

# Study of Transverse Myelitis in Veterans Health Administration Records

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[00:00:00] **GG deFiebre, PhD:** Hello everyone and welcome to the SRNA Ask the Expert Podcast Series: Research Edition. This podcast is titled "Study of Transverse Myelitis in Veterans Health Administration Records." My name is GG deFiebre, and I moderated this podcast. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at [wearesrna.org](https://wearesrna.org).

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[00:01:16] Horizon is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare autoimmune and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives.

[00:01:36] For this podcast, we are pleased to be joined by Dr. Michael Sweeney, Dr. Justin Abbatemarco, and Dr. Jonathan Galli. Dr. Sweeney is an assistant professor of Child Neurology and Neuroimmunology at Norton Children's Hospital and the University of Louisville School of Medicine. He completed his Child Neurology residency training at Cincinnati Children's Hospital and an Autoimmune Neurology fellowship at the University of Utah and is a former James T. Lubin Fellow.

[00:02:03] Dr. Abbatemarco is an assistant professor at the Cleveland Clinic Mellen Center, Neurological Institute. He completed his Neurology residency and neuroimmunology fellowship training at Cleveland Clinic and an Autoimmune Neurology fellowship at the University of Utah.

[00:02:17] Dr. Galli attended medical school at the University of Vermont followed by residency in neurology and fellowship in autoimmune neurology at the University of Utah. He also is a former James T. Lubin Fellow. He remains on faculty at the University of Utah, where he specializes in autoimmune neurological conditions, including MOGAD, NMO, autoimmune encephalitis in both clinic and hospital settings.

[00:02:40] So, thank you all for joining us today. We're really excited to talk about this new research and learn a little bit more about it.

[00:02:50] So to start, do you mind just explaining the purposes of this research and what it was about? Dr. Sweeney, do you wanna start?

[00:02:58] **Dr. Michael Sweeney:** Sure. So, when we first set off on this project, we were kind of hoping to expand on what we knew about the epidemiology of transverse myelitis. There were kind of some small studies that had been published with smaller type cohorts included and we had this VA healthcare system that spans the entire country with a whole lot of data that was really untapped. So, we set out to look at that data to see what we could learn about transverse myelitis incidents across the country, kind of in a more geographically diverse population.

[00:03:45] **GG deFiebre, PhD:** Great, yeah. And then, you know, obviously since, as, you know, the US doesn't have a national healthcare system, was your goal with kind of looking at the Veterans Health, was that kind of a way to not necessarily get the same sort of data you could from some place that has a national healthcare system, that has all this information kind of collected in one place? Or how was, how did that kind of thinking go?

[00:04:12] **Dr. Michael Sweeney:** Yeah, that's probably, that system is probably as close as we have in the US to a national healthcare database. Still those databases still don't exist. This study was started back in 2015. We still don't have any bigger data pools out there to draw from.

[00:04:39] **GG deFiebre, PhD:** And then, so what methods did you use to conduct this research? So, I know that it was a retrospective review, so if you could just talk a little bit about what that means as opposed to something like a prospective study, Dr. Galli?

[00:04:56] **Dr. Jonathan Galli:** Yeah. So, the methods of our study, we performed a retrospective review of charts, which will explain the process in a just a second here. But basically, a retrospective review is saying, "At this point in time we're going to look back over a time period." And in our case, it was from 1999 to 2015. And saying, "In that snapshot of time, we are going to study this group of patients." And that is in comparison to a prospective study where we say, "Here's time point A and we're going to follow any new cases moving forward and look at all the new cases at that standpoint."

[00:05:43] So we were able to look back on cases from 1999 to 2015, and the way that we were able to use the VA system is our colleague Dr. Stacey Hardy has her connections, for a lack of a better way to put it, through the Veterans Affairs Healthcare and through their national database. And what they're able to do is use, in this case, diagnostic codes, the ICD-9 codes for transverse myelitis and list every single patient within the VA system across the nation who's ever received that specific diagnosis.

