Why Is There No Cure for Tinnitus?

By David Stockdale

At the British Tinnitus Association (BTA), our vision is "A world where no one suffers from tinnitus." We believe this is possible now, for many, using the currently available management techniques. However, we also know that these are not adequate solutions for everyone and nothing short of a cure — or cures — will do.

One question I'm always asked, frequently in exasperation, is, "Why is there no cure for tinnitus?" People living with tinnitus can't believe we haven't yet found a universal solution to tinnitus. I'm not sure it reduces their frustration any to hear my answer: "It's complicated, there are a lot of factors." So, along with colleagues, I tried to give a more comprehensive answer in a recent paper.[1]

Tinnitus Services in the United Kingdom

Before I run through the findings of our work, I think it's important to highlight why we wanted to write that paper. The BTA has been working hard to put in place the right tools to empower researchers and clinicians who investigate tinnitus and offer better management, as well as the tools to campaign for more research funding.

We looked at what tinnitus costs the U.K. and how much it costs to offer a tinnitus service through the National Health Service (NHS).[2] This was an important question to ask, and one I understand the ATA is looking to answer for the United States, as well. What we found was heartening yet offered much food for thought.

We discovered that:

- Tinnitus services are cost-effective according to the thresholds set by the NHS.
- An "average" tinnitus patient costs the NHS £717 per year (US$880 million).
- Tinnitus costs the NHS £750 million per year (US$925 million).
- The societal cost of tinnitus to the U.K. is £2.7 billion per year (US$3.3 billion).
- There are 1,050,000 GP (primary care/family doctor) appointments made every year in the U.K. because of tinnitus.

These costs are comparable with those found in other similar studies (see Table 1).

Table 1. Comparison of the Cost per Person With Tinnitus per Annum in Different Countries

	Cost per tinnitus person per annum
Netherlands (Cima et al., 2012)	€1544 (US$1700)
USA (Goldstein et al., 2015)	$660
UK (Stockdale et al., 2017)	£717 (US$927)

So, the good news is that we could show current tinnitus services in the U.K. were effective, although with room for improvement. We believed it was important that we also published our calculations and process of deriving our figures so that others, with new or emerging treatments, could put their costs and outcomes into that model and see how their treatments compared.[3] An understanding of the numbers and financials was an important first step in building the case we wanted to make in the *Why Haven't We Cured Tinnitus?* paper.

"Although this growth in research activity and publication is very impressive, the volume of published papers on tinnitus lags behind that on other conditions, such as depression, anxiety, and deafness."

