#### PERSPECTIVES

# JARO



### The Current State of Tinnitus Diagnosis and Treatment: a Multidisciplinary Expert Perspective

Tobias Kleinjung<sup>1,2</sup> · Nicole Peter<sup>1,2</sup> · Martin Schecklmann<sup>3,4</sup> · Berthold Langguth<sup>3,4</sup>

Received: 28 December 2023 / Accepted: 31 July 2024  $\ensuremath{\mathbb{C}}$  The Author(s) 2024

#### Abstract

Tinnitus, the perception of sound without an external source, affects 15% of the population, with 2.4% experiencing significant distress. In this review, we summarize the current state of knowledge about tinnitus management with a particular focus on the translation into clinical practice. In the first section, we analyze shortcomings, knowledge gaps, and challenges in the field of tinnitus research. Then, we highlight the relevance of the diagnostic process to account for tinnitus heterogeneity and to identify all relevant aspects of the tinnitus in an individual patient, such as etiological aspects, pathophysiological mechanisms, factors that contribute most to suffering, and comorbidities. In the next section, we review available treatment options, including counselling, cognitive-behavioral therapy (CBT), hearing aids and cochlear implants for patients with a relevant hearing loss, sound generators, novel auditory stimulation approaches, tinnitus retraining therapy (TRT), pharmacological treatment, neurofeedback, brain stimulation, bimodal stimulation, Internet- and app-based digital approaches, and alternative treatment approaches. The evidence for the effectiveness of the various treatment interventions varies considerably. We also discuss differences in current respective guideline recommendations and close with a discussion of how current pathophysiological knowledge, latest scientific evidence, and patient perspectives can be translated in patient-centered care.

Keywords Tinnitus · Evidence · Guidelines · Meta-analysis · Treatment

#### Introduction

Tinnitus, which is characterized by the perception of sound without any external acoustic signal, affects approximately 15% of the population [1]. While the majority of individuals with tinnitus are not severely impaired, around 2.4% experience significant distress [1]. These individuals suffer from significant impairment and often have comorbidities such as hyperacusis, insomnia, anxiety, or depression, which adds to the complexity of their condition [2]. Recently, a new diagnostic classification has been proposed to distinguish

- <sup>1</sup> Department of Otorhinolaryngology Head and Neck Surgery, University Hospital Zurich, Zurich, Switzerland
- <sup>2</sup> University of Zurich, Zurich, Switzerland
- <sup>3</sup> Department of Psychiatry and Psychotherapy, University of Regensburg, Bezirksklinikum, Universitätsstr. 84, 93049 Regensburg, Germany
- <sup>4</sup> Multidisciplinary Tinnitus Clinic, University of Regensburg, Regensburg, Germany

between pure "tinnitus" and the more disabling "tinnitus disorder" [3].

In the field of tinnitus, a further distinction can be made between objective and subjective forms. Objective tinnitus, also known as "somatosound," refers to internally generated sounds such as sounds caused by muscle movements or blood flow. This review focuses on chronic subjective tinnitus, where the perceived sound has no identifiable external or internal source. According to a recent consensus, article chronic tinnitus is defined by a duration of at least 3 months [3].

In this review, we summarize current state of knowledge about the diagnostic work-up and evidence-based treatment options for tinnitus, with a particular focus on their implementation into clinical practice. With authors representing various disciplines (otology and neurotology (T. K.; N. P.), psychology (M. S.), psychotherapy (M. S.: B.L), and neurology and psychiatry (B.L.)), we want to emphasize the need for a multidisciplinary approach for tinnitus management.

Berthold Langguth Berthold.Langguth@medbo.de

#### Shortcomings and Challenges in Tinnitus Management

The diagnostic and therapeutic landscape for tinnitus patients varies considerably across countries and even within regions. Patients may receive different treatments depending on which institution they approach, reflecting the current lack of standardized, evidence-based care [4]. There are also differences in the assessment of individuals with tinnitus, influenced by factors such as point of contact, cultural differences, and variations in the healthcare system. Ideally, an evidence-based, stepwise diagnostic approach should be implemented universally, regardless of the first point of contact within the healthcare system [5]. Similarly, treatment decisions should be tailored to the individual patient rather than the treating clinician's specialty. Both patients and clinicians are dissatisfied with the current state of tinnitus management [4]. Given the prevalence, significant impact on affected individuals, and chronic nature of tinnitus, there is an urgent need for effective treatments.

The current unsatisfactory state of tinnitus management [4] is due to several factors. First, there is no treatment that can reliably eliminate tinnitus or reduce its loudness, which would be the main wish of most patients [6–9]. Although there are reports of single cases of tinnitus remission, no causal relationship has been established between specific therapeutic interventions and the disappearance of tinnitus in these patients [10]. However, there are many evidence-based options to reduce tinnitus suffering [4].

Tinnitus exhibits significant heterogeneity in terms of clinical features, pathophysiology, and response to treatment [11–13]. Efforts to classify different clinical subtypes have had limited success [14–16]. Profiling patients according to dimensions such as tinnitus severity, somatosensory impact, and hearing loss may be more pragmatic [16, 17]. Furthermore, the current understanding of the pathophysiology of the different forms of tinnitus is still incomplete [18], impeding progress in the development of effective treatments. Imaging, electrophysiologic, and genetic studies provide mixed results, and the limited power of animal models makes matters even more challenging [18]. Unlike serendipitous discoveries in other medical fields, such breakthroughs in tinnitus research have so far failed to occur [19].

The lack of established biomarkers and objective outcome measures complicates clinical research. Standardized questionnaires have been developed to assess various aspects of tinnitus, including distress, handicap, and functional impairment [20]. A longer-lasting reduction in tinnitus loudness, which is desired by most patients [6], can currently only be achieved by cochlear implants for unilateral deaf patients [21]. Reductions in tinnitus loudness due to phenomena such as residual inhibition are only short term and not permanent. Tinnitus loudness can be assessed by psychophysical methods such as loudness matching or minimal masking level or by subjective assessment using scales such as visual analogue or numeric rating scales. However, psychophysical measurements have a low reliability, and do not reflect subjective changes. As the subjective assessment of loudness can be affected by distress, the determination of tinnitus loudness remains complicated [22].

