



# Introducing the Ultimate MS Treatment Guide: Expanding Your MS Shared-Management Tool Repository

Presented by:  
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## **Alexis Kline:**

Hello and welcome to the Multiple Sclerosis Association of America's Educational Webinar. My name is Alexis Kline, and I'm the Director of Mission Delivery and Research Implementation. On behalf of MSAA, we greatly appreciate the opportunity to connect with you. Next slide, please. We're extremely honored to have Dr. Augusto Miravalle here to host this evening's presentation on the Ultimate MS Treatment Guide and Shared-Management. We very much look forward to introducing him and handing the evening over, but I have just a few items to touch on first. Next slide, please.

As you know, MSAA is a US based national nonprofit organization dedicated to improving lives today for people living with MS and their care community. If you've connected with MSAA before, it's likely that you've already met these wonderful individuals, but MSAA features a toll free helpline that is staffed by individuals with backgrounds in social work or counseling and are familiar with multiple sclerosis. They're available to help provide support related to MSAA's free programs, such as the MSAA durable medical equipment program, cooling garment program, and MRI access program, as well as share available resources from the broader support community. If you have questions about these or any of our programs or services, you can connect directly with an MSAA helpline specialist or visit our website at [mymsaa.org](http://mymsaa.org).

Also, as a friendly reminder, we invite all individuals viewing this program to complete the MSAA Patient Education Survey form. This information helps us to evaluate quality, impact and helpfulness of educational programs, as well as provide support for future educational funding.

Also, as a friendly reminder, this program is for informational purposes only and should not be taken as individual medical advice. The content discussed tonight is not intended to compare any specific therapies or specific treatment products. You should not use the information presented as a means of diagnosis for determining treatment. For diagnosis and treatment options, please consult with your trusted healthcare provider.

Next slide, please. Now for the part we've all been waiting for. I am delighted to introduce Dr. Augusto Miravalle. Dr. Miravalle is a board certified neurologist who sub-specializes in multiple

sclerosis and related neuroimmunological disorders that the brain and spinal cord. Dr. Miravalle has been involved in both clinical and science based research and is a member of many professional societies and advisory boards, including participating as a member of the MSAA Healthcare Advisory Council. Dr. Miravalla received his medical degree at the University of La Plata, Buenos Aires, Argentina, completed his neurology residency training at Loyola University, where he served as Chief Resident of Education, and subsequently completed a clinical neuroimmunology fellowship at Harvard University. Without further ado, I am delighted to introduce Dr. Miravalle.

### **Dr. Augusto Miravalle:**

Thank you, Alexis, for that wonderful introduction, and what an honor to be invited to share this amazing tool. I just wanted to make sure that I honor everyone that has been involved in the development of this amazing resource for our patients. And what you're going to hear today is the result of the efforts for multiple staff members at the MSAA, but also experts in the area of multiple sclerosis that came together and decided that our patients deserve to have access to unbiased information, but at the same time, a comprehensive tool to help you define what is the best course of action in your care. And as we always say, the best treatment for MS is one that is personalized and individualized to your needs. And the best team is someone that actually not only helps you understand your options, but actually honors your opinion. And you have to be the center of that opinion. You have to be educated and you have to understand all your options. And with the options you have, you also have a clear understanding of what are the benefits, what are the risks, and what are the expectations of that care.

So without further ado, I would like to start with a very brief review of multiple sclerosis. And as you all know, we currently don't have a cure for multiple sclerosis. However, there are many available therapies, if you compare to whatever was happening in the nineties. Currently, we have over 22 disease modifying therapies for the treatment of multiple sclerosis. And I want to pause for a second and encourage you to participate in today's talk by writing your questions in the Q&A chat box and so we can make sure to address those questions at the end of the presentation.

So, I mentioned before all of these therapies that we have available offer benefits. And that's why they were approved by the FDA. Right? But those benefits actually may vary between patients and actually the benefits of these medications, even with the same individual, may be different earlier in the course of the disease or towards the end of someone's life. So it's important to always discuss with your healthcare provider where you are in your course and your journey with multiple sclerosis and what is the risk-benefit ratio.

Let's go to the next slide. So this is the way I look at multiple sclerosis. There are different domains and all of those domains are going to affect your brain health and ultimately your quality of life. There are clinical features for multiple sclerosis that affect the course of the disease, and that's why not every patient is the same, every patient with multiple sclerosis will have a different journey and a different experience. There are environmental factors that are going to influence your journey and experience with multiple sclerosis. Among those we know that things like nutritional factors, vitamin D, recently re-emphasized the role of Epstein-Barr virus, or the virus that causes mono, as common factors that will influence the course of your multiple sclerosis.

Of course, this is why modifying therapies play a key role in the disease, and there is absolutely no doubt that the use of these medications have significantly changed the course of multiple

sclerosis. We also know that the use of highly effective therapies early on in the course of the disease has significant benefit and advantages over the use of low efficacy medications.

Of course, patient preference is important to discuss and whether that's based on the route of administration, the frequency, or things like pregnancy planning, or lifestyles - patients that actually travel for work may not like to take a daily medication. So those things are important. And recently we have re-emphasized the use of biomarkers, whether it's bloodwork results, or serum based biomarkers or spinal fluid biomarkers, MRI markers, genetic markers to help us determine what is the best course of action for your multiple sclerosis. Let's go to the next slide.

