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## Managing MS in Older Adults: Key Considerations for DMTs and Lifestyle Interventions

### Announcer Intro:

You're listening to *On the Frontlines of Multiple Sclerosis* on ReachMD. And now, here's your host, Dr. Charles Turck.

### Dr. Turck:

Welcome to *On the Frontlines of Multiple Sclerosis* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss the management of multiple sclerosis, or MS for short, in adult patients is Dr. Carol Swetlik, who's a neurologist at MetroHealth and an Assistant Professor of Neurology at Case Western Reserve University, as well as Dr. Kimberly DiMauro, who's a neurologist at the Mellen Center for MS Treatment and Research associated with Cleveland Clinic. The two of them contributed to the journal article we'll discussing today. Dr. Swetlik, thanks for being here today.

### Dr. Swetlik:

Thanks for having us.

### Dr. Turck:

And, Dr. DiMauro, it's great to have you with us as well.

### Dr. DiMauro:

Thanks so much. We're happy to be here.

### Dr. Turck:

Starting with you, Dr. Swetlik, what motivated you to focus on the management of MS in older adults? And what gaps in the literature did you aim to address with this review?

### Dr. Swetlik:

Our motivation to complete this review was really grounded in the changing demographics of patients living with MS and changing needs in their clinical care. Of the one million adults in the United States living with MS, the peak prevalence is now between ages 55 and 64, but many of the completed clinical trials have had enrollment limited to patients under the age of 55, so there is somewhat of a growing mismatch between patients who have been eligible to participate in research and the patients who are in our office seeking care. In our review, we focus on issues that are particularly relevant to caring for this older cohort, including initiation and discontinuation of disease-modifying therapies, or DMTs, the impact of physical and psychiatric comorbidities on MS severity as many patients have diagnoses in addition to MS by this stage, and wellness and lifestyle modifications.

### Dr. Turck:

Now, with that background in mind, let's turn to you, Dr. DiMauro, and focus on some key management strategies discussed in your journal article. How should patient-specific factors like comorbidities influence treatment decisions, in particular those involving disease-modifying therapies, or DMTs?

### Dr. DiMauro:

So comorbidities are relevant to both diagnosis and disease management in our older MS population. Older patients generally tend to have more medical comorbidities; thus, we need to carefully weigh in how these can impact the neurologic differential when we're making a diagnosis as well as when choosing an appropriate MS DMT. For instance, the S1P receptor modulators with agents, such as fingolimod, can exacerbate hypertension and bradyarrhythmias in those with underlying cardiac disease, as well as they have the

potential to cause conditions such as macular edema. And so in these patients with underlying cardiac or ophthalmologic conditions, this is something to be aware of. Another example would be an older patient with premorbid liver or renal disease who you may then want to avoid medications with potential risk of hepatotoxicity, for instance, such as with teriflunomide or natalizumab.

And then, essentially, all of our MS DMTs carry some increased risk of infection, with that risk being greater in our higher efficacy DMT groups, so this is also something to keep in mind: weighing that risk-benefit profile, particularly in older patients who tend to have increased infection risk rates at baseline. This is by no way an exhaustive list of our DMTs and potential adverse events or interactions but some examples to show how comorbidities can inform our DMT choice.

**Dr. Turck:**

And staying with you for just another moment, Dr. DiMauro, why is it so challenging to determine when to discontinue DMTs? And how would you recommend navigating the contours of that decision?

**Dr. DiMauro:**

That's a really great question. So we know in our learning that the risk-benefit ratio of our MS DMT treatments evolves for the individual patient over time, and the beneficial role of DMTs in patients later in the disease course with no evidence of active inflammatory disease becomes less clear. So given the shift to a more significant risk profile with likely diminished biological benefit for DMT use as MS patients age, transitioning older MS patients off their DMT has become a more common issue today in clinical practice. I will say there's no clear consensus guidelines on this, and I think this is in part why this decision can be so challenging. Ultimately, I think there's a need for very careful patient selection if you are considering discontinuation, and this is going to be a very individualized approach for each patient case. So factors such as age, MS stability, your patient's personal preferences, out-of-pocket costs of medications potentially, and DMT side effect profile in conjunction with the patient's comorbidities are all going to weigh in.

In terms of navigating this decision, as mentioned, there's likely going to be different opinions in the field depending on who you speak to, but generally, if you have an MS patient that is approaching their 60s or even in their sixth or seventh decade of life and they've been stable on their DMT with no clinical or radiographic disease activity in at least the past five years or so, then this is a topic that I think is reasonable to be introduced to your patient as a potential management strategy in the years to come, with of course being careful to counsel those patients on the potential risks of MS activation.

