



MIGRAINE WORLD SUMMIT

INTERVIEWS WITH WORLD-LEADING EXPERTS

# TRANSCRIPT



**IS MIGRAINE A PROGRESSIVE DISEASE?**

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**Introduction (00:05):** I say, "I have two bad migraines a month," right? So, if I have two really bad migraines a month, so how many days of work did I miss in the past month? I would say, "Two." OK, so we're at two. Then, you know, the next question would be, how many days a month were you unable to do household chores? "These migraines, they're very disabling, I'm not able to do that." So now we're at four. And how many days a month am I unable to participate in family activities? "Well, again, that's two more." So, now we're at six. But the questionnaire is about the past three months. So,  $6 \times 3 = 18$ ; that's ... moderate is 11+, and severe is 21+. So, with only two headache days a month, we're already far into the moderate. And if you have three, it could be severe disability. So that's a misconception I like to knock away that, hey, even if someone has low-frequency episodic migraine, it could still be very disabling.

**Amy Mowbray (01:00):** For many of us, migraine has taken such a heavy toll that we cannot ignore it. But that's not the case for everyone; some people have only one or two attacks per year, and they may be mild, while others are bedridden every single day. If we leave migraine alone, will it go away or is it likely to get worse? To help us uncover whether migraine is a progressive disease is Dr. Fred Cohen from Mount Sinai Center for Headache and Facial Pain. Dr. Cohen, welcome to the Migraine World Summit.

**Dr. Cohen (01:29):** Thank you.

**Amy Mowbray (01:30):** What is the prevalence of migraine disease in the general population?

**Dr. Cohen (01:35):** So, the prevalence of migraine is about 12% among the total population, and it's split between around 17 to 18% for women, and about 6 to 7% for men. And that has actually been about the same since as far back as the '80s when they were first doing epidemiology studies for migraine. And over time those trends have, sort of, gone up and down by maybe 1%.

**Amy Mowbray (02:02):** So, is migraine becoming more prevalent over time?

**Dr. Cohen (02:05):** Right now I would say no; I would say it's stable. The most recent studies — which were government studies — the National Health Interview [Survey], which up until about 2018 ... and those numbers have remained similar. They've sort of been bobbing up and down, but it has not been an upward or downward trend. Its prevalence, I would say, has been stable.

**Amy Mowbray (02:28):** Would you have expected this number to go up due to increased awareness and education resulting in more diagnosis and self-reporting?

**Dr. Cohen (02:37):** I would say yes. Over time, the criteria — ways we've diagnosed migraine — has changed, and I would say improved. Some would say since we're being more refined in how we diagnose it, there's more headache specialists in the country, etc., more word [about migraine]. But again, from the studies we've been doing — the epidemiology work — that has remained the same.

**Amy Mowbray (03:00):** How is the level of disability caused by migraine disease evaluated?

**Dr. Cohen (03:04):** The disability and impact, or burden, of migraine has been measured differently over time. In the early epidemiology studies, in the interview questions they would ask, "Is your migraine — is it moderate impairment? Is it severe impairment? Do you need bed rest?" It also would measure decreased productivity in missed workdays. For instance, it would



ask, "How many days in the past three months have you missed school or work?" And as years went on, questionnaires were developed to better assess. For instance, there's the Migraine Disability Assessment (MIDAS), which is now a common one, and that similarly asks about missed workdays, but it also asks about, "How many days were you unable to do household chores?" And, "How many days in the past few months have you been unable to participate in social, or leisure, or family events?"

**Amy Mowbray (03:56):** What patterns are being seen in the progression of migraine?

**Dr. Cohen (04:00):** So, the patterns, or rates of progression from episodic migraine to chronic migraine we've seen from epidemiology studies is about 2.5 to 3.1% of these study populations. But also of note, that number — because some people believe that number can be a bit misleading, for when they look at a subpopulation of people that were being seen in clinics — meaning the individuals that were being treated for their migraines, that group of people, it was about 15%.

