96| Polypharmacy in Older Adults – With Dr. Mike Steinman and Dr. Matthew Growdon

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NAVIGATING NEUROPSYCHOLOGY

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Speakers: Mike Steinman, Matthew Growdon, Steve Correia, John Bellone, Ryan Van Patten

Intro Music 00:00

John Bellone 00:17
Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior, brought to you by INS. I'm John Bellone...

Ryan Van Patten 00:26
...and I'm Ryan Van Patten. Before we get into today's episode, we have a quick announcement for you about the upcoming Minnesota Update Conference. Dr. Steve Correia will make the announcement. Steve is a board certified

neuropsychologist who's a former guest of NavNeuro and the former Chair of our advisory board. He's also part of the Planning Commission and the Steering Committee for the Minnesota Update Conference. So here's Steve.

Steve Correia 00:52

Thank you, John and Ryan, for letting me take a few minutes to talk with NavNeuro listeners about the upcoming Minnesota 2022 Conference to update education and training guidelines in clinical neuropsychology, referred to as the MNC. The conference is scheduled to be held at the University of Minnesota in September 2022. Almost certainly neuropsychologists and neuropsychology trainees have been touched by the 1997 Houston Conference guidelines. Those guidelines not only helped define the identity of our field, but also set the standard for training. They have served the field well. It is time, however, to update these guidelines to address current and anticipated changes in the world's demographic diversity and advances in computer technology and data science. The primary goal of the conference is to update clinical neuropsychology's training guidelines, developing detailed and measurable competencies, incorporating technological advances, and fully integrating multiracial, multiethnic, and multicultural knowledge, skills, and attitudes within all aspects of clinical neuropsychological competence. Launching a work-intensive and product-driven conference such as this is costly. It involves paying for our venue, accommodations for delegates, meals, logistics, and technical support. The conference organizers have obtained financial commitments from several organizations and allied industries, but more is needed, especially from those who have completed their training and are gainfully engaged in the profession. Your tax deductible donation can be made on the conference website, MinnesotaConference.org and click on the Donate Now button. That's one word, MinnesotaConference.org and click on the Donate Now button. The website allows you to donate in your name or anonymously. You can designate your donation in honor of someone who has been important in your training and career, for example a mentor, colleague, family member, or departed loved one. The Planning Commission and Steering Committee for the conference thank you in advance for your contribution to this important undertaking. Again, please consider contributing at MinnesotaConference.org and thank you.

John Bellone 03:26

And now for today's episode. Today we talk to two physicians, Drs. Mike Steinman and Matthew Growdon about polypharmacy in older adults. Mike Steinman is a geriatrician and a professor of medicine. Matthew Growdon is a geriatrician and research fellow, soon to be an assistant professor. Both Mike and Matthew are at the University of California San Francisco. They both do research in polypharmacy and deprescribing in older adults, as well as clinical work seeing geriatric patients.

We are excited to have their expertise as physicians, and they provide great information on the positives and negatives of various psychotropic medications in older adults. Throughout the episode, they focus on cognition and mental health and they discuss how these issues apply to neuropsychologists. So now we give you our conversation with Drs. Mike Steinman and Matthew Growdon.

Transition Music 04:26

John Bellone 04:36
All right. We're here with Mike Steinman and Matthew Growdon. Thanks for joining us on NavNeuro, we're excited to have you here.

Mike Steinman 04:42
Thanks for having us.

Matthew Growdon 04:42
Thanks so much.

John Bellone 04:42
There are multiple definitions of polypharmacy such as the use of more drugs than may be clinically indicated, the use of two or more drugs to treat a certain condition, the use of five or more overall medications, etc. Can you talk about the pros and cons of the different definitions and what you prefer?

Matthew Growdon 05:03
I think it's a really good question to kick things off. As you alluded to and I think as you read across the literature, there are a lot of different ways that people define this term “polypharmacy”. The most common [definition] that I've seen is the notion of taking five or more medications chronically. Then sometimes [there is] this notion of hyperpolypharmacy, with a cut-off of 10 [medications]. But I think your question implies that there is this notion that there are a lot of different ways to define it. One thing that I learned from Mike in a commentary he wrote from some years back was that it's actually not really that the numbers themselves are the enemy, but that we're really interested in getting at the medications themselves - whether they are unnecessary, whether they're ineffective, and whether they're harmful to patients. The numbers are really important for the studies and I think, depending on the context, using one that is within a category could be useful. So you might say that there's central nervous system polypharmacy and some people define that as three

or more meds in the CNS category, that might be especially interesting if you're looking at a patient population with those sorts of problems. But I think matching the number to whatever study or clinical use you're using is paramount. I guess the definitional confusion can also lead to a wide variety of studies that aren't exactly all using the same definition, which can be challenging in and of itself. Mike has a lot more perspective on that. [To Mike] I'm not sure if you want to add anything.

Mike Steinman 06:32

No, I fully agree with what you said. The one thing I might add is that polypharm basically just means a lot of meds. And then the question is, “Why do you care?” So if you're thinking from a pharmacologic perspective and the risk of things like drug-drug interactions or adverse drug events, clearly, the more medications, the worse. If you're looking at the ability of the patient to adhere to the medications, or their happiness, or their willingness to take medications, or their lived experience with taking medications, then you might end up with a different number. This can be much more patient specific. For some patients, four medications might be overwhelming. And for other patients, they might take 12 or 13 and be doing just fine. So my personal way of thinking about it is not to get too hung up on any one specific definition about a number, but just to think, “Why do I care about it?” And then think, "Is the number of the medications that the patient is on really meeting their needs or not from that specific perspective that I'm trying to focus on?"

Ryan Van Patten 07:38

Thank you. Despite this variability in definitions, the research I've seen suggests that polypharmacy is on the rise in the US and elsewhere. So how much has polypharmacy increased in the last 20 to 30 years? And do we know why?

Matthew Growdon 07:55

There was a really good study in JAMA Internal Medicine a few years back that showed that in a nationally representative sample, going back to those definitions, using the most standard definition of people taking five or more medications, that around 2005, 2006, about half of older adults in the United States were meeting that definition. It had risen to about two-thirds of older adults by 2010, 2011. That included the use of over-the-counter and dietary supplements, which have also been on the rise along with prescription medications. I think we'll probably delve into a lot of the reasons today but, demographically, the common causes are felt to be the general aging of the US population and also the rise of multimorbidity and overlapping reasons that people are taking chronic disease modifying medications for a host of common conditions that they may have all at once. Those are standard reasons. Then I think there's a whole tranche of other cultural things around our prescribing culture, around fragmented care in terms of people seeing potentially

many doctors or prescriber, that aren't necessarily thinking holistically about their overall medication use but kind of adding ad hoc. We can delve in as we go into some of the deprescribing work as well and to some of the other behavioral and psychological reasons that people may be taking more medications than either they want to or that they should be taking. But, yeah, it's definitely on the rise not just here, but pretty much across the world and definitely in European literature as well that I've looked into.

Ryan Van Patten 09:39

And Matthew, as you had clarified earlier, there's polypharmacy but then there's bad polypharmacy, and we can distinguish between those sometimes called inappropriate polypharmacy. Just because an older adult is taking multiple medications doesn't always mean that that's the wrong decision or clinical decision for that person. So, we want to make sure to, as best as we can, try to identify iatrogenic effects when they do occur. Do we know how much of a problem inappropriate polypharm is in the US and around the world beyond simple polypharm?

Matthew Growdon 10:15

You have two card-carrying geriatricians today, so a lot of my answers are targeted in older adult populations. My sense and from my read of the literature is that potentially inappropriate medication use is also highly prevalent and likely increasing, along with overall medication use. One of the things that studies have shown is that - and this is not a surprising finding, per se - but the more medications that you're taking, the more likely that you are going to be on one of these potentially inappropriate medications that we'll delve into later. So no matter what definition you're using, if the overall medication use is increasing, just across the population there's the likelihood that there's going to be some percentage of people who are taking these so-called PIMs, or potentially inappropriate medications. I think as to giving you an exact number, it often comes down to these definitions of how you are defining potentially inappropriate medications. But as a broad first look for this question, I've seen anywhere around half of older adults are taking one of these potentially inappropriate medications. But I think another thing to think about is that we don't want to just focus on overmedication, and that some of these adults may actually also be underutilizing the right medications. So, though we feel strongly that polypharmacy is often problematic and that you have to be thoughtful, it's not in and of itself the problem. Sometimes it's the mixture of medications. Maybe there are ones that they should be on that they're not on, and certainly there are ones that aren't appropriate that they are on.

John Bellone 11:53
In terms of the reasons for overprescribing, Matthew, you had mentioned a few of them before. Mike, I've heard you say in another podcast that inertia is a big factor here and the fact that, over time, medications seem to accumulate. There's a lack of coordination. I wasn't sure if you wanted to add anything there.

Mike Steinman 12:12
The one good analogy, which actually learned from Matthew, is that medications are like barnacles.

