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Hearing Loss, Social Engagement and Mental Health in Older Adults: Evidence from Population-Based Studies

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- [Christy] It's my pleasure to welcome back Dr. Jennifer Deal. She'll be resenting today, "Hearing loss, social engagement, and mental health in our older adults: evidence from population-based study." If you'd like to learn more about Dr. Deal, you can read her bio on the course registration page. And at this time, I'll hand the mic over to you.

- Thank you so much, Christy. It really is a pleasure to be here. Thank you very much for having me back. So these are my disclosures and the content disclosures. I'll just note that part of the content today includes discussing topics that includes social isolation, loneliness, depression, and anxiety. The goal is to evaluate the current public health literature that looks at the relationship between hearing loss and social engagement and with mental health outcomes in older adults. We have three learning objectives. So first, we'll start by summarizing and interpreting that evidence, and then we wanna think about some potential explanations to help with the inference from all of those studies. And then finally, we'll talk about some key questions that we still don't know the answer to that pertain to this topic.

So I wanna start our, you know, really we have two of our learning objectives really center around understanding the literature that's out there, at least from the public health literature, the population-based studies. And so I wanna start by giving just a little bit of a framework for us to do that, to think about the evaluation. And then I'd like to get into the content, which is the association between hearing loss and social connection and the association between hearing loss and mood disorders, focusing primarily on depression. And then a couple thoughts for us to think about as we wrap up and hopefully to have some discussion about. So just starting with that interpretation and evaluation. The goal of this section, as I said, you know, our goal is really to think about evaluating population health studies.

So I just wanna start by introducing some key methods considerations that's gonna provide a framework for us to do that successfully. So when I talk about public health studies or population health studies, really, I'm talking about those that have been designed from an epidemiologic perspective because epidemiology really is the science of public health. Certainly we partner very closely with biostatistics, but we really are focused on the design and the interpretation of those population studies. Epidemiology is defined as the study of how disease and other health states are distributed in populations and what factors influence or determine that distribution. And what's really important about epidemiology is that it is a population science. So we look at averages, comparing a group who's exposed, so for example, with hearing loss to a group who's not exposed, so for example, older adults with normal hearing.

And when we make those comparisons, we can actually start to see some really interesting patterns. And those are patterns we can't always detect at the individual level. So for example, I have no idea what my cause of death will be. Certainly, I will die at some point, but I don't know when, and I don't know what that cause will be. But if we look at mortality at the population level, we are really good at discerning those different causes of death and predicting those causes of death, as well. So what we can't predict at an individual level, sometimes when we look at the population, that gives us a lot of insight. So that really is the whole idea behind epidemiologic studies.

Let's look at the population, see the population averages, and that can help give us some ideas about potential causes of disease. So when we think about the types of epidemiologic studies that exist, there really are two broad types. The first is our experimental design, and this is a randomized trial. And then we also have observational study designs. So when we think about an experimental study, this is where there is a treatment and some sort of comparison, some sort of control group. It can be a placebo, it could also be standard of care. But each participant is randomly assigned to get either that treatment or that control. And the random assignment is

very important because what that means is it doesn't have to do with any of the characteristics of that individual.

So it doesn't matter the age or the sex or the race ethnicity of that individual. It's a random chance, whether they go to the treatment or the control group. And that's important because sometimes those factors are associated with the outcome. So for example, if we had a comparison group of individuals who all had a very good diet, no one smoked, they followed a healthy exercise regimen, and we compared them to a group of individuals that didn't have quite so healthy habits, then it's hard for us to know, right? Is it those factors in the treatment group, like the healthy exercise, like the good diet? Are those the factors that are making us see an association between the treatment and the outcome?

Or is it actually the treatment? And so we wanna try to break that link between the treatment assignment and any of the other factors in the individual person. And so what that means is that our treatment group and our control group, on average, will be balanced with respect to those factors. And by balanced, I mean it'll be a similar proportion in each group. And that's really powerful because if that's done well, and it's a well conducted study, then if we see a difference between the treatment and control, we can actually ascribe that difference to the treatment itself, not to any of those other factors. And so that's really why our randomized trial is our experimental design.

It's kind of the gold standard study design in epidemiology for determining if we can prevent an outcome by having a certain intervention. But we also have a number of observational designs. And unlike the the randomized study, here, we're just observing individuals. So we're not assigning any treatment, there's no randomization. We're just recruiting participants, measuring some exposure, some outcomes, following them over time to see what happens as they age. So observational study designs, there's many different types, but some examples you may read in the literature include cohort,

case-control, and cross-sectional. So we can't determine cause from observational studies, and that's because every observational study has bias. And we'll talk a little bit more about that in the coming slides.

So for that reason, when we're interpreting the evidence today as it relates to hearing loss and social connection and mood disorders, we're really gonna focus on randomized controlled studies. And that's gonna give us our inference in terms of the impact of hearing loss treatment to either improve social engagement, improve connection, social connection, or to decrease depressive symptoms. But we can't randomize people to have hearing loss or not, right? Obviously, that's very unethical. So if we're interested in comparing individuals who have hearing loss to individuals who don't, we need an observational study design. And so our focus for thinking about those different associations will all be based on those observational designs. But that really means when we interpret them, we have to think carefully about potential sources of bias and how they might be influencing those associations that we see.

