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Investigating the Prevalence of Comorbidities in MS Clinical Trials

Ashley Baker:
This is *NeuroFrontiers* on ReachMD. I'm psychiatric nurse practitioner Ashley Baker and here with me today to discuss her recent study on the prevalence of comorbidities in multiple sclerosis clinical trials is Dr. Amber Salter, who is an Associate Professor of Biostatistics at the University of Texas Southwestern Medical Center.

Dr. Salter, thank you for joining me today.

Dr. Salter:
Thank you for having me.

Ashley Baker:
So let's jump right in. Starting with some background, can you tell our audience about the objectives of your research?

Dr. Salter:
Sure. So when we do clinical trials, we're generating evidence to support clinical decision-making, and often clinical trials have restrictive inclusion and exclusion criteria, which raises some concerns about the generalizability of studies or how well the results of those trials will be applicable to the broader patient population. So factors such as age, racial diversity, and having comorbidities are generally thought to be excluded from trials, thus reducing the generalizability of study results to these individuals.

So this is a problem because comorbidities or having a disease other than MS, in our case, are common in individuals with MS. So some of the most common comorbidities are depression, anxiety, hypertension, hyperlipidemia, and chronic lung disease. In 2016, an International Advisory Committee on Clinical Trials in MS recommended that comorbidities be more clearly and consistently described in enrolled clinical trial populations for common comorbidities so we can better understand the applicability of these clinical trial findings to those in clinical practice. So with this study, we were looking to describe the prevalence of comorbidities in MS disease-modifying therapy phase III clinical trial populations.

Ashley Baker:
So for the study that you did, can you walk us through the exact study design and the methods behind your research?

Dr. Salter:
So this study was a two-stage meta-analysis of individual participant data from these phase III clinical trials of MS disease-modifying therapies. So what this means is that first, we requested clinical trial data from the sponsors of these trials, and then we use the individual-level participant data to classify comorbidities and other demographic and clinical factors within each trial. Thus, with the benefit of having some of the individual-level data as opposed to say, using a meta-analysis from published to data where everything is already summarized, this allowed us to kind of classify the comorbidities and then do what we needed to do within each trial.

The next stage involves summarizing the data across all of those trials using a meta-analysis approach. We obtained 17 phase III clinical trial data sets of MS disease-modifying therapies. It was quite a lot of data to manage, and we used the Maelstrom guidelines for retrospective harmonization to make sure that the data were consistently prepared across each of these trials. And then to get the comorbidities, we used the medical history data reported from the trials and went through a process to classify all of the chronic comorbidities. We had 15 of interest that we reported here, and we also considered the number of the comorbidities that an individual had. And then using that data, we ran the meta-analysis to summarize the proportion of participants in these trials or the prevalence of these comorbidities to report a pooled or an overall summary of the prevalence of these conditions across all of the 17 trials. We also compared the prevalence of the comorbidities by age groups, sex, disability level, race, and treatment using what we call prevalence

ratios.

Ashley Baker:
You mentioned hyperlipidemia. What other specific comorbidities were included in the trial?

Dr. Salter:
We had 15 that we considered for this analysis. We focused on chronic conditions and those conditions that were recommended by the International Advisory Committee on Clinical Trials in MS, and that included depression, anxiety, hypertension, hyperlipidemia, migraine, diabetes, and chronic lung disease. Then we also looked at a few additional comorbidities that we wanted to consider, and that was autoimmune thyroid disease, cerebrovascular disease and other cardiovascular diseases, peripheral vascular disease, other miscellaneous autoimmune conditions, skin conditions, and other psychological disorders. Some of these were selected because they have been shown in systematic reviews to be more prevalent in the MS population, so they're the ones that we generally see in the broader MS population. Some of these have been shown to have association with outcomes, and some of these are treatable too.

Ashley Baker:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Ashley Baker, and I'm speaking with Dr. Amber Salter about her research that investigates the prevalence of comorbidities in MS clinical trial populations.

So now that we reviewed the setup of this study, Dr. Salter, I'm curious now to hear about the results. What did you uncover?

Dr. Salter:
So we ended up being able to examine the comorbidity status of nearly 18,000 participants with MS enrolled in these seventeen phase III clinical trials. When we looked at the pooled prevalence, there were about 46 percent of the trial participants that had one or more comorbid condition of the ones that we considered. In addition, we saw that depression, hypertension, migraine, anxiety, and hyperlipidemia were the more prevalent comorbidities that were observed in these trials. We also observed an increase in the prevalence of diabetes and hypertension in the trials over this 15-year period that these trials were conducted, but most of the comorbidities decrease or remain the same over time.

Next, we looked at the differences in the prevalence by some different demographic factors, and we saw that the burden of comorbidity was higher at older ages in females and those at higher disability levels. The prevalence of hypertension, hyperlipidemia, and diabetes were higher in older age groups, and migraine was more prevalent in female participants and younger age groups. When we looked at differences in racial groups across these trials, we saw that other racial groups had a higher prevalence of diabetes and cerebrovascular disease and of other autoimmune conditions compared with the white racial groups. Female participants also had a higher prevalence of autoimmune thyroid disease and chronic lung conditions, and for depression and anxiety, female participants and those in older age groups had a higher prevalence of these conditions.

Ashley Baker:
How do you think these findings will potentially impact future clinical trials?

Dr. Salter:
It would be helpful for future clinical trials to think about the makeup of comorbidities moving forward, especially as we consider more progressive MS trials, which have older participants and higher disability levels which likely also will be associated with an increased prevalence of some of these comorbidities. There are also some studies and some accumulating evidence that suggest that comorbidities may affect outcomes, and if this is true, this has a potential impact on how we might design clinical trials moving forward.

Ashley Baker:
So we're almost out of time for today, and I'd like to wrap up by hearing any final takeaways that you may have for our target audience.

Dr. Salter:
So I'll say in our study, while it varied by trials, people with comorbidities were included in these trials, and they were potentially somewhat underrepresented compared to the general population, but it was still encouraging to see that there were some people with comorbidities present in these trial populations. The prevalence of these conditions varied somewhat by demographic and clinical characteristics.

There are studies that suggest that the presence of comorbidities is associated with MS clinical outcomes, such as disability progression and relapse rate. And given the prevalence of the comorbidities we've observed in these trial populations and the previous studies suggesting that it affects outcomes, it will be important to further understand the influence of the comorbidity on outcomes in the clinical trial setting.

Ashley Baker:

With those final thoughts in mind, I want to thank my guest, Dr. Amber Salter, for joining me to share her important research focusing on comorbidities in MS clinical trial populations. Dr. Salter, it was wonderful having you on the program.

Dr. Salter:
Thank you very much for having me.

Ashley Baker:
For ReachMD, I'm Ashley Baker. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.