nature reviews disease primers

https://doi.org/10.1038/s41572-026-00702-0

Primer

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Tinnitus

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Abstract

Tinnitus is the perception of sound without a corresponding external sound source. This condition affects approximately 14% of adults, with approximately 2% experiencing severe symptoms. Underlying mechanisms of tinnitus suggest involvement of both peripheral and central processes, in which cochlear injury and deafferentation may trigger maladaptive plasticity, increased central gain, and thalamocortical dysrhythmia, modulated by limbic and salience networks. Neuroinflammation, somatosensory–auditory coupling and other factors, such as stress, may contribute to chronicity. Clinical expression is heterogeneous. Tinnitus is often comorbid with hearing loss, hyperacusis, migraine, anxiety, depression, mild cognitive impairment, insomnia and temporomandibular disorders, influencing assessment and care. Diagnosis comprises distinguishing objective (including pulsatile) from subjective tinnitus, recognizing red flags (for example, pulse-synchronous tinnitus requiring vascular imaging), quantifying hearing with audiometry and screening for modulating somatic factors. Multimodal management can reduce the effect of tinnitus: tinnitus-focused counselling and cognitive behavioural therapy are first-line treatments, and hearing rehabilitation and targeted treatment of somatosensory contributors are valuable adjuncts. Moreover, emerging neuromodulation, including bimodal stimulation, benefits selected subgroups. New areas of research include biomarkers, deciphering tinnitus genetic architecture, inner ear regeneration, closed-loop neuromodulation and digital therapeutics.

Sections

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Introduction

Tinnitus is the conscious perception of sound in the absence of an external acoustic source. Tinnitus affects almost 15% of the global population and is one of the most prevalent and distressing auditory phantom percepts[1–3]. Tinnitus must be distinguished from other auditory phenomena, such as auditory hallucinations seen in psychiatric or neurological disorders, because these disorders have other treatments and prognoses[4]. Subjective tinnitus, the most common form, reflects central auditory dysfunction and is considered a phantom percept analogous to central neuropathic pain (that is, a sensory experience generated in the absence of peripheral input).

Subjective tinnitus arises through a complex interplay between peripheral and central neural mechanisms[5]. Damage to cochlear structures through noise exposure, ototoxic agents or ageing often leads to auditory deafferentation and consequent maladaptive plasticity within the central auditory system. These changes include increased spontaneous firing rates, abnormal neural synchrony and tonotopic reorganization within the auditory cortex[5]. These alterations contribute to the persistent generation of 'neural noise', which the brain misinterprets as sound[6].

A key clinical feature of tinnitus is the heterogeneity of its perceptual characteristics and degree of associated distress. While some individuals experience mild or transient symptoms, others develop chronic tinnitus (whereby symptoms are present for more than 3 months) and intrusive tinnitus (persistent and distressing tinnitus that interferes with daily life, sleep, concentration or emotional wellbeing) that substantially impairs quality of life, sleep, concentration and mood[7]. The severity of tinnitus-related distress is influenced by sensory factors and affective and cognitive dimensions, including anxiety, depression, and attentional bias towards the phantom percept.

Despite its high prevalence and considerable impact, effective treatment options for tinnitus remain limited[8]. Available pharmacological and non-pharmacological therapeutic strategies often provide incomplete relief. This challenge stems partly from an incomplete understanding of the complex neural mechanisms underlying the generation and persistence of tinnitus, which involve dynamic interactions across sensory, limbic and cognitive networks.

This Primer provides an overview of the epidemiology, clinical presentation, diagnostic assessment and pathophysiological mechanisms of tinnitus. The Primer also summarizes available treatment approaches and highlights emerging strategies aimed at improving diagnostic precision and therapeutic efficacy for this challenging and multifaceted condition.

Epidemiology

Case definition and ascertainment

Estimating the epidemiology of tinnitus is particularly challenging as prevalence estimates depend on how tinnitus is defined and assessed. The identification of tinnitus in epidemiological studies typically relies on self-reported symptoms collected through questionnaires or interviews. As a result, differences in survey wording, response options, recall periods and thresholds used to define a case can substantially influence reported prevalence estimates[1,3,9,10].

Across studies, tinnitus has been defined using a wide range of questions, from broad items assessing whether individuals have 'ever experienced ringing or buzzing in the ears' to more restrictive definitions requiring the perception of sound lasting for a specified duration or occurring with a certain frequency[3,9]. Some studies classify tinnitus simply as present or absent, whereas others distinguish between different clinical categories, including any tinnitus, chronic tinnitus (commonly defined as lasting ≥6 months), bothersome or severe tinnitus (tinnitus causing significant distress or interference with daily activities) and medically diagnosed tinnitus.

Prevalence and incidence

Prevalence. Numerous studies worldwide have attempted to estimate the frequency of tinnitus in the general adult population. Most cross-sectional studies have shown a prevalence of 10–15% for tinnitus and 1–2% for severe tinnitus in adults[2,8–11].

A major advancement in assessing tinnitus epidemiology came from a comprehensive systematic review that included only studies based on samples representative of the general population and excluded studies limited to high-risk groups or clinical samples (for example, patients recruited from otolaryngology or audiology clinics or from speciality tinnitus centres)[3]. This systematic review found a pooled adult prevalence of 14.4% for any form of tinnitus (95% CI 12.6–16.5%). Individual study estimates ranged from 4.1% to 37.2%. Prevalence did not differ significantly by sex (14.1% in males versus 13.1% in females) but increased sharply with age: 9.7% in those aged 18–44 years, 13.7% among those aged 45–64 years, and 23.6% among those aged ≥65 years[3,10]. Most of the available prevalence data was from Europe (overall tinnitus prevalence of 14.7%), followed by North America (13.4%) and Asia (15.2%). Data from other regions remain limited, with only a few studies conducted in Oceania (16.2%), Africa (5.2%) and South America (21.9%). Regarding tinnitus severity, the pooled prevalence estimates were 2.3% (95% CI 1.7–3.1%) for severe tinnitus, 9.8% (95% CI 4.7–19.3%) for chronic tinnitus and 3.4% (95% CI 2.1–5.5%) for diagnosed tinnitus[3,10]. Pooled prevalence in children and adolescents was 13.6% (95% CI 8.5–21.0%), with a broad range from 0.7% to 66.9%, probably reflecting substantial methodological variation and differing criteria for tinnitus awareness in younger populations[3,10]. The systematic review did not report pooled tinnitus prevalence stratified by ethnicity or race[3].

Other studies have reported differences in tinnitus prevalence by race or ethnicity. For example, a nationally representative analysis in the USA found a higher tinnitus prevalence among non-Hispanic white adults (about 13%) and lower prevalence among Black (~8%), Hispanic white (~8%) and Asian (~4%) adults; however, after adjusting for age, otological or medical conditions and noise exposure, most race or ethnicity differences attenuated (with Asian ethnicity still showing lower odds)[12]. Another study reported similarly higher odds of tinnitus in non-Hispanic white adults compared with other racial or ethnic groups[13].

Incidence. Longitudinal data suitable for estimating tinnitus incidence remain relatively scarce[10]. One systematic review found a pooled incidence rate of 1.16% per year (95% CI 0.48–2.83%)[3]. Although these data are based on relatively few cohorts and exhibit high heterogeneity, they nonetheless confirm tinnitus as a common and recurrent condition in adult populations[3].

Tinnitus burden

Overall, prevalence estimates suggest that tinnitus affects >740 million adults worldwide, with more than 120 million perceiving it as a significant or debilitating condition, particularly among older adults. These figures place tinnitus among the most prevalent conditions worldwide[3,10,14,15]. The prevalence of tinnitus, and particularly of severe tinnitus, is expected to increase in the coming decades owing to the ageing global population[16].

Risk factors

Risk factors for tinnitus vary in strength and causal proximity (Fig. 1). Some factors directly affect the auditory system and are strongly associated with tinnitus onset, whereas others may act indirectly through pathways such as hearing loss, comorbidity or environmental exposures. For clarity, risk factors are presented from proximal auditory determinants to more distal medical, genetic and socio-demographic factors; however, this ordering does not necessarily reflect their relative importance. For several factors (such as migraine, temporomandibular joint (TMJ) disorders and sleep disorders), the direction of the association with tinnitus remains uncertain, as these conditions may act both as potential risk factors and as consequences of tinnitus-related distress. Evidence on the determinants of tinnitus remains limited, largely because relatively few case–control studies based on incident cases and prospective cohort studies have been conducted[17].

Auditory and otological factors. Auditory and otological factors represent the most proximal and well-established determinants of tinnitus. These factors directly affect cochlear function or auditory neural pathways and are therefore considered central in the pathogenesis of tinnitus.

Hearing loss is strongly associated with tinnitus, although the relationship is not linear: some individuals with severe tinnitus exhibit audiometrically normal hearing, and many individuals with hearing loss do not experience tinnitus[8,10,18]. A meta-analysis of case–control and cohort studies reported a pooled relative risk of 1.94 (95% CI 1.41–2.67) for unspecified hearing loss and 3.68 (95% CI 2.93–7.04) for sensorineural hearing loss, which is characterized by damage to the inner ear or auditory nerve[17]. Cochlear injury and the resulting reduction in auditory input are thought to trigger maladaptive plasticity within central auditory pathways, contributing to tinnitus perception[19–21].

Importantly, normal hearing thresholds in conventional audiometry do not necessarily exclude cochlear damage[22]. Hidden hearing loss, also referred to as cochlear synaptopathy, involves the loss of synapses between inner hair cells and auditory nerve fibres and may occur despite normal audiometric thresholds within the conventional frequency range (0.125–8 kHz). Individuals with tinnitus and normal audiograms may exhibit subtle deficits detectable in extended high-frequency audiometry (8–20 kHz) or reduced auditory brainstem response wave I amplitude, indicating underlying cochlear damage[23].

Noise exposure is a well-established risk factor for tinnitus, particularly occupational exposure to high-intensity sound[17,24]. Recreational noise exposure, such as through concerts or personal listening devices, has also been investigated, although the epidemiological evidence remains less consistent[17,24]. Electromagnetic exposure (for example, mobile phone use) has not been convincingly associated with tinnitus[25].

Ageing is also associated with progressive degeneration of cochlear structures and auditory nerve fibres that may increase the risk of tinnitus. Age-related cochlear degeneration includes loss of hair cells, synapses and auditory nerve fibres, often occurring alongside presbycusis (age-related hearing loss). Individuals with tinnitus and clinically normal hearing may exhibit reduced cochlear nerve responses and altered auditory reflexes, suggesting underlying cochlear neural degeneration and compensatory hyperactivity in central auditory pathways[26].

Several otological conditions are associated with tinnitus, including Ménière disease, acoustic neuroma, otosclerosis and otitis media[10,27]. Evidence from longitudinal studies confirms a direct link between otitis media and the risk of tinnitus[17].