**Amy Mowbray (04:33):** And how many people have chronic migraine in the general population?

**Dr. Cohen (04:36):** That is about 1%.

**Amy Mowbray (04:38):** And is this number increasing?

**Dr. Cohen (04:40):** That number overall, per se, isn't increasing. But what we're seeing is the ratio of chronic migraine to episodic migraine, meaning from the overall group of people with migraine, that is going up.

**Amy Mowbray (04:57):** How does the burden of migraine disease differ between high-frequent episodic and chronic migraine patients?

**Dr. Cohen (05:04):** So, to give you numbers, there was a recent epidemiology study called OVERCOME, and they saw that the MIDAS scores three to four — three being moderate, four being severe — those respondents who had high-frequency episodic migraine. And high-frequency episodic migraine are individuals who report about eight to 14 headache days a month; and chronic is 15 or more. The people with high-episodic migraine, 68% of them reported moderate-to-severe disability, and those with chronic migraine reported about 78%. This also compares to individuals with low-frequency episodic migraine, and they reported about 24% moderate-to-severe disability. And one thing I just want to highlight: When we did this systematic review of all these epidemiology studies evaluating migraine burden over time, a lot of questions and things I got is, "Hey, over 50% of these individuals have low-episodic migraine. It's only three headache days a month. How are you saying burden is going up when so many have only two to three headaches a month?"

**Dr. Cohen (06:10):** And that's very misleading, and unfortunately a very big stigma issue, because to bring it back to MIDAS, what does MIDAS, this questionnaire, ask? Let's say you have... I say, "I have two bad migraines a month," right? So, if I have two really bad migraines a month, so how many days of work did I miss in the past month? I would say, "Two." OK, so we're at two. Then, the next question would be, how many days a month were you unable to do household chores? "These migraines, they're very disabling, I'm not able to do that." So, now we're at four. And how many days a month am I unable to participate in family activities? "Well, again, that's two more." So, now we're at six. But the questionnaire is about the past three



months. So,  $6 \times 3 = 18$ ; that's ... moderate is 11+, and severe is 21+. So, with only two headache days a month, we're already far into the moderate. And if you have three, it could be severe disability. So, that's a misconception I like to knock away: That even if someone has low-frequency episodic migraine, it could still be very disabling.

**Amy Mowbray (07:16):** Is migraine becoming more disabling, or are we better at reporting symptoms, or being diagnosed?

**Dr. Cohen (07:22):** Now, that's sort of a big question I've been asking. So, as I stated before — myself and my group — we did a systematic review looking at all these U.S.-based epidemiology studies. And while these studies show that prevalence has remained stable, MIDAS scores have been going up. To give numbers, for example, one of the first studies that employed MIDAS was what we called the "Henry Ford" study, which was back in 2001 in the Henry Ford Medical System in Detroit. And they reported 30% MIDAS grade three to four. Then came a very large-scale study, the American Migraine Prevalence and Prevention study (AMPP) in 2004 and '05, they reported about 22%. Moving on to 2012, we have what was called CaMEO, which was looking a lot at chronic migraine, and they reported 39%. So — that's 22 to 39% — we have a big increase.

**Dr. Cohen (08:15):** In 2016, with what was called the MAST study that reported 43% moderate-to-severe disability. And then lastly, [the] OVERCOME [study], recently, in 2018, reported 42.4%. So, it's been going up. And that [begs] the question: Well, what's going on here? And that fell into two camps with us. The first being: Well, what trends are there? And that's what we sought out to seek, to examine. And we looked at various things. So, for instance, we were talking before about progression to chronic migraine. So, we looked [at]: What [are] the changes in the number of headache days a month people are reporting? And what we found is: There is, that over time — from 2005 to 2018 — to these studies the amount of people reporting 15 or more headache days has increased from 6.8% to 11.7%.