Ryan Van Patten 12:20
[laughs]

John Bellone 12:20
[laughs]

Mike Steinman 12:20
Sail through the seas of life, lots of stuff sticks to you. And once it's stuck on, it's really hard to remove. [laughs] So, for me, that's been a nice visual image because it really reflects the sticky nature of medications and how they can accumulate and really potentially drag you down over time. To really scrape off those barnacles can be worthwhile, but it is not a small thing to do. So it definitely requires dedicated effort and skill to figure out how best to kind of clean off your own hull.

Ryan Van Patten 12:55
[laughs]

John Bellone 12:55
[laughs] Yeah. I love that.

Matthew Growdon 12:57
I'll jump in just to make sure it's correctly attributed. Hopefully I'm not doing this incorrectly, but I believe that Jerry Avorn, who you and your listeners may know as a formative figure in this pharmacoepidemiology field, I think he may have come up with the barnacle idea and then incepted it into my mind at some point.

Ryan Van Patten 13:14
[laughs]

Matthew Growdon 13:14

But it is very apt. One thing I find really helpful is to think about polypharmacy, overprescribing, and then later as we get into deprescribing as more of a social, socioecological model of all these different layers of things that lead to this outcome of overprescribing. Everything from the culture, like Mike was talking about in terms of inertia, but also the lack of nonpharmacologic options, and we're going to talk about that later. They exist, but people often can't get access to them or we don't make it easy for them to get them. We have a culture that is very attuned - we have a huge drug industry so there's a lot of power behind medical options. So everything from that cultural level to a more organizational level. We have a lot of disease guidelines that are disease focused. So they say, “You have COPD, you should be on all these things. You have depression, you should be on these things.” But they don't say, “You have six conditions, and the Pareto optimal number of medications for you to be on is these ones.” Then it gets down to more personal things like what is the doctor doing? What is the prescriber or pharmacist doing? Do they ever take people off meds? Does the patient have capacity and cognition? There's all sorts of layers and I think together they lead to this end result.

John Bellone 14:33

It's an excellent point. I want to talk a lot about deprescribing a little bit later. Before we get there while we have you card-carrying geriatricians, like you mentioned, Matthew, I wanted to ask about the age-related changes that lead older adults to become particularly vulnerable to polypharmacy compared to younger adults.

Matthew Growdon 14:53

I think there are a myriad ways in which the body changes as people age that has a lot of bearing on how medications are both acted on by the body and how they act on the body. We talked about pharmacokinetics in terms of when you take a drug, what a body does to it in its processing. There are a lot of major changes with aging in terms of how the liver metabolizes those drugs, sometimes into their active agents. A really key one is how the kidney clears those drugs. One of the big takeaways in that kind of central preceptive prescribing in older adults is the notion that medicines that in middle life may have a certain half life will often have a much longer half life in people who are older. So, for your readership, a great example is something like diazepam can have a much longer half life in an older adult showing up in an emergency room. It could be significantly more than if they were 40 or maybe when they started the medication. And then similarly, in terms of pharmacodynamics, which is the word we use to describe how the drug is acting at the level of the receptors, those things can also change so that people are more exquisitely receptive to or responsive to medications. So that things like the dose that you would give someone in the middle of life may have a much more potent

effect in terms of some of these downstream harms. We often think about this notion of starting low and going slow in geriatric prescribing. So using the lowest possible dose and going up as slowly as possible just to take into account some of these changes.

John Bellone 16:33
Can you talk about some of the negative outcomes associated with polypharmacy in older adults?

Mike Steinman 16:39
John, before we get there, I just want to add one quick thing to what Matthew said.

John Bellone 16:42
Sure.

Mike Steinman 16:43
I think another key and often underappreciated difference in risk of medication side effects for older and younger adults is the concept of frailty, which effectively means decreased ability to adapt to a stressor. The analogy I like to think of is if you have a healthy 20-year-old and they're standing up and you give them a big shove, they won't fall down. They've got good muscle tone, they've got good balance, they'll maybe stumble back for a sec, but they'll stay upright. And then you do the same to a weak and infirm 90-year-old, it's likely they'll fall down with the same degree of pushing because their balance is less and because they have less muscle strength to compensate and adapt to that stressor. The same thing happens with medication. Say you give a healthy 20-year-old a medication that's prone to make them lightheaded. They might feel a little annoyed when they stand up and they get lightheaded, but it's not such a big deal. [If] you do the same thing to an older person who's got impaired blood pressure regulation, whose balance is off, whose cognition is not so great, and that person, when they take that medication, they're more likely, even with the same degree of symptoms, to fall down and break their hip. It's this general sense of frailty and decreased ability to react to stressors that really makes it so that even if a drug has the same degree of negative effect, its end result for the person can be much more severe.

Ryan Van Patten 18:10
I love that analogy for frailty. The push, like you described, really brings it home. Of course, frailty is strongly correlated with age, but not perfectly. You could have a 60- or 65-year-old who's quite frail and a robust 85-year-old, relatively speaking. Frailty is a good way to think about how people react to medications. So…

Matthew Growdon 18:34
You guys have got me - oh, sorry.

Ryan Van Patten 18:36
No, go ahead.

Matthew Growdon 18:36

I was just going to add one other thing that I find really relevant clinically and have wanted to start to explore from a research standpoint as well. That, as people age, their social circumstances will often change and the medications that we put out into the world maybe thinking that someone has a caregiver to help them or thinking that they have a well-kept place to keep track of those meds, or that they have the cognitive wherewithal to use medications that have narrow therapeutic indices, like anticoagulants or insulin, or that they can see and manipulate the pills or manipulate the syringe. Those things are all dynamic, and they're changing. So when I write a prescription that comes with all that. On top of just why am I giving this medicine for the medical reason, I'm often much more worried as a geriatrician about, are they going to be able to adhere to this safely? If they have a side effect, are they going to be able to get the care they need? Are they going to be found two days later because they were hypoglycemic and no one was there to find them, which, unfortunately, is an admission I've seen a number of times.

John Bellone 19:43

I think that's excellent. While we're on the topic of adherence, that's something that's come up for us too in how we think about this and in terms of polypharmacy. The more medications, the more difficult it will be for a patient to maintain the regimen. If they have to take it morning and night and at meals, it gets more and more complex. I know geriatricians think about this quite a lot. Do you think other physicians are also having this on their mind? Or not so much?

Matthew Growdon 20:11

I can't speak for all physicians, but I think it writ large I do think there is not enough thought given to the medical complexity of the regimens that we send people on. Part of it is to adhere to the meds to get the benefit from them, but another that I think about a lot is also the medicalization of people's lives and the amount of the day that is spent adhering to meds that maybe could be a little bit simpler. So instead of three times a day, maybe you could get down to two times a day. I think, in general, it would be good if we could generalize this notion of looking at the whole med list, but the incentive structure isn't necessarily there. The subspecialist doesn't own the meds that some other subspecialist is prescribing. So I think there

can be a lot of deference to the regimen as it is. It takes a holistic provider perspective to start thinking about simplifying it or taking those sorts of matters into consideration.

John Bellone 21:12
How about some of the negative outcomes associated with polypharmacy in older adults?

Matthew Growdon 21:16
I think there are a lot of associations that have been made in the literature between different definitions of polypharmacy. But, again, let's use the five or more [medications] as the mean definition and the number of adverse outcomes. So these range from everything like you were talking about adherence to medications to becoming harder to do things that are very important to older adults and their quality of life and well being. Polypharmacy has been associated with falls, it has been associated with ED visits and hospitalizations, and hip fractures. There's a lot of data there. I know we'll talk a little bit about how it's difficult sometimes to know exactly if and how polypharmacy is causing these things or not. Mike, I welcome your perspective on this, but I think as a newbie into the field, I was like, "Oh my gosh, I want to find these associations." I think it can be a little bit harder to both add to what's already known and also to really delineate why it is. But the association is quite strong across a number of studies.

Mike Steinman 22:24
That's a really interesting topic. It's a little hard to pin down because, of course, the people who end up taking lots of medications tend to be sicker than the people who don't. So how can you tease that apart? You can't do a randomized trial where you randomize somebody to take 20 meds and someone else to take two. But that said, I do think there is really something there. The things that lead me to come to that conclusion are, first of all, if you look across a series of studies for all sorts of bad outcomes in older adults that are related to medications, far and away the strongest risk factor across this whole series of studies is the number of medications. It is more strongly associated with bad outcomes than age, or number of comorbidities, or renal function, or any of these other factors. Is that proven causality? No, but it certainly strongly suggests there's something there. Then the other thing, which is a fascinating study - I mentioned before that we can't randomize people to take fewer drugs versus amending drugs, but you can do that with animals. There's actually a colleague, Sarah Hilmer in Australia, who did this amazing study where she took mice and she randomized the mice to either getting no drugs or getting a cocktail of five commonly used drugs in people - stuff like a beta blocker or ACE inhibitor. I don't remember the exact drugs, but things that people commonly take, [like]

statins, in appropriate mouse doses. She just randomized people to mouse polypharmacy versus mouse no-polypharmacy. The mice who got the cocktails of these commonly used medications did a lot worse. I don't recall offhand the exact outcomes, but there were noticeable differences in clinically meaningful outcomes between those mice. That does comport with other studies which suggest that there was something synergistic about the effects of multiple medications that seem to result in people having worse outcomes across the board in a way that's hard to pin down to any one medication. There's probably hundreds of different interactions that occurred, some of which we understand [and] some of which we don't, but it does suggest that there is something real about increasing numbers of medications truly being associated with harm. [It] doesn't mean you shouldn't be taking many medicines, a lot of them have benefits, too. But it does provide a note of caution.