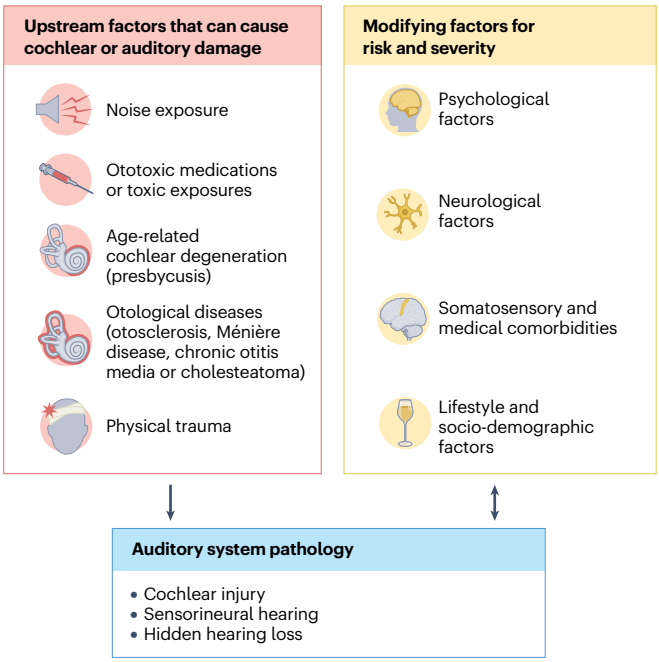

Fig. 1 | Pathway-based contributors to tinnitus. Auditory system pathology, including cochlear injury, auditory deafferentation, sensorineural hearing loss and hidden hearing loss (also known as cochlear synaptopathy), is a central pathway in tinnitus. Several factors, including noise exposure, use of ototoxic drugs, age-related cochlear degeneration, trauma to the ear or head, and otological diseases, may contribute to tinnitus primarily by inducing or worsening auditory system pathology. Other factors, such as psychological, neurological, medical, lifestyle and socio-demographic factors, may modify risk, severity or persistence of tinnitus. The strength and direction of associations vary across factors, and not all act independently.

Medical and neurological factors. TMJ disorders are frequently reported among individuals with tinnitus[28]. Beyond simple co-occurrence, epidemiological evidence from at least one case–control study and a cohort study suggests that TMJ dysfunction may increase the risk of tinnitus[17,29,30], consistent with previous suggestions[31], possibly through somatosensory–auditory neural interactions[32,33]. Physical therapy treatment of the TMJ disorder can lead to reductions in tinnitus perception[31].

Cross-sectional and longitudinal studies consistently demonstrate a relationship between tinnitus and headache, particularly migraine[34–37]. In a Swedish population-based study, headaches were reported by 14% of individuals without tinnitus compared with 26% of those with tinnitus and 40% among participants with severe tinnitus[34]. This relationship probably reflects common pathophysiological mechanisms[38], although a few prospective studies showed that migraine is a risk factor for the development of tinnitus[34–36].

Poor quality of sleep (not necessarily meaning sleep impairment) affects most patients with tinnitus[39]. Severity of tinnitus correlates with sleep disturbance[39], suggesting a bidirectional relationship. However, a large case–control study showed that the risk of tinnitus is higher in people with sleep disturbance, in particular with sleep apnoea[40]. Other factors that may be associated with tinnitus include autoimmune disorders, arthritis and steroid use in conditions such as asthma[13,41].

Pharmacological and toxic exposures. Ototoxic medications, including certain oral or intravenous antibiotics, chemotherapeutics, and high-dose aspirin (taken acutely or for sustained periods), may contribute to tinnitus development[10,42]. A large retrospective cohort from the USA found a statistically significant association between the use of statins and the risk of both hearing loss and tinnitus, indicating the potential ototoxicity of statins[43]. A direct association between tinnitus and ototoxic platinum-based chemotherapy has been confirmed by a few cohort studies[17].

Genetic susceptibility. Genetic factors may also contribute to tinnitus susceptibility. Epidemiological studies in European cohorts, including twins[44,45], adoptees[46] and familial aggregation studies[47], have reported significant tinnitus heritability[44,48]. A genome-wide association study also indicates that the genetic architecture of tinnitus differs from that of hearing loss[49].

Sequencing studies focusing on individuals with severe tinnitus have identified rare variants with potentially large effects. Gene burden analyses in exome datasets suggest that rare allelic variation contributes to severe tinnitus[48,50] and have identified several implicated synaptic genes, including *ANK2*, *AKAP9* and *TSC2* (refs. 48,51). Individuals with rare missense variants in *ANK2* and severe tinnitus may exhibit an endophenotype characterized by hyperacusis (increased sensitivity to normal everyday sounds), persistent noise-like tinnitus, high-frequency hearing loss, and decreased amplitudes in auditory middle latency response[52]. In addition, common variants in *WNT11* (rs2846071) and *TNFRSF1A* (rs4149577) have been associated with susceptibility to noise-induced tinnitus in a Chinese population[53].

Socio-demographic and lifestyle factors. Tinnitus prevalence rises with increasing age, primarily due to age-related hearing loss[2,3,8,10]. Socio-economic status also plays a role, with lower educational attainment[13,41] and income[54] associated with tinnitus prevalence[11]. Certain occupations, such as military service[55] and musicians[56], are at higher risk, possibly due to occupational noise exposure, but a cohort study showed that unemployment and specific occupations (not necessarily noisy ones) can also be predictors for tinnitus[57].

Tobacco smoking has been consistently associated with an increased risk of tinnitus in cross-sectional studies[1]. A systematic review reported a pooled relative risk for current versus never smokers of 1.27 (95% CI 1.12–1.43)[1]. However, the only cohort study carried out did not confirm this relationship[1,17]. Regarding alcohol consumption, a systematic review found no evidence of an association between alcohol intake and tinnitus[1]. Associations with diet, caffeine consumption and physical activity remain inconsistent[1,17,58,59], and the limited longitudinal evidence available[60–62] does not allow for firm conclusions. Similarly, while cross-sectional studies suggest that obesity may increase the risk of tinnitus, this finding is not consistently supported by prospective studies[1,17].

Comorbidities

The relationship between tinnitus and its comorbidities is complex and often bidirectional. In many cases, the temporal sequence between tinnitus and the associated condition remains unclear. The most commonly reported comorbidities are auditory hypersensitivity, mental health disorders, sleep disturbance, cognitive impairment and suicidal ideation.

Auditory comorbidities. Tinnitus frequently co-occurs with hyperacusis. An odds ratio of 3.51 (95% CI 2.99–4.13), rising to 12.1 among participants with severe tinnitus, has been reported[20]. Severity of hyperacusis correlates directly with tinnitus intensity, reaching an odds ratio of 77.4 in those with the most severe hyperacusis[3]. Although the direction of causality remains uncertain, available evidence suggests that tinnitus and hyperacusis are distinct yet comorbid conditions sharing common neurophysiological mechanisms[63].

Mental health conditions. The neuroticism personality trait is consistently associated with tinnitus[64]. Depressive and anxiety symptoms are highly prevalent in patients with tinnitus, especially in the early stages of tinnitus, possibly due to the distressing nature of the condition[10,24,65–68]. Psychological factors can also exacerbate the perception of tinnitus, creating a feedback loop. Tinnitus severity correlates with the number of depressive symptoms[65,66]. Notably, some prospective cohort studies showed that anxiety and, particularly, depression are predictors of a tinnitus diagnosis[17,30].

Sleep disturbance and cognitive disorders. As noted above, sleep disorders have been associated with an increased risk of tinnitus[40]. At the same time, tinnitus itself frequently disrupts sleep, suggesting a bidirectional relationship between these conditions.

Chronic bothersome tinnitus has been linked to deficits in attention, executive function and working memory, presumably due to the continuous attentional load required to suppress or cope with the tinnitus sound[67,69,70], although the issue remains under debate[71]. Furthermore, mild cognitive impairment has been associated with perceived tinnitus handicap, measured by the Tinnitus Handicap Inventory (a survey used to evaluate the effect of tinnitus on daily life), and with high-frequency hearing loss[64], although the direction of causality remains uncertain.

Suicidal ideation and behaviour. Tinnitus is not a direct cause of mortality. However, several studies have documented an association between tinnitus and increased suicidal ideation and suicide attempts[72,73]. A comprehensive review of 23 studies confirmed a relationship between tinnitus and both suicidal thoughts and behaviours in tinnitus populations overall (that is, not restricted to those with comorbid depression)[72]. At the same time, the review found no evidence of a direct link between tinnitus and death by suicide[72]. Furthermore, in a large epidemiological study, the association between tinnitus and suicidal ideation persisted after adjustment for socio-demographic factors and relevant comorbidities[74]. The only study specifically analysing death by suicide was a large retrospective cohort of veterans in the USA, which counterintuitively showed lower suicide rates among those with tinnitus compared to those without[72]. More recently, a systematic review reported that individuals with tinnitus have a significantly higher risk of suicidal ideation (relative risk 2.1, 95% CI 1.6–2.8) and suicide attempts (relative risk 1.8, 95% CI 1.3–2.4) compared with those without tinnitus[73].

Data gaps and methodological challenges

Despite the increasing body of epidemiological research, several challenges remain. Differences in tinnitus case definitions and survey instruments hinder comparability across studies and across countries. To improve population-based surveillance of tinnitus prevalence, severity, hearing difficulty and healthcare resource use, the adoption of a standardized set of four questions, already implemented in several countries[2] and available in multiple languages[75], is recommended.

Most studies on risk factors come from cross-sectional data[17], limiting causal inference. Well-conducted prospective cohort and

case–control studies based on incident cases are needed to clarify the risk factors of tinnitus. Pooling existing cohort data with standardized follow-up information would allow for robust longitudinal analyses, potentially identifying modifiable predictors and informing preventive strategies. Furthermore, most studies are based on European cohorts, which limits the findings to certain ethnicities, especially regarding genetic variants of tinnitus. Indeed, the comorbidities and risk factors of tinnitus in other ethnicities are unclear, particularly in communities in the Global South.

Mechanisms/pathophysiology

Until the 1990s, tinnitus was thought to be an 'ear problem'[5]. However, animal studies, functional neuroimaging research and pathophysiological models have shown the involvement of auditory and non-auditory pathways in the generation, maintenance and intrusiveness of tinnitus. Thus, tinnitus results from a complex bidirectional interplay between peripheral and central mechanisms of action.

Peripheral mechanisms

Approximately 80–90% of people with tinnitus present with hearing loss that may or may not (hidden hearing loss) be detected by audiography[76]. Damage to different cochlear structures, including the basilar membrane, outer hair cells, inner hair cells and stereocilia, due to exposure to noise or ototoxic drugs can produce mechanical (decoupling of stereocilia from the basilar membrane or damage to inner and outer hair cells), electrical and chemical abnormalities[77]. These changes are hypothesized to be perceived by the brain as 'sound' or tinnitus. A seminal study severing the auditory nerve as a treatment for tinnitus improved the perception of tinnitus in 45% of patients, suggesting that tinnitus can have a peripheral origin at the level of the auditory nerve[78]. However, the remaining 55% of patients reported that their tinnitus was the same or worsened, suggesting that tinnitus has a more central origin in some patients.

Central mechanisms

A decrease in spontaneous activity of the auditory nerve is accompanied by an increase in spontaneous activity or synchronous neural firing at the dorsal cochlear nucleus and higher up in the auditory pathway[79] (Fig. 2). This increased spontaneous activity is hypothesized to be perceived as 'sound' or tinnitus. Several models and findings support this theory of tinnitus, namely, central gain increase, thalamocortical dysrhythmia, neuroinflammation and the stochastic resonance model.