So it's true that bias exists in every observational study. It doesn't matter if it's a cross-sectional study. It doesn't matter if it's a prospective cohort design. No matter what the study design is, if it's observational, there's bias there. And bias can really come in at any point of the study. So it can come in at the design, when we collect the data, when we analyze the data or write the paper and try to publish the data. So bias really comes in at all those different steps. So if we do see an association between an exposure and an outcome, so for example, between hearing loss and social connection, we really need to consider all those possible reasons why we might be seeing that association.

And that includes bias. So if we see an association, hearing losses associated with social connection in our study, what are some possible reasons why that might be? Why might we see that association? And so there's three kind of big groups of things

to consider. The first is chance. The second is bias, and there's different types of bias. We'll talk about selection, information bias, and confounding. And then finally, there's a cause. So it could be that actually the exposure causes the outcome. If we see the result due to bias, or if we see the result due to chance, that's means the exposure is not a cause of the outcome. But if it is a cause, then what that means is if we intervene on that exposure, we can actually prevent the outcome from occurring down the line.

So we have to first think, you know, how likely is our our finding due to chance? Or how likely that we have this finding, just because there's some bias that we didn't account for? And if we feel pretty confident that it's not chance and that we've kind of addressed all the sources of bias that we need to, then we can start to say, "Well, maybe it's chance." We can't determine that from an observational study. We need a trial for that. But at least we can say that we don't think the association is solely due to chance or solely due to bias. Okay, so a little bit more on chance. If any of one has taken a epidemiology course or a population-based health course or a biostatistics course, you may have talked about sampling variability.

And this is exactly what I'm talking about with chance. So when we conduct a study, obviously we cannot study everyone. We have to, because we have a limited budget, a limited time, there are only so many people who are interested in participating, we have to sample people into our studies. And in that sample, they may have different population characteristics than the larger true population that we sampled from. And so what that means is, in our study, we might find an association, but maybe actually there isn't one in the true population, or maybe we don't find an association, and there actually is one. So just based on sampling, associations in our study may differ from the true association.

And that's why repeating the same study, same research question, but in different populations at different times, that's very, very important. We call that replication. And

so replication is really key when we're thinking about interpreting observational designs. If we see a study with an association, but every other study that's looked at that failed to find an association, right, it's probably more likely that that first study was just chance. It was just based on the sampling, right? It's not the true relationship in the broader population. So truthfully, you know, whenever we submit our papers, we're always supposed to say what's novel and what's important and what this study adds. But the truth is, from my perspective, for the reasons that we just talked about, novelty is really overrated.

And replication is not just good, it's great. And so because of that, when we focus on the literature today, thinking about the associations between hearing loss and our outcomes of interest, we're really gonna focus on designs that go to the literature more broadly and conduct a systematic review so there's detailed methods so that the review would be reproducible, it looks across a variety of populations, across a variety of different settings, and then tries to synthesize that information into what it seems like most of the studies are suggesting. So our focus today is really gonna be on that type of review, a systematic review, and if there's enough, if there's not too many differences in terms of the methods that were used for the individual studies in that review, sometimes the results are combined into one overall effect estimate.

And that type of study is called a meta-analysis. So those are the the types of studies that we'll be focusing on. And the reason we're focusing on that, again, is just to try to make sure that we're not highlighting a study finding that maybe is just due to chance, it's not consistent with what the other literature has found. In terms of bias, so I'm gonna start with selection bias. And that really is beyond the scope of this presentation. Selection bias is fascinating, and it can cause huge error in our study and in the effect estimate that we generate. And so if you have questions, I'm very happy to talk about it. But what I do wanna focus a little bit on is not selection bias, which is a

systematic error in our study findings, based on the way that we select people to participate in our study.

But as we said already, we have to select people to even have the study to start. And sometimes that selection, not all of that is due to bias. And there are some issues related to selection that I think are worth considering today. So for example, where are you finding your participants? You may be recruiting them from a clinic, so perhaps an audiology clinic where you conduct your work and see patients. Or it could be a random sample of the population at large. So a random sample of the United States, for example. I think what's important to keep in mind is that clinic samples, although it is often convenient for us to use them because we're interacting with them already and can be very beneficial to understand what patients who are coming to the clinic, what are their needs, what are associations in that population, what's different about people who are there is that they have self-selected to be there.

And we know that not everyone with hearing loss chooses to seek hearing care. So a reminder, then, that clinic samples include patients who self-select to seek and participate in healthcare. And those patients may be very different from people who choose not to engage in hearing healthcare. And so when we find results in a clinic study, that's fantastic, but we may not be able to apply those more broadly, or the term that we use is generalized. Those findings may not apply to the general population. So just something important to keep in mind. And that's why, today, we're really focusing on the evidence from the population-based public health literature, not so much on patients who recruited into clinical studies.