Ryan Van Patten 24:48
Yeah.

Matthew Growdon 24:49
I think it is a very interesting epidemiologic question. Is polypharmacy causing these outcomes? But, also if you just step back from that, you can say it is definitely a very strong signal of risk. So, clinically, the more meds someone's on, the more - and, you know, I will routinely see people who are on 20 or even 30 meds. My level of risk goes much higher. I'm much more concerned about either adding new meds to them or trying to figure out how to be thoughtful about taking them off of medications.

Mike, just to add a finer point to the Sarah Hilmer study, I think for the audience of this podcast, one of the five meds that they put those mice on was citalopram, so they did have a common SSRI in there. The outcomes were things like mouse mobility, mouse balance, mouse strength. To amplify what Mike was saying, all of those things are, as are so many geriatric syndromes, they're great integrators of many body systems. It's not just a disease that one drug is treating. Like [for] mobility, you need to have neurologic function, you'd have to strengthen your muscles, you need to have energy. There's something about this complex over-interaction of multiple drugs on multiple pathways that is rolling up to affecting these global functions like mobility, or balance and strength. So, a lot to be worked out, but I think that mouse study is really a great proof of concept.

Ryan Van Patten 26:17

Fascinating. We have some evidence in that direction. We can't "prove causality," and it probably goes both ways for different people. For some people, the complex interactions and side effects are causing negative outcomes. For those same

people, or other people, a lot of medications as a marker of medical complexity and being sicker. But, yeah, the mouse study is very interesting. I'm wondering if we know anything about health disparities in polypharmacy? Like, are people of color and/or people of lower SES experiencing more especially inappropriate polypharm than people from other groups?

Matthew Growdon 26:57

I think this is like a really, really important area of inquiry. I think it can be a little bit complicated because you also have to think about the background of access to care and whether people are getting equitable access to care because in some way, to be prescribed, you also have to be accessing the system and being exposed to prescribers who can give you the medications. I have come across some really interesting work that suggested that there may be disparities, specifically in an interaction between [groups]. In one study looking at African American versus white respondents and then also looking at their lower versus higher socioeconomic status, finding an interaction in that people who in that study were both African American and lower income had a higher risk of polypharmacy. But I think, in general, that there's also been a history of literature looking at whether there are disparities in whether people are being put on newer or better versions of meds. There's some data to suggest that African American patients that were in these studies were less likely to receive the new or more effective, simplified medication combinations and they were kind of on more legacy type medications. I think there's still a lot of questions to be answered there. I'd definitely be interested in Mike's perspective, but that's some that I've gleaned from my reading.

Ryan Van Patten 28:24

Mike, you're welcome to add anything there or we can move on. Whatever you prefer.

Mike Steinman 28:29

I think the only other thing to say is it's a super complex issue, as Matthew was alluding to. Some of the literature, particularly some of the more early literature, suggested in some ways that older adults who came from historically disadvantaged backgrounds might have been in some cases less likely to get potentially inappropriate medications because they were also less likely to get appropriate medications. They were just less likely to be prescribed across the board because of discrimination, lack of access, etc. So it sort of cuts both ways. The other thing that's, I think, an important thing to consider is it's probably not just an issue of being able to access clinical care, although that's certainly part of it, or subtle discrimination but that's likely part of it too. But also issues of trust between

patients from different communities and the healthcare system. So I know, for example, that some people from African American and in some cases other minority communities are, for example, less likely to like hospice or comfort care than people from Caucasian backgrounds. Part of that might be issues of trust in the healthcare system to let your loved one go or withdraw care be perceived as doing less. So the same can also extend to medications because one of the key concerns about deprescribing is that you're taking something away from someone or that you have to proceed by not caring for them because you're not giving them something. Of course the intention is the opposite, but it is understandable that it was perceived that way. So whether or not that results in more or fewer inappropriate medications in people from disadvantaged backgrounds, it's hard to say offhand, but it is a really important issue to think about when we do prescribe. So much of it is mediated by the relationship, and that's something that's important to be attentive to.

Ryan Van Patten 29:13

Let's move into deprescribing now that we've set the stage. What can healthcare providers do about inappropriate polypharmacy? Tell us about some of the best interventions to deprescribe and reduce harm in older adults.

Matthew Growdon 30:42

I'm really glad that we're switching into this part. I would say, as a relatively new geriatrician in clinical practice, one of my most rewarding things I do clinically is the act of deprescribing. I think it can be very hard for some of the reasons that we're talking about, but when it is done successfully and with the right patient interaction, it can be a very rewarding interaction and one that patients and families are grateful for. But a couple of motivating thoughts. One is that there's been some very interesting work using national surveys that has shown that a lot of older adults, in fact, like more than 9 out of 10, are willing to stop medications and well over half of them want to reduce their medications. So, this is definitely an opportunity area where we know that potentially inappropriate polypharmacy is common. We know that polypharmacy is common and now we also know that people, at least in terms of reacting to a survey, are interested in addressing this. The broad scope of literature would suggest there are definitely ways that we can get people to come off of medications. There have been lots of different ways that people have taken a crack at this, whether it's general medication reviews - so set someone up either with the prescriber or pharmacist who does a very comprehensive look at all their medications and then give some sort of feed out of these are the potentially inappropriate ones and these are ones you can come off of. So that's one tranche of interventions. Then another tranche is more category by category. I know we're going to talk today about some that are specifically in the psychotropic categories,

but there are protocols, whether it's proton pump inhibitors or benzodiazepines, where there are ways that different people have studied getting people off of these medications. I think the literature is quite heterogeneous. There's probably the strongest evidence in the nursing home setting where we geriatricians work that we can make a difference not only in getting people off of potentially appropriate medications, but that we might be able to prevent falls, that we might be able to prevent hospitalizations, or even mortality in the nursing home population. I think the jury's still out in a way in terms of at the hospital level and especially in the outpatient level. There's more conflicting data about how these different interventions work. One takeaway, from my perspective, is that we often can show in these sorts of studies that we can reduce the number of potentially inappropriate medications that people are taking, but we haven't yet shown that it has another downstream clinical benefit. We always want to get to things like mortality or reducing hospitalizations. So we're moving the number in some cases, but it's not clear yet that we're reducing falls or that we're reducing hospitalizations, if that makes sense. Mike, I don't know if you want to talk a little bit about some of the randomized control trials in this area. I'm also happy to, but there's been some really interesting randomized controlled trials from in particular a group in Canada working on benzodiazepines and looking at other kinds of high risk medications, antidiabetics and things like ibuprofen, that have shown that these team approaches, not just focused on prescribers but actually using pharmacists and sending things out to patients directly, hold a lot of promise to activate people to come off medications.

Ryan Van Patten 34:13

This is very exciting work. I love the idea of deprescribing as an intervention. Prescribing the right medication can be an intervention or a treatment, and deprescribing the wrong medication can be a good intervention, too. So the work you guys are doing in this area is great. Mike, I was hoping to get you to talk a little bit about the US Deprescribing Research Network. I believe you're the co-PI of this. I'm curious what this organization is and what its purpose is.

Mike Steinman 34:42

Great. I'm always happy to talk about the US Deprescribing Research Network. [laughs] As you mentioned, I am one of the co-Principal Investigators of it, working with my close colleague and friend Cynthia Boyd at Johns Hopkins. The US Deprescribing Research Network is an NIH-funded research network that is focused on enhancing the quality and the quantity of research on deprescribing specifically for older adults. This is in response to a growing interest and concern about overmedication and the opportunities to deprescribe. There's this mismatch between the growing awareness that there's something we need to do and then

figuring out how best to actually get it done, because it doesn't get done very often. There's clearly a gap between where we should be and where we are right now. So the goal of the Network is to stimulate research and support and promote research that can help us to answer those questions. So some of the things that we do through the Network are to help support early stage investigators through educational programs by awarding pilot grants, by providing different supports and activities, and having meetings and webinars that will provide people information about best practices and the current state of science around deprescribing, and then also help people form collaborations and share ideas and knowledge and skill sets with one another to help all of us advance our work concurrently. Another big pillar of what we do is really to make sure that we're representing the voices of stakeholders. The stakeholders include older adults and their caregivers, and they also include people like health systems, leaders and policy makers, and the government because they are very important in this process as well. A lot of research historically has ignored the perspective of stakeholders. Doctors, like me, go off and do our doctor things and we think we kind of know everything, but we are often missing the boat. So one of the things we're really trying to do through the Network is to bring in those people who can represent those perspectives and make sure that they are infused into the research that gets done. Although the Network is not focused specifically on psychotropic medications or people with, for example, cognitive or mental health issues, clearly that is a very big topic in which a lot of our investigators have a strong interest.

