2021 Podcast Series

Podcast 4. Kevin Munro. "The curious incidents of the pandemic in our lifetime: COVID-19 and the auditory system".

This text is an edited transcript of a recorded podcast.

Hello and welcome once again to a ManCAD / British Academy of Audiology podcast. You might well know that ManCAD stands for Manchester Centre for Audiology and Deafness and that we are located at the University of Manchester in the UK.

I am Gabrielle (Gaby) Saunders. I'm a Senior Research Fellow at ManCAD and I moderate these podcasts.

We always try to address the topics pertinent to the practice of audiology but also want to make sure that they are relevant to audiologists, researchers and anyone interested in hearing and hearing loss.

We will record a new podcast each month each one will be about 20-30 minutes long and we will post the audio recording along with a transcript on our University of Manchester webpages.

You can find information on the ManCAD website.
http://research.bmh.manchester.ac.uk/ManCAD/Podcast/

Today Kevin Munro is going to be discussing "The curious incidents of the pandemic in our lifetime: COVID-19 and the auditory system".

You might have heard it's a topic that's been getting quite a lot of publicity recently so we're taking this opportunity to spend some time clarifying what the research data indicate. Kevin has a multitude of roles and titles, including Ewing Professor of Audiology, Director of the Manchester Centre for Audiology and Deafness, Deputy Director of the NIHR Manchester Biomedical Research Centre and Theme Lead for Hearing Health. Kevin, do you want to add something about your research interest?

Kevin: Thanks for the invite. I guess my research covers a continuum from trying to prevent hearing loss. Looking at assessment and diagnostic procedures, through to interventions and outcome. A lot of my work previously has been focused on kids and I also do some adult work. I suppose you could describe it as being translational and applied research. By way of example, one of the biggest studies we're doing right now is called FAMOUS, funded by the Health Technology Assessment Programme. That's looking at interventions to increase the uptake and the use of hearing aids in adults.

Gaby: Thank you. Alright so now let's get on to the business of today. That is discussing what the data show about COVID-19 and the audio vestibular system.

We're going to talk about the findings of a systematic review that Ibrahim Almufarrij and Kevin conducted and that they've recently published.

Before we talk about the results. Tell me what was your motivation for carrying out the review?

Kevin: Well I guess just over a year ago when the pandemic started, I didn't know very much about corona viruses at all. I didn't realise even then that they account for about 20% of the common colds that we that we get over winter, but I'm certainly aware that some viruses can cause hearing loss.

Actually over the last year, a good review that I've referred to frequently by Brandon Cohen that was published in Trends in Hearing about five years ago, gives a good overview of the different viruses and what part of the ear have been damaged.

We also know that about 10 or 20 per 100,000 adults each year report a sudden hearing loss, usually single sided and in some of them it is explained by a virus. So we're certainly aware that viruses can damage the ear.

I started to receive inquiries from the public saying that they thought their ear had been damaged and they had COVID. That made me sit up and take notice. At the same time a number of professionals, I can think for example of a GP that contacted me to say that he thought he was seeing more patients complaining of hearing loss and tinnitus . It was that combination that made me think we should sit up and take notice and do something about it so that was the motivation for this work.

Gaby: I know that what you did was a systematic review. Could you just tell us what a systematic review is and particularly how it differs from a standard literature review?

Kevin: So a literature review is where you search and evaluate studies on a particular topic. A systematic review is a particular process, it's almost like a recipe that you follow and it's formulaic.

It guides you how to do a review starting with how to really clearly identify the research question you want to answer by reviewing studies that are published in the literature. How to assess the quality of the individual articles, how to assess the quality of the overall evidence and because it's somewhat formulaic and you're following pretty much a recipe I suppose it means it should be reproducible if other people go off and try to do the same thing. So it's trying to minimize the risk of bias and often these systematic reviews have what's called a meta-analysis. If there's numerical data there, there's a way of pulling the numbers that come from a whole collection of studies to give you the best estimate and that's one thing that we have included to get the best estimate of audio vestibular symptoms.