So as we were talking before, MS is a common disease, it affects over a million individuals in the US and over 4 million people in the world. We know that most of MS patients are going to develop their symptoms early on in life, and it's still a female predominantly risk, with a ratio of 3 to 1. We also know that if we don't intervene with our medications MS could lead to significant disability, to the point that up to 50% of individuals may require support for ambulation within the first 10 years of the disease, and up to a third of people may require the use of a wheelchair.

And again, this happens without any type of interventions which has led to disease running its natural course. In the past, we used to say that it also decreased life expectancy by over five years. But these numbers are now no longer true since we have instituted disease modifying therapies and other interventions for multiple sclerosis patients. Unfortunately, MS is also a costly disease, not only due to direct healthcare costs of medications and treatments that we use, but also the indirect cost of having a high degree of disability in our patients, leading to less productivity and less engagement in society. That's why we always say not only for your own personal development and mental health, it's important that you stay engaged in society, but also for your finances. It's important to take care of you and your family. Let's go to the next slide.

So this is a cartoon that tries to exemplify the typical clinical course of multiple sclerosis. But as I mentioned before, everyone is different. We always say that most patients with MS start with relapses and those relapses are very frequent early on in the course of the disease, and we anticipate that an average patient with MS will have approximately one relapse every 18 months to two years, and that's without treatment. The frequency of relapses decreases over time and that is likely as a consequence of the immune system, which is one of the main factors behind relapses, also becoming older, a process that we like to call immune senescence. And that is nothing else but just saying that immune cells also become older with age, and the consequences, or the good consequences of immune reactions to the brain become less frequent.

However, we also see that MS patients may continue to accumulate disability, the so called progressive phase of the disease. And that progressive phase may be influenced by the inflammatory phase of the disease, by relapses, by the lesions found on the MRI. However, we may see that sometimes affecting that inflammatory phase may have little, if any, effect on progression, and that varies between patients. And we always like to say that by being aggressive in the way we manage multiple sclerosis early on with our antiinflammatory therapies, we are optimizing the care and doing everything we can to try to prevent future accumulation of disability.

At the bottom of this slide, you can see these vertical bars, and that tries to represent the MRI activity. And there are things we can see on MRIs and things that we can't see on the MRIs, or are more difficult to see. The most typical finding on an MRI with someone with MS is lesions,

and those lesions are those white dots that we like to count to have an idea of how fast MS is progressing in someone's disease. But there are things that absolutely we sometimes struggle to measure, things like brain atrophy or shrinkage of the brain, that unless we have some research available to us, we may not be able to identify early signs of atrophy. Interestingly, atrophy is one of those markers that actually strongly predicts disability.

Let's go to the next slide. And actually, this is just to highlight that early on in the course of the disease, at the bottom, you have these numbers and those represent years of age, anywhere between the early diagnosis phase of the disease until your 50s, that's the prime time in which we have the highest chances of affecting the course of the disease with our interventions, among those with the use of disease modifying therapies.

Let's go to the next slide. So this brings me back to why we are here today, and which is, again, an honor for me to present to you what we decided to call The Ultimate MS Treatment Guide, and that is intended to provide you with the information that has been available through peer-reviewed research, research that has been very rigorously designed, and information that has been approved by the FDA and all the medications that you have available. And the goal for this is to design and develop an interactive tool with the targeted goal of improving your self-advocacy. This tool was intended to identify the primary treatments that we use in all the stages of multiple sclerosis, whether it's relapsing-remitting MS, secondary progressive MS, or primary progressive MS, and to allow you to compare the risks, the benefits, the cost effectiveness and the availability of these to patients. And just to make it more interactive and more and more user friendly, the foundation of this tool is to make custom videos featuring physicians or experts in the field of multiple sclerosis who use these medications and prescribe them on a day to day basis. So we hope that this tool not only allows you to be more educated, but also more engaged in your own care. Let's go to the next slide.

So this is just a summary of all of the disease modifying therapies, and I like to group them into different mechanism of actions, into the class of what we call monoclonal antibodies that work in different targets on the cells, and anti cell therapies like ocrelizumab and ofatumumab, OCREVUS or KESIMPTA, those are the brand names. Of course, Rituximab is available but is not FDA approved, but we've been using that for a long time. Alemtuzumab and Natalizumab, those are the typical monoclonal antibodies. In terms of the oral category, we have the, now a large class, very popular class of the S1P modulators, Fingolimod, Ozanimod, Ponesimod, and Siponimod, what I like to call the antimetabolites, which is oral cladribine and teriflunomide. They work in different ways, even though they are in the same category, they have different mechanism of actions. And then the large subgroup of the Fumarates: Dimethyl Fumarate, Monomethyl Fumarate, and Diroximel Fumarate. And then we have the good old injectable therapies. These ones were the first available therapies back in the '90s that are still available, for some patients may be appropriate, which are the Interferons and the Glatiramer Acetate. Let's go to the next slide, please.