Okay, so that was selection. Another type of bias is called information bias. And this really just means that we are measuring something with error, and it's a systematic error in the way that we're measuring. So imagine if we have a blood pressure cuff, if that isn't calibrated correctly or an audiometer isn't calibrated correctly, we may be

mis-measuring. So that's a good example. And it can occur in the exposure, the outcome, or any other factors in the study. And so it really is important, when we're looking at these observational data, to make sure we're using a validated instrument to measure those factors in our study. And we're gonna talk about some validated measures and instruments for thinking about social connection, as well as for depression.

But I also wanna think a little bit about it in terms of hearing. So certainly, there are lots of different facets to hearing. There are many ways we could measure hearing. The two that are most common in the population-based literature are audiometry, so we are objectively measuring the function of the cochlea, or we can ask participants. And this, of course, is much faster, and so many more studies have self-report, compared to audiometry. But what's important to realize is that they actually really do measure different things. And we know that not everyone with hearing loss, especially older adults, recognizes that they have a hearing loss. In fact, the older you are, the less likely you are to report your hearing in a way that matches audiometry.

You're more likely to say, "I don't have any hearing loss," or, "I have just a little," when maybe you have more. And then there are some other studies that are quite interesting that suggest that if you have higher levels of education, then you may actually over-report your hearing loss, compared to the way it would be measured on audiometry. And so really self-report is about the way a person perceives their hearing and then that has to be within their own social context. So if they're out and about, if they're in an office or a noisy environment, they may perceive hearing loss if they're having trouble understanding speech for example. But the same person, the same value that we would get measuring their threshold using audiometry, if they're in a quiet setting, they may not notice as much, right?

So what's key is that audiometry and self-report really do measure different things. Both are really important, but a lot of times, we use self-report to try to approximate the audiometric values 'cause we don't have those there. And I think we can get ourselves into a little bit of trouble when we do that without thinking carefully about it. And so let me show you an example. This is data that came from a nationally representative survey. It was cross-sectional, so everything was measured at the same point in time. It's conducted in the United States. It's called the National Health and Examination survey, pooled a couple of different waves of data. On the same individuals, they had their hearing measured using audiometry, and then they also had self-report of hearing loss.

And it was, how would you rate your hearing? And it's a Likert scale, so they could say, you know, that deaf is on one side of the scale, and then it's, you know, I don't have any trouble, would be on the other side. So no trouble, little trouble, a lot of trouble, those types of questions. And so those are all measured in the same exact individuals. And then there were a number of different outcomes that were measured, as well. Some of those were measured more objectively. So something like measuring physical activity using an accelerometer. So think about your Fitbit, counting your steps, something like that, right? So that's an objective measurement. We're not asking the participant to report.

And then the number of hospitalizations that they've experienced in the past year. That's also something that we can count. But then there are some subjective measures too. And these are where we're just asking participants, "So how much physical activity are you participating in?" for example. What about disability? So do you have any difficulty climbing up 10 stairs, for example? Or do you have any concerns about your memory or any issues with confusion? So that's another example of you're asking someone how they feel about their health. And in the middle there we can see that we have the audiometric results. So these are associations. They're odds ratios, so

estimated risk looking at one point in time. We're comparing, in the first column, mild hearing loss to normal hearing.

In the second column, we're comparing moderate or greater hearing loss to normal hearing. Here, this was a four frequency pure tone average from, you know, 0.5 up to four kilohertz. And what you can see that the odds ratios themselves aren't as important as the shade because the shade of the box tells you whether the association was statistically significant, in which we would say, "Yes, we found an association between audiometric hearing loss and with whatever outcome is of interest." So for example, if we were to interpret that moderate or greater hearing loss under audiometry for accelerometry, that number, that odds ratio is 1.9. That means that individuals, on average, who had moderate or greater hearing loss, compared to individuals with normal hearing, on average, had 1.9 times the odds of lower physical, or lower physical activity as measured by accelerometry.

So we see associations there, and I'll point out that when we measure hearing objectively using audiometry and when we have our objective outcomes, you can see we see associations, but we don't see those same associations. They're not statistically significant when we use self-report. But if we move down to where we have our subjective outcomes, so physical activity, disability, and memory and confusion concerns, you can see that there are a lot more shaded boxes under the self-report. And there's a phenomenon, and we actually have a specific name for this. So just summarizing overall, when we measure an outcome objectively, we tend to see associations with the audiometry.

But when we measure something, an outcome by self-report, we saw stronger associations when we measured hearing by self-report, compared to by audiometry. And this bias has a special name, and the name for it is called same-source bias. And what this means essentially is if we're measuring hearing by self-report, and we're also

measuring an outcome by self-report, we may see a correlation, but that correlation is because it's coming from the same person, the same person is measuring those. They're reporting their hearing. They're also reporting the outcomes. I think an easier way to think about this is that the level of one measure could actually influence how someone reports the other. So for example, imagine someone who has clinical depression, they perhaps might be more likely to say they have hearing loss, maybe even if they don't, or we would not be able to detect that using audiometry, right?