It's an approach that is used by Cochrane; Cochrane library uses systematic reviews. NICE use this approach when evaluating the evidence. Just a great skill to have. Great I would think for hearing health professionals to have as well. It's a bit like riding a bike, once you understand how to use the recipe, you can then apply it to different research questions. Not only is a good skill to have, they are very valuable when you can give a good summary of the literature that is unbiased and it doesn't take a lot of resources. I've often said to people who want to get involved in research. Just collaborate with someone who's already done systematic reviews. They have the skills to enable them to guide you through. It's a good way to move forward so I don't know what you think and you've done systematic reviews?

Gaby: I have not.

Kevin: But you think that's a good idea and a useful skill for hearing professional staff.

Gaby: I do and I think it's a really good way of getting a rigorous evaluation of what's out there. What did the review show?

Kevin: Well we've actually conducted two reviews. Let me just mention in passing, we did our first review last April or May time so very early on in the pandemic. At that time, we identified about seven articles. Not great quality, but we were still somewhat amazed to find that they were already talking about potential hearing problems, tinnitus and balance problems. At the end of last year in November / December time. I should just mention Ibrahim again to make sure he gets credit. He did a lot of the donkey work for this. We did a new systematic review. We identified 56 articles that were looking at a link between COVID-19, or the virus that causes COVID-19 and problems with the audio vestibular system. About half of these studies were individual case reports, the other half were observational studies or cross section of the population who have COVID. In a nutshell. The best estimate from all of these studies. Was that 7% of people with COVID were reporting hearing loss. Double that were reporting tinnitus and again about 7% reporting vertigo. So that was our best estimate based on what other people have already published.

Gaby: There some indication that there's some association there. Were there any factors that seem specifically to be associated with the balance problems and by that I mean is it with anything to do with people's age or severity of COVID or I don't know presence of other medical conditions.

Kevin: We're looking specifically at that, I guess in a word, no.

Interestingly last night, I was listening to a free online seminar from the Royal Society about long-COVID. These people who are, weeks or months after having the acute episode were still

experiencing fatigue or shortness of breath. One of the conclusions from last night was that actually there doesn't seem to be a pattern.

Sometimes its people who weren't especially ill that were managed at home, and sometimes people who would appear to be asymptomatic then reported problems further down the road and not tested positive for COVID. So it didn't seem to be related to age. It didn't seem to be related to the severity of the symptoms. I think I would say the same when we look at all these studies, there's nothing in particular that jumps out, except people with comorbidities which is kind of well-known with COVID people with other health problems are more likely. That's about the only thing that that I would say stands out just know.

Gaby: And was there any particular comorbid condition or just generally being less healthy.

Kevin: One of the limitations actually of the articles is sometimes they don't specify what the comorbidities are they just list them and say, you know, X percent had one comorbidity or two or three; diabetes cropped up quite a lot but I can't be absolutely sure because it wasn't always explicit.

Gaby: Presumably there must be something ultimately we just haven't measured it or noted it.

Kevin: One would think so, yes.

Gaby: One advantage of a systematic review you mentioned before is that you rate the quality of the studies in your review. So what can you tell us about this as regards the review that you did? What are some of the limitations of the current studies how, what was the quality like and can we be confident in the overall findings?

Kevin: So let me just make this clear when we're doing systematic review we're looking, we're trying to address a very specific question so we're looking at the quality of the evidence to answer a question.

It could be, there's a study where we say you know the quality to answer our question isn't great. It doesn't mean it's reflecting badly on the study because maybe their aim was slightly different from our one. There's certainly an improvement in quality between the studies we identified last April / May time and what we identified this time. I would say it moved up from being poor quality where we couldn't have an awful lot of confidence in the findings to moderate level.

The limitations would be; there is often limitations in the design or the methodology of the studies so for example, most studies use self-report. So there could be pros and cons to that. It could be that there is bias because of difficulty with recall. It could be that the person asking the questions has a vested interest in knowing about, for example, hearing problems. We have to be careful how we interpret that. Not many of the studies have a control group. If I can give you an example let's say 5% of people say, I have now got tinnitus or my tinnitus is worse since having COVID-19. Without a control group you don't know what that may be in the general population. So we've all been through a pandemic and we've all had some mental emotional stress and anxiety, particularly in the early days when we didn't know what was going to happen so without a control group for all you know, maybe 5% of the general population who never tested positive for COVID might be reporting these symptoms.