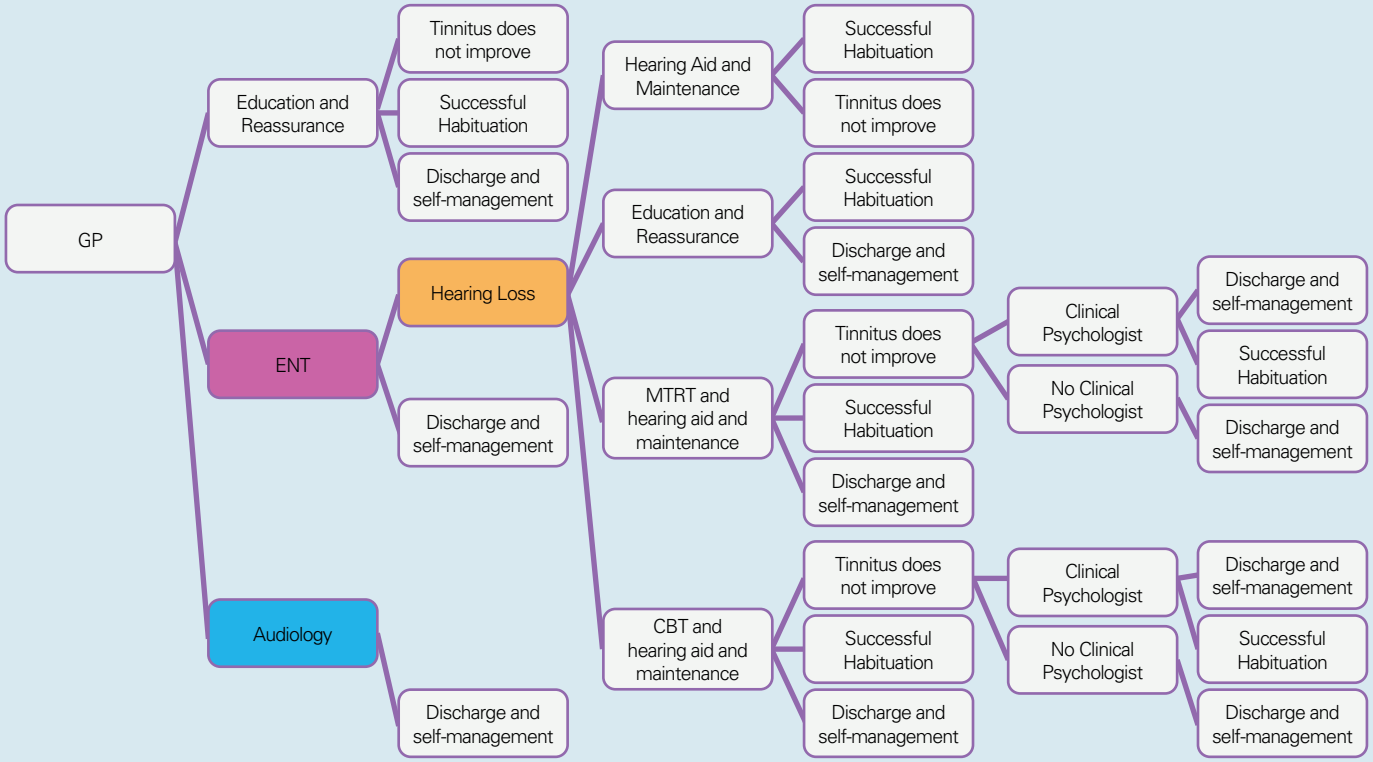
We found a myriad of pathways and routes patients might take to the tinnitus clinic. We wrote the costs paper on the basis of our experts' opinions of which services were typically provided for tinnitus patients. Figure 1 shows half of the pathways we found and maps possible patient journeys for those with tinnitus associated with hearing loss. Where the expert panel didn't know or couldn't agree on a particular point, we surveyed BTA members to find the answer. We have since published these results as a paper, too.[4] This research uncovered some troubling findings:

- Patients experienced "revolving door" healthcare — two in five patients discharged by ENT or audiology found themselves back at their family doctor (GP) asking for help.
- One in five patients said their GP took no action when they visited with tinnitus for the first time.
- More than two-thirds of patients were discharged at ENT, meaning they had had two diagnostic appointments for their tinnitus (GP and ENT), but no support with managing tinnitus (which would usually be provided by audiology services in the NHS system).
- A range of interventions were offered, with no clear rationale why some were prioritized over others.
- When patients were asked who they found helpful or unhelpful on their tinnitus journey, audiologists and hearing therapists were found to be the most helpful, and GPs were the most likely to be found unhelpful.

Both papers reached the conclusion that the U.K. has a health system that delivers tinnitus management cost-effectively — but it could be better. What we really need are more effective treatments and a better understanding of which types of treatment are best for different groups of patients.

What do people consider an effective treatment? Researchers Fatima Husain and Philip Gander found patients and audiologists have different aims for tinnitus treatment. Patients want a reduction of tinnitus loudness (63%) or elimination of the tinnitus (57%), whereas audiologists

Figure 1. NHS patient pathways for tinnitus associated with hearing loss.



Source: McFerran, D., Hoare, D. J., Carr, S., Ray, J., & Stockdale, D. (2018). Tinnitus services in the United Kingdom: A survey of patient experiences. *BMC Health Services Research, 18,* 110. doi:10.1186/s12913-018-2914-3

saw treatment success as decreased awareness (77%) and stress/anxiety relief (63%).[5] These results may help explain why people with tinnitus think current treatments are unsatisfactory and why prospective treatments should be designed to meet patient expectations.

The final piece of this background story happened in March 2018, when the U.K. charity Action on Hearing Loss (AoHL) organized an excellent meeting titled "Translational Hearing Research Summit: Biological and Pharmacological Approaches."[6] Here, for the first time, negative results of recent pharmaceutical trials in tinnitus were presented. This might sound disappointing, but these findings were put forward alongside suggestions of why these trials had failed and what needed to change for future drug-based research to have an increased chance of success.

So, Just Why Haven't We Cured Tinnitus?

Having given you the context in which the BTA is working, why did we decide to write a paper about what we *haven't* done? I, alongside colleagues, felt it was important to raise awareness of the issues, and we looked to work across the tinnitus community to give a holistic view of progress to date and — more importantly — how to move forward. The paper's authors represent charities — the patient voice — clinicians, academia, and industry. What follows is only a summary of key themes. If you'd like more detail, the full paper can be accessed at https://www.frontiersin.org/articles/10.3389/fnins.2019.00802/full

Would Patients Want a Drug?