This is a summary of what I like to see as the most common categories of patient preference factors that we need to take into account, anywhere from the route of administration, some patients like to have oral therapies or injections or vice versa, or also mechanism of action, some patients like to be more educated on what is this drug doing to me? And I want to understand exactly what are the consequences of that mechanism of action. There are medications that cause, most of them actually, what we call chronic immunosuppression. Some medications will cause immune modulation. And some medications, like cyclophosphamide, for example, cause an intermittent immune suppression, in periods in which the immune system is affected but then we allow the immune system to recover and restore to baseline levels. Also,

it's important to look at safety. In any intervention medicine, you want to know your risks and your benefits. And as I mentioned before, pregnancy is a common factor that we always have to discuss with our patients. Let's go to the next slide.

And this summarizes what I already mentioned before, which has to do with the route of administration, mechanism of action, and safety. Those are important factors. We recently, we all were exposed to a pandemic, and that brought a new wrinkle into our discussion with multiple sclerosis patients in terms of not only the risk of infection with COVID 19, but also response to vaccines. So those are important factors to discuss with your healthcare provider. Let's go to the next slide.

So, and this is perhaps one of the most important decisions that an MS patient can make. Right? So I would like for you to take... I always tell my patients, take your time. There is no rush in making the decision. I want you to be aware of all your options, educated in any decision that is being done with a patient in the center of the discussion, and conversation always leads to better outcomes. So that's the vision that each therapy is featured in its own page with patient friendly language. A lot of people have been behind this tool to make sure that the language used is something that anyone can understand and the language is actually inclusive to demonstrate the mechanism of action of the medication, as well as the safety and efficacy features. But it is also a video clip that has experts, as I mentioned before, that will feature each medication along with additional information. And we hope that this not only benefits our patients but also our providers, this should be a constant conversation between you and your provider. Let's go to the next slide please.

Something I want to highlight is a recent meta analysis of multiple studies that has been done with multiple medications in multiple sclerosis. And you have them listed there, and apologies for a small font, but you can see that each color of these circles represents a different medication, and the same color is the same medication. So you can see in yellow is ocrelizumab, in light blue are interferons, in green is glatiramer acetate. So the purpose of this study was to look at age and response and this concept of the younger you are, the more benefits that you're going to get of all of these medications, regardless of what that medication is. Right? Even though we like to look at the medications and kind of group them into, you know, highly effective therapies, kind of middle efficacy or low efficacy. Regardless of the category, age is an important factor that will also determine that efficacy, even in the same class of medications. So as you can see that over age, this same medication may lead to less clinical efficacy, whether it is relapse outcomes, whether it's clinical progression, or MRI based outcomes. So this is a factor that is always important to discuss.

The other thing to consider is as we age, our immune system also ages, as I mentioned before, and that process of immune senescence can also lead to an increased risk of infections. And so not only the efficacy of medications may go down, but the side effects and the safety, particularly when it comes to infections, may go up. So it's always important that as you reach certain age, and we usually start thinking about, you know, mid-fifties, mid-sixties, and certainly in the seventies, that perhaps the benefits that someone is getting from the medications are not as relevant as perhaps the side effects and the safety concerns that may outweigh those benefits. Let's go to the next slide, please.

So this is a typical patient journey and someone that is diagnosed with multiple sclerosis and he's trying to understand what the options are. And we hope that that individual lands into the ultimate treatment page. And we hope that that allows the patient to understand that Treatment X is perhaps the best for that individual. We hope that with any information that individual will

bring this back to the healthcare provider and then between the two may discuss the different options. So, perhaps this is a good time in the presentation to see if our wonderful staff behind the scenes can provide us with a link and we can do a live demonstration of how that tool looks in real life.

So while they do that, I'm going to keep sharing with you the hopes, which is that, you know, this tool is something that not only patients see once, but actually is a constant reminder of, you know, the different options you have. And as your disease continues and you go through this journey of multiple sclerosis, you keep going back and refer back to this guide to not only learn more about your current therapy, but also what other therapies are available. And this is a moving target. We hope that we can continue to update information in this tool so our patients have always access to up to date information.

So the first thing that we see is colleague and wonderful mentor and friend Dr. Barry Hendin, and he is the Chief Medical Officer for MSAA. And he gives you a very warm welcome to this wonderful tool. So I encourage all of you to listen to his presentation. And he's going to explain not only the vision behind this tool, but also the details on how to best take advantage of this resource. And if you scroll down, you will have, and this is in alphabetical order, all of the different options. So those are all the different disease modifying therapies that are approved. And you can see that they are color coded and each color represents a route of administration, so you have the orals in blue, you have the injectables in purple, and the intravenous medications in pink, I believe that's a pink color. And then what you can do is click on each name of the medication, and that will bring you to its own page. And each page will have a video, as I mentioned before, of an MS expert that is going to explain to you more details about the medication. But also we'll have text information that gives you a sense of the route of administration, how frequent you administer, what are the potential benefits, what are the potential side effects, who is the manufacturer. So how the medication works, what is the mechanism of action. When was this medication approved. What are the potential side effects. So all of that information is going to be available, but also information about, you know, when to test, how to test, how to monitor safety and efficacy data on each of these medications.