John Bellone 37:13

That's really exciting work, that Network. I've also heard about some computerized decision support systems to assist physicians and pharmacists in determining potential interactions and adverse effects of medications and potentially reducing polypharmacy. I've seen some discussion of combining the systems with relevant patient data [and] genetic profiles to achieve some kind of precision medicine in prescribing. Can you tell us anything about what you know about this area?

Matthew Growdon 37:43

Mike, please chime in later if you have more insight on this, but I think there definitely has been promise in computerized decision aids. In the hospital setting, they've definitely been shown to reduce serious medication errors. I know clinically, I work mostly in the inpatient setting nowadays, and I find it very helpful when I'm working with older patients in the hospital to know if I'm adding medication or reviewing medications, what the relevant drug-drug interactions are. Sometimes there can be a nuisance factor for prescribers, of clicking through things in their EHR interface. I think that has been an Achilles heel of some of these things in terms of whether they really get to some of those barriers that Mike was referring to

earlier in terms of inertia. If people encounter things in their prescribing practice that are annoying, like a little alert that says, “Don't do this", some of the data on that more broadly outside of the hospital has, I think, been more mixed in terms of whether it really makes a difference. I know, for example, [there are] some studies in long-term care facilities that these sorts of clinical decision supports didn't actually reduce the rate of adverse drug effects, which is kind of the whole point of the intervention in a way. So I think it has great promise. And, obviously, we've gone from paper charts not that long ago to a fully computerized system in a lot of ways, and so there's a great promise there. But it's really in a way that it needs to meet people behaviorally with the way they practice and lower the barrier to how much work they're doing to really lead to uptake. Mike, I'm not sure if you have any other thoughts.

Mike Steinman 39:27

Maybe just echoing what you said. My understanding of the literature is that these decision support systems tend to have small effects on overall quality prescribing, but less than we would all want or hope that they would. I think maybe some of the reasons why are that they are good if I want to prescribe a drug at a certain dose and then I get this big flag "Oh, your patient's kidney function is such and such and that dose is too high," you know, it's fairly easy. "Okay, give a lower dose." But if you've already made the decision to prescribe a medication, I've already had that internal conversation in my head and then I tried to enter it and I got some flag about it. Well, unless there's like some crazy bad interaction, a lot of times I might just want to go and prescribe it anyway. I've already made the decision, it's too late to intervene. Or through a lot of other factors that those electronic health record systems are not able to address. For example, is my patient going to end up taking three times the dose of the medication I prescribed because they don't understand the directions? No EHR is going to help with that, at least as they're currently configured. So I find they're useful for addressing very certain, specific technical aspects of prescribing, but so much of prescribing incorporates these whole other domains that this is ill-equipped to address The global effects on quality tend to be fairly small as a result. It doesn't mean that they're not important and there's not going to be a one size fits all solution, but maybe this is one of many different things that we need to be doing to really reach our end goal of improving prescribing quality and outcomes.

Matthew Growdon 41:05

There's some really exciting work bringing in more behavioral economic type theory into these computer decision aids. So that it's not just kind of a nanny thing that says like, "Don't do this!" or "Watch out for this!", but it's kind of like "Other doctors do this!", or, you know, "These adverse drug events are going to happen" or other

incentives to get human beings over their inertia or to jog that decision making that Mike's talking about. I know of at least one trial of a more pragmatic way of rolling this out in a large health system. So it'll be interesting to see if it leads to anything different because though there's a lot of promise, I don't think we've really gotten there with the paradigm.

John Bellone 41:47
It'd be interesting to see how that unfolds over the next few decades for sure. There's lots of applications. I want to talk about the Beers criteria and, correct me if I'm wrong Mike, I believe you were involved in the 2019 revision of that.

Mike Steinman 42:00
Yes, I'm one of the co-chairs of the criteria guideline panel.

John Bellone 42:05
Great. Could either or both of you tell us a little bit about it? Just the elevator pitch of the Beers criteria, utility, and purpose?

Mike Steinman 42:15
Sure, I can maybe take that one. The Beers criteria are designed to be a list of medications that are potentially inappropriate in most older adults. It doesn't mean that any medication that's on the list is bad for every single human adult who has ever graced this planet. It just means that for many older adults, these drugs are not good choices. The reason they're not good choices is either they're ineffective, that their harms exceed their benefits, or there are readily accessible, better alternatives that have a better balance of benefits and side effects. So some of the drugs that are on these criteria include things like benzodiazepines for older adults, because we know that benzodiazepines and also the Z drugs, things like zolpidem or zopiclone, these other sleep aids have serious side effects - falls, worsening cognition, motor vehicle accidents, etc. We also know they're not super effective in actually improving sleep. And finally, we know that there are alternative treatments that can help people sleep better and are safer, some of them pharmacologic and most of them nonpharmacologic. That is a good example of how a drug gets on this list and why it's on the list. The most well known part of this list is for drugs that are just inappropriate or potentially inappropriate for older adults, or just in general. There are other tables in this multicomponent series of criteria that are focused on people with specific conditions. So, for example, for older adults with falls, there's another list of medications that are particularly important to avoid because they increase the risk of falls. For older adults with heart failure, there's other drugs to avoid because they can worsen heart failure. There's some other aspects in there

about drug-drug interactions and drug renal function interactions that we should be worried about for older adults. But the key idea behind the list is really they should be viewed of - if you ever see a patient taking one of the drugs on the list or thinking of prescribing one, it doesn't mean you should never prescribe that medication or always stop it, but it should set off that little warning light in your head, like "danger ahead." Does this patient really need this medication? Is it really the right choice? Now, the answer might be yes. But it should stimulate that internal conversation to really take a close look and see if that medication is the right choice [or] if there's something that's going to be safer, more effective to help the patient. And, like I said, the alternative may be pharmacologic or maybe nonpharmacologic.

Ryan Van Patten 44:49
That's consistent with how I've heard you describe the Beers criteria, Mike. As a yellow light, not a red light. It's not a hard stop, it is raising a warning flag, which I think is a great analogy.

Mike Steinman 45:00
Orange light, maybe. [laughs]

Ryan Van Patten 45:01
Orange light. [laughs]

John Bellone 45:04
Well, we'll talk a little bit more in a second about the different classes that are potentially relevant to neuropsychologists. I know, Mike, you mentioned benzos, the non-benzo sedatives, the Z drugs. I know anticholinergics and antipsychotics are also on the list of medications that geriatricians love to hate. I want to talk about those in a minute. But is there anything you wanted to say about the STOPP/START criteria and the Medication Appropriateness Index and how they might differ from the Beers criteria?

Mike Steinman 45:35
Sure. So the STOPP criteria is the same animating idea behind the Beers criteria. Beers criteria were developed in the US, STOPP criteria were developed in Europe. But it’s the same general idea - here's a list of potentially inappropriate medications. The main difference between the two criteria is that the STOPP criteria tend to be a little more clinically nuanced, and the Beers criteria tend to be a little more broad in a way. One of the reasons that Beers criteria have been designed in a way that makes them amenable to being implemented in large scale health systems, whereas the STOPP criteria tend to be a little more clinically nuanced and some of

that nuance is sometimes harder to get out of a health system. So they're both good. There's a lot of drugs and clinical scenarios that are common across the two, there are some differences. But I think, globally, they're much more similar than different. There are these other ways of measuring medication appropriateness. For example, the Medication Appropriateness Index tends to be a research tool, not really a clinical tool. The Medication Appropriateness Index basically requires an expert review of each of a person's medications and you're graded on the score of is this medication really necessary, is it causing side effects, is it meeting certain cost criteria, is it a duplicate of therapy? And so, like I said, that's been used for measuring quality in research studies, but it's not really practical for use in clinical work, although a lot of the things that go into that integrated research assessment are the kinds of things that our clinicians are thinking about perhaps in a less structured way. The one thing I'll say is also about these Beer criteria and the STOPP criteria is that they're really useful, but they are certainly not the end point. They're useful for identifying the specific list of medications that are commonly problematic, but the majority of medications that older adults take which end up causing them problems are not on either of these lists, because those are medications that aren't necessarily inappropriate for many people, but might be inappropriate for that individual person. So, for example, some anticoagulants. Anticoagulants tend to be underused, they tend to be really good medications, but if someone is taking an anticoagulant and they don't really have a very strong indication and they're bleeding all over the place, then maybe that's not a good choice. But anticoagulants tend not to be in these lists because there are many situations in which they are useful and it's hard to create a criterion around that. So just keep in mind that the Beers criteria or STOPP criteria are a good starting point for thinking about potentially inappropriate medication use, but by no means should they be the end all and be all. It's like an entry into the area, but a more holistic assessment to see how the medication is actually working for that patient, whether they actually need it, is going to go far beyond where you can get to with either one of these explicit criteria.