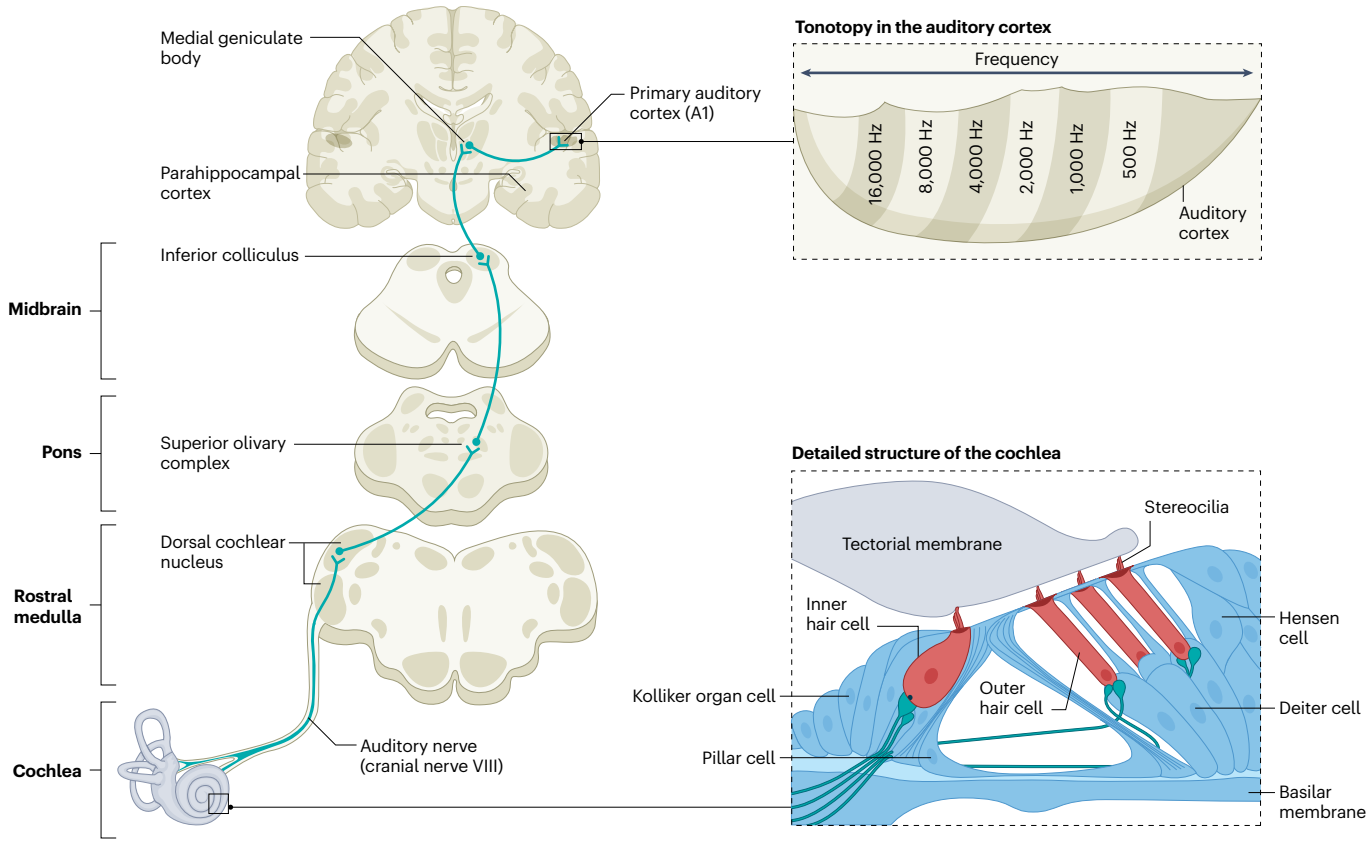

Fig. 2 | The human auditory pathway. Sound is detected by the sensory epithelia of the cochlea in the inner ear. Inner hair cells in the organ of Corti – running along the spiral length of the cochlea – convert sound-driven vibrations into receptor potentials and release glutamate. Glutamate activates type I spiral ganglion neurons, whose axons contribute to cranial nerve VIII (the cochleovestibular nerve). Outer hair cells support auditory processing by amplifying sound. The primary (lemniscal) lateral auditory pathway begins with a first synaptic relay in the dorsal cochlear nuclei of the brainstem, which receive input from type I spiral ganglion neurons. Most auditory fibres then cross the midline and synapse in the superior olivary complex, the second relay. The pathway continues to the inferior colliculus in the midbrain (third relay), and then to the medial geniculate body of the thalamus, the final relay before projections reach the auditory cortex. The lemniscal pathway is organized tonotopically: individual hair cells are tuned to particular frequencies, and this frequency mapping is preserved through the brainstem relays and into the primary auditory cortex, located in the temporal lobe. Adapted from ref. 5, Springer Nature Limited.

Central gain increase. As previously mentioned, reduced auditory nerve firing at the auditory periphery as a direct consequence of cochlear damage leads to increased activity at higher levels of the auditory pathways[5]. This increased activity may occur as a result of Hebbian (activity-dependent synaptic strengthening when presynaptic and postsynaptic neurons are co-active) or non-Hebbian homeostatic (activity-stabilizing adjustments such as changes in intrinsic excitability that globally increase neuronal responsiveness when input is reduced) synaptic plasticity and compensates for decreased peripheral activity[80]. This central gain is hypothesized to preserve the stability of neural activity and neural coding efficiency, and this increased 'neural noise' is perceived as tinnitus[81]. At the systems level, hyperactivity in the auditory cortex is seen as an increase in gamma oscillations and is correlated to tinnitus loudness[82].

Thalamocortical dysrhythmia. Hyperactivity in the auditory cortex following sensory deprivation may also be a result of incoherent thalamocortical rhythms. A key feature of accurate sensory perception is the brain's ability to enhance relevant inputs while suppressing neighbouring activity that could degrade the sound. This suppression, termed lateral inhibition, is mediated by local GABAergic interneurons[83]. In states of sensory deprivation to the auditory cortex, GABAergic interneurons in the auditory cortex have reduced activity, leading to a loss of lateral inhibition and increased neural activity, which distorts sound perception[84]. From a neural oscillatory standpoint, lateral inhibition is coded by alpha rhythms[85]. A loss of lateral inhibition is characterized by the slowing of alpha oscillations to theta oscillations and an increase in gamma oscillations in the immediate vicinity[85]. This simultaneous increase in theta–gamma activity is characteristic of a disruption of thalamocortical rhythms in the auditory cortex and is correlated with tinnitus loudness[86,87].

Neuroinflammation. Tinnitus may also be related to low-grade neuroinflammation in the central auditory pathways[88–90]. This neuroinflammation is thought to be triggered by peripheral auditory injury, which may promote immune signalling via oxidative stress, excitotoxic neurotransmission and damage-associated molecular patterns[88–90]. However, in humans, the initiating cause is often not directly identifiable and may be multifactorial[88–90]. While acute inflammatory processes may be beneficial for repair, chronic neuroinflammation may be detrimental and may contribute to tinnitus by promoting a state of chronic hyperexcitability and reduced inhibition within central auditory pathways[91]. This process is hypothesized to involve persistent activation of microglia and astrocytes and the release of inflammatory mediators such as pro-inflammatory cytokines (for example, TNF, IL-1β and IL-6), chemokines (for example, CCL2; also known as MCP1) and downstream effectors, including prostaglandin and COX2 signalling, nitric oxide (inducible nitric oxide synthase-related) and reactive oxygen species[89,91]. Persistent inflammatory signalling may stabilize maladaptive plasticity by shifting synaptic and intrinsic excitability towards a more excitable state (for example, enhancing glutamatergic drive, reducing GABAergic inhibition, altering receptor or ion-channel expression, and changing synaptic scaling or pruning), thereby reinforcing changes such as increased central gain and disrupted thalamocortical rhythms and 'locking in' the aberrant hyperactivity that is perceived as tinnitus[91].

Stochastic resonance model. The stochastic resonance model (also known as the Erlangen model)[92,93] argues that increased neural noise occurs to compensate for hearing loss, and could partially restore hearing ability and improve sensitivities to perception of weak signals through the addition of noise to a non-linear system[94]. By adding this noise, weak signals are better able to reach perceptual threshold, thereby improving hearing. This model also hypothesizes that neural noise is generated in the dorsal cochlear nucleus.

Tinnitus-related pathways — changes in excitation–inhibition balance

Similar to chronic pain, tinnitus has been hypothesized to be generated and maintained by three different pathways — two ascending pathways (lateral and medial) and one descending pathway[95]. The lateral pathway is hypothesized to follow the ascending auditory lemniscal route from the cochlea to the cortex. The distress component of tinnitus is hypothesized to be encoded by the medial, extra-lemniscal pathway that projects to the anterior cingulate cortex, the insula and other regions of the limbic system[95]. The ascending and extra-lemniscal pathways are hypothesized to be countered by a descending pathway that originates in the ventromedial prefrontal cortex, extending into the pregenual anterior cingulate cortex and descending via the thalamus to the auditory brainstem.

Evidence for the existence of the three pathways has been shown through animal and human studies. A decrease in synchronous activity in the auditory nerve compensated by an increase in synchronous activity in regions higher up in the auditory pathways supports the presence of the lateral pathway of tinnitus[96]. Functional MRI studies confirm the involvement of non-auditory regions in tinnitus, particularly those encoding tinnitus-related distress, such as the anterior cingulate cortex, anterior insula and other regions of the limbic system[97]. An important extra-lemniscal route for the generation of a certain type of tinnitus, called 'somatic tinnitus', is facilitated through auditory–somatosensory interactions at the dorsal cochlear nucleus[98]. Evidence for this interaction has been repeatedly shown in animal and neuromodulation studies[99]. Moreover, hyperactivity in the ventromedial prefrontal cortex in tinnitus has been consistently demonstrated via MRI[100,101] and electrophysiological studies[102]. This hyperactivity has been proposed to be part of a fronto-striatal gating[103] or 'noise cancellation' system[104], which reduces aberrant 'neural noise' and hyperactivity of the thalamus[105] (as described by the thalamocortical dysrhythmia model; Fig. 3a).

Analogous to pain[106], an imbalance between the excitatory (primarily through the ascending lateral pathway) and inhibitory (primarily through the descending pathway) processes, both at a cellular[107] and systemic[108] level, is hypothesized to lead to the generation of tinnitus. This imbalance is disrupted by neuroinflammatory processes[89]. At a systemic level, this model explains why both hyperactivity and hypoactivity, as detected on functional imaging, are associated with tinnitus, depending on whether the imbalance is based on a decrease in noise cancelling, an increase in auditory activity or a combination of both (Fig. 3b).

Tinnitus networks

The pathway-based models described above (lateral, medial and descending systems) are embedded within, and dynamically interact with, large-scale intrinsic brain networks that consist of auditory and non-auditory regions[109,110]. Chronic tinnitus is therefore not only a disorder of specific auditory–limbic pathways but also of network-level reorganization[111,112].