In clinical trials, therefore, the gold standard for primary outcome measurement is the use of tinnitus questionnaires, which provide a more comprehensive and reliable assessment of the multiple manifestations of tinnitus [23, 24]. In contrast, measures of tinnitus loudness, although valuable, are of secondary importance as outcome measures in such trials. The clinical relevance of score reductions of existing questionnaires [25] and whether they adequately cover all relevant domains of tinnitus impairment [26] are the subject of ongoing debate.

## Comprehensive Diagnostic Assessment of Tinnitus as a Basis for Treatment

Usually, recommendations for diagnostic assessment by means of history taking and clinical examination are based less on evidence from systematic controlled trials but rather on expert recommendations. This is also the case in the tinnitus field. Here, we summarize recommendations from guidelines [27] [28] and the authors' clinical experience [29, 30].

At the beginning of each assessment, it is crucial to realize that tinnitus can create a high degree of uncertainty and psychological stress. Patients may fear that tinnitus may indicate a serious underlying condition, even though such cases represent only a small minority. The initial case history interview, therefore, requires a high degree of seriousness, reliability, and empathy. It is equally important to conduct this conversation carefully in order to avoid unnecessary sensitization and to prevent an excessive focus on the symptom and the development of unnecessary fears. An essential goal is to live with chronic tinnitus without handicap, which means with a minimum of emotional and physiological stress and without avoiding activities, which improve quality of life. It is important to find a balance between awareness for tinnitus conditions at the beginning of the diagnostic process (e.g., to find out relevant causal and modulating factors) and the long-term strategy of avoiding sensitization to the symptom, as it is the therapeutic idea in psychosomatic disorders.

Subsequently, it is important to ask about the circumstances that led to the onset of tinnitus, such as noise exposure, ear infections, or stressful situations. The duration of the symptoms and the examination of accompanying otological symptoms such as perceived hearing loss, dizziness, or otalgia are also important parts of the diagnostic process. The laterality and quality of the sound are of critical importance, as unilateral sounds may indicate a structural origin, which can potentially be treated causally. Determining whether the sound is continuous, rhythmically pulsatile, or pulse synchronous provides valuable information about the nature of the tinnitus, with pulsatile symptoms warranting imaging, particularly if they persist for more than 3 months.

Pure-tone audiometry should be performed in every tinnitus patient, even if no impairment is perceived, as it can reveal subtle hearing loss that may impact speech comprehension or occur in ultrahigh-frequency ranges [31]. In addition to its diagnostic value, pure-tone audiometry provides guidance for potential therapeutic interventions such as hearing aids and informing discussions about the conceptual development of tinnitus. For non-pulsatile unilateral tinnitus, imaging, such as MRI of the temporal bone, is recommended, especially if an asymmetrical hearing loss is ipsilateral to the tinnitus side.

Active exploration of possible psychological distress related to tinnitus and previous distressing circumstances is crucial. By supplementing interviews with standardized questionnaires, such as Tinnitus Handicap Inventory (THI) [32] and Tinnitus Functional Index (TFI) [33], the severity of distress can be quantified, providing clinicians with guidance towards psychiatric/psychotherapeutic assessment and treatment.

Active questioning for possible modulation of tinnitus through manipulation of the neck and masticatory muscles is recommended. Such modulation suggests a somatic tinnitus component and opens up possibilities for physiotherapeutic interventions [34, 35].

Finally, it is important to identify the primary source of distress related to the patient's tinnitus, as this serves as an important guide for treatment. For instance, if a patient's primary complaint is tinnitus-induced insomnia, the treatment plan should incorporate strategies to address and alleviate insomnia. The question about the primary source of distress should be complemented by exploration of comorbidities such as anxiety, depression, insomnia, hyperacusis, communication difficulties, temporomandibular joint disorder, headache, or neck pain. These comorbidities can have a negative impact on tinnitus and also increase the overall burden of the patients. Therefore, the treatment plan should also address these comorbidities.

In summary, a comprehensive diagnostic work-up should explore underlying mechanisms and comorbidities of tinnitus in auditory, somatosensory, and psychological domains. Establishing an understanding of atmosphere is essential for fostering a therapeutic relationship. Based on the diagnosis, informative counselling sessions can be initiated, and potential somatic therapy approaches can be evaluated. For persistent and severely impairing tinnitus symptoms, a specialized interdisciplinary team provides an ideal setting for a comprehensive assessment and treatment to improve overall quality of life.

#### **Treatment of Tinnitus**

Many different tinnitus treatments have been proposed. Box 1 provides a (possibly incomplete) overview of therapeutic interventions, which have been investigated in clinical trials. Due to the limited knowledge of the pathophysiological mechanisms of tinnitus, most approaches have only a weak pathophysiological rationale and follow a "trial-and-error" approach.

Box 1 Therapeutic interventions for tinnitus that have been evaluated with randomized controlled trials (listed in alphabetical order; treatments recommended by most guidelines are listed in bold and marked with "recommended by guidelines"; see also Table 1, modified from [36]).