Ryan Van Patten 48:22

Great. We've alluded to specific classes of medications a few times now and I think probably the biggest one that comes up for psychologists and neuropsychologists would be benzodiazepines, like you had referenced. So benzos bind to the GABA A receptor and work in concert with GABA to allow chloride into the neuron. This leads to a hyperpolarization, fewer action potentials. This is an inhibitory effect. We often see benzos prescribed for anxiety and/or sleep, especially psychologists. So how well do benzos work in older adults? And when should they be used, if ever?

Matthew Growdon 49:01

I think benzodiazepines are in a way kind of a poster child for a medicine that, with older adults, we really are careful with and that jumps out whenever I look at a medication list. A couple of general thoughts on it in terms of their utility and when they should be used. I think in terms of when to use them, it really should be a very, very last resort and it should be at the lowest possible dose and for the shortest period of time possible. What we see a lot, though, is that people are on them from a legacy use. So maybe they were placed on them even chronically at an earlier time before some of the downsides of benzos were known and they've been on them for many years. A very common interaction for me is someone who says, "Oh, but I've been on it for X amount of time." And the answer is inevitably a hard one but it's basically, “You have changed over time, your body has changed. This medication, especially at the dose you were at, is no longer safe for reasons that we can get into. And there are ways to come off of it, which we can also talk about, that are not easy, but are doable.” I think there definitely is a place for them in the right patients, but I would say nonpharmacologic interventions and perhaps other drug classes like SSRIs for some of the indications you talked about may be a slightly safer and better first option. I almost never prescribe them newly but a lot of times, I'm working more on getting people off of them. I'm talking about this more as benzos not for their antiepileptic indication, but more in the psychotropic use. Then the last thing I would say is that you mentioned how they work, which is basically similar to having a shot of alcohol. So you have to be really careful when people are mixing them with either alcohol use, which is prevalent in older adults, and also with other medications that are very common, like opioids and other CNS active meds. I think benzos are amongst the top handful of drug-related deaths in the older adult population for that reason, because of respiratory depression.

John Bellone 51:15

I've seen a number of poor outcomes associated with benzos in older adults. You mentioned mortality in general, hip fractures, falls, motor vehicle accidents, risk of dependency, delirium, cognitive impairment. Of course, the causalities are not clear in many of these cases. I wanted to see if you had anything else to say about the relationship between benzos and those outcomes in terms of correlation or causality.

Matthew Growdon 51:42

I think... Oh, go ahead, Mike.

Mike Steinman 51:44

Oh, no, you first.

Matthew Growdon 51:45

I was going to say I think, for a number of those, it's pretty strong, even though like Mike was alluding to before, a lot of these sorts of studies are observational research where we have to use different sorts of research methodologies to glean from what is happening in the world, whether we think it is actually causing the problem. But I think a lot of those more short term things like falls or fractures or motor vehicle accidents, you can see clinically. Like, you can see someone showing up in the emergency department who is intoxicated from a benzodiazepine. So it's easy to assign at least on a case by case basis causality. I think that the data behind those are pretty strong. There's more debate in the literature around, for example, like the short term effects are clear. cognitively, people may become delirious when they take it or they may have lapses in their memory. But I think it's more of an outstanding question as to whether the benzos themselves cause dementia or cause irreversible cognitive decline. Part of that may be that people who take benzodiazepines may be taking other medicines that have other properties, like anticholinergic effects. There have been some fancy studies to try to really disentangle that dementia causality question, but my sense is that the short term risks are felt to be pretty strong based on the observational data.

Mike Steinman 53:03

Yeah, that's my understanding as well. One of the things I might add is that one of the challenges with benzodiazepines, as well as a lot of other drugs in older adults, is that the effects aren't necessarily super dramatic, but even small or subtle effects can add up over time. So, for example, we know benzodiazepines and the evidence is pretty strong that they increase the risk of falls and fractures and increased risk of motor vehicle accidents. But it doesn't mean that you take a benzodiazepine and suddenly you're falling down all over yourself like you're a rip-roaring drunk. The effect might be more subtle, but over time that might double your risk of a fall. But someone might think, "Oh, this is just the way I walk. This is just normal for me." Or the same thing with cognition. They might have a hard time remembering things or maybe not feeling quite as clear as they were. They might just chalk that up just to getting older. It can be very difficult to tease apart which of these symptoms are just due to age and other chronic conditions or which are due to the benzodiazepines. And particularly if people feel like the medications are helpful for them and they've already been taking them, they might be very reluctant to stop because they don't really see the harm. It's always hard to know if the harms are really there. But because those risks do exist, and we know at the population level they do exist, that, for me, reinforces the need to stop the medication even if the patient doesn't perceive that they're having problems. The final thing I'll say there is that that does need to be done as a shared decision making capacity. It will not work if I just tell the patient, "I'm not going to write that benzo script anymore. See ya later." They're

just going to find another doctor who will write that script. [laughs] So what it really comes to is a process of working with that person to help identify the potential harms and help them meet their needs, whether it be controlling their insomnia or anxiety or whatever in a way that works for them but exposes them to a safer treatment modality.

Ryan Van Patten 53:10

I'd like to follow up on the non-benzo or so called Z drugs you had mentioned - Ambien, Lunesta, Sonata. They have generic names with a prominent Z like zolpidem. My understanding is these medications are chemically distinct from benzos, but still operate at that GABA A receptor similar mechanism of action. I've read literature on the problems with them. What are their therapeutic indications and side effects in older adults?

Matthew Growdon 55:31

These drugs, as you were alluding to, I think were developed in a way to get some of the therapeutic benefit of the benzo class but maybe with a slightly different mechanism that might be safer. The data, however, over time as they've been collected, they're primarily used to answer your question, they're primarily used for insomnia - trouble falling asleep and also trouble staying asleep. That's the indication that they're approved for, as I understand it, but there have been studies linking them to some of the similar outcomes we were talking about with benzodiazepines. So things like delirium, falls, fractures, going to the hospital or going to the emergency department. And also, objectively, that maybe they don't actually provide that much improvement in sleep - how long it takes people to fall asleep and how long they stay asleep. So, in my mind, I treat them pretty darn similarly to benzodiazepines in terms of thinking of them as something that I'm worried about clinically and that I try not to start people on and I often try to get people to come off of. But for a lot of the reasons Mike was talking about, they can be challenging medications to take away because people's sleep, obviously, is very important to them. A lot of times people have arrived at these medications after trying a lot of other things, so they may feel like there's nothing for them if you take it away.

Mike Steinman 56:55

There's a common misconception, like Matthew was saying, that they're safer than benzodiazepines, but they're really not. They have a similar risk profile. The way I like to think about that is they've got this extremely clumpy drug class name, which is like the non-benzodiazepine receptor agonists. Whenever I try to write that in a paper, I have to find the abbreviation to be long to write out. [laughs] But the key thing there is like they're acting on the benzodiazepine receptor. They're not

chemically benzodiazepines, but they're acting on the benzodiazepine receptors. So they're basically doing the same thing as a benzodiazepine.

Ryan Van Patten 57:25

Well said. I feel like there was a PR or marketing attempt there to say non-benzo when [laughs] it's a very similar mechanism. While we're on meds for sleep, briefly, what are your thoughts on melatonin for sleep?

Matthew Growdon 57:40

Ooof. I just let out a big sigh because I feel like we use it a lot, but I will personally plead my feeling that I don't really know the evidence in and out as to exactly how efficacious it is or what dose to give people. But I will reach for melatonin before these other meds for sure. Part of me wonders if there's a large placebo effect with all of these medications with insomnia because it is so tied to people's mental state and psychological status in terms of what's going on in their life. But still low dose melatonin is something I use. I think there have been mixed studies, for example, like using it in the intensive care unit, does it reduce delirium? Maybe in a small study it did, but not in all studies. There's a lot of variances of practice in terms of what dose do you give people. I would be the first to say I'm not totally sure what the totality of the evidence would point to, but some patients say it helps them and some patients say it's useless. I know that's not great evidence, but that's what I hear.

Mike Steinman 58:43

I'm certainly no expert on the evidence. My understanding is that the effects are minimal to none actually [laughs] on hard sleep outcomes. But, nonetheless, it can have some effects but, globally, it's a pretty safe medication. So I've noticed a lot of patients seem to be taking it and it's not always the first thing I try to withdraw. Sometimes I will offer it for the psychological reasons that Matthew mentioned. It's a pretty safe medication, especially if you're not giving mega doses, and the psychological effects around insomnia are so important that people feel like they're getting something that's helping them and that there's value to that.

Ryan Van Patten 59:34

Let's move on and touch on anticholinergics. This is a diverse set of medications, cuts across multiple classes. Talk about the impact of acetylcholine on the CNS and the negative effects of anticholinergics in older adults.