It is clear people with tinnitus would like a drug. Fifty-two percent of tinnitus patients said they would try a drug for tinnitus if it reduced tinnitus loudness by half; 62 percent, if it eliminated their tinnitus.[7] However, currently no drug is approved for the treatment of tinnitus by the FDA or EMA (European Medicines Agency).[8] We need more rigorous research to fully understand a patient's motivation to take a drug for tinnitus and what would be acceptable — a topic I'm hoping the BTA will be able to work on in the near future.

We know the potential market size for a drug for tinnitus is huge. A study published 15 years ago estimated that a tinnitus drug would have an estimated value of US$689 million in its first year.[9] This is likely now to be an underestimate, not only because of inflation but also because of an aging population in the Western world that is leading to a growing tinnitus population. The BTA estimates there will be 14 percent more adults living with tinnitus in the UK over the next decade.[10] There's a market and a willingness of patients to take a drug — so why hasn't it happened?

How Much Is Spent on Tinnitus Research?

Analysis of spending on tinnitus, both in terms of amount spent and volume of projects approved, shows that it pales in comparison to spending on other conditions. Research from 2012 shows that funding by the major statutory healthcare funders in the United States and Europe is much lower than the funding of comparable conditions.[11] (See Table 2.)

Table 2. Tinnitus Research Funding: Average Annual Funding by Major Funding Organizations in 2009–2011

	Diabetes	Hearing	Tinnitus
USA (NIH)	$913m	$214m	$5m
EU (FP7)	€60m (US$66m)	€3.3m (US$3.6m)	€0m

Note: US figures $ millions; EU figures € millions. FP7, 7th Framework Programme for Research and Technological Development; NIH, National Institutes of Health.

Source: C. R. Cederroth, B. Canlon, & B. Langguth. Hearing loss and tinnitus – are funders and industry listening? *Nature Biotechnology.* doi:10.1038/nbt.2736

The volume of papers published on the PubMed database with *tinnitus* in the title, abstract, or as a major topic has increased several hundred-fold since the formation of the BTA in 1979. (See Figure 2.) This reflects the growing interest in tinnitus as a research topic and the progress that is being made in the field.

Although this growth in research activity and publication is very impressive, the volume of published papers on tinnitus lags behind that on other conditions, such as depression, anxiety, and deafness. (See Figure 3.)

The reason for this lack of activity is unclear, and we tried not to speculate on it in the paper.

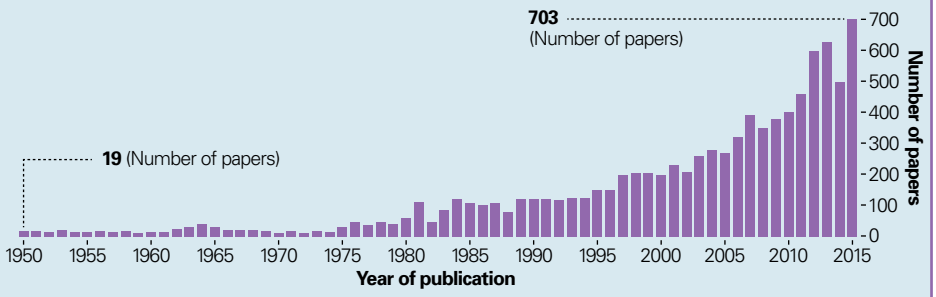
However, we did reference the need for tinnitus research to be undertaken across disciplines, and currently two European Union (EU)-funded projects are looking to address this, each with 15 PhD students working in a cross-disciplinary way on a range of questions to progress our knowledge and understanding of tinnitus.[12,13] This is an important first step, but more cross-disciplinary work and closer working relationships with academic institutions, industry, and patient bodies are needed to truly drive forward research.

Is *Tinnitus* Too Much of a Catch-All Term?

It appears that subtyping tinnitus — finding and defining the different types of tinnitus — will be essential to progressing research. Tinnitus is often seen as too varied to result in reliable, repeatable outcomes, especially when looking at drug trials. Many recent tinnitus drug trials have performed well in preclinical trials (the stage before studies in humans), yet have failed in later stages. Conversely, it may be that we already have highly effective strategies to manage or treat certain types of tinnitus, but these effects are hidden if the treatments are delivered to people with different types of tinnitus. If we can understand how to categorize these different types, we may be able to identify the most effective solution for each one.