#### Pharmacological interventions • Antidepressants Amitriptyline Nortriptyline Paroxetine Sertraline Trimipramine • Anticonvulsants Carbamazepine Gabapentin Lamotrigine Selurampanel Benzodiazepines/GABAergic drugs Alprazolam Baclofen Clonazepam Diazepam • Glutamatergic drugs Acamprosate Esketamine Memantine Neramexane Muscle relaxants Cyclobenzaprine

Table 1 Evidence	for several tinnitu	s treatments and r	ecommendations of	the various guidelin	nes (listed in alphabe	tical order; modified	from [36])		
Intervention	Source of evi- dence	Number of study partici- pants	Efficacy (immedi- ate)	Efficacy (long term)	Potential harm	US (2014)	European (2019)	NICE (2020)	German (2021)
Anticonvulsants	Cochrane [59]	453	Insufficient evi- dence	Not reported	Side effects reported in 18% of participants	Clinicians should not routinely recommend anticonvulsants for a primary indication of treating persis- tent, bother- some tinnitus (recommenda- tion against)	Weak recommen- dation against pharmacologi- cal treatment	Not mentioned	Strong recommen- dation against pharmacological treatment
Antidepressants	Cochrane [60]	610	Insufficient evi- dence	Not reported	Side effects com- mon	Clinicians should not routinely recommend antidepressants for a primary indication of treating persis- tent, bother- some tinnitus (recommenda- tion against)	Weak recommen- dation against pharmacologi- cal treatment	Not mentioned	Strong recommen- dation against pharmacological treatment
Auditory training	Systematic review [48]	269	Available evidence of insufficient quality to make conclusion about efficacy	Not reported	Not reported	Not mentioned	Not mentioned	Not mentioned	Recommendation for auditory training
Betahistine	Cochrane [74]	303	No significant effects on tin- nitus loudness or distress	Not reported	Side effects on placebo level	Not mentioned	Weak recommen- dation against pharmacologi- cal treatment	Do not offer betahistine to treat tinnitus	Strong recommen- dation against pharmacological treatment
Cochlear implant	Meta-analysis [75]	674	Tinnitus score (SMD: – 1.32)	Not reported	not reported	Not mentioned	No recommenda- tion for coch- lear implants	Not mentioned	Strong recommen- dation for coch- lear implants in patients with tinnitus and severe hearing loss/deafness

Table 1 (continue	(p								
Intervention	Source of evi- dence	Number of study partici- pants	Efficacy (immedi- ate)	Efficacy (long term)	Potential harm	US (2014)	European (2019)	NICE (2020)	German (2021)
Cognitive behav- ioral therapy	Cochrane [42]	2733	Tinnitus severity (SMD): – 0.56 THI: – 10.91	No evidence due to lack of data	Adverse effects are rare	Clinicians should recommend CBT to patients with persistent, bothersome tinnitus (recom- mendation)	Strong recom- mendation for cognitive behavioral therapy	If tinnitus is still causing an impact on emotional and social wellbeing, and day-to-day aday-to-day aday-to-day aday-to-day arguer approach as follows: 1. Digital tinnitus-related cognitive behavioral therapy (CBT) 2. Group-based tinnitus-related psychological interventions including mindfulness- based cogni- tive therapy, acceptance, and commitment therapy or CBT 3. Individual tinnitus-related CBT	Strong recommen- dation for cogni- tive behavioral therapy
Dexamethasone (intratympanic administration)	Meta-analysis [76]	220	No significant effect compared with placebo	No significant effect compared with placebo	Complications such as hearing loss, eardrum perforation, and middle ear inflammation are rare	Clinicians should not routinely recommend intratympanic medications for a primary indication of treating persis- tent, bother- some tinnitus (recommenda- tion against)	Weak recommen- dation against pharmacologi- cal treatment	Not mentioned	Strong recommen- dation against pharmacological treatment

Table 1 (continu	(pa)								
Intervention	Source of evi- dence	Number of study partici- pants	Efficacy (immedi- ate)	Efficacy (long term)	Potential harm	US (2014)	European (2019)	NICE (2020)	German (2021)
Ginkgo biloba	Cochrane [58]	1915	Little to no effect at 3 to 6 months compared to placebo, but the evidence is very uncertain	Little to no effect at 3 to 6 months compared to placebo, but the evidence is very uncertain	Incidence of side effects, low	Clinicians should not recommend Ginkgo biloba, for treating patients with persistent, both- ersome timnitus (recommenda- tion against)	Weak recommen- dation against pharmacologi- cal treatment	Not mentioned	Strong recommen- dation against pharmacological treatment
Hearing aid	Cochrane [47]	290	No significant effects on tin- nitus loudness or distress	No data	Not reported	Clinicians should recommend a hearing aid evaluation for patients with hearing loss and persistent, both- ersome tinnitus (recommenda- tion)	Weak recom- mendation for hearing aids	Offer amplifica- tion devices to people with tinnitus who have a hearing loss that affects their ability to communicate Consider ampli- fication devices for people with tinnitus who have a hearing loss but do not have difficulties communicating Do not offer amplification devices to people with tinnitus but no hearing loss	Recommendation for hearing aids in case of hear- ing loss
Hyperbaric oxygen	Cochrane [77, 78]	392	No significant improvements in tinnitus for chronic tinnitus	No significant improvements in tinnitus for chronic tinnitus	Not reported	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Sound therapy	Cochrane [47]	590	No significant effects on tin- nitus loudness or distress	No data	Not reported	Clinicians may recommend sound therapy to patients with persistent, both- ersome tinnitus. (option)	No recommenda- tion	Recommendation for research	Recommendation against sound generators, recommendation against specific sound therapies

 $\textcircled{ } \underline{ \widehat{ } }$  Springer

Table 1 (continue	(þí								
Intervention	Source of evi- dence	Number of study partici- pants	Efficacy (immedi- ate)	Efficacy (long term)	Potential harm	US (2014)	European (2019)	NICE (2020)	German (2021)
Tinnitus retrain- ing therapy	Meta-analysis [56]	1345	Significantly increased treat- ment response	Significantly increased treat- ment response	Not reported	Not mentioned	No recommenda- tion	Not mentioned	Can be considered for long-term treatment
Transcranial direct current stimulation	Meta-analysis [79]	1031	Loudness (SMD) – 0.35 Distress (SMD): –0.5	Not reported	Not reported	Not mentioned	No recom- mendation for transcranial electrical stimu- lation	Recommendation for research	Recommendation against transcra- nial electrical stimulation
Transcranial magnetic stimulation	Meta-analysis [63, 80]	945	Tinnitus severity (SMD): – 0.45	Tinnitus severity (SMD): – 0.42	Not reported	Clinicians should not recommend TMS for the routine treat- ment of patients with persistent, bothersome tinnitus (recom- mendation against)	Recommenda- tion against transcranial magnetic stimu- lation	Recommendation for research	Recommendation against transcra- nial magnetic stimulation
Zinc	Cochrane [81]	209	No evidence for improvement of tinnitus severity by oral zinc supplementa- tion	No evidence for improvement of tinnitus severity by oral zinc supplementa- tion	Not reported	Clinicians should not recom- mend zinc, for treating patients with persistent, bothersome tinnitus (recom- mendation against)	Weak recommen- dation against pharmacologi- cal treatment	Not mentioned	Strong recommen- dation against pharmacological treatment