Matthew Growdon 59:49

Acetylcholine, as many of your listeners know, is a central neurotransmitter in the central nervous system. There's a whole hypothesis, for example, behind Alzheimer's disease dementia, that there's a cholinergic deficit that develops. This comes from many decades ago of early phenotyping and studying people with Alzheimer's disease that found they had less cholinergic transmission happening or less cholinergic burden overall in their brain. The anticholinergic class of medications, broadly speaking, causes a dysfunction in that acetylcholine transmission. So, in terms of negative effects, I think this is another big poster child class mixed with the benzodiazepines of something, particularly in older adults, with any form of cognitive impairment, especially people who have mild cognitive impairment where you're trying to do everything you can to preserve and prevent progression of their cognitive impairment. This is a class of drugs to be very aware of because the side effects can include memory impairment, confusion or delirium, hallucinations. Something that I see a lot actually that is very bothersome to some older people is dry mouth. They'll say, “I have a really dry mouth.” And one of the things I find, really again, going back to that thing that I find to be very rewarding about this area of deprescribing is saying, "Hey, you know, you're taking this medicine" for example, "you're taking oxybutynin for your bladder symptoms, and maybe it's not even helping you that much, but it's definitely giving you the dry mouth." I've had a patient or two come off and say, “My gosh, my dry mouth is much better.” Urinary retention, there's all these things that they are associated with. I think one of the main areas of research you asked about dementia with benzodiazepines is that it does feel like the data would suggest that use of anticholinergics may be associated with onset of dementia in terms of the cumulative dose over time. So that can be another talking point with patients if you're trying to talk about whether medicine is really giving them more benefit than harm.

Ryan Van Patten 1:01:58

Is that anticholinergic dementia reversible? Do we know?

Matthew Growdon 1:02:01

I think the feeling for a long time has been that anticholinergics may be reversible in terms of their cognitive decline when you take them away. But there have been some large cohort studies, in particular one out of the Kaiser Group in Seattle, that looked at cumulative use of benzodiazepines, or sorry, of anticholinergics over time and found that it was associated with all cause dementia, so that would argue against its reversibility. In general, I want to use the term dementia as a potential downside of anticholinergics, I, unfortunately, am referring to an irreversible neurologic decline. So I do worry about that with anticholinergics. Maybe not if

they've taken them for a little while, but if you have someone who has been on something for a long time, I do think it's a contributing factor.

Ryan Van Patten 1:02:49

Thus far, we've talked a lot about polypharm negative outcomes, these drug classes that have negative cognitive effects. But while we have you both, I wanted to briefly ask about SSRIs for depression in older adults. Do they work? How often do you use them, etc?

Matthew Growdon 1:03:06

I think the antidepressants are, there's definitely a place for them in pharmacotherapy in older adults for depression and potentially for other indications like anxiety disorders. And there are studies showing that they're efficacious. I think that a few pearls in general, again as a geriatrician prescribing an SSRI, is to be very mindful of the dose. The dose may often work well for a patient at a much lower dose than you might think of in say someone in the middle age group. And then it's really important to be aware that they do have side effects and they show up in the Beers list in different ways. So one way is that they can contribute to what we call the CNS or central nervous system polypharmacy. So if they're being used in conjunction with opioids and benzos and something else, they can contribute to things like falls. I think, again, like a precept is like, “Is it really necessary that this patient be on a drug for this treatment of depression?” There definitely are older adults with depression that's refractory to nonpharmacologic management, in which case I do think an SSRI is a good thing to reach for with the right prescriber. But you should watch them carefully and watch for side effects. And, again, start low and go slow.

Mike Steinman 1:04:27

The other thing I would add to that is that I definitely use them frequently to help me manage my patients who have depression. Anecdotally, but I suspect this is true across the board, a lot of my patients who have depression or symptoms of depression, their spouse died, they're living alone, they've got impaired mobility, their life is just hard and they have understandable reasons. That's not an excuse for having depression. It doesn't mean we shouldn't treat it, but it means that just giving a pill is not going to solve all their problems. So I think of it as part of a more comprehensive strategy where I will push a lot to try to get them into individual and group therapy. My clinical practice is at the VA and we have some great resources around that, as well as trying to help them engage with their social networks to help improve socialization and the sort of things which are making them feel down in the first place. I think of it as complementary, but I do use them often. The one other thing I'll say is I think a common mistake is because we start low in older adults to

avoid side effects and we ramp up the dose slowly to avoid the risk of adverse effects, sometimes people start low and stay low. For someone who has responded, that's great, but a lot of older adults will need the same full dose as a younger adult to get the full therapeutic effect. So I try to remind myself if I've started someone on a low dose that if they're not doing great, then it does mean I need to try to increase that dose and not just let them slide along.

Matthew Growdon 1:06:06

The last thing I'd add is just that there's a lot of different medications in this class, and they have different half lives and they have different ways that they metabolize. So this is an area where it can be really helpful to be thoughtful about drug-drug interactions. In general I would say we don't, for example, go to fluoxetine or Prozac, which has a relatively longer half life. Often you see people more on sertraline or citalopram in this population. I'm by far not a geriatric psychiatrist who really has a lot of expertise in the pharmacopeia of each individual one, but there's a lot of thought to these differences.

John Bellone 1:06:43

Great. I'm glad you both mentioned the non-pharmacotherapy options, too. You don’t need to sell therapy to a bunch of psychologists. [laughs] But before we can move on to the neuropsych specific questions we have, let's just round out the topic by talking about antipsychotics quickly and the use of antipsychotics to treat behavioral symptoms like dementia and potential problems with this approach. The idea of a so-called “chemical straightjacket”. Can you talk a little bit about that?

Matthew Growdon 1:07:15

I think this is a really critical area. So just to reformulate what you asked in the question, there is a common - not common, per se - but there is a practice that is off-label in the treatment of patients with dementia where in some cases, if they're having what are often referred to as behavioral or psychological symptoms of dementia, things like agitation or wandering or obsessive compulsive symptoms that are bothersome to themselves or to others, or hallucinosis that is causing problems, that medications in the antipsychotic class whether they be - more often now I see these new atypical or second generation ones things like Seroquel or quetiapine, but previously there were the first generations like haloperidol or Haldol - used theoretically as this last resort. It is definitely a very problematic approach. A lot of attention has been cast on some of the major downsides and potential side effects of this medication class. In general, it has a blackbox warning on it that it is associated in patients with dementia with a risk of mortality and death related to treatment. Just a couple other reflections. I would just say, actually, Mike and I have been working on an analysis that looks at people with dementia in the Medicare

dataset. About 1 in 10 of the people with dementia that are going to the hospital in this dataset are already on one of these medicines. So, obviously, despite these red flags that we put around it, there are situations where prescribers are finding themselves reaching for them. In some of those cases, I definitely think those prescribers are aware of the risks and they have thought a lot about it. They didn't want to do it, but they're doing it because they really are at a last resort. But there's going to be some percentage of them that are also inappropriate in the sense that they haven't availed themselves of other things. And again, speaking to your neuropsychology audience, that would be non-pharmacologic management. So things like music therapy, having caregiver support. A lot of times I think about when people are using these antipsychotics as a failure of our social system around the patient. So, maybe someone doesn't have anyone to help them take care of their loved one because it's very expensive and they don't have the social support for that. Or it's not safe for them to go to an adult daycare system. Or the adult daycare was closed down because of the pandemic. Then in this situation, sometimes the drug becomes like Mike was referring to with depression - like, is this one pill going to fix all these problems? It's really just a stopgap for all these other things. Things that we need to be providing to support people, in my mind. The last thing I'll say is, while there's not a lot of evidence that it even really helps too much, there is evidence again, going back to the SSRIs, that some of these behaviors can be improved through the use of [SSRIs]. There was a big trial that looked at citalopram for the behavioral and psychological symptoms of dementia. That would be safer for sure than using an antipsychotic. So if I am reaching for a medication to treat these problems in patients with dementia, I'm far more likely to use an SSRI than I am to use antipsychotic. Sorry, that's a long winded answer, but something I've thought a lot about.

John Bellone 1:10:40

Excellent. We'll have to do a full episode eventually on behavioral strategies for managing agitation, too, because it's something I deal with a lot in the inpatient facility I work at. Before we leave the deprescribing topic, I think we should make a blanket statement for any patients that might be listening. If you are hearing of a medication class and you want to get off of it, this obviously needs to be done in concert with your prescribing physicians.

