This left 8 outcomes for individual voting.

### **Voting on the remaining individual domains**

Table 1 Q8-15 shows the voting scores for Acceptance, Concentration, Coping, Difficulties getting to sleep, Mood, Negative thoughts and beliefs, Sense of control, and Tinnitus intrusiveness.

**Table 1. Questions discussed and votes cast during the consensus meeting**

	Agree (%)	Disagree (%)	Unsure (%)
Q1) Today's discussion will focus on the 24 outcome domains that all 3 groups (Members of the public with tinnitus, Healthcare professionals, and Clinical researchers) agreed to include in the COS. The remaining 46 domains will not be discussed	79	11	11
One participant said that they selected 'unsure' just to see what would happen if they press this option!			
Q2) Do you agree to put 'anxiety', 'impact on social life' and 'annoyance' on the list for further discussion?	68	21	11
Those voting 'unsure' indicated that 'annoyance' was an outcome which they felt could be moved to the category of outcomes to be set aside from further discussion.			
Q3) Do you agree to put 'anxiety' and 'impact on social life' on the list for further discussion?	79	21	0
Q4) Do you agree to put aside: 'annoyance' 'catastrophising' 'fear' 'helplessness' 'irritable' 'impact on relationships' 'quality of sleep' 'suicidal thoughts' 'tinnitus-related thoughts' 'worries/concerns'	74	21	5
Q5) Do you agree that the definition of 'mood' includes feelings of anxiety and depression?	100	0	0
The group agreed that it was acceptable to set aside 'anxiety' and 'depressive symptoms' if these feelings were captured by 'mood'			
Q6) Do you agree that the definition of 'intrusiveness' includes 'impacts on everyday life'	100	0	0
The group agreed that it was acceptable to set aside 'impact on relationships' and 'impact on work' if 'intrusiveness' captured specific ways in which tinnitus can intrude in your everyday life. Furthermore, an important facet of 'intrusiveness' was also considered to be the impact on 'concentration'. The group agreed that a lot further discussion is needed about how 'intrusiveness' should be measured, because it impacts on so many situations/scenarios as well as at different times of the day.			
Q7) Do you agree to put aside: 'ability to ignore' 'depressive symptoms' 'anxiety' 'impact on work'	95	0	5

'impact on activities' 'impact on social life'			
Those voting 'unsure' were not sure that 'ability to ignore' should be put aside.			
Q8) Do you agree that 'mood' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: Consensus 'in' reached - include</b>	100	0	0
Q9) Do you agree that 'Sense of control' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: Consensus 'in' reached - include</b>	84	5	11
The outcome name generated a lot of disagreement. Some felt that it implies that a goal should be about controlling tinnitus whereas the concept is actually more about sensing there is a choice and about the feelings generated by having a sense of control. The individuals who voted disagree/no to Q9 felt that 'acceptance' was more important than 'sense of control'. They were partly compelled by the group discussion, but not enough to vote in favour.			
Q10) Do you agree that 'Intrusiveness' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: Consensus 'in' reached - include</b>	95	5	0
Q11) Do you agree that 'Difficulties getting to sleep' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: No consensus, set aside</b>	39	58	11
The clinicians noted that not all patients report sleep difficulties, but for those patients who do have sleep problems, then this outcome is one of <b>the</b> most important since it is fundamental to health and well-being.			
Q12) Do you agree that 'Coping' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: No consensus, set aside</b>	63	16	21
A hearing therapist in the group felt that this outcome name needed to be revised to encompass all aspects of coping (especially emotional and problem-focussed coping) otherwise psychologically speaking the concept is incorrect. The description was felt to be acceptable.			
Q13) Do you agree that 'Acceptance of tinnitus' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: Consensus 'in' reached - include</b>	84	5	11
Q14) Do you agree that 'Negative thoughts and beliefs' is critical to be measured in every clinical trial for a psychology-based tinnitus treatment? <b>Decision: Consensus 'in' reached - include</b>	79	5	16
Hearing therapists in the group felt that this outcome name was overly negative and it omitted to concept relating to the process of evaluating those thoughts. There was also some concern that it might be more relevant for some psychological approaches than others.			
Q15) Do you agree that 'Concentration' is critical	11	84	5

to be measured in every clinical trial for a psychology-based tinnitus treatment?			
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**Decision: No consensus, set aside**

The group agreed that changes in 'concentration' are captured by 'intrusiveness'. "When your tinnitus is less intrusive, your concentration will improve".

Table 2.