Tinnitus loudness is primarily associated with hyperactivity of the auditory cortex[82]. Moreover, changes in tinnitus-related pitch

are characterized by changes in gamma activity in the right parietal, frontal and left temporal cortices[113]. Hearing loss is characterized by changes in grey and white matter integrity in the auditory regions but has a complex relationship with tinnitus. In the absence of tinnitus, hearing loss is characterized by increased alpha activity in the ventromedial prefrontal cortex and increased alpha connectivity with the

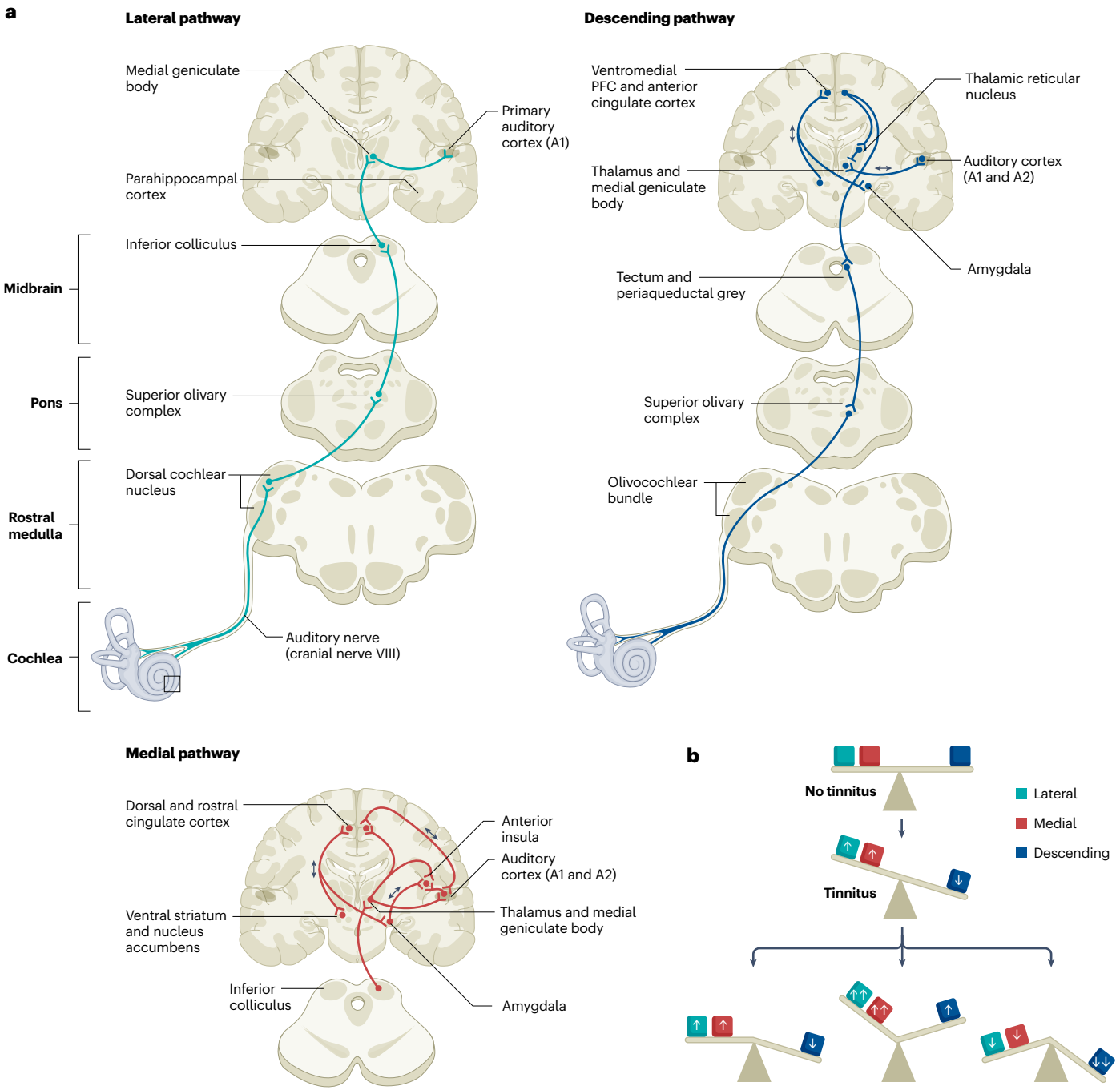

Fig. 3 | Pathway- and network-level mechanisms of tinnitus. a, Tinnitus emerges from distributed networks rather than a single hyperactive node, requiring a pathway and network perspective. The lateral ascending (lemniscal) auditory pathway conveys altered activity from the cochlea to the auditory cortex. The medial (extra-lemniscal) pathway links auditory structures to limbic or salience hubs (anterior cingulate cortex, insula and amygdala), providing a route by which the percept acquires distress and salience. Opposing this is a descending prefrontal gating ('noise cancellation') pathway originating in the ventromedial prefrontal cortex (PFC), projecting via the thalamus to the auditory brainstem; failure of this top-down fronto-striatal gate permits aberrant 'neural noise', consistent with thalamocortical dysrhythmia. **b**, The lateral (bottom-up) and descending (top-down) pathways can be disrupted independently or together, depending on the degree of hearing loss: with no clinically detectable hearing loss, tinnitus primarily reflects descending (gating) dysfunction; with hearing loss, both ascending and descending pathways are engaged, and with greater loss the medial temporal lobe or auditory memory contributes to 'filling in' missing input.

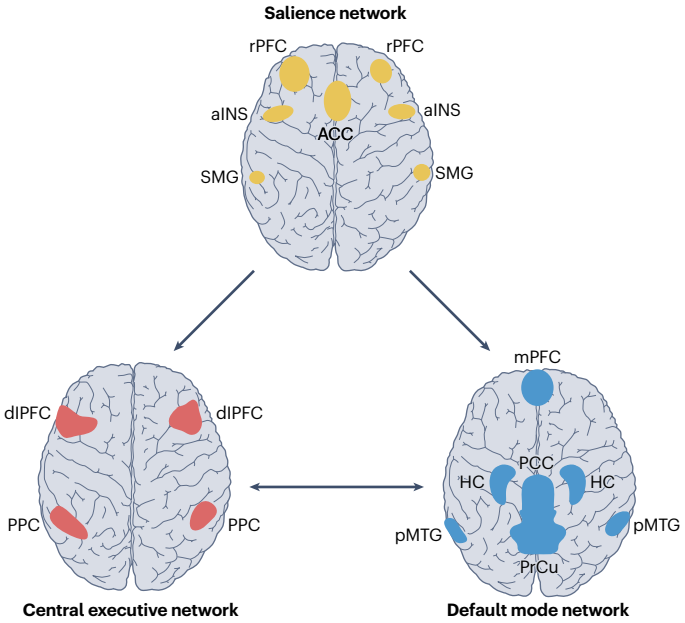

Fig. 4 | Brain regions and resting-state networks. The relationship between the central executive network and the default mode network, both of which are regulated by the salience network. Tinnitus-related distress engages the salience network and limbic regions, with altered connectivity in the default mode network and changes in the central executive network. These large-scale network interactions may encode, internalize and maintain the tinnitus percept, consistent with cognitive difficulties such as impaired concentration, working memory and task performance. ACC, anterior cingulate cortex; aINS, anterior insula; dlPFC, dorsolateral prefrontal cortex; HC, hippocampus; mPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; pMTG, posterior middle temporal gyrus; PPC, posterior parietal cortex; PrCu, precuneus; rPFC, rostral prefrontal cortex; SMG, supramarginal gyrus.

auditory cortex. In people with hearing loss who have tinnitus, this activity changes to low-frequency theta oscillations together with increased low-frequency theta oscillations in the medial temporal regions, suggesting an involvement of the auditory sensory memory to 'fill in' the missing sensory information[108].

PET and magnetoencephalography studies have characterized tinnitus duration as changes in activity and connectivity between the right inferior frontal gyrus, right ventromedial prefrontal cortex and right posterior cingulate cortex[114–116]. After correcting for age and hearing loss, tinnitus duration was characterized by changes in fronto-striatal connections between the nucleus accumbens and ventromedial prefrontal cortex[117]. Age of onset of tinnitus is characterized by neural changes in the anterior and posterior cingulate cortex as well as in the orbital frontal cortex and changes in functional connectivity between primary and secondary auditory and non-auditory regions, such as insula, anterior cingulate and precuneus, in both the theta and alpha bands[117].

Tinnitus-related distress activates regions of the salience network (anterior cingulate cortex and anterior insula) and other regions of the limbic system, including the amygdala, nucleus accumbens, parahippocampus and hippocampus[118]. Moreover, tinnitus-related distress is associated with increased connectivity in the default mode network (including medial prefrontal cortex and posterior cingulate–precuneus). Changes in the central executive network (including dorsolateral prefrontal cortex and parietal cortices) together with changes in cognitive tasks are also reported with tinnitus[119,120]. The salience network, default mode network and central executive network are hypothesized to respectively encode, internalize and maintain the tinnitus percept[121–124] in a maladaptive triple network model[125]. This finding is consistent with the frequently reported difficulties in concentration, working memory and task performance in people with tinnitus, even when tinnitus loudness is moderate. Therefore, large-scale network dynamics characterize the activation of different subnetworks in the brain, hypothesizing tinnitus to be a unified percept of dynamically interacting components (Fig. 4). With increasing tinnitus-related distress, these large-scale networks appear to lose flexibility: their dynamicity decreases and connectivity patterns become more rigid or 'hard-wired'[126,127].

Tinnitus and stress

Stress is a key mechanism in the chronification of tinnitus. Stress-related neural circuits partially overlap with the salience, unpleasantness and suffering networks[106] that are involved in tinnitus, especially within the medial (extra-lemniscal) system. Chronic stress is associated with a reversible reduction in the volume of the ventromedial prefrontal cortex and pregenual anterior cingulate cortex[128], regions that form the core of the 'noise cancellation' or gating system described earlier[104]. Structural and functional compromise of these regions weakens the descending tinnitus-suppressing pathway, thereby reducing its ability to counteract aberrant auditory activity.

Stress also enhances activity within the medial system (salience network), identifying tinnitus as behaviourally relevant and aversive. This heightened salience is closely linked to tinnitus-related distress[129,130] and the subjective loudness of tinnitus[131]. Stress has also been suggested to contribute to the generation of tinnitus[132,133]. Stress affects the hypothalamic–pituitary–thyroid and hypothalamic–pituitary–adrenal axes and the autonomic nervous system. These systems induce plasticity changes in the limbic system, the auditory system and the reticular systems, all of which have been proposed to be generators of tinnitus[134,135]. Patients with tinnitus show delayed or sub-optimal responses to stress and higher levels of hormones such as norepinephrine and the serotonin metabolite 5-hydroxyindoleacetic acid[132]. Taken together, stress alters the balance between tinnitus-generating (lateral and medial) and tinnitus-suppressing (descending) circuits, promoting the persistence and exacerbation of tinnitus, but it may also be a risk factor for its origin.

Other models of tinnitus generation — predictive coding

More recently, tinnitus has been conceptualized from a more fundamental perceptual standpoint of the brain. Perception is considered an active process where the brain maintains an internal model of the sensory world and constantly predicts the next upcoming input, while comparing the sensory input it receives to its internal model[136]. The difference between its prediction and received input is called prediction error — if the prediction error is small, it is ignored; however, if it is severe, it is used to change the internal model. Three different accounts have been proposed that use predictive coding to explain tinnitus generation. One account proposes the existence of a tinnitus precursor signal that reaches a certain threshold due to changes in the auditory pathways and is then perceived as tinnitus[6]. In this model, tinnitus is hypothesized to be driven by changes in sensory input to the brain. Another model posits that changes in sensory input or changes within the brain (due to stress) cause the brain to look for ways to minimize the prediction error and generate tinnitus as a compensation mechanism[137].

This is in accordance with the active inference standpoint proposed by another group. The third model suggests that patients with tinnitus create strong predictions about their sensory world, which is difficult to adapt to changing sensory demands[138]. Therefore, instead of adapting to the sensory world, they create phantom percepts to minimize the prediction error arising due to the difference between their strong predictions of the world and incoming sensory input.

Diagnosis, screening and prevention

Diagnosis

Tinnitus is a heterogeneous condition with various subforms, which require specific management[139]. Therefore, a comprehensive diagnostic assessment is important. The diagnostic examination should determine the aetiology of the tinnitus, whether the tinnitus is the symptom of a severe underlying disease, whether the patient is impaired by the tinnitus, and any relevant comorbidities[8]. At the same time, the doctor's attitude during the diagnostic process can meaningfully influence how patients perceive and evaluate their tinnitus.

Physician attitude in the diagnostic process. Tinnitus frequently causes a high degree of uncertainty and psychological stress, and the way in which the diagnostic process is performed and communicated to the patient can have a major effect on how patients perceive and evaluate their tinnitus[140]. Many patients worry that tinnitus signals a serious underlying disorder, although this is uncommon. Clinicians should therefore combine appropriate screening for red flags with clear, reassuring communication about likelihoods and next steps. During the initial medical history, it is important to guide the conversation in a way that gathers relevant information without inadvertently amplifying the patient's attention to, and concern about, the tinnitus percept. In this context, 'sensitization to the symptom' refers to increasing the salience of tinnitus through repeated monitoring, threat-focused interpretation and heightened emotional arousal, which can reinforce attention to the sound and contribute to distress over time.