So Alexis, let's go back to the main page, and what I like in most about this tool is like, you know, similarly when you're looking for cars, right, you can click different options and then you can compare them. And so let's say that you are in between these first three ones. And again, this is in no particular order other than alphabetical order. And you can click compare and that will take you to a chart that will give you a snapshot of all of this information at once. So you can see when the drug was approved, whether it's a pill or an injection, how often are you going to receive the medication, the approval class, whether it is for relapsing-remitting multiple sclerosis or clinically isolated syndrome. And you can read the rest. So it's very self-explanatory and we hope it's going to facilitate the process, the very important process, of decision making for your disease modifying therapy.

So I'm going to make sure that I look for potential questions and feel free to ask questions in the chat box. We will be happy to address those in case you have any questions. Otherwise, Alexis, we can perhaps go back to the presentation, and I was looking at some questions from before and there were quite a lot of questions about aging in multiple sclerosis. Right? So there was a common theme about, you know, how long can someone with MS receive medications and what is the right age to stop them? And I wish I had a straightforward answer to that very important question. And just to summarize the pretty complex answer let me tell you that every patient is different. So the recommendation is that please discuss this with your healthcare provider.

We recently had a publication from one of the, perhaps, the most organized, better organized, study looking at this particular topic, which is the discontinuation trial called DISCO-MS, and the data from that study was released recently. And and we didn't get a lot of answers that actually we can generalize to everyone. However, the study was designed to see whether patients over the age of 55 can safely discontinue disease modifying therapy. So there were two groups of patients, patients who continued and patients who discontinued. And then the statistical analysis was done in a way called non-inferiority study, trying to say, well, the patients who discontinued were not inferior in terms of outcomes, whether it's relapse rates, MRI progression, or disability progression, to the patients who continued. Right? And so the non-inferiority design means that you look at these prespecified outcomes and you see how each group behaved. And if the group that has continued behaved worse, then you conclude that they were inferior. If the group who discontinued didn't behave worse. You could say they were not inferior. And there's always a margin of error that you allow, which leads to this gray zone.

And unfortunately, or fortunately, depending how you want to look at it, the results fell into the gray zone. Ultimately patients who discontinued had a 7% chance it was higher to have disease activity than those who continue. But that 7% was considered still within that margin of error to not be considered inferior. So it's hard to translate that to a particular individual. Perhaps the most concrete outcome that we can say is that perhaps that there is a 7% increased risk of activity, whether it's relapses or MRI, in those who actually discontinue medications after the age of 55. So, you know, it's a very personal decision, it's something that I always recommend talk to your healthcare provider, because factors like how aggressive was your MS early on, and when was your last relapse or when was your last change in MRI. It's going to truly determine this process of predicting what could happen in the future. Like many things in medicine and actually life, past behaviors often predict future behaviors. Right. And so we would always say, well, if your MS has been very, very stable, that no changes in MRI, no disease activity for over ten years, well, perhaps your chances of having any of those activities if you discontinue are very low. However, if you have consistently new lesions on MRI or you have difficulties keeping your MS stable, perhaps your odds of having disease activity after you discontinue are significantly higher. So those are factors that are important to actually discuss with your healthcare provider.

And this leads to the final thought, which is this concept of precision medicine in multiple sclerosis. And precision medicine is something that is very popular and perhaps developed in the field of oncology in which doctors use certain markers of the cancer, the type of cancer that patients have, to guide therapies. And, you know, even within the same type of cancer, and by looking at these markers in cells or different other biomarkers they have, they can actually guide treatments that are very specific to that particular cell.

So we would love to have that in multiple sclerosis and something that we can actually say, well, based on your age, based on your race, your ethnicity, your cultural background, your nutrition, your family history, comorbidities, you having hypertension, I mean, all of these factors together, plus results of your blood work. This is your best bet. Right? And that would be something that will fit into what we call precision medicine. Unfortunately, we are not there and actually we are getting there, but not quite. We are starting now to understand how different factors influence the disease course, things like nutritional factors. Right? So we know that certain diets are what we call pro-inflammatory diets, like the diets are rich in saturated fats, those processed fats and the fats are solid at room temperature. Right? The bacon, the animal based fat. Right? Those are pro-inflammatory fats. We also know that poly unsaturated fats are good for MS patients. Right? The fats that are present in the good oils, the fat that is present in fish. Right? So those

are little pieces of information that we are getting from research that tells us that those interventions may be beneficial.

We also are learning that the content of salt in diet is not beneficial for MS patients. So high sodium diets are linked to more inflammation and worse clinical outcome. So we always recommend keep your sodium intake in check and try to minimize the use of salt with a recommendation of do not exceed more than two grams per day. We also know that smoking cigarettes has a negative impact in MS. Vitamin D deficiency, hopefully by now you're familiar with story of vitamin D, which there may be some controversies, but the truth is that supplementation with vitamin D when it's deficient, may have some benefits.

There is no doubt and controversy in the role of exercise in multiple sclerosis. We know that individuals who are active and engaging in exercise activities do better. And now we are starting to understand what type of exercises help what type of problems. So exercises, perhaps, that are better for balance or for core strength or exercises that are better for brain health and cardiovascular health. So the recommendation is work with a physical therapist to try to find a formula for exercise that is better for you and your particular needs. And don't wait until you're in trouble to exercise. Right? So you can divide the field of exercise into rehabilitation, which is restoration of function after someone loses a function, or pre- habilitation, which is use exercise to actually improve brain health and improve your brain reserve in order to be better prepared in case you get into trouble in the future. So don't wait until you're in trouble to start exercising.