**Dr. Cohen (09:06):** You know, a little less than double. This is where I was saying the ratio of chronic migraine has gone up. And as well, the amount of people reporting moderate-frequency episodic migraine, which is 4-to-7, and high frequency 8-to-14, also go up. Moderate being 17.7% to 19%, so we have about a 2% increase; and 7.8% to 10.8% in high-frequency episodic migraines, that's a 3% increase. So, we are seeing that. Other trends we've looked at [are]: What about employment? So, this questionnaire is all about reduced productivities as well as missing workdays. And we thought if more people are employed, well then they're going to be reporting more missed workdays. And we actually do see that: That the [number] of individuals [employed] with migraine — because in the studies that was a question asked in their demographics: Are you full-time, part-time employed? And we see that from 2005 to 2012, there are more people reporting employment. And even so to 2016.

**Dr. Cohen (10:08):** Then the weird sort of thing with that trend is, in OVERCOME, the 2018 study, employment actually comes down, but burden remains the same. So the first half of that does account for it, but then it doesn't later on. We also thought about: What about triggers? Are triggers worse for migraine these days? Because one thought that was put forward is: Well, what about weather triggers? Which is very common — people report in bad weather that they get a bad migraine attack. And there was recently an article in *Headache* that reported an increased incidence of worsening of migraine frequency after a natural disaster. So the thought is: Maybe climate change is taking a part in this?



**Dr. Cohen (10:48):** We also looked at: What about treatments going on? For instance, it is known that opioid use is a risk factor for going to chronic migraine. Is opioid use getting worse? And we see that, among these studies I mentioned, it's actually not going up, really. And one thing we're examining now — that unfortunately, I don't have a direct answer for is: What about the use of acute medication? Because we also know medication overuse headache is another component leading to chronic migraine. And then the last thing of this group of thought is: What about cultural changes? We've been talking about over time: The word of migraine's been getting out, we've been getting better at detecting it, talking about it. And there's a whole talk about the stigma of migraine. Unfortunately, there's a large stigma to it, and we're doing everything we can to decrease that and have people be more forthcoming to talk about it.

**Dr. Cohen (11:39):** And also, what's happening in society, for instance, in the late '80s, early '90s, it wasn't really talked about on TV. And nowadays there's a commercial with Serena Williams for a treatment of migraine. So it's definitely being talked about more, and it's that ... allowing people to be more forthcoming with how their migraine affects them. And then the other school of thought is: Well, is this all artifact? Meaning that, is this just a product of changing how these surveys worked? Overall, these surveys I mentioned, their methods, the methodology, has changed. The earlier ones like the American Migraine Study I and II in the early '90s, and AMPP in 2004, these were mailed questionnaires. Not only were they mailed questionnaires, they were directed to the head of the household. So meaning if, in the '90s, when a house got this, the head of the household would fill it out for the other participants in the house. Then, in 2012 with the CaMEO study, it became online modules. And it's been that way since. So, is it that now we have a different way of interacting with these participants of the study? Has it sort of changed how things are answered, and that's the data we're getting? So, it's sort of distinguishing: Are there actual trends that account for this, or is it just a change in how we're doing our studies?

**Amy Mowbray (12:54):** Going back to the role of education and awareness, what role do you think migraine education awareness play in the accurate reporting of migraine symptoms, and the burden of disease by patients?

**Dr. Cohen (13:07):** I would say an extremely high level. I can't tell you how many times I've met patients, I've met people, and I'm talking to them, or it's so common when I'm talking to new people and they're like, "What do you do?" And I tell them I'm a headache specialist, they're like, "I get this really bad headache like once every two weeks." And talking to them and [I] say, "You have a migraine. That's not just a bad headache, you're having a migraine, and there's stuff we could do about it." So awareness is a major, major factor. We know that no, or suboptimal, treatment of migraine is a risk factor going into chronic migraine. So, people who just aren't aware of this disease they have, this condition that is causing this high level of burden ... [are] like, "Oh, this is not just a bad headache." This is something that ... you could see someone, and there's resources, and things we could do for it, and give you lost time.

