

**Supplementary file 5.** Comments in favour and against, explaining the reasons for setting aside those outcome domains which failed to reach the 70% consensus in the face-to-face meeting for pharmacology-based interventions. Votes represent the % of the 16 participants who agreed that these outcome domains were *not* critical to be measured in every clinical trial for pharmacology-based tinnitus treatments (threshold  $\geq 30\%$ ). \*Note that participants voted to replace ‘anxiety’ and ‘depressive symptoms’ by the concept ‘mood’ during this face-to-face meeting.

Pharmacology-based exclusions	Vote	Comments in favour	Comments against
Ability to ignore	88	<i>No strong views expressed.</i>	<ul style="list-style-type: none"> <li>• ‘Ability to ignore’ was considered much less ambitious than ‘Intrusiveness’. ‘Ability to ignore’ merely suggests helping people to manage, ‘intrusiveness’ suggests seeking a cure.</li> <li>• The concept could be interpreted differently by different people.</li> </ul>
Adverse reaction	100	Agreed important to always measure for drug trials.	Adverse events are already a necessity by the regulatory authorities for any properly conducted double-blinded randomised controlled pharmacological trial, and so on that basis the group felt that it was pointless to include as a COS.
Annoyance	88	<ul style="list-style-type: none"> <li>• Concept of annoyance can be easily explained and interpreted.</li> <li>• Can have an impact on a variety of activities (e.g. social interaction)</li> </ul>	<ul style="list-style-type: none"> <li>• Some considered this too ‘mild’ or ‘trivial’.</li> <li>• The group felt ‘annoyance’ could be covered by other domains (e.g. ‘intrusiveness’).</li> <li>• Some believed it to be too subjective and personality-dependent.</li> </ul>
*Anxiety	88	People with tinnitus are often in a state of anxiety, which is separate from depressive symptoms, but may be related.	<ul style="list-style-type: none"> <li>• ‘Anxiety’ is a secondary consequence of tinnitus.</li> <li>• It can be treated by anxiolytics, not a direct target for tinnitus drugs.</li> <li>• Both anxiety and depressive symptoms could be captured together as feelings related to mood. The definition of ‘mood’ indicates a sense of well-being rather than having a psychiatric classification.</li> </ul>
Concentration	88	<i>No strong views expressed.</i>	<ul style="list-style-type: none"> <li>• Concentration problems are not specific to tinnitus.</li> <li>• Some felt this was covered adequately by ‘tinnitus intrusiveness’.</li> </ul>
Confusion	100	<i>No strong views expressed.</i>	Too general, may not necessarily be specific to tinnitus.
Coping	88	<i>No strong views expressed.</i>	<ul style="list-style-type: none"> <li>• Coping techniques felt to be less relevant to pharmaceutical interventions.</li> </ul>

*Depressive symptoms	88	People with tinnitus often experience depressive symptoms, which is separate from anxiety, but may be related	<ul style="list-style-type: none"> <li>• ‘Depressive symptoms’ are a secondary consequence of tinnitus.</li> <li>• It can be treated with antidepressants, not a direct target for tinnitus drugs.</li> <li>• Both ‘depressive symptoms’ and ‘anxiety’ could be captured together as feelings related to mood, since they are more about having a sense of well-being than having a psychiatric classification.</li> </ul>
Difficulties getting to sleep	100	<i>No strong views expressed.</i>	<ul style="list-style-type: none"> <li>• Difficulties getting to sleep can be part of a hierarchy of sleep problems that is better captured by ‘quality of sleep’. Quality of sleep is more encompassing.</li> <li>• Not all people with tinnitus have problems with sleep and a good core outcome will be relevant to everyone.</li> </ul>
Impact on individual activities	31	<ul style="list-style-type: none"> <li>• Recognises the World Health Organisation ICF framework (i.e. activity limitations) and is an indicator of well-being.</li> <li>• May be less influenced by personality type (introvert vs extrovert).</li> <li>• Some felt it could be sensitive to change in the short term (i.e. during a clinical trial)</li> </ul>	<i>No strong views expressed.</i>
Impact on social life	88	Recognises the World Health Organisation ICF framework (i.e. social participation) and is an indicator of well-being.	<ul style="list-style-type: none"> <li>• Tinnitus interventions can only partly influence this outcome. It may be more to do with the number of social interactions the individual has.</li> <li>• May be influenced by extrovert more than introvert personality type.</li> <li>• Some doubted that people with tinnitus could show a change on this parameter over a short time period (i.e. during a clinical trial).</li> </ul>
Impact on work	88	<i>No strong views expressed.</i>	Not applicable to those who are in education, retired, or otherwise not working
Mood (replaced ‘anxiety’ and ‘depressive symptoms’)	75	<ul style="list-style-type: none"> <li>• The group noted that regulatory bodies typically seek evidence of quality of life benefit in clinical trials, so ‘mood’ could be an indicator of therapeutic benefit.</li> </ul>	<ul style="list-style-type: none"> <li>• The definition of ‘mood’ is too unspecific.</li> <li>• The impact of ‘mood’ on quality of life can be captured by ‘intrusiveness’.</li> <li>• ‘Mood’ is a secondary consequence of tinnitus. It implies emotional issues that may not be specific to the tinnitus.</li> </ul>

			<ul style="list-style-type: none"> <li>• It can be treated with other drugs, not a direct target for tinnitus drugs.</li> <li>• Could be more useful as a stratification tool when interpreting data from clinical trials.</li> </ul>
Quality of sleep	62	<ul style="list-style-type: none"> <li>• 'Quality of sleep' captures all different aspects of tinnitus-related sleep complaints.</li> <li>• Disruption of sleep quality is described as a major complaint associated with tinnitus.</li> <li>• Some suggested that poor sleep quality could directly modulate tinnitus intrusiveness and loudness so it is therefore important to understand changes in these aspects.</li> </ul>	<ul style="list-style-type: none"> <li>• Not all people with tinnitus have problems with sleep and a good core outcome will be relevant to everyone.</li> <li>• The group felt that inclusion of 'quality of sleep' in the COS may weaken the power of the trial because it is not common to all people with tinnitus.</li> </ul>
Tinnitus unpleasantness	100	<i>No strong views expressed.</i>	<ul style="list-style-type: none"> <li>• The group had doubts that a drug therapy could change the degree of 'pleasantness' (i.e. believed unlikely to change tinnitus quality or pitch).</li> <li>• There were mixed feelings about 'unpleasantness' since what is deemed to be unpleasant is quite individual and may be more driven by personality.</li> <li>• Individual interpretations of the construct could make it hard to come up with a reliable measure.</li> </ul>
Treatment satisfaction	88	<i>No strong views expressed.</i>	This is not specific to the tinnitus.