[00:06:32] once that list was compiled, which was over 4,000 patients, our team then went through each chart and reviewed the patient's presentation diagnostic evaluation, treatment, and outcomes, and really that way we were ensuring that the patient's diagnosis truly was consistent with transverse myelitis versus an alternative diagnosis. And from there we were able to record different sets of data and then down the road kind of go through the statistical analysis of that.

[00:07:12] **GG deFiebre, PhD:** Great. Thank you for that overview. And then in terms of the, I don't know if there's any additional kind of comments about the methods that you used but what were the inclusion and

exclusion criteria? You pulled all these potential people who had that ICD code attached to them. How did you decide kind of who to include and look into more detail with and who to exclude? Dr. Abbatemarco?

[00:07:42] **Dr. Justin Abbatemarco:** Yeah, absolutely. So, as Dr. Galli kind of explained, we took the entire health system and tried to look at that population. Again, it's really unique because it's comprehensive. It includes the whole country and it's a system that doesn't you know, impact all members or kind of equitable access to the healthcare system, which is kind of unique in the US. And so, it offers us some advantages. The VA system has some downfalls. You know, one is it's a very homogenous kind of population. So, we're dealing with like older Caucasian men with a high propensity of smoking. It doesn't have pediatric cases. So those are some of the kind of pieces that are not as available within the VA system, right?

[00:08:29] Other things that we excluded, if there were other kind of noninflammatory causes to their spinal cord disease. So sometimes we can have arthritis or degenerative disease. Sometimes there can be abnormal clusters of vessels that can cause trouble with the spinal cord. So, we really just wanted to look at cases of transverse myelitis, which at its most basic principle just means that there's inflammation in the spinal cord region, and we can kind of define that.

[00:08:59] **GG deFiebre, PhD:** Great. Thank you. And so, you did report on a point prevalence which you know, it was, I think, 7.86 cases per 100,000 people. And so that's the estimate of the number of people with transverse myelitis at a given point in time. So, can you talk a little bit about what this means and maybe how it compares to prior studies? I think some prior studies maybe showed a, a little lower prevalence. Dr. Sweeney?

[00:09:33] **Dr. Michael Sweeney:** Sure. So, you know, the point prevalence is an important piece of data to take out of this study. I think that it's difficult to compare that number to other studies because of the wide differences in the subjects that were included in the study. So, if you have other studies that compared or looked at their entire population that had maybe a less homogenous group of subjects included. In the US there are some, there's a few studies that were across single healthcare systems or the Olmsted County Study from the Mayo Clinic which also has its own kind of limitations and kind of referral biased.

[00:10:25] So it was a little bit higher than what is reported in some of the other studies, but it's, it's not overall too surprising. This also included the subjects that went on to get a multiple sclerosis diagnosis or other kind of secondary diseases that can present with myelitis which probably was a big factor in that higher number.

[00:10:57] I do think it probably represents maybe a closer kind of a realistic number of what we see day-to-day. So when, when a patient comes in and has myelitis, we don't know if they're going to have multiple sclerosis. We don't know if they're going to have NMO, MOG disease, or an isolated myelitis. So, it kind of gives us a number for that.

[00:11:22] **GG deFiebre, PhD:** Yes, for sure.

[00:11:24] **Dr. Justin Abbatemarco:** And just-

[00:11:25] **GG deFiebre, PhD:** Yeah, go ahead.

[00:11:25] **Dr. Justin Abbatemarco:** I just had a follow up with that piece. Some of those older studies that Dr. Sweeney was mentioning, there's an oft-cited study out of Israel. But that was looking at criteria between, it was 1955 to 1975. I mean, that was when they were collecting cases, and we're talking about that on the scale, they collected 60 cases, I think. And so that's why we kind of set out to do this project, to kind of give

like a modern look at this, right? Because the numbers that we were looking at were from a long time ago and a lot has changed. They didn't have MRI as a diagnostic kind of part of this evaluation, so I don't think it's too surprising that we got higher numbers because we're much adept at diagnosing and managing these patients than we were back then. And it's true for some of the other studies in the US. We're talking about things that were done in the late '90s early 2000s.