")

Counselling/psychoeducation ("recommended by guide	elines
Mindfulness-based therapy	
Hypnosis	
• Sound therapy	
Noise generator (complete masking)	
Noise generator (partial masking)	
Enriched acoustic environment	
Fractal tones	
Auditory training	
Tailor-made notched music training	
Coordinated reset auditory stimulation	
• Virtual reality-based approaches	

#### **Tinnitus Counselling**

Tinnitus counselling is a therapeutic process in which individuals with tinnitus are supported and guided by a trained professional to help them cope with the psychological and emotional aspects of their condition. Counselling aims to reduce the impact of tinnitus on the individual's quality of life by providing information about tinnitus, discussing coping strategies, exploring stress management techniques, and offering relaxation exercises, emotional support, and selfefficacy enhancement [30, 37]. Tinnitus counselling is considered a fundamental therapeutic approach recommended by all guidelines, although evidence from randomized controlled trials is limited [36, 38]. Recent studies exploring counselling via smartphone apps [39] promise wider accessibility and increased patient involvement.

#### **Cognitive Behavioral Therapy (CBT) for Tinnitus**

Cognitive behavioral therapy (CBT) for tinnitus is a treatment that incorporates cognitive, behavioral, or a combination of components in a structured time-limited program, aiming to change the negative thought patterns and behaviors associated with tinnitus [40]. CBT typically involves identifying and challenging negative thoughts related to tinnitus, developing relaxation techniques, and habituation to the tinnitus sound by distraction techniques. Another approach for cognitive restructuring is the systematic exposition to the tinnitus sound through a mechanism similar to the treatment of phobias. The goal of CBT is to help patients better control their emotional reactions and improve their ability to cope with the impact of tinnitus on their daily lives [41]. CBT for tinnitus treatment has been investigated in a large number of clinical trials [42]. The results of a Cochrane meta-analysis suggest that tinnitus questionnaire scores are effectively reduced after CBT treatment with minimal adverse effects. Both face-to-face and Internetdelivered CBT demonstrate comparable efficacy [42]. As there are various behavior modification techniques, it would

Orphenadrine Tizanidine Sodium channel blocker Lidocaine • Others Atorvastatin Betahistine Chinese medicine Cilostazol Cyclandelate Deanxit Ginkgo biloba Melatonin Misoprostol 3,4-Methylenedioxymethamphetamine (MDMA) Naloxone Ondansetron Oxytocin Piribedil Pramipexole Vardenafil Vitamin B12 Zinc Non-pharmacological interventions

Acupuncture/acupressure

• Bimodal stimulation

Electrical vagus nerve stimulation plus sound therapy Electrical skin stimulation plus sound therapy Electrical tongue stimulation plus sound therapy

Brain/neural stimulation

Transcranial magnetic stimulation

Transcranial direct current stimulation

Direct electrical stimulation

Vagus nerve stimulation

Transcutaneous electrical neural stimulation

• Combination approaches

Tinnitus retraining therapy (directive counselling plus sound therapy) Neuromonics (counselling plus sound therapy)

• Electrical stimulation of the ear/cochlea

#### **Cochlear implants**

("Recommended by guidelines" in case of profound hearing loss) Electrical stimulation of the tympanum or the outer ear canal

#### • Hearing aids

("Recommended by guidelines" in case of hearing loss)

- Hyperbaric oxygenation
- Low-level laser therapy
- Music therapy
- Neurobiofeedback
- Physiotherapy
- Psychotherapy

Cognitive behavioral therapy (individual, group, or online setting) ("recommended by guidelines")

be desirable to identify predictors to determine the best CBT technique for the individual patient. For example, exposure as a treatment technique is supposed to have best effects in patients who fear their tinnitus and therefore avoid silent environments [43]. Mindfulness-based interventions, considered as part of CBT, are a promising way to reduce tinnitus distress, as recent systematic reviews indicate [44]. However, the long-term effects are still uncertain, and further research is needed to determine their effectiveness.

#### **Auditory Treatments**

Auditory treatments include a wide range of interventions, such as devices for hearing improvement, sound generators for masking or for distracting from tinnitus, and various auditory stimulation techniques. In cases of profound hearing loss, cochlear implants have demonstrated a significant reduction in tinnitus perception and distress [21, 45]. Consequently, unilateral burdensome tinnitus in single-sided deafness may indicate the need for cochlear implantation, even if the ability to communicate is preserved in most acoustic environments by the normal contralateral hearing function. Hearing aids are recommended when there is an indication due to comorbid hearing loss [36]. However, the use of hearing aids as a tinnitus treatment in patients with adequately preserved communication skills, e.g., mild hearing loss or hearing loss in the high-frequency range, is controversial due to the low quality of evidence [46, 47]. Similarly, there is insufficient evidence supporting the effectiveness of sound generators or other forms of sound therapy, although clear benefits have been observed in a subset of patients [47]. Music therapy and hearing trainings have been proposed as an option for the treatment of tinnitus with or without hearing loss, but the evidence base for their effectiveness is limited [37, 48].

Various individualized auditory stimulation approaches tailored to an individual's tinnitus frequency or hearing profile have been proposed [49–51]. These approaches aim to induce specific neuroplastic changes and have shown promising pilot data, but the effects have not yet been validated in independent larger controlled studies. Either such studies are still missing or they revealed negative results [52–54].

In general, many patients seem to benefit from acoustic distraction, be it music, white noise, or natural sounds, in certain situations such as falling asleep or concentrating.