**Dr. Cohen (13:56):** I'll give you an example of myself: Growing up, I got migraine attacks. And once a week, growing up — since I was a little kid, since I can remember — I would get a migraine, once a week, and that was just it. I would get this attack once a week, and everyone was like, "It's a bad headache," and I lived my life like this. Until I was in med school where I was in a lecture, and they talked about migraine. I'm like, "Hey, it sounds like me." And seeing someone completely changed everything. So it's sort of a mission of all headache doctors, the American Headache Society, the American Migraine Foundation, Miles for Migraine, to bring



more awareness to make people aware that, "Hey, this is what this is, and there's things that we could do." And I feel that could definitely decrease the level of burden that we see.

**Amy Mowbray (14:43):** With this migraine awareness and education, and people realizing migraine is not just a bad headache, would you have expected the prevalence of migraine to have also risen?

**Dr. Cohen (14:56):** Yes, in some regard, you would think that more individuals are coming forth. One thing that the studies do, do — these epidemiology studies — is they do have a good criteria of diagnosing. And that sort of brings this question: Is there a problem? Meaning that, maybe that from our numbers, of me here saying that, "Prevalence has remained the same," is that truly what's happening? Or it could just be, we need to make a better tool; maybe we have to do a better job. This is what happens every time. These large-scale epidemiology studies are conducted: What can be done to improve it? Again, from the data that we have now, through these various different kinds of epidemiology, migraine and headache studies, it says, "No, it's stable." But it could very well be, "Hey, we have to change something up to better assess our surveillance."

**Amy Mowbray (15:59):** We have better treatments for migraine than ever before, and you would hope the burden of migraine would be going down instead of rising. Why are we seeing the opposite?

**Dr. Cohen (16:08):** So, the quick answer to that is OVERCOME, which the current data ... OVERCOME is over multiple phases, I believe three of — I don't want to say the wrong thing — 2018 to maybe 2021? In the systematic review that we did, we only used Phase 1, the 2018 data, and these new treatments we talk about, the calcitonin gene-related peptide monoclonal antibodies, and whatnot. That was when it came out that year. So these studies don't capture that. And that's a big question we had that, "Hey, if we did one now, what would it show now that these treatments have been out for three, almost four years?" We also have gepants out now: Nurtec, Ubrelvy are also treatments that weren't in use when the last study was conducted that we looked at. How would that affect it, but then, also how would the pandemic affect it?

**Dr. Cohen (16:58):** That's something I've brought up to my colleagues all the time, is: Now that ... with the pandemic going on, what's that going to show in our studies? Like I said — missed workdays, we allow people working from home — is that going to affect what our MIDAS numbers show? But also, MIDAS accounts for a decreased productivity. So, there's a lot of, I'll say, "what ifs," and what can we do? Because let's say we do a new study, and we account for these drugs, but what if ... the pandemic is — I think I could say for everyone — is a very stressful time. I know myself, and all the headache advisers, we've definitely seen a lot of different kinds of cases from it. What would it show? Would it act as a confound? Or would it be like, "Oh yeah, look, migraine burden is even getting worse now." And also, what has it done to prevalence? Is it worse now from the pandemic? These are all good questions, and hopefully we'll have answers for that soon.

**Amy Mowbray (17:55):** So, in your opinion, maybe the negative impact of the pandemic might outweigh the positive impact of the anti-CGRPs and gepants?

**Dr. Cohen (18:03):** Yes, it very well could. And I mean, we first have to do it. You can ponder and debate all you want, but until we have those numbers, that data, that's when that will be meaningful. But then it will beg the question, all right, someone can look at that. Let's say we do



another study and we say, "Yeah, more people are reporting moderate-to-severe disability. These treatments aren't doing anything." That would be an unfair statement, because what we do know from the trials, that — again, MIDAS was used in these trials, and — they did see that with all these new treatments, MIDAS scores [have] come down. But again, a lot of these were done before the pandemic. So, it's a very good question and we'll have to see what the data tells us.