[00:12:17] **GG deFiebre, PhD:** Sure, yeah. We, unfortunately, have been relying on these very old data at this point, so it's great to get this more up to date and current estimate. And so, kind of jumping off of that, Dr. Abbatemarco, you talked a little bit about the fact that MRI wasn't available for some of these older studies. You did in this paper talk a bit about what diagnostic tests people got what treatments they got. Do you mind just kind of summarizing a bit about what you found in terms of that in the charts that were reviewed?

[00:12:54] **Dr. Justin Abbatemarco:** Yeah, absolutely. So, patients really require a really extensive evaluation when transverse myelitis is kind of a part the differential. So usually that includes a lot of blood work, MRI, and in most cases, it should probably include a spinal tap or CSF analysis. And so, we looked at all of those components. I think one of the more striking things that we found was only 42% of our patient population that we were able to identify had CSF testing, which could be an under reporting, right? Not everyone who goes to the VA gets all of their care there, and so there are some challenges. But we're still looking at a really, you know, less than half of the cohort, somewhere around there, not kind of obtaining a full evaluation.

[00:13:41] As Dr. Sweeney said, right, multiple sclerosis, NMO are on the differential, and CSF is really imperative to kind of help differentiate that, out that piece. And those numbers are in line with other studies that have been done at the Mayo Clinic or Hopkins, these big referral centers for transverse myelitis. And so, though they're striking, not too surprising for our end.

[00:14:03] Other things that we were kind of looking at, we looked at treatment, so what are patients kind of being treated with? About 70% of our population was treated with steroids. Usually that's IV methylprednisolone. Sometimes corticosteroids like Prednisone. So still of, it's a good portion of patients that weren't receiving any treatment. And there are a fair number of cases where we sometimes will use other interventions like plasma exchange apheresis. And it was only a small percentage of our population receiving those interventions. When analyzing kind of that subgroup who got either steroids or some other treatment, we were seeing them do a little bit better so that was encouraging. But we're still having these kinds of gaps in both diagnostic evaluation and treatment.

[00:14:55] **GG deFiebre, PhD:** Yeah, just, I can't remember from the paper, did you happen to look at whether these trends kind of changed over time? So, for some of the earlier cases, if they were less likely to receive, you know, some of these acute treatments or diagnostic testing than maybe people who were diagnosed a little bit later? Or was that something that wasn't included in the study?

[00:15:18] **Dr. Justin Abbatemarco:** I don't think we did a time analysis, though it is interesting where we did, you know, investigate outcomes from like 1999 all the way to 2015, and we're hopeful that things have gotten better throughout that time period. And more awareness is brought, but I think still think we have a ways to go, and I don't think we looked at it particularly in those time chunks.

[00:15:38] **GG deFiebre, PhD:** Got it. And so, were there any findings that surprised you or were something you didn't expect Dr. Galli?

[00:15:49] **Dr. Jonathan Galli:** So, some of our findings I would say, are not overall shocking. One of the things that we were able to kind of look at was in patients who had more disability, was there anything that related

to that? And not surprisingly patients with longitudinally extensive myelitis, so anybody with a spinal cord region really over three spinal segments long had more disability, which makes sense, because the more of the spinal cord you involve a, the more likely your disability is. And so, things like that were not overall very surprising in that sense.

[00:16:40] But there, I think, when we were going back through the data as a team, one of the things that I think surprised all of us was actually the lack of diagnostic data that was available as, as a whole. You know, as Dr. Abbatemarco had mentioned less than half of our patients had had documented spinal fluid results. Which, you know, as times have changed, we hope that that's improving. But that really points to these patients were having, you know, less of a complete workup than they really should have had that may change long-term management. And the same also goes for the serum evaluation in these patients as well. And so, I think as a whole, our group is really surprised most by the kind of lack of evaluation that patients as a whole got.