Outcome domain reaching consensus in the Delphi	Comments in favour	Comments against
Ability to ignore	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>Might be better captured by tinnitus intrusiveness</li> <li>Some patients are able to cope with their tinnitus without trying to ignore it</li> <li>Some psychological treatments specifically aim not to ignore the tinnitus</li> </ul>
Acceptance of tinnitus	<ul style="list-style-type: none"> <li>This is a point from where the patient can move on</li> </ul>	<ul style="list-style-type: none"> <li>Some felt this was a more 'passive' domain that does not accurately reflect a reduction of the impact of/ distress caused by tinnitus</li> </ul>
Annoyance	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>
Anxiety	<ul style="list-style-type: none"> <li>When a patient is anxious, this has a big impact on him/her life</li> <li>Identified as a major focus of psychology-based treatments</li> </ul> <p><i>Note: Agreed that final domain "Mood" would capture anxiety and depressive symptoms</i></p>	<ul style="list-style-type: none"> <li>If anxiety is thought of as a clinical anxiety disorder (as the definition says) this applies to a very limited number of tinnitus patients</li> <li>Can be captured in 'Mood'</li> </ul>
Catastrophizing	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>
Concentration	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>There might be other reasons for lack of concentration than just the tinnitus alone. Might not be a very sensitive measure for effect of psychological treatment.</li> <li>Some considered this as similar to tinnitus intrusiveness</li> </ul>
Coping	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>Improving on a coping scale (as in using different coping strategies) does not always mean that the patient is improving</li> </ul>
Depressive symptoms	<ul style="list-style-type: none"> <li>When a patient is depressed, this has a big impact on him/her life</li> </ul>	<ul style="list-style-type: none"> <li>If depressive symptoms are thought of as a clinical depression (as the definition says) this</li> </ul>

		<p>applies to a very limited number of tinnitus patients</p> <ul style="list-style-type: none"> <li>• Can be captured in 'Mood'</li> </ul>
Difficulties getting to sleep	<ul style="list-style-type: none"> <li>• One participant mentioned that sleep is fundamental to general health</li> <li>• Identified that this is often a big focus for psychology-based treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Can be captured in 'tinnitus intrusiveness'</li> <li>• Not everyone has 'difficulties getting to sleep', therefore it should not be measured in every study</li> </ul>
Fear	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Helplessness (lack of control)	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Impact on individual activities	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• This can also be captured in the 'tinnitus intrusiveness' domain</li> </ul>
Impact on relationships	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• This can also be captured in the 'tinnitus intrusiveness' domain</li> </ul>
Impact on social life	<ul style="list-style-type: none"> <li>• One participant was quite sure that this item was the most important item to question, because ones social life is essential for well being</li> <li>• Tinnitus is widely acknowledged (by community) to have a large impact on social activities (e.g. can cause isolation)</li> </ul> <p><i>Note: Group agreed that core intrusiveness domain would capture impact on QOL aspects such as social life</i></p>	<ul style="list-style-type: none"> <li>• This can also be captured in the 'tinnitus intrusiveness' domain</li> </ul>
Impact on work	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• This can also be captured in the 'tinnitus intrusiveness' domain</li> </ul>
Irritable	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	
Mood	<ul style="list-style-type: none"> <li>• Subclinical 'anxiety' and 'depressive symptoms' should be added to the description of 'mood'</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Negative thoughts/beliefs	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• It is more a process in the therapy than an outcome measure</li> <li>• More relevant to some psychological treatments than to others</li> </ul>
Quality of sleep	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• For some people with</li> </ul>

		tinnitus this is a very important item, but for many others it isn't
Sense of control	<ul style="list-style-type: none"> <li>• Crucial outcome measure</li> <li>• A construct that covers many aspects relating to tinnitus</li> <li>• Considered most important when symptoms are severe (e.g. sleep difficulties)</li> <li>• One patient felt that this an 'active' domain (unlike acceptance) that can represent a strong motivator for a patient to use a treatment</li> </ul> <p><i>Note: Sense of control was interpreted very differently in the context of sound based treatment. In this context, participants felt that it was possible to directly 'control' tinnitus with sound therapy.</i></p>	<ul style="list-style-type: none"> <li>• 'Acceptance of tinnitus' seems more important for some</li> <li>• Some felt that the application of coping techniques was more important than a feeling of control</li> <li>• Too broad</li> <li>• Encapsulated by other aspects</li> <li>• Some clinicians disliked the term "control" as this is not aligned with psychological treatment (i.e. tinnitus cannot be switched off)</li> </ul>
Suicidal thoughts	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Tinnitus intrusiveness	<ul style="list-style-type: none"> <li>• The definition should describe in more detail in which way tinnitus can be intrusive (e.g. impact on social life, impact on work, impact on relationships, impact on individual activities, difficulties getting to sleep, quality of sleep)</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Tinnitus related thoughts	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
Worries/concerns	<ul style="list-style-type: none"> <li>• N/A</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>