#### **Tinnitus Retraining Therapy (TRT)**

Tinnitus retraining therapy (TRT) is a combination of directive counselling and sound therapy, either through hearing aids or noise generators, aiming at habituation [55]. Despite its widespread clinical use, evidence for its efficacy is limited [56]. In a large randomized controlled trial, TRT and its components were compared with standard of care treatment. Patients were randomly assigned to either TRT (counselling + sound therapy), partial TRT (only counselling), or standard treatment with no significant differences found between groups [57]. A recent meta-analysis indicated a potential positive long-term effect of TRT, but further welldesigned studies are needed to clearly demonstrate its effectiveness [56].

#### **Tinnitus Pharmacotherapy**

Despite numerous studies, pharmacotherapy for tinnitus has produced predominantly null results in meta-analyses [58–60]. Accordingly, there is no drug that has been approved by the Food and Drug Administration (FDA) or the European Medical Agency (EMA) for the treatment of tinnitus [61, 62]. Current guidelines recommend pharmacological treatment only for the therapy of comorbidities such as insomnia, depression, or anxiety [36].

#### **Neurobiofeedback and Brain Stimulation**

Neurobiofeedback is promising based on controlled studies, but more extensive confirmatory research is needed. Noninvasive brain stimulation, including transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS), demonstrates positive effects with small to moderate effect sizes and offers potential therapeutic opportunities [63]. Currently, it is not recommended by any guideline, also due to the fact that most studies are rather recent, and that the required level of evidence for innovative treatments to be included in guidelines is particularly high [36, 64]. Invasive brain stimulation remains highly experimental, with beneficial outcomes reported in case series but insufficient data to support routine clinical use [65].

#### **Bimodal Stimulation**

Bimodal stimulation approaches, in which auditory stimuli are combined with various forms of neural stimulation, are promising for reducing tinnitus severity. Auditory stimulation combined with electrical stimulation of the tongue has shown beneficial effects in first studies in large samples [66, 67]. The combination of auditory stimulation with electrical face or neck stimulation [68] or vagus nerve stimulation [69] indicates substantial benefits in pilot studies, highlighting the need for further investigation.

#### **Complementary and Alternative Therapies**

Among complementary therapies, acupuncture is one of the best studied but has shown mixed results [70]. Many other techniques have been proposed and tested (see also Box 1),

mainly in small uncontrolled trials. The evidence is inconclusive and requires more rigorous research.

#### **Physiotherapy and Manual Therapy**

Based on the knowledge about somatosensory influences on tinnitus [71], physiotherapy and manual therapy have been investigated in patients with somatosensory tinnitus [35], with promising results [34], and further systematic studies are warranted [72].

#### **Self-Help Interventions**

Traditional self-help interventions, facilitated through mutual self-help groups, emphasize social integration and psychosocial relief. However, clear evidence regarding their efficacy for tinnitus remains elusive. The term "self-help" has also been applied to online CBT and other smartphonebased interventions where the potential for tinnitus management is currently being explored [73]. The concepts of self-help should be defined in detail for the research perspective. First, a clear distinction should be made between online-guided treatments and mutual support for patients in self-help groups. Secondly, a differentiation should be established with regard to the type, nature, and content of self-help activities.

### Overview of Treatments, Their Results, and Guideline Recommendations

Table 1 provides an overview of the best-studied tinnitus treatments, their evidence, and the respective recommendations in current guidelines.

In summary, treatment options for tinnitus are diverse and range from traditional counselling to innovative technology-based interventions. Whereas some modalities show promise, further in-depth research is needed to establish robust evidence-based guidelines for more effective tinnitus management.

#### **Advancing Tinnitus Management**

#### **Inconsistencies in Tinnitus Management**

Tinnitus management varies widely around the world, reflecting differences between countries, medical disciplines, and healthcare institutions [4, 82]. Given this diversity, the development of treatment guidelines based on current evidence represents a crucial step towards establishing a standardized approach [5, 36, 38, 83–85]. The evidence-based treatment options currently available are limited,

highlighting the urgent need for improved and innovative solutions.

#### **Challenges in Guideline Development**

Guidelines tend to be conservative by nature and focus on established treatments based on experience, eminence, and evidence. However, this should not discourage the exploration of innovative approaches [36]. Overcoming this dilemma requires strategic considerations. Practically, all meta-analyses in the field of tinnitus emphasize the need for larger studies with higher methodological rigor. In addition, clinical trials should take into account the inherent heterogeneity of tinnitus. There is always a certain risk of bias in guideline committees, as most experts have material or immaterial conflicts of interest. One solution would be for the evidence to be assessed by independent guideline committees with methodological expertise, as is the case with the NICE guidelines. It is possible that AI applications might be developed in the near future to facilitate this time-consuming work. The methodology of guideline development contains a certain bias towards established treatments. Therefore, care should be taken to ensure that that guidelines remain open to novel therapeutic options. For example, rather than advising against innovative interventions due to insufficient safety or efficacy data, guidelines should emphasize the need for research. A good example of this are the NICE guidelines, which make explicit recommendations on research priorities based on the lack of evidence for the aspects of management they review. Faster update cycles should also be introduced. Adherence to the concept of a "living guideline" allows timely incorporation of new evidence and improves adaptability to emerging treatments. Finally, it is important to actively involve tinnitus patients in guideline development to ensure that their perspective contributes to a comprehensive understanding of the condition and its treatment [86].

#### **Development of Decision Support Systems**

The current treatment landscape for tinnitus is characterized by a variety of options, each with varying outcomes. While some patients experience significant improvement from a particular treatment, others achieve no benefit. This variability is not surprising given the diverse nature of tinnitus. However, predicting response to treatment based on specific clinical or demographic factors remains challenging. Consequently, patients often go through a trial-and-error process, attempting multiple treatments until they experience relief [87]. This approach is both burdensome and costly. There is hope that the situation can be ameliorated in future through the development of decision support systems. These systems, which use artificial intelligence to analyze large databases, aim to predict treatment response by taking into account a combination of various individual characteristics [88, 89].