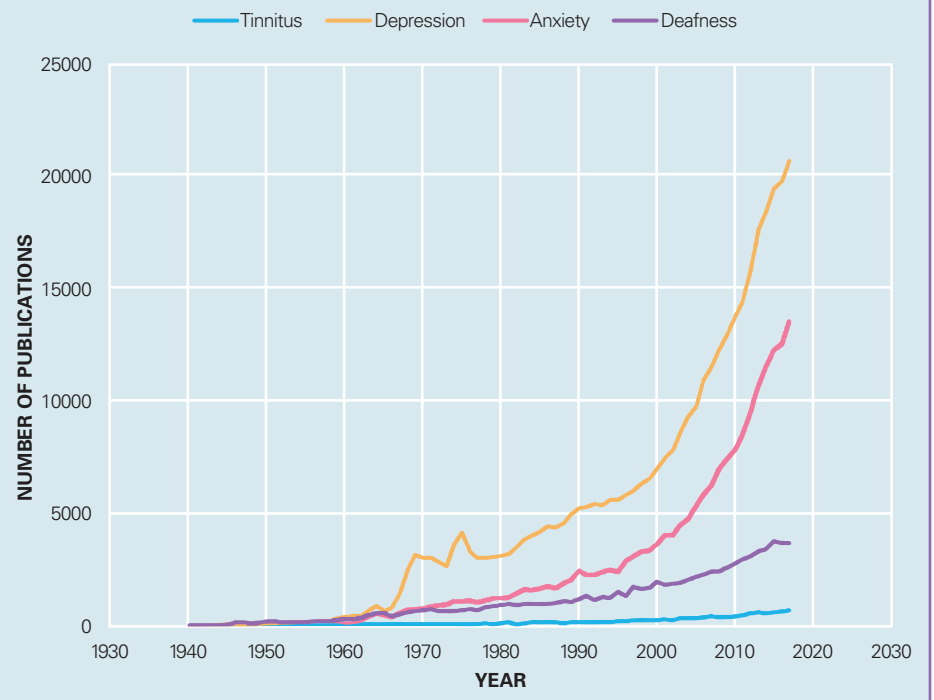
Subtyping tinnitus is a priority many sources have identified, and doing so will then enable research to progress at pace. However, if subtyping is not possible, or if research is to happen before subtypes have been established, then allowing for the different types of tinnitus in people taking part in research trials will be necessary. This presents its own challenges — the need for internationally standardized, large, well-designed randomized controlled trials for tinnitus has already been recognized.[14] Work is ongoing on developing a standardized set of outcome measures, and much work is being done on identifying tinnitus subtypes. It may also be possible

Figure 2. Number of articles published on PubMed with tinnitus in the title, abstract, or as a major topic per year.



Source: D. M. Baguley & N. Wray (Eds.). (2016). Introduction. *British Tinnitus Annual Tinnitus Research Review 2016*. Sheffield, England: British Tinnitus Association.

Figure 3. Publications listed on the U.S. National Library of Medicine PubMed database for the conditions tinnitus, deafness, anxiety, and depression in the period from 1940 to 2017.



Source: D. M. McFerran, D. Stockdale, R. Holme, C. H. Large, & D. M. Baguley. (2019) Why is there no cure for tinnitus? *Frontiers in Neuroscience*. Advance online publication. https://doi.org/10.3389/fnins.2019.00802

to revisit past trial data and analyze by subtype once subtypes have been identified for a quicker solution to identifying the most effective treatment by subtype.