So those are examples of things that we are starting to learn. We are far from being able to apply that in a way that we can determine the best course of action in terms of therapies based on these factors. But I think the more we learn, the better we can help our patients optimize their brain health in multiple sclerosis. So with that, I would like to perhaps end this conversation and open up to questions.

**Alexis Kline:**

Well, thank you so much, Dr. Miravalle, we have a whole boatload of questions. That was a really wonderful presentation and we really appreciate the overview and now we're ready for the really exciting part. So one of the first questions that we wanted to ask, and it came up a couple of times, is how can someone be more proactive in regards to preventing or slowing progression with their MS?

**Dr. Augusto Miravalle:**

Good question. Yes. So choosing the right medication is one step, but it's not the only one. And so, I will always say, you know, it's a combination of be educated and try to learn as much as you can. There are wonderful resources through MSAA, but through other organizations that you can actually try to get, you know, as much information as you can.

And then remember that brain health is something that is... you have control. Right? So we talked about the role of exercise, the role of nutrition, that there are other pillars, we we call, in brain health, like sleep. It's important to keep a good sleep hygiene. And, you know, if you have difficulties, let's say in the morning, early morning, you wake up with headaches or you wake up tired and fatigued. That might be a sign that your sleep is not allowing your brain to restore function. So that might be something to discuss with your doctor. And they may do a sleep study. Right? Look at comorbidities like depression or anxiety and treat them, be proactive about it. Have your team, your healthcare team, don't do it alone. Whether it is through health care providers or your social network, your significant other, your family, try to find people that is with you that will be there and ready to help you in case you need help.



**Alexis Kline:**

Mm hmm. Thank you so much. And this might be a plug, but I think making sure, too, that folks can advocate for themselves. Right? When they're looking for the right thing that's right for them. As a provider, do you think that's important for them to communicate and share?

**Dr. Augusto Miravalle:**

Absolutely. When patients advocate for themselves, they treat not only better for themselves, but for other patients. Right? They become role models, which is so inspirational to see.

**Alexis Kline:**

Yeah, that's great. Thank you so much. So, if there's someone who is considering or has questions about which therapy is the right one for them, is there anything that comes to mind that you think is important that folks should be thinking of when they're deciding on a starting therapy, whether it's the type of therapy or the administration mode and things like that?

**Dr. Augusto Miravalle:**

Yeah. And I think all of those factors are included in this wonderful resource that we just discussed today. And to be completely honest, I've been waiting for something like that for decades because the patients need this. And so this is unbiased, this is based on peer reviewed information that is being based on evidence and is something that we hope that will help you facilitate that process of deciding what's your best therapy.

**Alexis Kline:**

So that leads me to another question. Someone asked in the question about whether the medical community, whether you think the medical community will use this tool and we'll look at it and leverage it.

**Dr. Augusto Miravalle:**

Yeah, I hope so. Yeah. Yeah, exactly. And you know, this came during the design of this tool. Right? So this was, as I mentioned before, a team of experts and staff members behind this. Right? And this was a team of individuals that represent a very broad, you know, diverse community of famous providers. And I think the consensus was that we want to make sure that it's something that is helpful not only for patients but also for providers.

**Alexis Kline:**

Thank you so much. Yeah. And so moving into another topic, kind of talking about decision making and when it might be time to know if you're on the right therapy or not. So the first question we have is how can someone better understand the side effects of their DMT and how do they know if it's safe or okay that they're experiencing side effects or they need to start discussing it with their health care provider?

**Dr. Augusto Miravalle:**

Right. Always we say when in doubt, please talk to your healthcare provider. Right? So don't make assumptions. But it's always good to keep track of patterns. Right? So with that, I mean, well, let's say you have headaches. And what's important to know is where's the pain. Right? Location of the headache. What are your triggers, whether it's food or weather or menstrual cycles or medications. Right? Whether it's something that you can see a pattern in the day, like when you wake up in the morning or at the end of the day. So a headache that usually comes at the end of the day and in the entire head it may be a tension headache, headache that comes

with, you know, menstrual cycles and has more of a throbbing quality is maybe a migraine. So be your own detective. Right? So, when you have a side effect or a symptom, it's always good that you pay attention to patterns. You try to describe that as eloquently as you possibly can, take notes, keep a diary of symptoms, and then discuss that with your healthcare provider.

**Alexis Kline:**

Thank you so much. Yeah, that's that's a great suggestion. At MSAA, we have the My MS Manager, which can help you track, if you need to track symptoms and your treatments and things like that. So that might be helpful to you to keep notes on. So another question was kind of in the same line, are there signs that someone should be mindful of when it might be time to look at changing their treatment? Are there certain things, physically or emotionally that they should be cognizant of?