**Amy Mowbray (18:48):** What is the difference between nonmodifiable and modifiable risk factors for migraine progression?

**Dr. Cohen (18:54):** Sure. So, a nonmodifiable risk factor is sort of what it sounds like: One you can't modify. Something that you can't just say, "All right, I'm going to stop doing this." And those being: The female sex, and also low socioeconomic status, are ones that are nonmodifiable. Modifiable would be ones that something that could be changed. So, obesity is very — is highly associated with worsening migraine — leading to chronic migraine. And that's because we know that a lot of adipose tissue is pro-inflammatory, and migraine is a disease of neurogenic inflammation. So, any other condition that promotes widespread inflammation we hypothesize is a risk factor to going to chronic migraine. For example, asthma. We've seen through all these epidemiology studies that those with asthma have a higher likelihood of progressing to chronic migraine than those that don't, because asthma is a disease of inflammation.

**Dr. Cohen (19:55):** And then also, those with other pain conditions is another risk factor, as well. Depression is a very common comorbidity we see, and also having a major or stressful life event, as well. As I was saying before, poor or suboptimal treatment, not getting any treatment, is a major risk factor. And also, too much treatment — medication overuse is very common. People who are taking over-the-counter pain medications every day, using triptans a lot, opioids ... These are all factors that could be changed, that could lead to chronic migraine. Sleep disorders: insomnia, sleep apnea — I always ask lots about sleep — very underdiagnosed. And then actually one that is not as big as a risk factor is age. Age is commonly thought to be a risk factor, but actually, the age is not really set. Over time, we see people who, because people get chronic migraine that we think, "Oh, it's because they're getting older." No, it's just ending up over time, but just because someone is getting older doesn't mean that they're at a high risk of progressing to chronic migraine.

**Amy Mowbray (21:07):** You touched on depression there. What role do psychiatric comorbidities play in the progression of migraine?

**Dr. Cohen (21:13):** A very, very high level. Depression: There are a lot of studies that would even say depression is the highest rate of something leading to the progression to chronic migraine. It's commonly seen a lot — depression, as well as anxiety. And again, just like I said, I ask about sleep at all my patient visits. I always talk about their mood, and what's going on. And you can see the two play on each other, and it's not surprising: A disease that is causing such burden, of course will be having an influence on someone's mood and how they're feeling. And [if] you want to treat one, you also have to address the other. It's not as simple as, "Yeah, I want to make your headache feel better," and then, "Oh, your depression's going to wait." Both need to be treated. And I always make sure that all my patients are like ... I screen them for depression and make sure they're getting the proper resources for that. Either they're being seen by a therapist, they're being seen by a psychiatrist, or psychologist. But it's something that should never be missed in anyone suffering with migraine.



**Amy Mowbray (22:16):** Does MIDAS capture the impact of the psychiatric comorbidities?

**Dr. Cohen (22:22):** MIDAS does not ask about that, however, I've seen in all these epidemiology studies — one other question that's brought forward is PHQ [Patient Health Questionnaire], which is a depression screener. It asks anywhere from four to even nine questions about a patient's mood and what's going on. And that — while MIDAS doesn't do that — these studies do accomplish that from asking that kind of questionnaire.

**Amy Mowbray (22:52):** What role does central sensitization play in the progression of migraine?

**Dr. Cohen (22:57):** I could talk a long time about that. But you know what, first let me describe what's happening in a migraine. One of the components is — during a migraine attack — what we call central sensitization. Think of a pain pathway, like, the way I describe, "Why am I feeling pain?" to a patient is: Let's say pain is a train, right? When you're on the road, and you get to a train crossing, so when you get to a train crossing, the signs come down, it's very loud and annoying, and the train's coming. Well, pain is the train. Then, let's say someone hits me — the pain, the pain train comes; the pain passes, and the crossing goes up.