We Need Better Ways to Measure Tinnitus

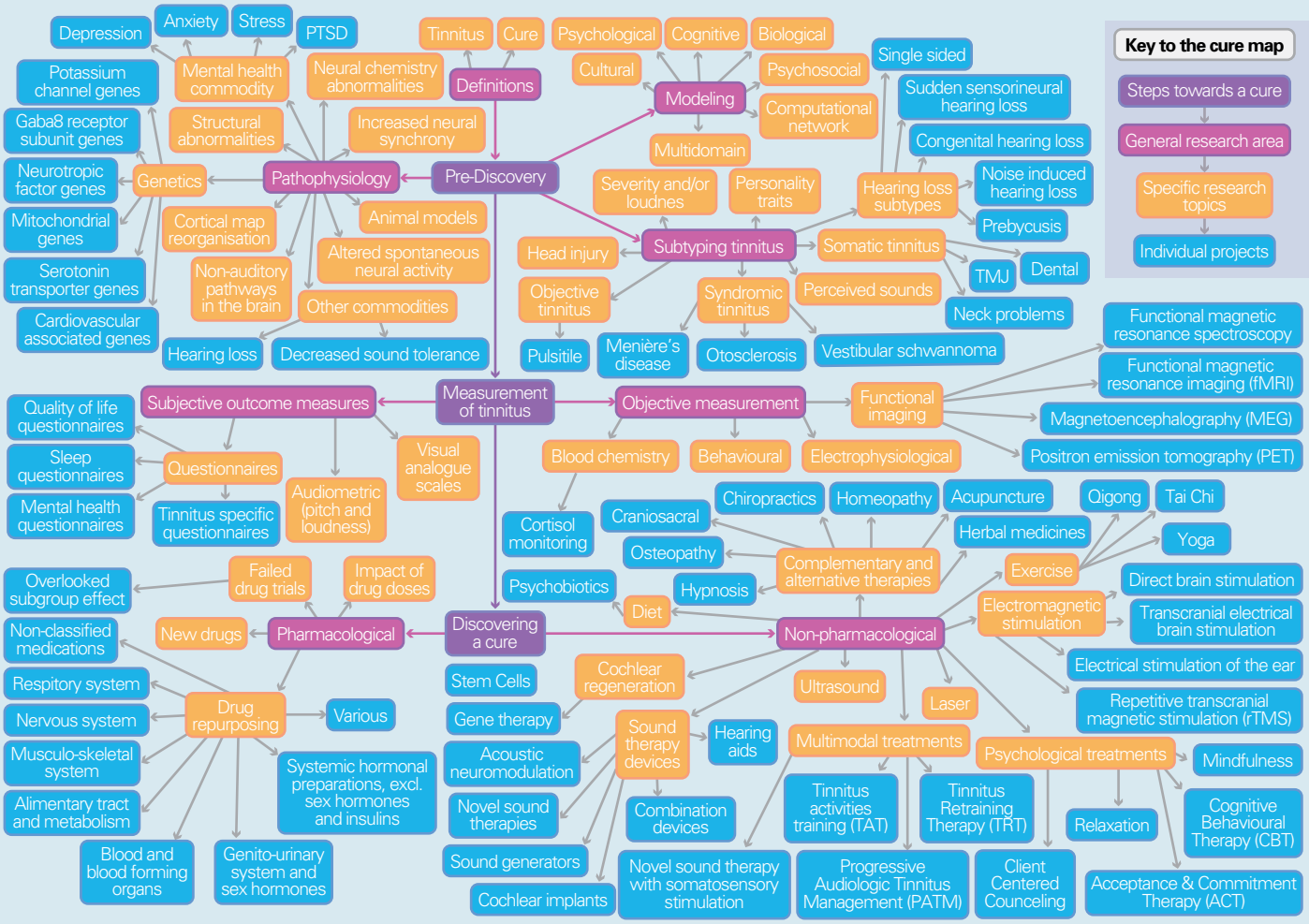
If you have consulted a medical professional for your tinnitus, they will have taken a history of your condition and probably asked you to complete a questionnaire about your tinnitus.

In completing that questionnaire, you thought about your tinnitus and the impact it is having on your life. At that time, a lot of other factors influenced how you answered the questions, from your life experiences to how frustrated you felt finding a parking spot before your appointment. To put it crassly, how you scored your tinnitus might differ very much from how the next person scores theirs, yet the sound or volume at which you hear the tinnitus or the distress you feel about it may be the same.

What is needed to really move forward is a way to objectively measure tinnitus, for example, in a similar way to how blood sugar levels are measured — there's an absolute figure, not one based on how you are feeling at the moment.

Research has probed how to do this, and so far, an objective measure has not been found, but it is an area we think the research community

Figure 4. The British Tinnitus Association *Tinnitus Cure Map*. V10, June 2019. A representation of tinnitus research areas.



Source: D. M. McFerran, D. Stockdale, R. Holme, C. H. Large, & D. M. Baguley. (2019) Why is there no cure for tinnitus? *Frontiers in Neuroscience*. Advance online publication. https://doi.org/10.3389/fnins.2019.00802

should be prioritizing. A promising early study, funded by the BTA, has already been published.[15]

The Tinnitus Cure Map

For the past two years, the BTA has been working on how to represent all of the challenges above. We've been trying to summarize the current state of tinnitus research, show where our knowledge gaps are, and pinpoint where we feel confident that we have sufficient insight. We have plotted these areas on a diagram we call the *Tinnitus Cure Map*. (See Figure 4.)