Differentiation between subjective and objective tinnitus. During diagnosis, objective and subjective tinnitus must be distinguished. Objective tinnitus (also termed 'somatosound') is rare and refers to internally generated sounds such as of blood flow or contractions of the middle-ear or palatal muscles. The distinction between objective and subjective tinnitus is made based on whether an internal sound source is physically present and can be detected independently of the patient (for example, by the examiner on auscultation (listening to the internal sounds of the body), inspection, recording or by imaging). If no externally detectable sound source is found and the percept is reported only by the patient, the tinnitus is considered subjective[140,141].

Pulsatile tinnitus. Pulsatile tinnitus is a form of objective tinnitus when patients hear a rhythmic sound that usually matches their heartbeat or are generated due to muscular sources. Vascular sources of tinnitus include arteriovenous malformations and fistulas, arterial or venous stenosis or dehiscence, or increased blood flow due to anaemia and typically present as pulse-synchronous pulsatile tinnitus. Muscular sources can be spasms or myoclonia of the middle-ear or palatal muscles and are often described as clicking, fluttering or tapping. Therefore, patients presenting with pulse-synchronous pulsatile tinnitus should undergo an appropriate neurovascular work-up (usually MRI, 4D flow MRI and/or CT-based imaging). Following proper diagnosis, treatment of the source might resolve the pulsatile tinnitus[142–145]. In addition, numerical simulation models for pulsatile tinnitus use patient-specific 3D geometries derived from imaging (MRI or CT) and computational fluid dynamics[144] to identify abnormal blood flow (turbulence and pressure) as a sound source, particularly in the transverse and sigmoid sinuses. These models can also be used for validating surgical outcomes, often showing reduced turbulence and pressure after interventions[145,146]. Notably, even with a thorough diagnostic evaluation, no specific aetiology is identified in approximately 30% of patients with pulsatile tinnitus and, in such patients, an increased perception of otherwise normal vascular flow (via bone conduction) has been proposed as a contributing mechanism[147]. Long-term tympanometry refers to continuous recording of tympanic membrane immittance or compliance over time (often using a 'reflex decay' or long time-base setting) to capture cyclical or intermittent tympanic membrane movements. This technique can be useful for identifying middle-ear muscle spasm or myoclonus and for demonstrating tympanic membrane excursions synchronous with respiration in patulous Eustachian tube[148].

Aetiological factors in subjective tinnitus. Subjective tinnitus is much more frequent than objective tinnitus and is defined as the conscious perception of sounds in the absence of both an external and an internal sound source. Most patients with subjective tinnitus have some form of hearing loss. Additional factors that contribute to the development of tinnitus include increased muscle tension in the neck and masticatory muscles. This form of tinnitus is referred to as somatosensory (also known as somatic) tinnitus, a subtype of subjective tinnitus[149]. As previously mentioned, psychological stress and increased arousal frequently play a role in the development of subjective tinnitus[140]. Often, several aetiological factors are involved. For example, a person with slowly progressive presbycusis and chronic cervicalgia (ongoing or frequently recurring neck pain) may develop tinnitus in the context of an emotionally stressful situation.

Medical history and clinical examination for subjective tinnitus. Identifying relevant aetiological factors is particularly relevant in cases of newly occurring tinnitus, firstly to rule out a potentially dangerous underlying pathology (Fig. 5), and secondly because successful and timely treatment of the aetiological factor increases the chance of tinnitus remission. For example, if an individual develops tinnitus alongside sudden hearing loss, recovery of hearing function increases the chances of tinnitus remission[150].

Accordingly, enquiring about the circumstances surrounding the onset of tinnitus is essential, including potential triggers such as noise exposure, ear infections, cervical trauma or periods of significant stress. Other essential features of the diagnostic work-up of tinnitus are asking patients about the duration of symptoms and assessing associated otological features (such as subjective hearing loss, vertigo or otalgia (ear pain)). Particular attention should also be given to the laterality, as unilateral symptoms may point to a peripheral structural cause, such as cerumen impaction, middle-ear effusion or chronic otitis media, cholesteatoma, or otosclerosis. Less commonly, unilateral tinnitus may be associated with lesions such as middle-ear paragangliomas (glomus tumours) or vestibular schwannomas, which may be amenable to treatment[142,143].

Additionally, clinicians should assess whether tinnitus can be modulated by movements or manipulation of the neck and masticatory muscles. The presence of such modulation suggests a somatic component to the tinnitus and may indicate a role for physiotherapeutic management[149]. The degree of distress related to tinnitus is also

Medical history

- Tinnitus onset associated with hearing change, acoustic trauma, otitis media, head trauma, whiplash, dental treatment, stress or other?
- Pattern: pulsatile? Intermittent or constant?
- Site: right ear? Left ear? Both ears (symmetrical)? Inside head?
- Quality of the sound: pure tone or noise? Uncertain or polyphonic?
- Pitch: very high, high, medium or low?
- Proportion of awake time aware of tinnitus
- Proportion of awake time annoyed by tinnitus
- Previous tinnitus treatments
- Can the tinnitus be masked by sounds?
- Aggravated by loud noise?
- Altered by head and neck movement?
- Effect of nocturnal sleep and daytime nap on tinnitus
- Effect of stress
- Effect of medications
- Hearing impairment?
- Noise annoyance or intolerance?
- Noise-induced pain?
- Hyperacusis?
- Vertigo or dizziness?
- Temporomandibular disorder?
- Headache? Neck pain?
- Under treatment for psychiatric disorder?

Clinical examination

- Otological exam
- Auscultation
- Cranio-mandibular and neck examination

Audiometric tests

- Pure tone audiometry
- High-frequency audiometry
- Speech audiometry
- Tinnitus frequency matching

Red flags

Clinical features in tinnitus that suggest a potentially serious underlying condition and warrant urgent evaluation

Clinical feature	Potentially serious underlying condition	Recommended diagnostic procedure
Pulsatile tinnitus (including 4D flow MRI)	Vascular aetiology (for example, arteriovenous malformation, vascular tumour, venous anomalies, intracranial hypertension or carotid dissection)	CT and/or MR angiography
Unilateral (asymmetric) tinnitus ± hearing loss on the respective side temporal bone	Vestibular schwannoma or other retrocochlear pathology, middle ear disease (otosclerosis, chronic otitis media)	MRI of the brain and temporal bone, high-resolution CT
Tinnitus associated with focal neurological abnormalities	Possible central nervous system pathology	MRI of the brain
Sudden hearing loss	Sudden SNHL	Audiometry and treatment of SNHL
Tinnitus with vertigo or imbalance	Ménière disease, vestibular schwannoma or other central causes	Vestibular evaluation, MRI of the head
Tinnitus following head or neck trauma	Vascular injury (dissection) or temporal bone fracture	CT, MRI, MR angiography
Tinnitus with otological symptoms (for example, ear pain or drainage)	Infectious, inflammatory or neoplastic ear disease	Otological evaluation
Tinnitus with severe psychiatric symptoms	Suicidal ideation	Immediate psychiatric evaluation

Counselling

Bothersome tinnitus (tinnitus disorder)?

Yes

No

Reassure the patient, provide information and safety-netting, and advise re-presentation if symptoms change or worsen

Tinnitus characteristics that suggest a potentially treatable underlying condition and warrant targeted evaluation

Symptom	Underlying condition	Recommended procedure	Treatment options
Clicking sound	Objective tinnitus due to myoclonus of middle ear muscles or palatal muscles	Otological evaluation	Surgery, botox
'Typewriter tinnitus'	Neurovascular conflict	MRI brainstem	Pharmacotherapy (carbamazepine), surgery

Tinnitus comorbidities

Comorbidity	Recommended procedure	Treatment options
Hearing loss	Referral to audiology and otolaryngology	Hearing aid or cochlear implant
Temporomandibular joint disorder	Dental referral	Dental splint or physiotherapy
Neck pain	Orthopaedic or physiotherapeutic referral	Physiotherapy
Anxiety, depression, insomnia	Psychiatric referral	Psychotherapy or pharmacotherapy

- Sound therapy
- Cognitive behavioural therapy
- Neuromodulation

Fig. 5 | Diagnostic and therapeutic management of tinnitus. Assessment of individuals with suspected tinnitus begins with medical history, targeted clinical examination and audiometric testing to define tinnitus characteristics, associated auditory and vestibular symptoms, somatic modulation and relevant comorbidities. Red flags, including pulsatile tinnitus, unilateral or asymmetric tinnitus, focal neurological findings, sudden hearing loss, vertigo, head or neck trauma, otological symptoms, or severe psychiatric symptoms, prompt urgent targeted investigation for serious underlying pathology. In patients with bothersome tinnitus, subsequent management includes counselling, identification of potentially treatable tinnitus subtypes and comorbidities, and individualized treatment with hearing rehabilitation, dental or physiotherapeutic interventions, psychotherapy or pharmacotherapy, sound therapy, cognitive behavioural therapy, or neuromodulation. MR, magnetic resonance; SNHL, sensorineural hearing loss.

important. Clinicians can ask the patient a simple question ('How much does your tinnitus affect you?') or use standardized self-report questionnaires for quantification, such as the Tinnitus Handicap Inventory[151] or the Tinnitus Functional Index[152]. Asking the patient about the primary cause of distress is also useful, as it provides important guidance for treatment. For instance, when a patient's main concern is insomnia related to tinnitus, management should specifically include interventions aimed at improving sleep. Identifying the primary source of distress should be accompanied by a thorough assessment of relevant comorbidities, including anxiety, depression, insomnia, hyperacusis, communication difficulties, mild cognitive impairment, TMJ disorders, headaches or neck pain, and vertigo. These associated conditions may exacerbate tinnitus symptoms and contribute substantially to the overall disease burden experienced by patients[153]. Therefore, the treatment plan should also address these comorbidities.

Hearing assessment in those with subjective tinnitus. As hearing loss is the most relevant aetiological factor for tinnitus, an examination of the ear and audiometric testing should be performed in every patient with tinnitus[154]. In many patients, hearing loss occurs in the high-frequency range[155] and may not be perceived by the patients themselves[10]. Depending on age, pure tone audiometry can be supplemented by speech intelligibility testing or ultrahigh-frequency audiometry[156]. This approach can reveal hearing loss that also affects speech comprehension or detect hearing loss in the ultrahigh-frequency range that remains hidden in standard audiometry. In addition to their diagnostic value, audiometric tests provide guidance for potential therapeutic interventions, such as hearing aids, and may help the patient to understand tinnitus as a compensatory mechanism of the brain in response to hearing loss.

Imaging in people with subjective tinnitus. Imaging is recommended in individuals with persistent unilateral subjective tinnitus, especially in those with ipsilateral hearing loss and/or vertigo, because, while most tinnitus is 'benign', a one-sided symptom pattern raises concern for a localized ('structural') problem affecting the ear, temporal bone, or the cochlear or vestibular nerves on the side of the tinntius. Conditions causing these problems may be treatable[143,157,158]. MRI is particularly useful for detecting nerve-adjacent, vessel-adjacent or brain-adjacent causes (for example, vestibular schwannoma and other retrocochlear lesions), whereas CT of the temporal bone is better for bony and middle-ear or inner-ear abnormalities (for example, otosclerosis, cholesteatoma complications or canal dehiscence)[143,157,158].

Screening

Routine screening for tinnitus in the general population is not typically recommended[159–161]. Unlike conditions with established biomarkers, tinnitus is defined by subjective perception, and most cases are transient, mild or non-bothersome. Thus, population-wide screening risks overdiagnosis, unnecessary anxiety, and downstream testing with limited clinical benefit[162]. Screening is more useful when it is embedded within risk-based surveillance programmes whose primary aim is to prevent or detect cochlear injury (for example, occupational hearing conservation or ototoxicity monitoring), rather than to detect tinnitus[159–161].