So that's called a bias, same-source bias. It's not a true cause there. And although self-reported measures, I think, are very important, it is important for us to realize that this can happen. If we measure two things by asking people about both the exposure and the outcome, sometimes we'll just see a correlation because the same person is reporting. And then, so that's information bias. Our third and final source of bias is confounding. And this is something where we have a third factor. It's associated with our exposure, it causes our outcome, and it's not caused by the exposure. So it's not what we say on the causal pathway from the exposure to the outcome. And so what that means is the arrow is going from the confounder to the exposure.

So let's give a real example of this. I do a lot of work in hearing and cognition. So if hearing loss is my exposure, cognitive function or dementia is the outcome, I wanna make sure, in all of my studies, I'm trying to account for vascular disease. Because we do know that things like hypertension, things like obesity, things like smoking, all of those are associated with hearing loss. There are also causes of dementia. And so we need to make sure that we're accounting for that. Otherwise, we're mixing the effect between hearing and these different factors, like smoking, for example. And we don't know what's the effect that's due to hearing and what's the effect on cognition that's due to smoking.

And so we do have to think carefully about how we account for confounders in our analysis. And there's different ways we can do that in the methods, also in the analysis. So we can restrict. So for example, if we're worried about smoking being an important confounder, we can only conduct a study in non-smokers, for example. Or we could stratify. We could do separate estimates in people who smoke versus people who do not. Another thing we can do that you'll often see, sometimes in retrospective cohort studies, using claims data primarily, or in case control studies, is we can match. So we can try to make sure our cases and controls, for example, are matched on important confounding factors like age.

And then finally the most common way is to adjust in our regression analyses. And so that's why we so commonly include that whole list of additional variables in our models. So to kind of summarize this section, our focus today, we wanna try to really maximize what we're able to gain from the literature. And so we wanna look at population samples here. You know, clinic samples, of course, very important. But our focus today is on population samples. We're gonna focus on studies that measure hearing using audiometry instead of self-report. Because when we're talking about something like loneliness, we do worry about that same-source bias. We wanna try to focus on studies that are using validated instruments to measure our social connection outcomes, so it's not just a random question.

It's a instrument that was really designed to get at whatever construct we wanna be measuring. And we're gonna also look at studies that adjust for possible confounders. So these are the factors, these are the criteria by which we'll be evaluating the studies today. Okay, so just putting it all together, summarizing, we're gonna gonna review studies that have the strongest possible level of inference for us. So we'll use an observational design if we're looking at associations. But if we're trying to look at treatment effects, specifically hearing aids, we wanna look at randomized trials. We're gonna look at studies that are population-based and that address those important

sources of bias we discussed. Okay, so with that, let's move on to the more exciting part of the talk where we actually talk about some of this research and what we know about the association between hearing loss and social connection.

And so I wanna start just by defining social connection, and what I mean, and it's an umbrella term, it encompasses the different conceptual and measurement approaches that are represented in the literature. And there are multiple components, structural, functional, and quality. And so this is a figure that's looking at the framework, so these three components of social connection. Starting with the structural components, what that means is the existence of and the interconnections among different social relationships and roles. And when we think about ways we might measure the structural aspects of social connection, those questions may have to do with living alone. Sometimes we will see things related to marital status because that goes so tightly in terms of whether you're living alone or with someone else.

When we think also about a structural component, social isolation is one of the biggest, most important, most commonly studied structural component of social connection. And so the definition, social isolation, it is the objective lack or limited social contact with others. It's marked by few social network ties, infrequent social contact, or potentially living alone. In terms of some of the functional aspects for social connection, that just means the functions that are provided by or perceived to be available because of those social relationships that exist under the structural component. So for example, questions relating to receiving support or feeling as if you have someone from which you can receive support, that's a functional aspect of connection. Loneliness is another really important functional aspect of social connection.

And so loneliness is different than social isolation. It is the perception of social isolation or the subjective feeling of being lonely. It's marked by a discrepancy between the

person's actual social connections and their needed or wanted social connections. So just to drive that point home a little bit, when we compare isolation versus loneliness, social isolation is the number, it's the quality of social connections. So for example, there's a commonly used scale in the epidemiologic literature that's called the Lubben Social Network Scale. And a question on this scale says, considering the people to whom you are related by birth, marriage, adoption, et cetera, how many relatives do you feel close to such that you could call on them for help?

And then the answer options are none, one, two, three or four, five through eight, or nine or more. So here we're talking about an objective measure of the number of individuals that people feel they can connect with, excuse me. Our second, you know, measure that I wanna make sure we talk about is loneliness contrasted to social isolation. And again, loneliness is the perceived lack of social connection. So it's not about the number of individuals you have in your network, it's how you feel about the quality of those people. And certainly these are related measures, but they're very distinct. So you can imagine someone may have lots of people they can turn to, but if they don't feel like the quality is very high of those relationships, they may still feel lonely.