#### Balancing Evidence-Based Practice and Therapeutic Freedom

It is crucial to recognize that guidelines are not rigid laws but rather a dynamic framework based on the available evidence. In the clinical situation, guideline recommendations have to be translated into treatment options for the individual patient. Clinicians should keep in mind that evidence for diagnostic or therapeutic interventions should not be considered as categorical ("yes" or "no") but rather as dimensional ("more" or "less"). In order to make informed treatment decisions, clinicians need to balance the existing evidence and guideline recommendations with individual factors and patient's preferences. Clinicians' therapeutic freedom also includes the option to offer treatments that are not or not yet recommended by guidelines. However, this requires good reasons, either new evidence for innovative treatments that has not yet been included in guidelines [67] or pathophysiological considerations, e.g., offering migraine medication for episodic tinnitus, which is similar to a symptom of cochlear migraine [90] or carbamazepine for "typewriter" tinnitus [91, 92]. For all therapeutic recommendations, but particularly for off-label treatments, the chances of improvement, treatment risks, and alternative options must be weighted and discussed with the patient.

#### **Striving for Quality Improvement**

In conclusion, following these strategies can elevate the quality standards of tinnitus management through evidencebased guidelines while creating an environment conducive to innovation. The ultimate goal remains patient-centered care, where guidelines serve as valuable tools rather than rigid directives. By integrating the latest evidence, patient perspectives, and innovative approaches, the healthcare community can collaboratively advance the field of tinnitus management and improve outcomes for those affected by this difficult condition.

Author Contribution All authors drafted the manuscript and reviewed and approved the final version of the manuscript.

Funding Open Access funding enabled and organized by Projekt DEAL.

#### Declarations

**Conflict of Interest** T. Kleinjung received honoraria for consultancy and speaker's fees from Sonova and Schwabe and travel and accommodation payments from Cochlear. His research was funded from the Tinnitus Research Initiative, the Swiss National Science Foundation, the European Union, the Zurich Hearing Foundation, and Cochlear. N. Peter received travel and accommodation payments from Cochlear. Her research is funded from the Zurich Hearing Foundation. M. Schecklmann received honoraria for consultancy, reports, and speakers' fees from Aureliym, MAG & More, Medical Tribune, Neuromod, and Schwabe; research funding from the Tinnitus Research Initiative, the German Research Foundation, the German Bundesministerium für Bildung und Forschung, the American Tinnitus Association, Neuromod, and the European Union; and funding for equipment from Mag-Venture, MAG & More, NeuroCare, and Deymed Diagnostic. B. Langguth received honoraria for consultancy and speakers' fees from ANM, AstraZeneca, Autifony Therapeutics, Decibel Therapeutics, Desyncra, Gerson Lehrman Group, Lundbeck, Merz, MagVenture, Medical Tribune, Neurolite, Neuromod, Novartis, Pfizer, Rovi, Schwabe, Sea Pharma, Servier, Sonova, and Sound Therapeutics; research funding from the Tinnitus Research Initiative, Bayhost, the German Research Foundation, the German Bundesministerium für Bildung und Forschung, the American Tinnitus Association, AstraZeneca, cerbomed, Neuromod, and the European Union; funding for equipment from MagVenture and Deymed Diagnostic; and travel and accommodation payments from Eli Lilly, Lundbeck, Servier, and Pfizer. He owns shares of Sea Pharma.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

#### References

- Jarach CM et al (2022) Global prevalence and incidence of tinnitus: a systematic review and meta-analysis. JAMA Neurol 79(9):888–900
- Langguth B (2011) A review of tinnitus symptoms beyond 'ringing in the ears': a call to action. Curr Med Res Opin 27(8):1635–1643
- De Ridder D et al (2021) Tinnitus and tinnitus disorder: theoretical and operational definitions (an international multidisciplinary proposal). Prog Brain Res 260:1–25
- Hall DA et al (2011) Treatment options for subjective tinnitus: self reports from a sample of general practitioners and ENT physicians within Europe and the USA. BMC Health Serv Res 11:302
- Langguth B, Kleinjung T, Landgrebe M (2011) Tinnitus: the complexity of standardization. Eval Health Prof 34(4):429–33
- Husain FT et al (2018) Expectations for tinnitus treatment and outcomes: a survey study of audiologists and patients. J Am Acad Audiol 29(4):313–336
- 7. Pryce H et al (2018) Patient preferences in tinnitus outcomes and treatments: a qualitative study. Int J Audiol 57(10):784–790
- Tyler RS (2012) Patient preferences and willingness to pay for tinnitus treatments. J Am Acad Audiol 23(2):115–125
- Rademaker MM et al (2021) What tinnitus therapy outcome measures are important for patients?- A discrete choice experiment. Front Neurol 12:668880
- Sanchez TG, Valim CCA, Schlee W (2021) Long-lasting total remission of tinnitus: a systematic collection of cases. Prog Brain Res 260:269–282