In practice, 'screening' for tinnitus in high-risk groups is usually implemented as brief, standardized case-finding alongside audiological assessment[1,75]. This applies particularly to individuals with sustained occupational noise exposure (industrial workers, military personnel or musicians), people receiving potentially ototoxic therapies (for example, platinum-based chemotherapy or aminoglycosides) and individuals with progressive or asymmetric hearing loss. Screening can be carried out with one or two standardized questions (for example: 'Have you had ringing or buzzing in your ears in the past year?' and 'If yes, how much of a problem is it?'), ideally using harmonized wording to support comparability across settings and over time. Positive screens should prompt review of exposure history (noise or ototoxic drugs), audiometry (often already carried out as part of surveillance) and triage based on the effect of tinnitus on the individual. Those who report bothersome tinnitus (for example, sleep disturbance, concentration problems or distress) can then be assessed more fully with validated questionnaires (such as Tinnitus Handicap Inventory or Tinnitus Functional Index) and evaluated for modifiable contributors and 'red flags' that warrant diagnostic work-up, as described above[151,152].

Prevention

Prevention of tinnitus primarily focuses on preventing or reducing auditory deafferentation and cochlear injury, particularly from noise exposure and ototoxic insults, as these are among the most consistently supported modifiable risk factors. Because tinnitus aetiology is multifactorial and not all cases are preventable, preventive strategies are best framed as risk reduction and early mitigation rather than as guaranteed prevention.

Noise exposure. Noise exposure is the primary risk factor for cochlear damage and is largely preventable through increased awareness of the risks of noise-induced hearing loss and its irreversible nature. The most evidence-based approach is a 'hierarchy of controls' that comprises reducing noise at the source, limiting exposure duration, regular monitoring of hearing abilities with audiometric measurements and using personal hearing protection when exposure cannot be sufficiently reduced. In occupational settings, consistent use of properly fitted hearing protection (earplugs, earmuffs or ear defenders, or double protection for very high levels, customized to fit the individual external ear canal) is expected to reduce the risk of noise-induced hearing loss[163] and, by extension, noise-associated tinnitus[164]. For recreational exposure (such as attending concerts or clubs, using power tools or firearms, or home-working with loud machines), practical prevention includes using high-fidelity earplugs, increasing distance from speakers, taking quiet breaks, and avoiding prolonged high-volume headphone listening.

Ototoxic exposures. Where clinically feasible, tinnitus risk can be reduced by avoiding unnecessary ototoxic medications, using the lowest effective dose and duration, and selecting less ototoxic alternatives when available. For unavoidable exposures (for example, certain chemotherapy regimens), structured ototoxicity monitoring supports early detection of auditory change and enables treatment teams to consider risk–benefit adjustments. This monitoring combines symptom checks (including new tinnitus, hearing loss and vertigo) with audiometry. Avoiding concurrent high-level noise exposure during ototoxic treatment is prudent given the potential synergistic cochlear injury.

Secondary prevention (early management of acute triggers). When tinnitus arises in the context of an acute and treatable otological event (for example, sudden sensorineural hearing loss or acute middle-ear pathology), timely evaluation and management of the underlying condition can increase the likelihood of tinnitus improvement or remission. Similarly, identifying and addressing somatosensory contributors (for example, temporomandibular or cervical dysfunction) and managing severe stress or arousal may reduce persistence and disability in susceptible individuals, although evidence for preventing incident tinnitus via these routes is less robust.

Management

Conceptually, tinnitus can be distinguished in two dimensions; first, the auditory percept with its characteristics, such as loudness, pitch or laterality, and second, its effect on quality of life involving emotional, behavioural and cognitive aspects. Notably, both aspects are purely subjective and therefore their assessment is challenging.

Several well-validated self-report questionnaires are available to evaluate the effect of tinnitus on various dimensions of quality of life[165]. Tinnitus loudness can be measured psychophysically by matching the tinnitus tone to the loudness of an external sound (tinnitus loudness match) or by determining the necessary loudness of a sound to mask the tinnitus (minimal masking level). Unfortunately, these measurements are not reliable and are therefore not useful as outcome parameters in treatment trials[166]. Loudness measurement by visual analogue scales is more reliable[165,167] but the subjectively perceived loudness depends on attention and salience.

Treatments that completely eliminate tinnitus are unfortunately only available for rare subgroups of objective tinnitus. Therefore, most of the procedures described below will not lead to the disappearance of the phantom sound or the reduction of its loudness but will rather improve the quality of life of patients by improving symptom management. Evidence for the efficacy of tinnitus treatments is based on the use of validated self-report questionnaires for assessing tinnitus-related functional impairment as the outcome measurement.

A synoptic summary of the most important therapeutic interventions, their evidence and recommendations included in the most relevant guidelines (American Academy of Otolaryngology–Head and Neck Surgery clinical practice guideline (2014)[159], European guideline (2019)[160], National Institute for Health and Care Excellence guidance summary (2020)[162], German guideline (2021)[168], United States Department of Veterans Affairs/Department of Defense guideline recommendations (2025)[161]) is provided in Table 1.

Tinnitus counselling

Tinnitus counselling comprises support and guidance delivered by a trained specialist, primarily otolaryngologists, audiologists, or psychiatrists and psychotherapists[169]. Counselling forms the basis of any tinnitus treatment and should always be the first step. The initial aim of counselling is to summarize the pathophysiology of tinnitus in a way that is understandable to the general public and to relate it to the available diagnostic measurements (hearing tests or physical findings). This allows a certain understanding of the symptom to be achieved and alleviates concerns about serious underlying diseases. The next step is to inform patients that the perception of tinnitus is not identical to the emotional reaction to it. This also means that reducing the negative effect of tinnitus on the patient's quality of life is possible, even if the tinnitus percept remains unchanged. Coping skills, stress management and relaxation techniques are then discussed as strategies for reducing tinnitus-related suffering.

Tinnitus counselling is recommended in all available clinical practice guidelines[159–162], although evidence from randomized controlled trials (RCTs) is limited. One meta-analysis demonstrated that educational counselling alone can improve tinnitus-related distress and functional effect, even if it does not typically reduce the perceived loudness of the sound, and has the same effect as other psychological or combination therapies[170]. The technique is usually offered during the initial consultation in a specialized clinic. However, various smartphone apps are now available that provide easier access, more intensive knowledge transfer and greater dissemination[171,172].

Counselling can also be combined with hearing aids for hearing loss or sound generators, as evidenced by reductions in tinnitus distress regardless of counselling type[161,173]. In this context, tinnitus retraining therapy (TRT) is a widely used combination of directive counselling and sound therapy, either through hearing aids or noise generators, with the aim of habituation[174]. Despite its widespread clinical use, TRT has limited supporting evidence and well-designed studies are needed to evaluate its effectiveness[169]. One review concluded that combining TRT with other interventions, such as cognitive behavioural therapy (CBT), pharmacotherapy or brain stimulation, may show greater efficacy than TRT alone[175].

CBT

Various structured therapeutic approaches have been developed for the treatment of tinnitus based on the cognitive and behavioural traditions in psychology, with the goal of changing negative thought patterns and behaviours associated with tinnitus. CBT encompasses cognitive restructuring to challenge negative beliefs, behavioural activation to modify avoidance behaviours, and relaxation and mindfulness techniques to reduce arousal and distress. Psychoeducation and exposure to feared situations are integral components, aiming to shift the patient's focus from tinnitus and improve coping strategies. CBT delivery formats are diverse. In-person CBT is typically administered in weekly sessions over 8–14 weeks, either individually or in groups.

A Cochrane meta-analysis based on a large number of RCTs confirmed the efficacy of CBT in reducing the negative effect of tinnitus on quality of life[176]. Based on these studies, CBT is considered the standard approach with the broadest scientific evidence[176], and is unanimously recommended by existing treatment guidelines[159–162]. However, long-term follow-up data are limited and do not consistently show lasting effects[176]. Moreover, treatment studies have included selected samples of patients who were suitable and willing to undergo CBT and the availability of tinnitus-specific CBT is limited. Internet-based CBT and smartphone-based CBT have demonstrated comparable efficacy to traditional formats, offering improved accessibility and sustained benefits over 3–9 months[176]. Thus, further development of

Table 1 | Tinnitus treatment options (in alphabetical order), their evidence and recommendations by the most important guidelines

Intervention	Source of evidence	Number of study participants	Efficacy (immediate)	Efficacy (long-term)	US: Clinical Practice Guideline Tinnitus (2014)[159]	European: A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment (2019)[160]	NICE: Tinnitus: assessment and management (2020)[267]	German: Clinical practice guideline: chronic tinnitus — diagnosis and treatment (2021)[268]	US VA/DoD: Clinical practice guideline for management of tinnitus: recommendations from the US VA/DoD Clinical Practice Guideline Work Group (2024)[161]
Auditory training	Systematic review[189]	269	Available evidence of insufficient quality to make conclusion about efficacy	Not reported	Not mentioned	Not mentioned	Not mentioned	Weak for	Neither for nor against
Cochlear implant	Meta-analysis[269]	1,285/853	THI: −23.2 TQ: −12.6 VAS: −4.5 (pooled over various follow-up periods)	THI: −15.4 TQ: −15.6 VAS: −2.9 (after about 12 months)	Not mentioned	No recommendation	Not mentioned	Strong recommendation for cochlear implants in patients with tinnitus and severe hearing loss/deafness	Weak for
CBT	Cochrane[176]	2,733	Tinnitus severity SMD: −0.56 THI: −10.91	No evidence due to lack of data	Clinicians should recommend CBT to patients with persistent, bothersome tinnitus (recommendation)	Strong for	If tinnitus is still causing an impact on emotional and social wellbeing and day-to-day activities, consider a stepped approach: (1) digital tinnitus-related CBT; (2) group-based tinnitus-related psychological interventions, including mindfulness-based cognitive therapy, acceptance and commitment therapy, or CBT; (3) individual tinnitus-related CBT	Strong for	Weak for
Counselling	Meta-analysis[170]	1,341	No difference in symptom severity compared to other psychological therapies	No difference in symptom severity compared to other psychological therapies	Strong for	Strong for	Strong for	Strong for	Weak for
Hearing aid	Cochrane[188]	590	No significant effects on tinnitus loudness or distress	No data	Clinicians should recommend a hearing aid evaluation for patients with hearing loss and persistent, bothersome tinnitus (recommendation)	Weak for	Offer amplification devices to people with tinnitus who have a hearing loss that affects their ability to communicate Consider amplification 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	Strong for in case of hearing loss	Weak for in case of hearing loss

Table 1 (continued) | Tinnitus treatment options (in alphabetical order), their evidence and recommendations by the most important guidelines

Intervention	Source of evidence	Number of study participants	Efficacy (immediate)	Efficacy (long-term)	US: Clinical Practice Guideline Tinnitus (2014)[159]	European: A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment (2019)[160]	NICE: Tinnitus: assessment and management (2020)[267]	German: Clinical practice guideline: chronic tinnitus — diagnosis and treatment (2021)[268]	US VA/DoD: Clinical practice guideline for management of tinnitus: recommendations from the US VA/DoD Clinical Practice Guideline Work Group (2024)[161]
Pharmacotherapy	Anticonvulsants: Cochrane[270]	453	Insufficient evidence	Not reported	Against	Weak against	Not mentioned	Strong against	Weak against
	Antidepressants: Cochrane[271]	610	Insufficient evidence	Not reported					
	Betahistine: Cochrane[272]	303	No significant effects on tinnitus loudness or distress	Not reported					
	Ginkgo biloba: Cochrane[273]	1,915	Little to no effect at 3–6 months compared to placebo but the evidence is very uncertain	Not reported					
Sound therapy (sound generators)	Cochrane[188]	590	No significant effects on tinnitus loudness or distress	No data	Weak for	No recommendation	Recommendation for research	Against	Weak for
Tinnitus retraining therapy	Meta-analysis[274]	1,345	Significantly increased treatment response	Significantly increased treatment response	Not mentioned	No recommendation	Not mentioned	Weak for	Weak for
Transcranial direct current stimulation	Meta-analysis[275]	1,031	Loudness SMD: −0.35 Distress SMD: −0.50	Not reported	Not mentioned	No recommendation	Recommendation for research	Against	Neither for nor against
Transcranial magnetic stimulation	Meta-analysis[209,276]	945	Tinnitus severity SMD : −0.45	Tinnitus severity SMD: −0.42	Against	Against	Recommendation for research	Against	Neither for nor against

As source of evidence, the most recent meta-analyses are listed (focusing predominantly on Cochrane meta-analyses when possible). CBT, cognitive behavioural therapy; NICE, National Institute for Health and Care Excellence; SMD, standard mean difference; THI, Tinnitus Handicap Inventory (range 0–100); TQ, Tinnitus Questionnaire (range 0–84); US VA/DoD, United States Department of Veterans Affairs/Department of Defense; VAS, Visual Analogue Scale (range 0–10).

such online-based approaches seems warranted to ensure widespread availability of CBT for tinnitus management.