And also someone may feel not lonely at all, but have very few actual number of social connections. So related but distinct important concepts. Just as an example for loneliness, the way that we normally measure this, there is a scale called the UCLA Loneliness Scale. And one of the questions on that is, how often did you feel left out, or how often did you feel completely alone? And then the answer choices might be often, sometimes, rarely, or never feel this way. So you can see it really is measuring something different than social isolation. Okay, and then finally, when we think about the last aspect of social connection, it's quality, and these are positive and negative aspects of social relationships.

So marital quality, relationship strain, social inclusion or exclusion. We're really gonna focus on the structural and functional components in the review today. And there really are many different ways that we can measure social connection. You'll see a lot of these in the literature. This is a, I think, a lovely figure that has structure in the top row, function in the bottom row. And then kind of starting from left, moving to the right, it's the degree of subjectivity that we're asking from the respondents. So starting with involvement, just how many people are there versus a perceived availability, perceived adequacy, and then related feelings. I have three here highlighted in blue. We just talked about the Lubben Social Network Scale as an example of how we measure social network.

The UCLA Loneliness Scale is another common one, as well as another loneliness scale too, the 11-item loneliness scale. So these are ones that will kind of resurface later in our discussion today. But you can see there are a lot of really validated measures for social connection, and that was one of our criteria. So we're in luck there. When we think about social isolation, it really is a large problem. So this is data that was taken from the National Health and Aging Trends study. It's a nationally represented survey. Individuals were recruited. They were followed over time. There are home visits to try to maximize participation. And importantly, they really try to over sample the oldest old, so individuals who are 85 and 90 and up, to try to make sure that they're represented in the study.

Here we have, on the y-axis, the proportion of the individuals who reported either feeling socially isolated, and that's the black circles, and then those kind of pink or mauve squares. That represents individuals who have social integration as measured by the scale that was used. And so here, you can see, overall, it was one in four US adults who are age 65 and older. The proportion of individuals, you know, it's kind of an inverse association. So actually, social isolation decreased over time and with age. But you can see that, most of the time, social isolation, once we're past 80, 85 and into

90s, even though the overall prevalence is declining from earlier age groups, more older adults are socially isolated, comparatively.

So this is something that predominantly impacts older individuals. And overall, the estimate, again, is one in four US adults have experienced social isolation, and that equates to about 7.7 million individuals. And then here's also nationally representative data. It's from a different study, the National Social Life Health and Aging Project. This is a study of community-residing adults. They were born between 1920 and 1947. This is based on that UCLA Loneliness Scale. And you can see the prevalence or the proportion is, again, on the y-axis. The first bar is for overall. And so overall in this population, it's around 30% of individuals reported being lonely, roughly one in three US adults. When we break it down by sex, we can see more women report being lonely.

And by age group, it's actually, again, the younger ages more likely to report being lonely. But even then, you can see the prevalence in older adults is still very high, right around 30. So social isolation and loneliness impact a lot of individuals, especially as we age. So as we age, that's a risk factor for isolation and loneliness. And so it impacts a lot of people. But these, you know, social connection measures are also really strongly associated with a lot of adverse outcomes. And there is a very robust literature showing that isolation and loneliness are associated with mortality. And so here is age and sex-specific mortality rates from all causes. This is from a study called the Social Network Index, the Human Population Laboratory Study from Alameda County.

This took place, so the data here is from 1965 to 1974. So really a seminal paper, but there have been many, many studies that have repeated this finding since. We have the percentage who die on the y-axis. And then we have age groups, starting with 30 to 49 on the left, 50 to 59-year old is in the middle, and 60 to 69-years old is on the right. And then the first three sets of age groups are for men. And the second three sets of

age groups are for women. The color coding goes that green is the most social connections and that yellow or gold is the least number of social connections. And so we can see some really striking patterns that hold across both sexes.

So for men, we can see that as the men in the study age, a much higher proportion of individuals with, you know, in terms of the percentage that are are dying. But we can see consistently across those different age groups that the mortality rate is much higher in the people who have the least number of social connections. And that's the same for women. So overall, a higher mortality in men than in women, but we see the same pattern, whereas the number of deaths increases with age, and the number of deaths in each each category is always most strong or largest in the group that had least number of social connections. So this is a systematic review on meta-analysis, so where they looked across a broad number of studies.

They identified 148 studies that have enrolled people, followed them over time, for a mean of 7 1/2 years, over 300,000 participants. And they did find then there was a 50% increased survival if you had stronger social connections, compared to weaker social connections. So that association first reported in the Alameda study we just reviewed, clearly there are a lot of studies that have shown this association since then. Same is true for loneliness. So another systematic review in meta-analysis. This included 35 studies, but the mean follow-up was much longer. It was 13 years. Still a lot of participants over 77,000 participants. And overall, it was estimated that loneliness was associated with a 22% increased risk of all-cause mortality, so both social isolation and loneliness associated with mortality.