Another point to consider is discontinuation with agents that have rebound potential, such as the S1P receptor modulators and natalizumab, and sometimes you may even see a deescalation approach be employed, although there's uncertainty that deescalation to a lower efficacy agent ultimately confers more safety.

And the last thing I would say overall is it's important to note that discontinuation of DMT still requires close ongoing monitoring, both in the neurology clinics as well as radiographically, for ongoing MS disease activity surveillance.

**Dr. Turck:**

For those just tuning in, you're listening to *On the Frontlines of Multiple Sclerosis* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Drs. Carol Swetlik and Dr. Kimberly DiMauro about how we can best treat older patients who have multiple sclerosis, or MS.

Coming back to you now, Dr. Swetlik, let's talk about lifestyle and wellness interventions for patients with MS. What role do factors like exercise and smoking cessation play in slowing disease progression in older adults?

**Dr. Swetlik:**

I think this question is so important as it really emphasizes both the need and the benefit of continued coordinated care between the neurologist, the primary care clinician, and all members of the care team for the MS patient. We know that wellness and preventative care are critical aspects of MS management in older adults, as many of these interventions are disease-modifying in their own right and as many patients enter the secondary progressive phase of disease and may look to begin discontinuing DMTs, as Dr. DiMauro mentioned. These factors become especially critical for helping patients maintain a functional status and have a high quality of life.

Smoking, in particular, is associated with accelerated brain atrophy and disability worsening. Following smoking cessation, the rate of patient-reported motor deterioration actually slows and eventually can match those who have never smoked. In other words, quitting now allows patients to course-correct and slow down their rate of disability progression. And I bring that point to the clinic often when patients are debating if it's worth trying to quit just one more time or if it's worth trying to quit now later in life to help counsel and motivate them regarding the impact of that decision.

Exercise has also been a topic of significant focus driven by very encouraging results across a number of smaller studies in patients with MS. Progressive resistance training, for example, has led to improvement on both MRI measures, such as cortical thickness, and improvement in clinical measures of motor and cognitive function. And while the precise mechanism isn't really well known, about half of

the available studies of physical training in people with MS do demonstrate improvement in vascular risk factors, and so exercise may be considered a component in the therapeutic management of those vascular comorbidities as well.

**Dr. Turck:**

Now, before we wrap up our program, I'd like to ask each of you one final question. Starting with you, Dr. Swetlik, are there any emerging therapies or research directions that you think hold promise for improving outcomes in older adults with MS?

**Dr. Swetlik:**

I do. I think there are many exciting developments going on in the field right now that are particularly relevant to older patients with MS. In general, there is a growing awareness of a need for data surrounding use of DMTs in older populations with a need for better representation in clinical trials, which we are starting to see as enrollments are expanded beyond age 55 for many trials of therapeutic agents. There is a huge need for therapies for secondary progressive MS, which overlaps quite a bit with this patient population. The phase III HERCULES trial of a compound called tolebrutinib did show significant effect on disability accumulation in a non-relapsing secondary progressive population, and excitingly, patients were more likely to have improvement in their clinical status as well compared with placebo. So while early, this is a hopeful trial, and the MS community is on the lookout for updates regarding approval and availability status, hopefully in the near future.

**Dr. Turck:**

And, Dr. DiMauro, I'll turn to you for the final word. If there is one key takeaway from your review that you hope neurologists incorporate into practice, what would it be?

**Dr. DiMauro:**

Yeah. I think, as we discussed, an important takeaway here is that MS in older adults appears to be increasingly prevalent, so this is something we're going to continue to encounter more and more in our clinics. And there's multiple considerations in this population that I feel are unique, such as their level of medical comorbidity and the role of immunosenescence in aging, as well as the choices on DMT length of treatment. And these are all important in this population when it comes to diagnosis and management. I also think it's critical to remember that these patients really require lifelong MS care, so even if MS-specific DMT isn't being actively prescribed, monitoring and ongoing symptomatic management is still of really great importance for older MS patients.

**Dr. Turck:**

Great insights for us to consider as we come to the end of today's program. And I want to thank my guests, Drs. Carol Swetlik and Kimberly DiMauro, for joining me to discuss strategies for optimizing the management of multiple sclerosis in older adults. Dr. Swetlik, Dr. DiMauro, it was great having you both on the program.

**Dr. Swetlik:**

Thank you.

**Dr. DiMauro:**

Thank you so much.

**Announcer Close:**

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