Treatments focusing on hearing improvement

As hearing loss is the most relevant aetiological factor for tinnitus, improvement of hearing represents an important therapeutic concept in tinnitus management.

Hearing aids are recommended for those with accompanying hearing loss. Hearing aids are very effective in improving speech comprehension but their effectiveness in alleviating tinnitus symptoms is less clear. Beneficial effects have been reported in the literature[177–179] but available data come mainly from observational studies and not from RCTs[180]. The use of hearing aids for alleviating tinnitus symptoms in patients with well-preserved communication skills (for example, mild hearing loss or isolated hearing loss in the high-frequency range) is controversial. This is due, on the one hand, to the poor data available and, on the other, to the limited effectiveness of conventional hearing aids at frequencies above 6 kHz. Future research should focus on extending amplification in the high-frequency range and evaluating the usefulness of hearing aids for this patient group[181].

In patients with severe hearing loss bordering on deafness, cochlear implants significantly reduce tinnitus perception and distress[182–184]. This applies to both unilateral and bilateral forms. Cochlear implants can achieve complete tinnitus suppression in up to 80% of patients as long as the device is active. This technique is therefore superior to most other tinnitus therapies in terms of its success rate. However, cochlear implants are only suitable for a small group of people with the most severe hearing impairment, and therefore their clinical use in tinnitus therapy remains limited. Despite this, as the clinical effect of electrical stimulation of the cochlea is successful, there is great potential for research into making this technique available to people with no or mild-to-moderate hearing loss[185].

Surgery can be considered for some patients with tinnitus and hearing loss (otosclerosis or chronic otitis media). In both conditions, a positive prognosis can be given with regard to a possible improvement in tinnitus in patients with otosclerosis after successful stapedotomy (in which the footplate of the stapes is perforated, the anterior and posterior arches of the stapes are removed, and a prosthesis is inserted to improve sound transmission from the incus to the inner ear) or tympanoplasty (surgery to repair the eardrum and/or rebuild the middle-ear sound-conducting mechanism, often performed for chronic eardrum perforation or chronic inflammatory middle-ear disease). However, supporting literature is sparse. One review assumes that approximately 80% of individuals with tinnitus and otosclerosis can expect postoperative improvement (partial or complete suppression of tinnitus) after stapedotomy[186]. In the case of tympanoplasty for the treatment of chronic otitis media (eardrum perforation), one review reports a reduction in tinnitus perception after surgery in 75% of patients[187].

Sound-based treatment

Sound-based treatment encompasses a variety of procedures, including noise generators to mask or distract from tinnitus, environmental sound, music therapy, auditory training, and stimulation techniques using sounds or music that are tailored to the tinnitus frequency of the patient. Sound generators, which usually play white or pink noise, are offered for masking tinnitus or for distraction and are also an element of TRT. However, evidence for the effectiveness of noise generators is insufficient[188,189], and guidelines differ in their recommendation for their use (Table 1). Music therapy approaches include the active generation of sounds by singing or by using specific instruments to mask the tinnitus sounds. Hearing training involves frequency discrimination training, sound localization training and the attention shift on specific sounds in the background. Evidence for these approaches is limited[189,190]. Passive listening approaches have been developed over the past decade that consist of music or sound stimulation, which is individualized depending on a person's tinnitus frequency or hearing profile[191–194]. These approaches aim to induce specific neuroplastic changes and have shown promising pilot data but results could not be validated in larger controlled studies.

In clinical practice, many patients seem to benefit from acoustic distraction in certain situations, such as when falling asleep or concentrating, whether through music, white noise or nature sounds. In this case, personal taste in the selection of suitable sounds seems to be more important than tailoring to specific tinnitus frequencies.

Pharmacotherapy

A large variety of pharmacological compounds have been investigated for tinnitus but none have demonstrated replicable and reliable efficacy in RCTs, and therefore none are approved by the FDA or EMA[195,196]. The failure of successful pharmacological tinnitus alleviation contrasts with the transient tinnitus suppression after intravenous lidocaine[197], demonstrating that, in principle, tinnitus can be influenced by pharmacological treatment.

Pharmacological treatment does have an important role in the management of comorbidities in patients with tinnitus such as for insomnia, anxiety or depression[159–161,198–200].

Therapy for specific subgroups of tinnitus

For very specific subgroups of subjective tinnitus (somatosensory tinnitus) or forms of objective tinnitus (pulsatile or pulse-synchronous), specific therapeutic procedures may be useful to alleviate or eliminate symptoms. For somatosensory tinnitus, these include physiotherapy and/or dental measures. These therapies aim to improve posture in the head and neck or to reduce abnormally increased muscle tension[33]. Dental measures mainly include conservative temporomandibular disorder management, most commonly occlusal stabilization splints (night guards), bruxism or parafunction counselling and habit modification, and other reversible occlusal (the way your teeth meet when you bite) appliances, and are typically delivered alongside physiotherapy and/or pain-reducing or muscle relaxant pharmacotherapy. For some pulsatile forms of objective tinnitus, anticonvulsive medication, physiotherapy, local botox injections and even tenotomy are used to treat myogenic causes (palatal myoclonus or middle-ear myoclonus)[201–203]. For vascular causes, the range of therapies extends from interventional neuroradiological interventions to open surgical procedures[204,205]. In cases of vascular irritation of the auditory nerve, which can manifest as so-called typewriter tinnitus, treatment with carbamazepine[206] or surgical microvascular decompression[207] can be helpful.

Neuromodulation

A wide variety of neuromodulation techniques have been evaluated over the past 25 years to positively influence tinnitus by changing the aberrant neural activity of brain areas. The techniques range from non-invasive approaches, such as neurofeedback[208], to minimally invasive procedures (transcranial magnetic stimulation (TMS) or transcranial electrical stimulation (TES)) and invasive neuromodulation (direct electrical epidural or deep brain stimulation (DBS))[209,210]. However, despite multiple studies and promising results, no procedure has yet been established

in the routine treatment of tinnitus[211]. In the past 10–15 years, various techniques of bimodal neuromodulation have been studied to improve tinnitus. This involves combining auditory stimulation with sounds and peripheral stimulation of cranial nerves (the vagus nerve, trigeminal nerve and C2 nerve)[212–214]. The proposed mechanism of action is using peripheral electrical stimulation to increase neuroplasticity in the brain. Bimodal stimulation consisting of electrical stimulation of the tongue surface in combination with auditory stimulation has shown promising effects in a large sample[215] and has received FDA approval.

Quality of life

Beyond the perception of sounds, the presence of chronic tinnitus has a profound psychological effect on the individual across several dimensions: sleep disturbances, psychological distress, including anxiety and depression, and daily functioning, which includes cognitive processing and participating in workplace activities as well as engagement in social activities. Patients often have complaints about one or more of these dimensions, and patient-centred, individualized treatment plans attempt to address the specific aspects of the patient's tinnitus. A comprehensive systematic review of the everyday problems faced by adults with tinnitus identified 42 discrete complaints spanning physical and psychological health, negative attributes of the tinnitus sound, and quality of life[216].

Tinnitus-related questionnaires often measure particular aspects of quality of life, for instance, the 'Function' subscale of the Tinnitus Handicap Inventory, which measures activities of daily life, or the 'Quality of Life' subscale of the Tinnitus Functional Index, although other subscales of 'Relaxation', 'Sleep' and 'Emotional Distress' may be considered as well. The 'Emotion' and 'Sleep' subscales in the Tinnitus Primary Function Questionnaire may be useful in this regard. Separate from tinnitus-specific questionnaires, quality of life can be assessed via validated self-report questionnaires and is an important measure for a chronic condition such as tinnitus[217–219]. These questionnaires have revealed a detrimental effect on quality of life[220–229].

The effect of tinnitus often extends beyond the individual, with family members and particularly partners experiencing increased stress, frustration or feelings of helplessness in supporting their loved one[216]. Detailed knowledge about the effect of tinnitus on partners and families remains limited. In one review, only 2 out of 86 studies reviewed considered the perspective of significant others[216]. Available studies demonstrated mismatched perceptions between patients and partners: patients with tinnitus reported greater confidence in their hearing yet wished partners would speak louder, tolerate higher volumes and face them when speaking[230]. Notably, tinnitus was seldom discussed openly; 56% of individuals with tinnitus and 53% of partners felt uncomfortable addressing it, highlighting a potential source of misunderstanding. Partners of patients with tinnitus also report making sound-related adjustments, limiting activities, facing increased demands, experiencing feelings of helplessness, and enduring a general emotional burden[231]. Among the 156 partners who completed the open-ended survey, 58% described negative effects, primarily due to communication difficulties. At the same time, 47% reported positive effects on family life, including greater health awareness, beneficial lifestyle changes, personal growth and a positive perspective on life. The severity of tinnitus experienced by the individual, measured using the Tinnitus Functional Index, was not associated with the level of effect on the partner, indicating that partners themselves may require support to help reduce the negative effects of tinnitus.

Of note, tinnitus often co-occurs with clinically significant hearing loss, which can also affect quality of life[232]. Some of the challenges reported by individuals with tinnitus, such as communicating in workplaces, may be attributed more to the accompanying hearing loss than to tinnitus. Similarly, co-occurring conditions, such as traumatic brain injury[233] or post-traumatic stress disorder[234], have meaningful effects on quality of life that may only be marginally related to tinnitus.

Ameliorating the co-occurring conditions improves the quality of life of those with tinnitus, and the treatment of tinnitus should always include the treatment of related comorbidities[235]. Improving hearing loss by providing appropriate amplification can improve communication, diminish focus on tinnitus and improve quality of life[236,237]. Similarly, the treatment of comorbid insomnia, depression, anxiety, headache, neck pain or TMJ disorder has a positive impact on the quality of life of patients with tinnitus[235,238].

Chronic tinnitus is a substantial economic burden for healthcare systems and individual patients. However, there has been limited use of commonly used economic measures to assess this burden and a paucity of studies in general in this regard[220]. The direct costs of tinnitus for healthcare systems in the European Union are reported to be between €1,544 and €3,429 per person annually. Indirect costs, primarily due to productivity loss, add a further €2,565 to €3,702 per person each year[221–227]. A 2024 study on the individual economic burden of tinnitus underscored the personal financial effect of the condition, showing that people with tinnitus incur substantial out-of-pocket expenses for treatment and management: approximately €368 annually for mild cases, €728 for moderate cases and €1,492 for severe cases[228]. Direct costs of the disability associated with tinnitus are difficult to ascertain in the USA. Available data indicate that approximately US$1,635 are paid per veteran due to tinnitus as a service-connected disability, accounting for US$2.6 billion annually by the Department of Veterans Affairs[229].