And it's not all-cause mortality, specifically, they've looked, and cardiovascular mortality is elevated, as well. And so this is a lovely quote by James House saying, "Social relationships, or the relative lack thereof, constitute a major risk factor for health, rivaling the effect of well-established risk factors such as cigarette smoking,

blood pressure, blood lipids, obesity, and physical activity." And we know when COVID hit and everyone needed to go into lockdown, social isolation and loneliness got a lot of press. It was very important. It was something that was real for all of us. But even before then, there were schools of public health, from data like this, talking about how loneliness was the next epidemic that we really should be thinking about addressing in public health.

So the downstream adverse effects of being lonely, of having few social connections is really well documented and well known in the public health literature. I'll just point out another outcome that social isolation is really important for, and that's dementia. So the Lancet Commission on Dementia Prevention Intervention and Care first published a report in 2017. They then updated that report in 2020, and they looked at all the different modifiable risk factors for dementia. And they found, overall, that social isolation accounted for about 2% of dementia cases worldwide, so an important risk factor and something that we can intervene on, something we can do something about. I'll just point out on this slide, too, that, of course, hearing loss is there as a risk factor for dementia as well.

An estimated eight to 9% of dementia cases associated with hearing loss. Okay, when we think about why social isolation and why loneliness might be associated with these outcomes like mortality, like cardiovascular disease, like dementia, well, we do know it's associated with mood disorders or depression. And so that relates to, you know, another part of our talk today. But there's actual some biological pathways, and they have to do with the stress response and inflammatory response. So a number of studies in animal models showing increased microglial activity. We see up regulations of the genes that control inflammation and the pro-inflammatory genes. And then we also see, there's a little bit more mixed results here, but we do also see increased levels of circulating cytokines.

So increased inflammation that we can measure in blood plasma in human studies. And so it's thought to be through these kind of biological pathways that isolation and loneliness might cause dementia, or cause mortality. As I mentioned, so loneliness has kind of been on the radar for a while. In 2020, the National Academies of Sciences, Engineering, and Medicine, or NASEM, released a consensus report. This report was chaired by Dr. Dan Blazer, who's a professor emeritus of psychiatry, who's at Duke. And they called this report "Social Isolation And Loneliness In Older Adults." And it really was motivated by knowing that loneliness was important for help, but thinking that it was really unappreciated as something that we should be tackling as public health officials.

And so they created this guiding framework thinking about different levels of intervention that could range from intervening at the individual level, the community level, or the societal level. Social isolation and loneliness certainly are distinct, but they are related. And then social support can help modify that as well, right? And then they also said, but there's also some important things. So we have health impacts. The mediator might be something like increased inflammation that then might cause something like cardiovascular disease that then could lead to mortality down the line. Importantly, they highlighted that there are several known risk factors for poor social connection. And when we look at those risk factors, they include chronic disease, disability, frailty, depression, cognitive impairment, disruptive life events, social factors, like transportation or housing, and, of course, sensory functions.

So hearing is known to be associated with loneliness and isolation in many studies. So it's kind of accepted as an important risk factor. And that's because hearing loss has the potential to impact communication and interpersonal relationships. And there have been some nice qualitative work that's been done, and here's an example of one study. The study title was "The worst my hearing got, the less sociable I got." This was from a UK clinic. They had seven hearing healthcare professionals that were interviewed and

six adults with hearing loss. And I'm highlighting some of the common themes that really had to do with the interview with the adults with hearing loss themselves. So in terms of the experience of social connection and hearing loss, you know, that one key point was that hearing loss can lead people to become disconnected and withdraw from social events.

It can also affect social roles and identity, and it can impede either forming new relationships or maintaining current relationships. There's complexity to the hearing loss experience. So also when we think about isolation, right? It can be difficult to know the exact cause. Hearing may be a part of that, people said, but it doesn't always have to be and that there's a lot of factors that might be contributing. And then there are important downstream effects. So hearing loss and social isolation can impair other aspects of wellbeing including mental health, like depression. And there was also a key point related to the stigma for both hearing loss and isolation from those adults. So individuals, when you interview them, recognize an association.

There have also been a number of quantitative studies. There really is an, excuse me, there really is an extensive literature, a lot of studies that have looked at this. A very important kind of seminal study led by Meg Wallhagen, again, took place in the Alameda County study. It had 356 participants. They were age 65 to 95, the majority female, 59%. Meg found that hearing loss was associated with an 80% increased odds of feeling lonely. So this was a really important study perspective, followed participants for over six years. Hearing loss here was self-reported, and then the number who reported hearing loss was 17%. So we can see that's a little bit less than we know we would get if we measured their hearing using audiometry.

So then when we move to thinking about reviewing the current state of evidence, there are a couple of nice systematic reviews and meta-analyses that have been done in this space. I'm highlighting one here that was called, "Hearing Loss, Loneliness, and Social

Isolation: A Systematic review." This was led by Dr. Aishwarya Shukla in conjunction with Dr. Nick Reed. They identified 14 population studies, but only three of those used audiometry. So let's take a look at each of those. The first study recruited 80 male veterans from a Veteran's Affairs Medical Center. They did not control for confounding variables, and then isolation was correlated with hearing measures, but, again, no control for those confounding variables. The second study used that nationally representative data from the National Health and Aging Nutrition Examination survey, or NHANES.