Mike Steinman 1:11:04

This is one of the things about the way I like to think about antipsychotics with dementia, and this is true for many other medications as well. I always think of the severity of behavioral and psychological [symptoms], such as dementia, as well as the severity of lots of other symptoms people have - pain, depression, anything else - is that it comes in waves, right? Just the course of these diseases is they get

better and then they get worse and then they get better. It just goes up and down over time, like anything. So when people come to see doctors like myself is when they're feeling worse, when their symptoms are at their strongest. So then I, as the doctor, prescribed medication, and then the symptom would have gotten better all by itself. But now they're on the medications and getting better, and I think, as the doctor, "Oh, I saved this person. They're doing better. The medication is working." And the patient or their caregiver might think the same thing. Then what ends up happening is, even for medications providing no benefit, we have the false perception that it provides benefit and the person stays on it forever. Which is not to say we should never treat, but it's a good reminder to me when I prescribe to think of the fact that the symptoms do tend to wax and wane over time. It does remind me as a prescriber to think about a trial of discontinuation. If I'm starting the medication and the patient's doing better, it was like, "Well, is that because of the medication? Or is that just because they just would have done better anyways?" There's often no way of knowing and the only way to really know is to stop the medication in a slow and safe, responsible way and see how they do. Some patients, their symptoms might come back and I'm like, "Okay, the medication is working. Maybe they need it for more time." But for a lot of patients, that won't. I think the key lesson there is, and this is of course done through regulatory mandates in nursing homes, to have regular trials that discontinue antipsychotics in people with dementia. But even in non-nursing home settings, I think it's a good reminder to try to taper people off of these medications after a period of time, after they're stabilized to make that assessment as to whether the medication is still providing benefit and whether it's needed long term.

John Bellone 1:11:06

I like that experimental approach on an individual basis. That's great. I want to wrap up the conversation by talking about the neuropsychologist's role here. As neuropsychologists, Ryan and I both see older adults, the following issue comes up frequently. I'm just going to give you a quick overview. We see an older adult patient with cognitive impairments. We identify maybe one or more Beers criteria medications with potential negative cognitive effects. We document that in our reports. We then want to help the patients to improve their cognitive functioning as much as possible, but we debate on how we might do that as non-prescribers. We also don't want to step out of our professional lane, so to speak, but we're highly motivated to help the patient. This is really an important issue to us. We'd love to get your take on what clinical psychologists and neuropsychologists can do in these kinds of circumstances.

Matthew Growdon 1:14:14

I think this is such a wonderful question. I feel honored to speak to you and your colleagues about it in the sense that I think the best approach to high quality prescribing and then for that matter high quality deprescribing is a multidisciplinary approach. The notion that it's on the back of primary care physicians, for example, alone or whatever prescribing physicians alone, I think is not the best way to tackle these issues. So, I think, to the extent that our systems can be set up so that neuropsychologists are empowered to be part of a team taking care of a patient that has been referred to them for a specific cognitive concern, but then to close the loop with the person who referred who presumably is the prescriber and to feel empowered to flag these issues, I think it's incumbent upon us to set up a system where that is the culture and that's the way it should be. But in a more finite way, I think that personally, I may be biased, I've found the neuropsychology reports on patients to be incredibly gratifying to read in the sense that they're very holistic and

in depth. Not just in terms of the domains that you've assessed with your exam, but also the very detailed history you've done. So I think it can be really helpful for busy providers who may not have had time to elicit how patients feel about their medications or the fact that medications may be linked to their cognitive concerns, that may not have even risen to the top at their chronic disease management visits in primary care. So the fact that you've done that is really valuable. I think it's a matter of getting it back into the prescribers mind. And then I think the last thing that's always a challenge, and I am curious what you guys think about this, too, is sometimes the reports because of how definitive they are, are very big and very long. I think in geriatrics, we also suffer from very long, holistic, large notes. I think that is challenging in a system where a lot of people are scanning. So I think if you have something about a Beers list med, it may be that you need to talk to the person separate from the note all together, or highlight it at the top of the note or find a way to make it relevant and catch their eye so it doesn't just get lost in all the prose.

Mike Steinman 1:16:31

I would 100% second that. For busy clinicians, having the top line recommendations, big and bold and making sure they're easily visible, I think it's super useful. The one other thing I would encourage is that if, as a

neuropsychologist, you see a patient taking a medication and you think it might not be a good choice for them, is to not just let the prescribing referring clinician know about the concerns, but actually raise it with the patient themselves. I'll sort of illustrate by example. So say I've sent a patient just for neuropsych testing, and then I get the report back and it's asynchronous with my next visit with the patient. So I get it and then I'm actually seeing the patient next month, and they come into my office and they're complaining of knee pain and might get totally distracted and

just focus on the knee pain, I might never get back to the neuropsych report, even if it's as thoughtful and as helpful as possible. And then the next time they see me it's for heart failure, and I just never get back to it. But what can help to short circuit that lack of follow through is by educating and activating the patient to raise those concerns. What I love as a clinician is when the patient comes in and says, "Hey, I really want to talk about this medication because I'm concerned about it." Because as the clinician, it may be item number 37 on the 50 item list of things I'm trying to take care of. So if you, as a neuropsychologist, if you see a patient and you have a concern that they're taking that anticholinergic or the antipsychotic and may not need it, let them know. "I have concerns about this medication. We have often seen patients like you, it causes problems, it's not helpful, whatever. You should really talk to your doctor and this is why." And if the patient feels reluctant to talk to the doctor, maybe give them some encouragement to do so. Then the patient can convey that message back to the clinician and can help support the follow up in a way that's often much more impactful than just sending the note to the clinician themselves. I wouldn't feel afraid of stepping on the doctor's toes. You're not actually changing the medication, you're just encouraging the patient to talk to their doctor about it and those conversations are often fruitful. So I wouldn't shy away from doing that.

John Bellone 1:18:59
That's nice to hear.

Ryan Van Patten 1:19:00
John and I have debates about this. John is very - he likes to reduce risk in a great way. But we've gone back and forth. Obviously every situation is different, each patient is unique, and there could be a scenario where we overstep our bounds and don't give appropriate caveats because we are not prescribers, but I appreciate the encouragement for us to raise these issues to you guys as physicians.

Mike Steinman 1:19:25
It's much appreciated when it happens, when a patient comes back, because I might have been telling the patient to stop that benzo for a long time and they're like, "No way, Doctor." And then they see you and you're the expert and you're telling them, and now they're like, "Oh, okay. Now, the experts told me." So it can be really helpful. [laughs]

Ryan Van Patten 1:19:44
[laughs]

John Bellone 1:19:44
[laughs] All right. Well, Ryan has some more fodder for his argument now.

Ryan Van Patten 1:19:48
[laughs]

John Bellone 1:19:49
I'm curious if the recommendations that you have for identifying potentially problematic medications are just as simple as looking at the Beers criteria. I know there are online calculation tools of anticholinergic burden, and hippocrate.com, and other tools. For us neuropsychologists, how do you recommend we go about identifying medications that could potentially affect cognitive abilities?

Matthew Growdon 1:20:17
I mean, Mike is obviously biased, so he can't answer this question. But I can say that I think the Beers list is a really good starting place. I do think, like you alluded to, there are a lot of resources in this realm. It's important to pick one and become familiar with it and integrate it into your practice. I think the Beers list specifically around neuropsych type complaints has a pretty good list, it has a good rationale for each of them, you can treat it like a yellow light, and not necessarily a red light. I think some of the other ones used, like anticholinergic burden, can be really useful in a research setting. I have not used it so much in my patients. I've seen it sometimes in notes and I don't find that it in and of itself really changes my behavior that much. Maybe it lumps together a group of meds and then maybe helps me figure out, "Okay, of these two or three meds, let's try to go after one of these." But the fact that the burden sums to a certain number doesn't change my behavior that much. It could be on the back end, like the EHR, that you might imagine a world in which some of these metrics are being tabulated and then used at more of a population health level, but I'm not sure so much at the individual level. But I think it's your question of how to identify problematic meds. In addition to having a tool like the Beers list, I think the other best tool at our disposal and I think that in neuropsychology, given how much time you guys allott to talking to patients, is that talking to our patients and asking them about their meds and asking them which meds are causing them problems is often a low hanging fruit. Because if you find an overlap in terms of a potentially inappropriate med and the med that the patient says is causing them a problem, you're off to the races. It's a little bit harder when there's a disconnect between the two. But I think I wouldn't discount the history and talking to people about the meaning of their meds and about what meds they're taking, why they think they're taking them. That can be very time consuming, but if you even did that specifically around meds with cognitive effect and it turned out

that they thought they were taking this Alzheimer's med for something else and it's causing a lot of problems and whatever, maybe it's not helping them, maybe that's something to go after. That's just kind of a random example.

Mike Steinman 1:22:35

The one other thing I've often found that would be useful is to call attention to is both the individual medications and the cumulative effect of multiple medications. It's not just anticholinergic burden scores, but how many CNS active medications are they taking? Because that person is coming in, they got a cholinetrate disinhibitor, they're got an SSRI, they've got an opioid, they're got Gabapentin for some pain syndromes they have. And suddenly they're on four or five psychotropics and no wonder they're not thinking at 100% capacity or falling down or whatever else. Because these medications are like barnacles, they accrue over time. This sort of might have crept up on the clinician and that clinician might not be thinking about it holistically. So I think maybe calling attention to the risks of CNS polypharmacy when you observe it, and where possible maybe identifying some specific strategies to reduce that CNS polypharmacy can be really helpful. One of the challenges, and Matthew was just alluding to this, it's like, “Okay, they're taking all of these medications, but which one do I stop? And how do I stop because they’re still having pain or they're still having depression, they still have dementia.” So it's not just enough just to say that, “Oh, they're taking a bunch of meds”, but giving possibly some suggestions or alternatives where appropriate can help direct the referring clinician about how they can reduce the meds and which meds might be most useful to prioritize reducing. I think, again, you're not stopping the meds yourselves so I wouldn't feel too shy about making recommendations to the extent to which you feel comfortable doing so because the more specific that a recommendation can be, the more likely the clinician will have something concrete to act on.