There are a lot of case studies so single cases, and they tend to be adults with a sudden sensory neural hearing loss. I mentioned earlier each year we expect to see about 10 to 20 adults per 100,000 that report a sudden hearing loss. So the question is, is it just a coincidence? Are the numbers really going to be higher than they were in previous years, or is it just a reflection that, because so many people happened to have COVID-19, it just so happened they had it at the time?

There are some studies that I would say have been relatively poorly executed so they might have had a control study but it wasn't well matched. I'll just give you a hypothetical example, might be a study where the people with COVID were aged 50, and compared to people without COVID that were age 20 and got perfect hearing thresholds. There's that sort of issue.

Also the general reporting, something that's not always clear are these symptoms that just occurred transiently or are they persisting. Did they occur during the acute phase or that they come at a later date?

And there are some studies that we've included, and we mentioned a word of caution in the article that we're just not 100% sure that they're measuring a change in hearing or tinnitus. It's just possible they're simply asking people if they've got hearing loss or tinnitus. We've tried to be very careful about that. For all of these reasons we just have to tread fairly cautiously.

Our review, the first one, was a meta-analysis, was a first stab at estimating these numbers. I guess it's likely to be refined over time, as you know just the nature of science. The last thing I can say on this is there are weight confidence intervals around our estimate. So for hearing loss we have 7%, but the 95% confidence interval. So the range where we say the true value is between these values, went from something like 2% up to 15% so you know it wouldn't surprise me if the actual number moves around a bit, it's somewhere inside quite a wide range really.

Gaby: It sounds like this is part of the problem with sort of doing research during the pandemic that you know one cannot do a fully controlled study and that really one needs to do this sort of step back and plan it and run the study. As I understand it, there is such a study planned at Manchester.

Kevin: We're just embarking on one and you're absolutely right. It's a study where we will be comparing individuals who had COVID. Actually individuals with quite severe symptoms, people who were originally hospitalized with people who were hospitalized but didn't have COVID. So we're trying to match them as closely as possible because just being very elderly and in hospital, can lead to all sorts of health problems that may or may not be related to the fact that you were admitted because you had SARS COVID 2 that resulted in COVID-19 so we're going to do a careful comparison between these two groups.

Gaby: So, if there is indeed a link between COVID and hearing loss. There must be some mechanism. Have people postulated what those mechanisms are yet and how the virus might affect the auditory system.

Kevin: It's not clear and I can give you some examples but the denominator when people have COVID-19 is that the virus enters the cells via a receptor called an Ace2 receptor.

We've come to learn over time that the virus can affect many parts of the body because this receptor, this kind of door into the cell that the virus creeps in and then starts reproducing, is present throughout the body. It's not at all clear to me that we have many of these Ace2 receptors in the inner ear.

I actually contacted people who are better informed about this me so. One of them was Professor Jonathan Gill, he's a Director at the Ear Institute. We had a discussion by email. There is a relative paucity of evidence that we have these receptors in the inner ear, we might have and if we do that could explain why the virus might directly damage the ear. It may be indirect damage because what we hear a lot about inflammation in the immune system. We're all getting to know / understand the immune system more and we hear about this cytokine storm where the body has this very strong stress response. We know that can damage the body and potentially could damage the ear. We've also been hearing a lot about the effect it has on the vascular system, making blood more viscous, more thrombosis, more clots and we have some narrow blood vessels capillaries in the inner ear.

Some people have been in hospital and in intensive care and as I said earlier, there's lots of things that can happen to you when you're seriously ill and unwell, including medications that potentially could be auto toxic.

Also, at least in the UK, we have not been familiar with wearing face masks up until this last year. I think sometimes just with wearing facemasks interferes with people's ability to communicate and I do wonder if there are some people who have a hearing loss that they didn't recognize until people were wearing a facemask and they realize that they're having these problems.