If you look carefully at the map, you will see that much of what has been discussed falls within the first two steps toward a cure, in the prediscovery and measurement of tinnitus phases.

Although we have published the *Tinnitus Cure Map* in the format you see here, we hope to raise the funds and publish it as an interactive online map in the next year or so. We will then expand it and increase the number of levels. The online version will link to the latest and best available research in each area, and we will be able to assess where we need more research and where a question has been answered. This map will be easily viewed so everyone can see how the drive toward a cure progresses.

So, What Next?

We concluded in our paper:

> Whilst an encouraging upturn in tinnitus research being performed is evident, it is also apparent that a step change will be needed to deliver progress towards truly effective treatments.[1]

"[The BTA and ATA] will continue to campaign for increased funding for tinnitus research and engage with the research community to encourage and support research that helps achieve 'a world where no one suffers from tinnitus.'"

The BTA is now looking to play its part in how to make this progress. We are seeking to do this in the following ways.

Funding Research

Much like the ATA, the BTA funds research into tinnitus, and our next funding rounds will focus on the recommendations from our paper and how we can progress these. Our current research priorities for funding are as follows:

- Identification of tinnitus biomarker(s) — finding a naturally occurring molecule, gene, or characteristic that indicates the occurrence of tinnitus
- Development of reliable objective measure(s) of tinnitus — moving away from questionnaires toward unbiased benchmarks
- A better understanding of animal models of tinnitus and their relevance to human tinnitus research
- Recognition that every individual's tinnitus is unique and being mindful of this when undertaking research
- Identification of subtypes of tinnitus[16]

Working in Partnership

We are working in partnership with academia and industry to push forward research in the areas we think will make a difference to our understanding of tinnitus. We hope to be able to say more about these soon; please keep an eye on our website for announcements.

Of course, we are working closely with our friends at the ATA! Torryn, the CEO of the ATA, and I continually collaborate to see how we can better support researchers to access funding and deliver high-quality, game-changing research. In that spirit, the ATA and BTA will be working in partnership to put on a networking event as part of the Association for Research in Otolaryngology's Annual Mid-Winter Meeting to encourage the cross-disciplinary research that is needed to really spur us forward.

There Is Hope!

The BTA and ATA are always campaigning for better and enhanced provision of services we know can help now and to make sure these are more widely available than is currently the case. We will continue to campaign for increased funding for tinnitus research and engage with the research community to encourage and support research that helps achieve "a world where no one suffers from tinnitus."

A compassionate and motivated research and clinical community out there is progressing our knowledge and building on this daily, seeking to offer the best management and support that are available now, while focusing on providing better treatments tomorrow. There are many challenges to overcome, but we are determined to succeed and we are getting closer to answering some of the outstanding questions.

The tinnitus research community is continually growing, improving, and refining how it works. The pharmaceutical industry is aware of the opportunities that exist and is keeping an active watch on developments in tinnitus research, hoping for those optimal conditions that will allow investment in tinnitus research to flourish.

In the meantime, proven treatments are available that can lessen the impact of tinnitus. Though we all hope for a cure, it is important to engage with the evidence-based management techniques that an experienced and compassionate audiologist and/or mental health provider can help you with, and to live well with tinnitus in the here and now.

David Stockdale is the chief executive of the British Tinnitus Association (BTA). His background is working in senior management positions in charities. He started on that path while completing his bachelor's degree in business studies at Sheffield Hallam University. His first role was working in youth consultation and advocating for better provision of services for children and young people. He joined the BTA in February 2010 and has sought to work alongside the global tinnitus community since then to promote better management of tinnitus, to enhance peer-to-peer support, to improve professional training, and, of course, to further research into tinnitus. He is most proud of increasing the number of tinnitus support groups in the U.K. from 34 when he started to 105 today. Having grown the team at the BTA, his focus is now on progressing research and looking at how the BTA responds to many of the points made in this paper.

1 McFerran, D. M., Stockdale, D., Holme, R., Large, C. H., & Baguley, D.M. (2019). Why is there no cure for tinnitus? *Frontiers in Neuroscience*. Advance online publication. https://doi.org/10.3389/fnins.2019.00802

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3 Supplemental material can be accessed here: https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-017-2527-2

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