Ryan Van Patten 1:24:25

That's a great way to end that answer because that segues right into my next question. I am interested in the two of you, as physicians who read neuropsych reports, if you can give us a little bit of feedback. Like the impression section or the recommendation section of our reports, if we've identified medications with potentially harmful cognitive side effects, is there a certain type of language that you've read that are especially helpful or less helpful? You mentioned highlighting and bold, capitalized, underlined font when we really identify a potentially problematic medication. But any other tips for us as we write a report with you as one of the primary recipients of the report?

Matthew Growdon 1:25:10

Obviously, the highlighting or bolding, by definition, needs to be used sparingly in order to bring certain things out. So if there happens to be potentially inappropriate med, great. If it happens to be, you know, they're driving and I have uncovered that they have incredible visual spatial deficits and no executive function and I'm very worried about their driving maybe that - so you guys will make that judgment. But another thing that could be useful is there are resources out there even through the Network Mike was talking about, the US Deprescribing Research Network. There's actually a section on there for clinicians for certain medications, there are actually algorithms that other research groups in this area have developed. So many clinicians are aware of them, some are not. But they can have things like for benzodiazepines - like what are the effective behavioral methods that have been used? What kind of patient facing materials have helped convince patients that maybe they should consider coming off of it? What would be an appropriate taper schedule, which would be very slow over a long period of time? So you could consider adding a link to those sorts of websites or information. But, yeah, I think, to me, the big challenge for the neuropsych report, as with other large and very detailed reports, is just drawing attention to your findings within the richness so it doesn't get lost.

Mike Steinman 1:26:37

I think the other way we corollary to that is we get so many other super long reports, which are not rich, which are just filled with tons of detail that's uninterpretable. For example, pulmonary function tests are like super long radiology reports and people just skip to the end. Just to tell me the top line result because there's all this little detail that's not really affecting my judgment. I suspect a lot of people are doing the same for the neuropsychology reports. So I would just take whatever your assumption is about a clinicians attention span and divide it by about 10 and it'll probably be an accurate one. [laughs]

Ryan Van Patten 1:27:14

[laughs]

Mike Steinman 1:27:15

So to the extent possible, if you can just have a bulleted list, like here are my five recommendations,1-2-3-4-5, or even three recommendations. You can have narrative above that, but sometimes having those bulleted lists for those clinicians who do have very limited attention spans or time. Just making it as easy as possible for them to get that top line results can be super useful. And then hopefully, people will go back and read some more of the details. But for those who don't, at least you've clearly communicated the key message.

Ryan Van Patten 1:27:48
This is a great topic. John and I have talked about neuropsych reports on this very podcast, and there is a movement in neuropsychology to work on shortening our reports for the very reasons you specified. So those are great points.

Mike Steinman 1:28:02
For what it's worth, I do the same thing with my own notes, too.

Ryan Van Patten 1:28:06
[laughs]

Matthew Growdon 1:28:06
Same here. My notes are so bloated. I cast no judgment.

Ryan Van Patten 1:28:12
[laughs] Fair enough. Well, this has been a wonderful conversation. Thank you both. Before we let you go, we have two bonus questions which are about the field of neuropsychology broadly. Your answers may or may not be related to medications. And, of course, we know you're physicians, so your perspective as an allied professional is valuable to us. The first one is if you can improve one thing about neuropsychology would that be?

John Bellone 1:28:41
And be as ruthless as you need to be. Don't spare feelings. Don't hold punches.

Ryan Van Patten 1:28:46
Yeah, good caveat. Please.

Matthew Growdon 1:28:47
I'm trying to - I mean, I guess it's a little bit biased by our recent discussion, but I think that, and I answer this as someone who within geriatrics has become very interested in neuropsych related conditions, things like dementia, and have spent time over the years training near neuropsychologists and neurologists and geriatric psychiatrists. But I think, actually, you've been talking about the thing that is the rub for me, which is that I actually am one of those people who will read your reports and read all the narrative in there. But they are very long, often. And I think that that's because you spend time with patients, which is of incredible value. But I think the challenge - and we also spend a little bit more time as geriatricians than the average doctor with patients, but I think both of us suffer from the result, which is

the potential for the long note that then when it goes to like the primary care physician, it just is lost. So, I know this is redundant, whatever can be done to streamline and bring to the top those really awesome things that you have distilled out of it, I think will be a service to your field.

Mike Steinman 1:29:53

I would just second that. The only thing I might add is that, and I don't know how widespread this is just anecdotally, I've noticed that sometimes it takes a really long time, up to several months for the reports to be generated. It's always nice when you get it, but typically the sooner the better. At least if there's a brief summary and the top line conclusions that I can then act on, it just allows me while the topic is fresh in mind. I mean, typically, when I refer to someone for neuropsychology I have an acute concern or the concern might be long standing, but it's really come to a head and is put to a point we really need to act. Like does this person need to be concerned? Or does this person really have dementia? And what are we going to do when this family is in crisis? They don't know how to deal with it. So having information sooner rather than later can be really helpful.

Ryan Van Patten 1:30:45

Yeah. There's a good study led by neuropsychologists on these very issues you guys mentioned, the Stakeholders Project, where they surveyed physicians and other referring providers trying to elicit feedback about our reports. And two of the big takeaways were just what you have both said - that attention spans are short and often there's not time to read the whole thing. Try to write shorter reports, if possible, and try to turn them around quickly if you can. So I think you're in good company and I hear that feedback from physicians.

John Bellone 1:31:18

For the last bonus question, what is one bit of advice that you wish someone had told you when you were training or maybe someone did tell you that really made a difference? Just an actionable step that trainees can take.

Matthew Growdon 1:31:29

Well, this is particularly meaningful because Mike has been a wonderful mentor to me in this latest step of my career. One piece of advice that he shared with me a number of times, and this is a little bit more in the research side of studying and working on issues related to polypharmacy, but I think it's also relevant to neuropsychology, Mike will often say to, “keep it simple.” Part of what is interesting about polypharmacy and geriatric medicine is the complexity of our patients and the complexity of these issues. We've talked a lot today about, like, is polypharmacy

causally related to these things? I think that there are a lot of really good study designs and research that support those things. But you can also zoom out sometimes and focus on from a clinical standpoint, things that are simple but highly relevant and very important. So that might be things like driving safety or if there is a medicine that may be of concern to focus on that. But not to get too lost in the weeds of localizing the lesion in the neuropsych report and all the very elaborate thinking that leads to our diagnostic idea. But at the end of the day, clinically, we just need a simple, actionable thing that the clinician can carry forward. I took the advice I've been using in the research world and these complex issues, and I think this notion of keeping it simple can often help cut through some of the complexity.

Mike Steinman 1:32:58

Just like my two cents on that question would be to follow your gut and take advantage of serendipity. There's a lot of decisions that people make, as they're embarking on their careers, like, what kind of practice do I want to do? Where do I want to practice? How do I want to practice? With who? What setting? And we might think we know in advance, but if your gut is telling you something, I would trust it. Then the other thing is, there are all these unexpected paths and turns that come up along the way. I've noticed sometimes people turn down really interesting opportunities because it wasn't part of their preconceived notion of what they wanted to do. Oftentimes I have found that following these interesting paths, even if I hadn't thought about them in advance, ends up being really enriching and productive. So as long as it feels like a good gut sense of where to go, even if it makes you a little uncomfortable, but it seems exciting, that can be really valuable to do. So don't overthink it too much.

Ryan Van Patten 1:33:57

Great advice. Well, thanks so much, Matthew and Mike, for your time, sharing knowledge. Your perspective as geriatricians will be very helpful for our audience as neuropsychologists, especially the issue of medications. So, thanks again.

Mike Steinman 1:34:12

Thank you. It's always a pleasure to work closely with neuropsychologists. It's a team effort and I love learning all sorts of cool stuff from my neuropsychology colleagues.

John Bellone 1:34:25

Glad to hear it.

Matthew Growdon 1:34:26
Thank you so much.

John Bellone 1:34:26
Take care.

Mike Steinman 1:34:26
Bye.

Transition Music 1:34:26

Ryan Van Patten 1:34:31
Well, that does it for our conversation with Mike and Matthew. We hope you enjoyed it as much as we did. And, as always, thanks so much for listening, and join us next time as we continue to navigate the brain and behavior.

Exit Music 1:34:44

John Bellone 1:35:00
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Ryan Van Patten 1:35:20
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