I also mentioned earlier about the sort of stress and anxiety and lack of sleep we are going through. This vicious spiral that I think Ross Coles was one of the original people that I used to hear talking about this link with tinnitus, constant stress and anxiety and not sleeping because I don't know about you. Actually you're maybe not old enough to have had the vaccine yet but I know when I got mine I kind of came out with a spring in my step so you know even subconsciously it clearly was weighing on me a bit that there was this virus going around so you know there's a whole range of things and we really need to be able to untangle them and find out what are the ones that are responsible for people reporting hearing loss, tinnitus and vertigo.

Gaby: You've referred a lot to people being seriously ill and in hospital. For those people who either have had asymptomatic COVID or COVID that didn't end up in hospital and you've talked about this risk of 7%. Is this something we should be worried about?

Kevin: The number probably includes as many people who had what I guess we would call mild COVID that weren't in the hospital, so it doesn't seem to just be the people who were severely affected and in hospital.

So I guess I wouldn't use the word worried. But I do think there's a need to be concerned and for us to take it seriously. Because, you know, we've already said, we know that somebody viruses can cause hearing loss for some people. We know that SARS COVID 2 that causes COVID-19 can affect a wide range of organs and systems in the body. We know that there's an issue, we published our most recent systematic review a couple of weeks ago and we've had about 150 people contact us.

Not all of them but the majority thinking the symptoms that are associated with COVID, we've got these numbers from our systematic review and we certainly know the impact of hearing loss can have on people's lives right and their ability to communicate with ease and how it can affect the quality of life so it. Let me turn it around, I think it would be wrong not to take it seriously, given all that background right.

I think we should take it seriously while we wait for better quality evidence to come along. It feels like I've used this analogy before, we're just in the foothills of this expedition and we've got a lot more adventuring to do yet but I do think we should be taking it seriously. What do you think looking at it more from the outside?

Gaby: I think it's something we need to look into. Seriously from the perspective of researchers working on it trying to understand it and the medical profession. We don't know if these effects, these auditory system effects are transient.

Kevin: I certainly know that at least for some people, it is transient. We can't say for all. I'm kind of intrigued by these adults who have this sudden onset sensorineural hearing loss. Was that going to happen anyway? I mean the ones that are reported, there is a close association that they felt unwell and they had COVID and they woke up the next day for example and had lost the hearing in one ear.

It's called Occam's razor isn't it, the most simple explanation is the most obvious one, that if they had a virus and were unwell and lost their hearing they probably are related but we cannot say for sure and we won't be able to say for sure until we look at the numbers and see on a time series analysis. Has it increased during the pandemic?

You would expect if it is because of the virus there should be a significant increase. If you look at the number of people in the world that have had the virus so time will tell. But there are people who have a sudden loss of hearing in one ear and that should always be considered a medical emergency because the treatment is steroids to reduce swelling and inflammation and if it's to have any chance of working at all and have a good outcome you need to start that treatment as soon as possible so you shouldn't delay if there's a sudden loss of hearing and unexpected loss of hearing in one ear.

Gaby: I'm just thinking about this risk in terms of the public perception of the topic. As I said earlier, we know that there's been a lot of press coverage about it. Do you think the press are generally sending the right message out to readers?

Kevin: I would be interested in your view on this but I'll tell you my thoughts first of all.

I personally have found it a little bit overwhelming that there has been so much interest, it seems like we've just touched the right nerve at the right time, because there's been over, it increases all the time, right but last time I looked was over 350 news stories. So that was in newspapers online. Live interviews I've done on radio and on TV. I'm always slightly anxious because you don't want to scare monger or be provoked into saying something totally outrageous or misleading, or stupid. On the other hand, if you're so guarded you come across as rather boring and don't have anything interesting to say.

I do think we have an important role in dissemination and I would like to think that we as researchers have pretty much got the balance right. When I look at the press coverage, I think mostly they've got it right but of course the press are trying to sell papers and trying to put a particular spin on it. It hasn't been as bad, I think it was last year, there was an article in a newspaper about the work we were doing in Manchester and the headline was Professor on verge of curing deafness.