**Dr. Augusto Miravalle:**

All right. So the traditional expectation for treatment is that the medication is going to keep your MS stable with minimal, if any, side effects. Right? So MS stable has a very broad definition, but we usually use a composite of NEDA, which stands for no evidence of disease activity or minimal evidence of disease activity, which means no relapses, no MRI activity and no progression. Right? So that's a simple kind of framework to look at MS stability. In terms of tolerability and side effects, we hope that the medication allows you to have a normal quality of life. Sometimes it's a compromise. Right? Saying, well, I do have some side effects, but actually I have so much benefit from that that I can tolerate that. Right? So that's, again, it's a conversation that is very individual, but of course, safety, we want to make sure that it's safe, that the medication is not putting your health at risk, and that's something that this tool will allow you to understand - what are the common side effects that you have to be mindful... and then if you have any of those things, and also the monitoring bloodwork that you need to do or your physicians need to do to make sure that we are on top of it.

**Alexis Kline:**

That's great. Thank you so much. So, and I know that you perused the questions beforehand, too, so you knew this was coming but we had so many questions about aging and kind of knowing at that time, do you stay on your therapy? Do you change? You know, how do you advocate for yourself when you're doing that? And we popped in the chat that wonderful article that you had shared some of the new research, but is there anything else to that you can add to?

**Dr. Augusto Miravalle:**

Right. So that research that I shared has perhaps the most up to date data on discontinuation. You know, some patients like to consider discontinuation, but they are not ready to go from, you know, a very effective therapy to nothing. Right? So there are other options in between, like I mentioned before, the use of, for example, intermittent immunosuppression. And that way you can use an intervention for a couple of years and then just see what happens with nothing else. Right? So that the use of intermittent immunosuppression may be an option for some patients. So I think it really depends on where you are. Usually after the age of 55, that's when the conversations start. It doesn't mean that we will stop medications in everyone at that age, but that's at least when we start having a plan. And and of course, if there are any side effects or any safety concerns, that sometimes expedites the conversation a little bit faster.

**Alexis Kline:**

Yeah. That's great to know. Thank you so much, and thank you for sharing that, the updated research with us. It's really exciting to...

**Dr. Augusto Miravalle:**

I believe there's a question about the link and it was included in the chat box, is that correct Alexis?

**Alexis Kline:**

Yeah and we can pop it back in, too, just in case, so that it's on top of everybody's chat box. Thank you so much. So, now we had a lot of questions too surrounding kind of symptoms and also nutrition. So one of the first symptoms, we have a lot of questions around fatigue, and if there's any research or things that are coming out that you think might be helpful for fatigue or anything that you would suggest for folks.

**Dr. Augusto Miravalle:**

Yeah, that's one of my favorite topics, to be honest, because it forces us to be comprehensive. Right? What I can tell is that you probably won't be able to address fatigue in MS with a single intervention. Fatigue is very complex. Patients with MS suffer from fatigue for many different reasons, and sometimes patients have more than one. For example, disease activity. The amount of inflammation is going to affect fatigue. The presence of sleep disorders, we talked before, but also bladder issues. Right? So if someone has what we call neurogenic bladder and has to urinate very frequently and that interrupts sleep, has to wake up two or three times in the middle of the night, of course sleep is going to be affected and then fatigue is the result. Depression is a common a factor that will influence fatigue. But also things like thyroid disorders and other metabolic disorders, vitamin deficiencies, nutrition. So all of those factors play a role in fatigue.

So often when a patient suffers from fatigue, one of the first things I do is try to diagnose why. There are questionnaires that we use in the clinic. I personally use the Modify Fatigue Impact Scale, that's 21 questions, people can answer that on their own and that allows you to have a score and also different sub scores, three different domains of fatigue: physical fatigue, cognitive fatigue, and psychosocial fatigue. So that gives you a little bit of a snapshot into how much fatigue you have. And I use that every time I see patients to kind of monitor and track fatigue levels and also do help guide interventions. Right? So if someone has physical fatigue, perhaps that tells me that they are deconditioned, and they need to have an optimal exercise training program. If someone has more of a mental fatigue, perhaps we need to look at sleep, we need to look at medication side effects. And so those are important tools to kind of start diagnosing why someone gets tired with multiple sclerosis.

**Alexis Kline:**

So that brings us to another question that someone had about it, about your experience with folks when they're making a decision between a disease modifying therapy or healthy lifestyle, one or the other, both?

**Dr. Augusto Miravalle:**

Well, the answer is both, right? I always encourage people to be as healthy as you can. And one of the things that I like when people say, well, I'm into natural medicines. Me, too! And I actually think that natural medicine or natural approaches bring a lot of benefits. But unfortunately, in multiple sclerosis, it's such a complex disease that most of the time natural medicine alone is not enough. So I'm all for healthy diet, healthy exercise. As you mentioned,

with my wife, we founded the Brain Health Center of the Rockies, and the reason behind that is because we endorse healthy activities for brain health. However, MS is complex and we know that there is an underlying immune process that is going to affect brain cells. And the most efficient way to stop that one process is through the use of these medications. So you need it all.

**Alexis Kline:**

Thank you so much. Yeah, and that kind of answered the next question we had, the immune system's response to nutrition and diet and if that does have a big impact on it and if that's kind of the reasoning behind why it's so important.

**Dr. Augusto Miravalle:**

Absolutely. We are what we eat. Right? So what we eat has an important influence and direct influence in our immune system. There's a lot of interest in research in what we call the microbiome, which is this bacteria that we have in the gut and how that is going to affect your immune responses and how our diet directly affects that.