[00:17:39] And I think that this may lead into kind of our next question a little bit. But where does that lead us into the future of diagnosis in treating transverse myelitis? And what I'm hoping that our paper can, you know, really boil down to is for clinicians to see that transverse myelitis, A, isn't as rare as we sometimes may think. With our point prevalence being what it is, it's more common than we might have initially thought.

[00:18:11] But also being aware that these patients really need a full evaluation. And whenever I'm talking to my patients, I will talk to them and say, "It looks like you have a transverse myelitis based on our evaluation." But what does that mean? That's still a very much umbrella term where we have to figure out what's caused this. Because if we're looking at transverse myelitis from something like NMO, that's going to change our management compared to if somebody has transverse myelitis for MS, versus somebody who we've ruled all of these things out and ultimately come down and say this looks like idiopathic transverse myelitis. What does that mean?

[00:18:54] And I think for the future, what I'm hoping our paper can really show is that there's a significant importance in doing a full evaluation to really make sure that we are having a good long-term game plan. And, you know, we weren't able to really break down from disease specific diagnoses and kind of outcomes there just based on what was not available to us. But I am hoping that we can at least show that a thorough evaluation, to really make sure that, for lack of a better way to put it, we know what we're dealing with and what caused somebody's transverse myelitis to begin with, will really allow us long-term to make sure that we have the right treatment plan for them.

[00:19:40] **GG deFiebre, PhD:** Definitely. And that's something just from the kind of patient advocacy side too, that we see frequently where people will join us. A number will send us an email and they haven't been tested for aquaporin-4 or the MOG antibody, or just got steroids and maybe are still not doing great and haven't been offered something like plasma exchange. So, you know, I definitely think, as you said, it kind of shows a gap there and where we can potentially move forward and make sure people are getting these full workups and that the diagnosis is correct, and they get timely treatment. Are there any other kind of additional points, Dr. Abbatemarco, or Dr. Sweeney, you want to make kind of about the future of diagnosing and treating transverse myelitis or why this kind of might a difficult diagnosis for, in some cases?

[00:20:27] **Dr. Michael Sweeney:** So, I'd like to point out, so during the time points that we studied our biomarkers were even more limited than they are now. So, we didn't have MOG testing. NMO testing was kind of spotty. The assays were kind of rapidly evolving during that time period, so we didn't include those. But I think moving forward, any study that's looking at outcomes in myelitis are going to have to kind of subtype their patients based on their different biomarkers. We know now that MOG patients tend to have a better outcome than NMO patients with myelitis. Multiple sclerosis is probably somewhere there in the middle. So

that's one thing. As somebody who was involved in kind of the initial data collection, I will point out that the heterogeneity of the data across the system is profound, so there was a very wide practice in ER physicians, primary care physicians, neurologists, and these patients presented to all of these different providers kind of as their first line person. And cases were missed early on by neurologists as well as primary care physicians. So, I think the education piece is really a big thing to focus on.

[00:22:09] Another, another limitation of this study that I should point out is that we did not look at the imaging data itself. We relied on the, the neuroradiologist or general radiologist that interpreted these studies. These MRIs were done on scanners that were variable strengths and different brands with different protocols. So, we can't really say too much about the imaging data itself or comment on the quality of those studies. But certainly in 1995 compared to 2015, there's a big difference in spinal cord imaging. Even now, it can be very difficult to interpret. So, the imaging standpoint of things is also something hopefully that improves as we move forward.

[00:22:58] **GG deFiebre, PhD:** Great, thanks. Yeah, and Dr. Abbatemarco, do you have anything to add?