That really frightened me and I was a bit embarrassed thinking are people really think I'm going around saying that. I've not seen that this time around. On average I think that probably got the balance right but it's quite difficult when you're sort of closely associated with something. What do you think?

Gaby: To be honest, I have not been reading all of the different things so I think my opinion is that it's really important the press come to credible scientists for input on whatever it is, because as you say, the information needs to get disseminated and it needs to be disseminated in a balanced way and so going to researchers is hopefully the way to do that.

The next part of this, audiologists. What is the need for audiologists to manage the situation? Is there something that they should do if a patient reports hearing loss following COVID. Is there anything we can do if it's not sudden hearing loss?

Are we at the point where asking about COVID needs to become a routine history taking question for audiologists?

Kevin: That's interesting, isn't it, I suppose the take home message would be we're in the foothills we've still got a lot to learn but we should take this seriously because of the potential impact that it can have on individuals and services need to know. Are there likely to be a big increase in the number of referrals coming through.

I would imagine that many audiologists right now, will be asking about COVID-19 or I suspect that new patients will be telling them I have had this change and it happened when I had COVID-19 so I think that information is likely to be made available.

If it isn't, I think it is something I would be asking about. And I think we need to be clear, did the person test positive for COVID on their PCR test, or do they just have a suspicion that it's related to COVID so I think it does make sense. That's how we spot trends right, talking to people who might have the symptoms and before we do fancy studies, we're looking for trends. So, I think I would be asking about it, noting it trying to be clear that the person definitely had COVID and when did the symptoms occur? Was it while they had the acute phase or was it sometime afterwards? Ultimately final thing is, if there are these people with sudden hearing loss, you know they shouldn't be hanging around they should be encouraged them to seek medical help as quickly as they can.

Gaby: Is there anything else is not being that situation but presumably tinnitus is tinnitus and you would use the same intervention, mild hearing loss is mild hearing loss, regardless of its etiology.

Kevin: Exactly, we just manage the symptoms appropriately as we do right now.

Gaby: Do you have any other final comments or things that you want to say about this very important topic.

Kevin: Not really. I mean I'm looking forward to seeing how things develop over time. It's always tricky when you're at the very beginning of something and there are not many studies, sometimes the results conflict and you know we always find over time when the dust settles the weight of evidence

will point us in one direction or the other, so I would think the more people who are investigating this and conducting good quality studies with carefully matched controls, the sooner we will get to the bottom of this. The better the service that we can provide to patients so we would know what sort of assessment procedures we should be carrying out, what part of the ear may be damaged, how severe it may be and how should that be managed.

Gaby: Thank you. Well that was very insightful, very interesting to hear. Hopefully everybody listening will have learned something about systematic reviews in general, which I think is really important.

So thank you, Kevin for sharing your time and thoughts with us.

To the listeners, there'll be a transcript of this, and will include the reference that Kevin mentioned, and also a reference to the systematic review.

If the audience have any follow up questions, feedback or share ideas for future topics please contact me.

You can send me an email. Gabrielle.Saunders@manchester.ac.uk

I hope you enjoyed this discussion and are going to come back to the next podcast. Until then farewell and stay well.

References:

Almufarrij, I., K. Uus, and K. J. Munro. 2020. “Does Coronavirus Affect the Audio-Vestibular System? A Rapid Systematic Review.” International Journal of Audiology 59 (7): 487–491. doi:10.1080/14992027.2020.1776406

Almufarrij, I., K. J. Munro. 2021. "One year on: an updated systematic review of SARS-CoV-2, COVID-19 and audio-vestibular symptoms." International Journal of Audiology Mar 22:1-11. doi: 10.1080/14992027.2021.1896793. Epub ahead of print. PMID: 33750252.

Cohen, B. E., A. Durstenfeld, and P. C. Roehm. 2014. “Viral Causes of Hearing Loss: A Review for Hearing Health Professionals.” Trends Hear 18: 2331216514541361. doi:10.1177/2331216514541361.

Young, Y. H. 2020. “Contemporary Review of the Causes and Differential Diagnosis of Sudden Sensorineural Hearing Loss.” International Journal of Audiology 59 (4): 243–253. doi:10.1080/14992027.2019.1689432.