Perhaps the Mediterranean diet has the strongest data as a beneficial diet for MS patients, but also for brain health. When you look at things like Alzheimer's and dementia, it's perhaps the one nutritional intervention that has the strongest data in order to help prevent cognitive decline.

**Alexis Kline:**

All right. Thank you. So if somebody is seeing they're a doctor and they're adherent with our treatment, is there an amount of time that they should be seeing their provider, that they might be expecting to get MRIs, and kind of is there something... what makes it so important to get those MRIs, and kind of how does that work within the entire treatment plan?

**Dr. Augusto Miravalle:**

Right. MRI is one of the many tools that we use in the clinic, not only to diagnose someone with MS, but also to monitor the disease process. It's perhaps one of the most important tools in the clinic. Right? Gives you that snapshot into what is happening, perhaps with asymptomatic lesions, lesions not causing symptoms. So particularly early on in the course of the disease, the recommendation is to have at least one MRI a year. Sometimes we do them more frequently. We try to monitor subclinical disease activity. You may not have to have with contrast, and it's perfectly fine if you have concerns about the use of contrast so frequently, to not do contrast with these surveillant MRIs, but at least have at least one MRI a year early on is important. When someone reaches a certain age, perhaps we can start spacing those MRIs out a little bit longer, 18 months to 2 years.

**Alexis Kline:**

Thank you so much. And, you know, another part of that is I think more people have heard that they've been asked to get spinal MRIs in addition to some of their other ones. And if you have any experience with that or thoughts about that kind of new option folks are including.

**Dr. Augusto Miravalle:**

You know, spinal cord MRIs are very important. For the most part, lesions in the spinal cord will cause symptoms. It's very rare that a lesion in the spinal cord will be asymptomatic. But up to 30% of the lesions in the cervical spine may be asymptomatic. Whereas 90% of the lesions in the brain are asymptomatic. So we'd often do a MRIs of the brain as surveillant, even if someone is stable because you could still accumulate lesions without symptoms. The spinal

cord is more rare to have lesions not causing symptoms. So sometimes we don't do the cervical spine MRIs unless someone has no symptoms. But, you know, more information is always better. So unless there are contraindications, I'm always in favor of doing MRI to see if there are clinical questions that perhaps we can answer through that tool.

**Alexis Kline:**

And is there someplace that folks can go to kind of find updated research or information if they're looking at the different disease modifying therapies? Can they kind of see what's going on in the background someplace and understand what research is being done?

**Dr. Augusto Miravalle:**

Yes. So a good research... Well, of course, you guys have, in the MSAA, have wonderful resources and these type of webinars give patients an opportunity to get up to date information. But also PubMed is an important tool, it's a part of the NIH and it's a way that you can raise a search option in PubMed and you just simply type pubmed.org and that gives you access to a database of all the trials open to enrollment in different disease categories. So you can simply type MS or multiple sclerosis and that will give you all of the current trials open to enrollment.

**Alexis Kline:**

That's great. Thank you so much. And so someone asked, and I thought this is an interesting question too, if there's a difference between the generic versions of DMTs and how they affect people living with MS or if there are considerations folks should make about that? I see that smile.

**Dr. Augusto Miravalle:**

Right. That's a kind of like a loaded question. But I have to be honest, my bias is I don't trust generics. I do value the fact that medications have to go through rigorous clinical trials and development and all the research behind the medications that, with some of these generics, we don't know. And there hasn't been a lot of research behind it to just give us some degree of certainty other than, you know, whatever the FDA states. So I trust the FDA, but at the same time, I like to see that there is research behind that. So for the most part, I'm skeptical about the use of generics, and that's my personal opinion. I try to discourage its use and I get concerned when insurance companies actually force us to use generics.

**Alexis Kline:**

Thank you. So this is another interesting question about MRI, and I've heard it more about kind of stress and anxiety about getting an MRI. It's a lot of time and it can be painful for folks. And so someone was asking if an open MRI is as effective as the three hour MRI and if maybe taking medication before they go or if there's something that they can do to prepare before their MRI because it's so stressful.

**Dr. Augusto Miravalle:**

And yeah, I agree. Getting an MRI is not pleasant. And that's a typical example of sometimes we have to compromise, right? So open MRIs certainly don't provide the same degree of fidelity to look at your brain as a closed MRI. So the quality of the image is not as good. So if you choose to do an open MRI, please know that the quality is not the same. So you may be in a situation in which there are lesions that you can't see. However, an open MRI is better than no MRI, right? So I always say, well, you know, why we're concerned and why we use medications and sometimes we use sedation and so we try to optimize the reasons and the strategies we

have to kind of address the reasons why someone, you know, gets nervous with an MRI. And if we can't, then, well, let's do an open MRI, and that's going to be better than nothing.

**Alexis Kline:**

Got it. Thank you so much. And so someone asked when they're comparing their disease... when they're comparing disease modifying therapies and they're considering transitioning, should they be considerate of the mode or any certain actionable items within the therapies that they're looking at? Does it make sense to transition from a similar therapy to a similar therapy? Should they be thoughtful about that?