[00:23:01] **Dr. Justin Abbatemarco:** I think just build off of that piece, you know? Just some of the numbers that we looked at, right? So, we identified 4,000 cases of transverse myelitis in the whole cohort but confirmed it in only 1,000. And that goes to Dr. Sweeney's point, right? The awareness of what that diagnosis truly is, right? We're only confirming it in a quarter of cases.

[00:23:21] And so there's a lot of confusion on what that diagnostic criteria is, what that diagnosis is and how to apply it. And then, you know, GG, to your point, patients kind of advocating for themselves about pushing their treating physician, "What's the cause for my transverse myelitis, the inflammation within the spinal cord? Have we done everything that we can?" And then patients should always feel free to get that second opinion. Ask, you know, for people with some expertise in those conditions help look over their case and help guide their care. Even if it's just in like a rehabilitation kind of perspective. There are some expertise there that can help.

[00:24:04] **GG deFiebre, PhD:** Definitely. And then just thinking about, now that this research has been conducted, any kind of further research you think that should be conducted to kind of follow up on some of these findings? Maybe in other populations or within the same population? Kind of we'll open it to the group.

[00:24:24] **Dr. Jonathan Galli:** Yeah.

[00:24:24] **Dr. Michael Sweeney:** Something... Oh, go ahead.

[00:24:26] **Dr. Jonathan Galli:** Sorry. Sorry, Dr. Sweeney. I think we've all talked about this kind of separately from this study. But one of the things we were unable to look at were treatments and treatment outcomes. And one thing I am hopeful of is that future research can really focus on prospective treatment outcomes. We know that there's been more and more evidence that's pointed towards not just using IV steroids alone, but also as adding plasmapheresis or other adjuvant therapies can lead to better outcomes. But really, how do we better define early in somebody's treatment course, who's going to need more aggressive therapies versus who's going to need just a shorter course of just steroids? And so that's one area that I'm really hopeful that we can go into and figure out.

[00:25:28] **Dr. Michael Sweeney:** Yeah, I agree that early stratification and looking at which patients need more aggressive therapy is going to be a helpful thing to look at and maybe we need to start with just a prospective treatment trial in general. I think that probably the time is right for that. And at the beginning we

talked about the lack of a healthcare system across the country that's unified. So, we're starting to become more organized, and we have kind of consortiums that organize across the country that has different modalities of unifying groups across the country to perform trials. So hopefully in the near future, these things will be much more possible.

[00:26:21] **Dr. Justin Abbateamarco:** Yeah, I think our patient population, right, that we're studying, even the studies that we've quoted from Olmsted County or John Hopkins, they're all looking at a similar group, right? Older, male predominant cohorts, Caucasian, and so how do we diversify the group that we're looking at to kind of better understand outcomes? We know outcomes are different in different groups of people in multiple sclerosis. That same concept is probably true in transverse myelitis but haven't identified that. And so, we need to get a more inclusive kind of research body of literature kind of out there to help inform care for those groups of people.

[00:26:56] **GG deFiebre, PhD:** For sure. Thank you. And then any final thoughts? Anything we didn't talk about that you think is important to mention about this research or future research or anything?

[00:27:08] Or we covered it all?

[00:27:13] Okay.

[00:27:13] **Dr. Michael Sweeney:** I'm offended we didn't talk about pediatrics, but that's for a different time.

[00:27:16] **GG deFiebre, PhD:** Yes, well, that's, yes, that's, pediatrics are important, too, and definitely obviously not something you could have covered in this research just based on the population.

[00:27:25] I don't think we're, yeah, kids are veterans at this point.

[laughs] But yeah, definitely an important area of future research and a place where, obviously also getting diagnostic and treatment and all of that is incredibly important, so thank you for bringing that up as well. But, yeah. But thank you so much for your time, I really appreciate it, and for doing this really important research. I know it was a lot of work, or I can only imagine it was a lot of work, so very much appreciated, so yeah. Alright. Well, thank you all.