Outlook

The tinnitus field is rapidly developing. The major challenge for the next decade will be the translation of growing mechanistic insight into clinically actionable tools. In particular, the marked heterogeneity of tinnitus, which probably reflects multiple partly overlapping pathophysiological mechanisms, drives the development of diverse treatment technologies. With this increased diversity, several promising avenues for future exploration have emerged, including new diagnostic approaches and treatments, as well as improved translational research.

Biomarkers

As the conscious tinnitus perception is accompanied by measurable alterations in brain function[82,116,239–241] and evokes autonomic responses[242] more objective diagnostics and the development of reliable biomarkers for tinnitus could be developed in the future. In principle, two categories of biomarkers could be developed: (1) a diagnostic biomarker capable of determining whether an individual perceives the tinnitus phantom sound, and (2) a quantitative biomarker that reflects the perceived tinnitus intensity and is sensitive to changes over time. The latter would represent a breakthrough for clinical research, enabling highly reliable assessments of treatment-induced effects with an objective end point in clinical studies.

Neuroimaging methods can identify abnormal tinnitus-related brain activity during the resting state, for example, classified by increases in alpha and gamma frequency bands together with decreases in slow wave activity[82,241], as well as alterations in functional brain connectivity[112,116,124]. Various experimental paradigms concentrating on evoked brain responses also identified promising features for biomarker development such as the auditory oddball design[240]

(a test where infrequent 'different' sounds are mixed into repeated standard sounds to assess detection of auditory change) or the gap pre-pulse inhibition of the acoustic startle[243–245] (a test where a brief silent gap before a startling noise usually weakens the startle reflex, indicating that the gap was heard). Furthermore, objective measures of the autonomic response might add information to a quantitative biomarker as pupil reactions to sound strongly correlate with the severity of tinnitus[242]. For objective measures of autonomic and brain activity, two key challenges remain. First, although available findings reveal significant group-level differences, sensitivity must be enhanced to enable reliable diagnosis at the individual level. Second, whether these objective markers are truly specific to tinnitus, rather than reflecting features shared with other conditions, is unclear.

Beyond diagnosis and outcome monitoring, biomarkers may also help identify mechanistically distinct tinnitus subtypes and thereby guide treatment selection. In this sense, the most clinically valuable biomarkers may be those that predict prognosis, treatment response or differential benefit from specific interventions.

Genetic diagnosis and gene therapy

Given the large contribution and effect size of rare genetic variation to the development of severe tinnitus[51], genetic screening and diagnosis could be applied in some collectives, such as in workers exposed to occupational noise or in individuals with mild cognitive impairment, to foster interventions that could prevent severe tinnitus. Although human gene therapy is still in its infancy in hearing disorders, the successful RCT in *OTOF* mutation carriers[246,247] paves the way for the development of gene therapy for individuals with hearing loss and tinnitus. Nevertheless, gene therapy for tinnitus remains years away.

Regenerative medicine

Advances in hair cell regeneration and cochlear repair hold potential for addressing the underlying causes of tinnitus. However, the complex cytoarchitecture of the organ of Corti is a considerable challenge[248]. Conversely, several studies have been performed to determine the transcription factors that control transdifferentiation of somatic cells into spiral ganglion neurons[249], including the mechanisms regulating glutamatergic synaptic properties[250]. This treatment approach is still in the exploratory phase.

Neuromodulation

Further development of non-invasive brain stimulation techniques is increasingly seen as a path towards new therapeutic options for tinnitus and related neuropsychiatric disorders[251,252]. While available non-invasive methods such as TMS, TES and bimodal stimulation show modest to moderate effectiveness[253,254], emerging research aims to refine these tools through better target engagement, adaptive dosing and personalized stimulation protocols guided by neuroimaging and electrophysiological biomarkers[255]. Closed-loop TMS (in which stimulation adapts in real time to brain signals) may enhance durability compared to fixed-frequency approaches[256]. Similarly, high-definition TES and state-aware transcranial alternating stimulation are being trialled to increase field precision and oscillatory entrainment, reducing variability linked to skull conduction and individual anatomy[257]. TMS and TES treatments are already in routine use at specialized tinnitus clinics.

At the same time, depth-capable non-invasive modalities, such as transcranial-focused ultrasound stimulation (tFUS) and transcranial pulse stimulation, are attracting attention as they promise DBS-like focality without the risks of electrode implantation[258]. Early-phase trials in depression and pain disorders show that MRI-guided tFUS can modulate deep structures, such as the thalamus and striatum, safely, which mirrors invasive DBS targets already explored in severe tinnitus[258,259]. If effective, these techniques could blur the gap between invasive and non-invasive neuromodulation, offering a middle path with high spatial precision but lower procedural risk.

Invasive techniques such as DBS are also evolving, moving towards adaptive or closed-loop systems that deliver stimulation only when pathological activity is detected[260]. Early findings from movement disorder research indicate that such adaptive DBS reduces side effects and prolongs battery life, and similar strategies could be applied to tinnitus by detecting aberrant thalamocortical rhythms or limbic hyperactivity and intervening only when necessary[260]. Future care models may therefore combine non-invasive priming sessions, such as TES, to increase neural plasticity, with targeted deep stimulation via tFUS or adaptive DBS to retune dysfunctional circuits more efficiently.

These parallel developments suggest that the boundary between invasive and non-invasive neuromodulation is becoming more fluid, with technology moving towards precision, personalization and integration across modalities. DBS, tFUS and transcranial pulse stimulation remain exploratory approaches for tinnitus.

Pharmacological targets

Developing a drug or a combination of drugs for the relief of tinnitus is desperately required. However, despite the large potential market, no pharmacological treatment for tinnitus has yet been approved, and pharma industry research and development remain minimal. The absence of chance discoveries of effective drugs beyond lidocaine may partly explain this stagnation. However, combining empirical strategies with advances in data science, such as big data-driven approaches in medicine, could help uncover promising therapeutic candidates in the future[261].

Digital therapeutics

Mobile applications and virtual reality platforms are increasingly explored as innovative tools for tinnitus management. They provide accessible, scalable and cost-effective treatment options available anytime, anywhere, thereby helping to bridge the treatment–demand gap. A review of tinnitus treatment apps available in the Apple and Google app stores revealed a wide range of categories of digital interventions, including chatbots, online CBT, sound stimulation, stress management, tinnitus masking and guidance for tinnitus self-management, which also includes psychoeducation[262]. Following this review, an additional treatment category was introduced in which patients with somatic tinnitus are guided through specific physical exercises designed to relieve tension in the neck and jaw muscles[263].

Although most of these approaches are implemented on smartphones and available in the app stores, an emerging class of digital therapeutics uses virtual reality headsets. In virtual reality environments, positive experiences, an internal locus of control, and active coping strategies can be trained in an immersive virtual environment. This is achieved, for example, by visualizing a 'tinnitus avatar' that represents the individual's perceived tinnitus and allows interactive engagement with it. Early studies have reported promising outcomes for such virtual reality-based interventions; however, this treatment is still exploratory[264].

Systematic research, particularly RCTs evaluating the clinical efficacy of digital therapeutics for tinnitus, is steadily increasing. Studies

have demonstrated encouraging effect sizes of the following approaches: app-based CBT (Cohen's *d* effect size 1.1)[265], smartphone-based structured counselling (Cohen's *d* effect size 0.8)[266], and physical exercises for somatic tinnitus (Cohen's *d* effect size 1.7)[263]. However, these are pioneering studies in a still-emerging field. Although early versions of digital therapeutics are already available in app stores, the field remains in its infancy and offers substantial scope for improvement through continued research. Their further integration into tinnitus care may also unlock new opportunities for more individualized treatment.

Translational research

Progress towards more personalized and targeted tinnitus care also requires changes in study design. Conventional trials that recruit broad and highly heterogeneous tinnitus populations may underestimate benefits that are confined to specific subgroups. Future studies may therefore benefit from enrichment strategies, biomarker-guided inclusion, adaptive trial designs, platform trials and longitudinal phenotyping. Such approaches will require close collaboration among auditory scientists, neurologists, psychiatrists, psychologists, engineers, data scientists and patients.

Overall, the future of tinnitus research is unlikely to depend on a single breakthrough therapy with a 'one size fits all' solution. Bridging the gap between heterogeneous pathophysiology and clinical practice will be essential for moving the field beyond symptomatic tinnitus management.

Published online: 21 May 2026

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Author contributions

Introduction (S.V., J.A.L.-E. and A.B.E.); Epidemiology (S.V., S.G., W.S. and A.B.E.); Mechanisms/pathophysiology (S.V., D.D.R., B.L., J.A.L.-E., A.B.E. and A.Y.-M.); Diagnosis, screening and prevention (S.V., B.L., T.K., J.A.L.-E., A.B.E. and F.T.H.); Management (S.V., T.K., W.S. and A.B.E.); Quality of life (S.V., B.L., S.G., W.S., A.B.E. and F.T.H.); Outlook (S.V., S.G., T.K., J.A.L.-E., W.S. and A.B.E.); overview of Primer (S.V.).

Competing interests

S.V. declares research support from the European Union, the Rainwater Foundation, Neuromod and Royal National Institute for Deaf People, and Nederlands Fond voor Wetenschappelijk onderzoek. S.V. has carried out paid consultancy for Neuromod and is an executive member of the Tinnitus Research Initiative (NGO, unpaid). D.D.R. declares research support from the Rainwater Foundation and is chairman of the board of directors of TRI. F.T.H. declares research support from the Rainwater Foundation, Department of Defense, USA, and Royal National Institute of Deafness. F.T.H. is a Scientific Advisor for Hyperacusis (NGO, unpaid), Tinnitus Learning and Health Network (NGO, unpaid) and SoQuiet Misophonia Advocacy (NGO, unpaid). B.L. declares research support from the European Union, the Rainwater Foundation, Neuromod and Sonova. B.L. has carried out paid consultancy for Neuromod, Sea Pharma and Sonova, holds shares of the company Sea Pharma, and has served as a scientific Advisor for consumer protection organizations (paid) and as a court-appointed expert (paid). B.L. is also Chair of the Tinnitus Research Initiative (NGO, unpaid), a scientific Advisor for the Royal National Institute of Deafness (NGO, unpaid) and a scientific Advisor for Tinnitus Quest (NGO, unpaid). T.K. received honoraria for consulting and lecturing activities from Sonova and Schwabe Pharma CH, as well as travel and accommodation expenses from Cochlear. His research was funded by the Tinnitus Research Initiative, the Swiss National Science Foundation, the European Union, the Zurich Hearing Foundation, and Cochlear. J.A.L.-E. received funds from the American Tinnitus Association (grant no. 1329287) and the University of Sydney (Meniere Disease Neuroscience Program). W.S. declares research support from the Rainwater Foundation and is an executive member of the Tinnitus Research Initiative (NGO, unpaid). A.Y.-M. serves as the Director of TRI Academy, the dissemination and communication wing of Tinnitus Research Initiative, is a member of the Tinnitus Detect (TIDE) consortium, and the Founder and Community Lead of Tinnitus Éire, an online community in Ireland for people living with tinnitus. A.Y.-M. is also the co-principal investigator for a grant received from the Royal National Institute for Deaf People. A.B.E. is a member of the Tinnitus Research Initiative (NGO, unpaid). S.G. declares no competing interests.

Additional information

Peer review information *Nature Reviews Disease Primers* thanks H. Schulze, Peng-Fei Zhao and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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