**Dr. Augusto Miravalle:**

That's a great question. So sequencing is an area that is becoming more popular in research now that we have so many options. And we are trying to understand if you have to change, will that make sense to not only change therapy from therapy, but also a different mechanism. And, you know, we, unfortunately, we don't have an answer that fits all. However, it does make sense. Right? So if someone, let's say, failed one of the AS1Ps. So whether it's GILENYA or Ozanimod or whatever drive in that category. Well, if there was disease activity or side effects, very likely the same drug and other drugs in the same category will offer a similar side effect profile. So in that case it will say, go to a different class. If someone is already on, and let's say, an Anti B-cell therapy and they have evidence of disease activity, which is rare but possible, then I will say, well, let's go to a different class. So I think there are situations or scenarios that will allow us to use common sense. But at the same time, we don't have a rule that actually can be applied to all patients.

**Alexis Kline:**

Thank you. So someone asked about acupuncture, incorporating acupuncture as a part of their treatment plan. And if you've heard anything about it in your experience?

**Dr. Augusto Miravalle:**

Yeah, acupuncture has been studied actually widely in MS and like any intervention, I always say, well, make sure to know who is doing it and then what are you expecting to get out of it? So it's very dependent on who does it, and they need to be knowledgeable, they need to be certified and they need to understand how to use this tool. It's helpful, particularly in situations of pain, central neuropathic pain, and spasticity. So those are the two areas that acupuncture has been used the most and it could be very beneficial.

**Alexis Kline:**

Thank you. And so I just have a couple more questions, if that's okay with you. So we got a couple about PML and health folks who might be at risk for that might navigate this treatment decision making or how to best manage their MS with that risk.

**Dr. Augusto Miravalle:**

Right. So PML is an infection that stands for progressive multifocal leukoencephalopathy. That infection is caused by a virus called JC virus. There are different ways we can mitigate this risk. One is there are certain medications that have a higher risk of PML and perhaps the highest comes with natalizumab. But other oral therapies like fingolimod and teriflunomide. I'm sorry, not... well, there were few cases, but Tecfidera has been linked to PML as well. So ways to mitigate this risk is by looking at the test results of your JC virus and whether you're positive or negative, that's going to determine a higher or lower risk. Even within that positive range, the

number of the titer is important. So how high that titer is also brings a higher risk. Things like the prior use of immune suppressants may increase the risk of PML as well as the treatment duration. Right? So how long someone has been on a given therapy. So those are factors that of course play into that algorithm to try to predict the risk of PML. We want patients to receive a therapy that has no risks of PML.

**Alexis Kline:**

Thank you so much. Yeah, that's really important. So, another question that we had, kind of going back to symptoms, was if you have any thoughts on this cionic neural sleeve, I don't know if you've heard of folks using that piece of equipment before.

**Dr. Augusto Miravalle:**

I don't have any personal experience on that. I will love if someone has experience to share it with me. I haven't used it.

**Alexis Kline:**

Perfect. No problem. Thank you. And so the last question before we ask you for your closing notes is someone's dealing with some really nasty heat sensitivity. And if you have any recommendations, because it just makes them feel like they shut down.

**Dr. Augusto Miravalle:**

All right. Right. So heat sensitivity is common in MS, it's something we call Uhthoff Phenomenon. It has to do with a sensitivity of abnormal myelin in the central nervous system to respond to increased body temperature. That could be due to external factors like weather or could be through internal factors like fever. Actually, MSAA has one of the best programs for cooling devices that actually folks can take advantage of that, which is one of the best strategies. Right? Just try to keep your body temperature down. Try to limit outdoor time if you go outdoors, try to be in shaded areas or try to bring cooling devices, there are a variety of them. Drink plenty of water. I mean, they're different things, but ultimately, it comes down to physics, right? We don't believe that overheating makes your MS worse, but it's just simply making you feel worse.

**Alexis Kline:**

Got it. Thank you so much. Well, we so, so, so appreciate you. You answered a boatload of questions for us. And we loved that. We got a great overview of the ultimate treatment guide. And before we close for the evening, I didn't know if you had any last notes you'd like to share. A closing thought for us.

**Dr. Augusto Miravalle:**

No, I just want to thank MSAA for inviting me. It's truly an honor. I know that with so many people behind this guide, I am truly... I'm biased when I say this is just a resource that we've been all waiting for. And so we can't wait to have our patients and the community overall taking advantage of that and hopefully get your feedback. We hope that this is a living product that will change over time. And so any feedback you have with all this, please share that with us so we can even make it better.

**Alexis Kline:**

Mm hmm. Yes, absolutely. Well, thank you so, so much for everything. Dr. Miravalle. We appreciate you taking time out of your extremely busy schedule to share this evening with us.

We truly appreciate that. And we just wanted to let everybody know if you'd like more information on MSAA's programs or services, we also will have this program available on demand on the [mysaa.org](http://mysaa.org) website in the upcoming weeks. And finally, as a friendly reminder, we ask again if you are viewing this, if you could complete the MSAA Patient Education Program survey. This information helps us evaluate quality, impact and helpfulness of these programs. On behalf of MSAA, thank you all so much for joining us this evening and we hope you have a wonderful rest of your week.