- 11. Langguth B et al (2024) Tinnitus: clinical insights in its pathophysiology-a perspective. J Assoc Res Otolaryngol 25(3):249–258
- Cederroth CR et al (2024) Editorial: towards an understanding of tinnitus heterogeneity, volume II. Front Aging Neurosci 16:1376600
- 13. Cederroth CR et al (2019) Editorial: towards an understanding of tinnitus heterogeneity. Front Aging Neurosci 11:53
- Tyler R et al (2008) Identifying tinnitus subgroups with cluster analysis. Am J Audiol 17(2):S176–S184
- Schecklmann M et al (2012) Cluster analysis for identifying subtypes of tinnitus: a positron emission tomography and voxel-based morphometry study. Brain Res 1485:3–9
- Genitsaridi E et al (2020) A review and a framework of variables for defining and characterizing tinnitus subphenotypes. Brain Sci 10(12):938
- Genitsaridi E et al (2019) Standardised profiling for tinnitus research: the European School for Interdisciplinary Tinnitus Research Screening Questionnaire (ESIT-SQ). Hear Res 377:353–359
- McFerran DJ et al (2019) Why is there no cure for tinnitus? Front Neurosci 13:802
- Langguth B, Elgoyhen AB, Cederroth CR (2018) Therapeutic approaches to the treatment of tinnitus. Annu Rev Pharmacol Toxicol 59:291–313
- 20. Hall DA et al (2016) Systematic review of outcome domains and instruments used in clinical trials of tinnitus treatments in adults. Trials 17(1):270
- 21. Mertens G, De Bodt M, Van de Heyning P (2016) Cochlear implantation as a long-term treatment for ipsilateral incapacitating tinnitus in subjects with unilateral hearing loss up to 10 years. Hear Res 331:1–6
- 22. Hall DA, Mehta RL, Fackrell K (2017) How to choose between measures of tinnitus loudness for clinical research? A report on the reliability and validity of an investigator-administered test and a patient-reported measure using baseline data collected in a phase IIa drug trial. Am J Audiol 26(3):338–346
- Langguth B et al (2007) Consensus for tinnitus patient assessment and treatment outcome measurement: Tinnitus Research Initiative meeting, Regensburg, July 2006. Prog Brain Res 166:525–536
- 24. Landgrebe M et al (2012) Methodological aspects of clinical trials in tinnitus: a proposal for an international standard. J Psychosom Res 73(2):112–121
- Langguth B, De Ridder D (2023) Minimal clinically important difference of tinnitus outcome measurement instruments-a scoping review. J Clin Med 12(22):7117
- 26. Hall DA et al (2018) The COMiT'ID Study: developing core outcome domains sets for clinical trials of sound-, psychology-, and pharmacology-based interventions for chronic subjective tinnitus in adults. Trends Hear 22:2331216518814384
- 27. Lewis S et al (2020) Assessment and management of tinnitus: summary of NICE guidance. BMJ 368:m976
- Cima RFF et al (2019) A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. HNO 67(Suppl 1):10–42
- 29. Langguth B et al (2013) Tinnitus: causes and clinical management. Lancet Neurol 12(9):920–930
- Kreuzer PM, Vielsmeier V, Langguth B (2013) Chronic tinnitus: an interdisciplinary challenge. Dtsch Arztebl Int 110(16):278–284
- 31. Vielsmeier V et al (2015) The relevance of the high frequency audiometry in tinnitus patients with normal hearing in conventional pure-tone audiometry. Biomed Res Int 2015:302515
- Newman CW, Wharton JA, Jacobson GP (1995) Retest stability of the tinnitus handicap questionnaire. Ann Otol Rhinol Laryngol 104(9 Pt 1):718–723

- Meikle MB et al (2012) The tinnitus functional index: development of a new clinical measure for chronic, intrusive tinnitus. Ear Hear 32(2):153–176
- 34. Michiels S et al (2016) Does multi-modal cervical physical therapy improve tinnitus in patients with cervicogenic somatic tinnitus? Man Ther 26:125–131
- 35. Michiels S et al (2018) Diagnostic criteria for somatosensory tinnitus: a Delphi process and face-to-face meeting to establish consensus. Trends Hear 22:2331216518796403
- Langguth B et al (2023) Tinnitus guidelines and their evidence base. J Clin Med 12(9):3087
- 37. Mazurek B et al (2022) Chronic tinnitus. Dtsch Arztebl Int 119(13):219-225
- Meijers S et al (2023) Analysis and comparison of clinical practice guidelines regarding treatment recommendations for chronic tinnitus in adults: a systematic review. BMJ Open 13(9):e072754
- Schoisswohl S et al (2021) Unification of Treatments and Interventions for Tinnitus Patients (UNITI): a study protocol for a multi-center randomized clinical trial. Trials 22(1):875
- Andersson G (2002) Psychological aspects of tinnitus and the application of cognitive-behavioral therapy. Clin Psychol Rev 22(7):977–990
- Schecklmann M et al (2023) Cognitive behavioral group therapy for chronic tinnitus in a German tertiary clinical real-world setting. Int J Environ Res Public Health 20(6):4982
- 42. Fuller T et al (2020) Cognitive behavioural therapy for tinnitus. Cochrane Database Syst Rev 1:CD012614
- Kleinstauber M et al (2013) The role of fear-avoidance cognitions and behaviors in patients with chronic tinnitus. Cogn Behav Ther 42(2):84–99
- Rademaker MM et al (2019) The effect of mindfulness-based interventions on tinnitus distress. a systematic review. Front Neurol 10:1135
- 45. Peter N et al (2019) The influence of cochlear implantation on tinnitus in patients with single-sided deafness: a systematic review. Otolaryngol Head Neck Surg 161(4):576–588
- 46. Hoare DJ et al (2014) Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Cochrane Database Syst Rev 1:CD010151
- Sereda M et al (2018) Sound therapy (using amplification devices and/or sound generators) for tinnitus. Cochrane Database Syst Rev 12:CD013094
- Hoare DJ, Stacey PC, Hall DA (2010) The efficacy of auditory perceptual training for tinnitus: a systematic review. Ann Behav Med 40(3):313–324
- Teismann H, Okamoto H, Pantev C (2011) Short and intense tailor-made notched music training against tinnitus: the tinnitus frequency matters. PLoS One 6(9):e24685
- Davis PB, Paki B, Hanley PJ (2007) Neuromonics tinnitus treatment: third clinical trial. Ear Hear 28(2):242–259
- Tass PA et al (2012) Counteracting tinnitus by acoustic coordinated reset neuromodulation. Restor Neurol Neurosci 30(2):137–159
- 52. Hall DA et al (2022) Systematic evaluation of the T30 neurostimulator treatment for tinnitus: a double-blind randomised placebocontrolled trial with open-label extension. Brain Sci 12(3):317
- Piromchai P et al (2021) A three-arm, single-blind, randomized controlled trial examining the effects of notched music therapy, conventional music therapy, and counseling on tinnitus. Otol Neurotol 42(2):335–340
- Therdphaothai J et al (2021) A Randomized, Controlled Trial of Notched Music Therapy for Tinnitus Patients. J Int Adv Otol 17(3):221–227
- 55. Jastreboff PJ (2007) Tinnitus retraining therapy. Prog Brain Res 166:415–423