It is a population study. They used different waves because hearing was measured in different ages at the different waves of the study. They did adjust for a number of demographic and clinical covariates, so they checked that box. And overall, they found each 25 decibel increase in hearing loss was associated with a twofold increased odds of social isolation here. Interestingly, they found it for only one age group. It wasn't across the board, and it was only for younger individuals. And they only found the association in women, not in men. So a little bit of confusing findings, I think, but interesting. And then the last study with audiometry used the exact same data, the exact same waves. Again, they adjusted for demographic and clinical covariates.

Here, again, they found an association with hearing loss, again in the younger age group but not in the older age group. So I'll just point out that even though study two and study three are separate papers, they actually used the same data, and they find the same answer, which is encouraging. But it really, I think there's only two studies that have really looked at this from the population perspective, excuse me. When we think about hearing loss treatment, so there have been two pilot studies that have been conducted, randomized studies. One is the Aging and Cognitive Health Evaluation in Elders study, and the other one is called Walk, Talk and Listen. In the ACHIEVE study, we had a small number of participants, 40.

They were all age 70 to 84. They all had untreated mild to moderate hearing loss. We had our hearing intervention, which included aids, as well as some hearing rehabilitation. And we compared that to a health education intervention control. And individuals were stratified one-to-one, so roughly 20 into the group that got the hearing intervention and roughly 20 into the group that got the health education control. And we followed them over time for six months. The goal of a pilot study is not to actually look at outcomes, but to instead think about feasibility. But we did take a peak, and interestingly we found association. So individuals who were randomized to the hearing intervention, the diversity of their social network increased over the six months.

And for the health education control, the diversity of their social network decreased. So it went in exactly the direction we would expect, and that was a statistically significant difference. So even though we weren't powered to see a change there in diversity, we did see. So here's the data just showing that we saw a difference in social network diversity for people randomized to the hearing intervention. For Walk, Talk and Listen, it was a 10-week single-masked randomized study. 58 adults self-reported hearing loss. They had a group exercise intervention with health education. They compared that to group exercise only. They were really interested in loneliness and combining both hearing intervention, as well as exercise. And here they used validated measures for loneliness.

And actually, they found no differences in social support. And that loneliness improved more in the control group than it did in the experimental group. So that was an a null finding there, no associations. But again, it was a small number of individuals, not powered to detect difference, but it really is one of the few examples we have of randomized studies in this area. So to kind of summarize, isolation and loneliness, very common between 1/4 and 1/3 of older adults. Associated with a lot of adverse outcomes, so it's important for us to try to intervene on. There's a large evidence base

for hearing loss as a risk factor, and it really is just accepted. You'll see people say that all the time.

But in truth, the study quality varies quite a lot, and there are very few studies that kind of met our criteria for evaluation. And then at the population level, and I'll just highlight that there, so not in clinic samples, but at the population level, the impact of treatment is unknown. In the last couple minutes, I'd like to just highlight hearing loss and mood disorders. The most common one, an important one is depression. This is using the Diagnostic and Statistical Manual of Mental Disorders. It's five or more symptoms during a two-week period. And the symptoms include depressed mood, diminished interest or pleasure in activities, weight loss or weight gain, slowing down a thought, reduction in physical movement, fatigue, feelings of worthlessness, diminished ability to think or concentrate, and suicidal ideation.

In older adults, actually, instead of having mood changes with depression, a lot of times, it's those physical changes that people experience more often. So you know, some examples, anecdotally, even talk about feeling like you're walking through water. It was so difficult for this patient to be able to move. Late-life depression, the prevalence is very high, so 10% of older adults, and it's even higher among individuals with hearing loss, nearly twice as high. When we think about hearing loss might cause depression, there was a lovely review that was conducted by Brett Rutherford, talking first about changes that happen in the ear and in the brain as we age. Those might then lead to some neural mediators, including, you know, compensatory recruitment of outside networks outside the primary auditory cortex area to kind of support trying to interpret that degraded auditory signal that's coming in.

Because of that lack of input, a lot of times, then we see atrophy in those areas where we're going to be processing those auditory signals. And then there's also, when we think about the connection between the ear and the brain, there is a direct connection

between the amygdala. It's part of the limbic system. It helps connect sensory information, including curing to the emotional response. And so you can get dysfunction in that connection when you don't have the auditory input and the auditory signals coming in. And what that means is that can lead to cognitive decline in particular executive function. It might also lead to kind of dysfunction in emotion regulation because of that connection to the amygdala, leading in altered emotion reactivity.