- Han M, Yang X, Lv J (2021) Efficacy of tinnitus retraining therapy in the treatment of tinnitus: a meta-analysis and systematic review. Am J Otolaryngol 42(6):103151
- 57. Tinnitus Retraining Therapy Trial Research, G, Scherer RW, Formby C (2019) Effect of tinnitus retraining therapy vs standard of care on tinnitus-related quality of life: a randomized clinical trial. JAMA Otolaryngol Head Neck Surg 145(7):597–608
- Sereda M et al (2022) Ginkgo biloba for tinnitus. Cochrane Database Syst Rev 11(11):CD013514
- Hoekstra CE et al (2011) Anticonvulsants for tinnitus. Cochrane Database Syst Rev 7:CD007960
- 60. Baldo P et al (2012) Antidepressants for patients with tinnitus. Cochrane Database Syst Rev 9:CD003853
- 61. Kleinjung T, Langguth B (2021) Pharmacotherapy of tinnitus. Curr Top Behav Neurosci 51:193–212
- 62. Langguth B, Elgoyhen AB, Cederroth CR (2019) Therapeutic approaches to the treatment of tinnitus. Annu Rev Pharmacol Toxicol 59:291–313
- 63. Lefebvre-Demers M, Doyon N, Fecteau S (2021) Non-invasive neuromodulation for tinnitus: a meta-analysis and modeling studies. Brain Stimul 14(1):113–128
- 64. National Guideline Centre (UK) (2020) Tinnitus: assessment and management. Evidence review 0. London: National Institute for Health and Care Excellence (NICE)
- 65. De Ridder D, Adhia D, Langguth B (2021) Tinnitus and brain stimulation. Curr Top Behav Neurosci 51:249–293
- Conlon B et al (2020) Bimodal neuromodulation combining sound and tongue stimulation reduces tinnitus symptoms in a large randomized clinical study. Sci Transl Med 12(564)
- 67. Conlon B et al (2022) Different bimodal neuromodulation settings reduce tinnitus symptoms in a large randomized trial. Sci Rep 12(1):10845
- Marks KL et al (2018) Auditory-somatosensory bimodal stimulation desynchronizes brain circuitry to reduce tinnitus in guinea pigs and humans. Sci Transl Med 10(422)
- 69. Tyler R et al (2017) Vagus nerve stimulation paired with tones for the treatment of tinnitus: a prospective randomized double-blind controlled pilot study in humans. Sci Rep 7(1):11960
- Huang K et al (2021) Acupuncture for tinnitus: a systematic review and meta-analysis of randomized controlled trials. Acupunct Med 39(4):264–271
- Shore SE, Roberts LE, Langguth B (2016) Maladaptive plasticity in tinnitus–triggers, mechanisms and treatment. Nat Rev Neurol 12(3):150–160
- Michiels S (2023) Somatosensory tinnitus: recent developments in diagnosis and treatment. J Assoc Res Otolaryngol 24(5):465–472
- Demoen S et al (2023) Effectiveness of telerehabilitation interventions for self-management of tinnitus: systematic review. J Med Internet Res 25:e39076
- 74. Wegner I et al (2018) Betahistine for tinnitus. Cochrane Database Syst Rev 12(12):CD013093
- 75. Oh SJ et al (2023) Cochlear implantation in adults with singlesided deafness: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 168(2):131–142

- 76. Chung J et al (2022) Effectiveness of intratympanic dexamethasone injection for tinnitus treatment: a systematic review and meta-analysis. Clin Exp Otorhinolaryngol 15(1):91–99
- 77. Bennett MH, Kertesz T, Yeung P (2007) Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database Syst Rev 1:CD004739
- Bennett MH et al (2012) Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database Syst Rev 10:CD004739
- Martins ML et al (2022) Effect of transcranial direct current stimulation for tinnitus treatment: a systematic review and metaanalysis. Neurophysiol Clin 52(1):1–16
- Yin L et al (2021) An updated meta-analysis: repetitive transcranial magnetic stimulation for treating tinnitus. J Int Med Res 49(3):300060521999549
- Person OC et al (2016) Zinc supplementation for tinnitus. Cochrane Database Syst Rev 11:CD009832
- 82. Jarach CM et al (2024) The out-of-pocket expenses of people with tinnitus in Europe. J Epidemiol (Online ahead of print.)
- Hoare DJ, Hall DA (2011) Clinical guidelines and practice: a commentary on the complexity of tinnitus management. Eval Health Prof 34(4):413–20
- Searchfield G (2011) A commentary on the complexity of tinnitus management: clinical guidelines provide a path through the fog. Eval Health Prof 34(4):421–8
- 85. Fuller TE et al (2017) Different teams, same conclusions? A systematic review of existing clinical guidelines for the assessment and treatment of tinnitus in adults. Front Psychol 8:206
- Hall DA et al (2021) Web-based discussion forums reveal the person-centered relevance and importance of tinnitus. Prog Brain Res 260:205–221
- Simoes J et al (2019) Toward personalized tinnitus treatment: an exploratory study based on Internet crowdsensing. Front Public Health 7:157
- Kikidis D et al (2021) Methodological aspects of randomized controlled trials for tinnitus: a systematic review and how a decision support system could overcome barriers. J Clin Med 10(8):1737
- Schlee W et al (2021) Using big data to develop a clinical decision support system for tinnitus treatment. Curr Top Behav Neurosci 51:175–189
- Umemoto KK et al (2023) Management of migraine-associated vestibulocochlear disorders. Audiol Res 13(4):528–545
- Levine RA (2006) Typewriter tinnitus: a carbamazepine-responsive syndrome related to auditory nerve vascular compression. ORL J Otorhinolaryngol Relat Spec 68(1):43–46
- 92. Sunwoo W et al (2017) Typewriter tinnitus revisited: the typical symptoms and the initial response to carbamazepine are the most reliable diagnostic clues. Sci Rep 7(1):10615

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.