So a really lovely review thinking about some of the biological reasons why we might see a link between hearing loss and depression. In terms of the epidemiologic evidence, so a systematic review and meta-analysis included 35 studies, nearly 150,000 participants, they did find, just looking at studies that looked over time, so they measured hearing, followed people over time to see who developed depression, there was a 39% increased odds in those 11 studies. But of those studies, most were self-report. Only one used audiometry. It was a really well conducted study, I think. So 1,611 adults, roughly the same percentage men and women from the Australian Longitudinal Study of Aging. They were seen at up to five visits over 16 years. There was good adjustment for covariates and potential confounders.

And they did find, over those 16 years, that, on average, individuals with hearing loss had faster rates of an increase, the change in depressive symptoms after hearing loss occurred. And they actually did a little bit of what we call a mediation analysis, which is where the results are explained by changes in social engagement. So what they found was that hearing loss led to changes in the way that people connected with each other, and then that led to depression over time. We also see associations with anxiety. I think that the evidence base is not quite as high, but there are associations there. And just one cohort study here. They didn't use audiometry. They used claims data, So ICD-9 codes to identify individuals.

But they did find that hearing loss was associated with a 2.4-fold risk of anxiety over 12 years. In terms of treatment, there are several studies to highlight. So one came from a Veteran's Affairs study. This was conducted back in 1990. Individuals were randomized to get hearing aids to a waitlist, and they did find that depression improved in the individuals who were assigned a hearing aid use over the four-month follow-up. Another study looked at, pilot study, looked at 25 participants, 60 years or older. They all had major depressive disorder and moderate to profound hearing loss. They were randomized to receive hearing aids, or they tried to have a sham hearing aid, although it really didn't help mask. Individuals knew whether they had hearing aids or the sham.

But unfortunately, they found no impact on depressive symptoms after 12 weeks. And then the final study, 61 patients, all older adults, these were recruited from an ENT. So it's more of a clinical sample, one-to-one hearing aids or control. And they did find, for individuals who were seeking care, that hearing aids did improve depressive symptoms over four weeks. So the study's mixed a little bit. But I would say, you know, depressive symptoms, in terms of the association with hearing loss, depressive symptoms we know are common. They impact 10% of older adults, related to social connection. There is evidence for hearing loss as a risk factor, but the study quality, again, varies. And at the population level, I would say we still need some evidence to know if really hearing aids make a difference.

And finally, just to conclude, you know, big picture, I think population studies do suggest an association, but, again, the quality varies. And so I do think we have some more work to do here. We do have unanswered questions. I don't think we know, at the population level, whether hearing treatment improves social connection in the general population. We do know, however, that patients may seek treatment because they feel isolated or lonely and feel like their hearing is related to that. And so it's very important for patient care when they seek treatment for that. We certainly hope that hearing aids

may improve that for them. But it's also important to remember that not everyone with hearing loss feels isolated or feels lonely or feels depressed.

Some people are okay. Something else to keep in mind, during this talk, we presented results of a systematic review. They suggested about a 40% increase in the odds or the estimated risk of depression associated with hearing loss. You know, when we think about how we communicate these types of findings to our patients, so let's say an 80-year-old patient with hearing loss wants to know their risk of depression, how would you respond? You know, you could say, "Well, your risk is 40% higher, based on the summary of the evidence," or, you know, it's much more long-winded, but you could say, "Compared to a group of people who had normal hearing, risk was 40% greater in participants with hearing loss, but your individual risk may be higher or lower."

And actually, that's the right approach because, remember, at the beginning, we talked about population studies, public health studies, they're designed to be at the level of the population, and that means the interpretation is at the level of the population, as well. And from an epi study, we actually can never determine an individual's risk. We only know, on average, in the population. And an individual's risk is zero or one. It's not 40%. They'll get it or they won't. We just don't know yet. So it's something important to try to remember when we're communicating these study findings to our patients. And then finally, I'd like to conclude by just saying there are a lot of interventions that already exist for social connection, obviously, for trying to help with depression and depressive symptoms.

You know, generally we see success with these studies, but the effect size is small. We're not sure how much they help. And again, we need more studies here. But what I think is important for us to realize is that they don't include hearing. And so we've been talking about treating hearing to prevent these things, but I think it's also important for

us to be able to say, "Okay, we already have interventions. Maybe hearing is part of the picture. Instead of solely focusing on hearing, maybe let's think about adding hearing to some of these interventions, as well." So just food for thought there. And with that, I know we're right at time, so thank you so much. Apologies for my voice today, and if we have time, I'm happy to take questions. Otherwise, here is my email, and I'm very happy to take questions by email, as well. So thank you.

- [Christy] So if anybody has any questions or comments for Dr. Deal, we'll go ahead and leave the classroom open, just for a couple more minutes.

- [Jennifer] Great.

- [Christy] And we wanna thank you so much for sharing all of your knowledge and all of that data. I know it was a lot to get through, but I think you broke it down and made it able for us to digest really well, so thank you Dr. Deal.

- Thank you, and again, well, if anyone has questions or wants further comments, I'm very happy to talk by email too.

- [Christy] We wanna thank you again for your time, Dr. Deal, and we appreciate your expertise. We hope that you all enjoyed this presentation and have a great weekend.

- Thank you. You too.