**Dr. Cohen (23:40):** Well, in migraine ... in these migraine attacks, what's happening is: Think of the train, the tracks — it's not stopping, they've been oversensitized — think of it like that. And therefore, the train crossing, the loud annoying — it's still going off and going off — hence the pain. We see these with the various pain pathways in the trigeminal vascular pathway. All these different areas of how we express and feel pain, it essentially just keeps going off. And what we see in chronic migraine from episodic migraine, it's just happening to a greater degree. We know in individuals with chronic migraine, that there is a larger degree of sensitization — that these pathways are releasing more of these neuroinflammatory markers. And it's just ... that's why the pain is more and more frequent.

**Amy Mowbray (24:34):** Are there any functional changes or differences in the brain that can be used to predict migraine progression?

**Dr. Cohen (24:40):** We do see functional changes in those with migraine. We know that areas of the brain — such as the brain stem, the cerebral cortex, the hypothalamus — we know changes are there. And in chronic migraine, those changes are more prominent. Areas of pain processing, such as the periaqueductal gray matter, is an area in migraine we know is more affected; it's even more so affected in chronic migraine. And also in that same area, if you were to look, in an individual with migraine and someone who doesn't [have it], there is what we see as iron accumulation. And that's likely from — there's just more metabolism from all these nerves firing off — and in those with chronic migraines we see even more iron accumulation.

**Amy Mowbray (25:24):** Why are treatment and early interventions so important to stopping migraine from progressing?

**Dr. Cohen (25:30):** Just as we said before, oh, it's more sensitization. It's sort of ... it's easier to prevent a fire than to put a raging fire out. As far as these changes happen — to get a patient to proper treatment before these changes happen, before there's more sensitization to these pain pathways. And just as I described before, poor or suboptimal treatment is a risk factor for going from episodic migraine to chronic migraine. And it's getting patients with a proper treatment plan before that can happen.





**Amy Mowbray (26:09):** What tips would you give to individuals who would like to prevent their own migraine condition from getting worse?

**Dr. Cohen (26:17):** The answer I would say is, it's sort of individual for everyone. I could talk to ... and this is something I talk about with every patient, because there's so many factors that are involved. But I say, I would say overall all these factors I was describing: Dealing with [and] getting a proper treatment for depression, decreasing your BMI, treating obesity, and seeing someone — it's actually such a big problem that as the headache society we're working on, is getting patients the proper treatment. In the recent — in OVERCOME, this recent large epidemiology study — we see that way more patients are seen for migraine in the emergency room or urgent care. Somewhere to 30%, compared to being seen in a primary care specialty setting, which is about 12%. That's a very big difference.

**Dr. Cohen (27:08):** And on top of that, we see in individuals with episodic migraine, only 22% are getting a triptan. And that's way — that, just saying, "Oh, triptans don't work." And that number doesn't account for it, but that signals to us there's a lack of guideline-based care — not enough people getting proper treatment. And on top of that, in the OVERCOME study, of individuals who were deemed eligible that they should receive preventative care, only 16% got that. That number is way off. And that just goes back to getting patients proper treatment. I mean, a lot more people need to get more proper treatment. So, it's on getting other conditions with the patient treated, but also on us as providers to get better access for our patients with migraine.

**Amy Mowbray (28:00):** Do you consider migraine to be a progressive disease? If so, do you think if more patients knew migraine was progressive, that it might encourage them to seek their healthcare professionals sooner?

**Dr. Cohen (28:10):** Definitely. You know, definitely the data shows migraine being left untreated is a major risk factor for migraines to become more frequent, more severe — leading to chronic migraine. As I was describing before, it's every day I hear it, it's like: "Oh, yeah, I get things like this, it's just a headache." No, it's not "just a headache." No, it's not: "Just drink more water." No, not: "Just take Advil or something like that." This is a disease; there's stuff that could be done. Like I said, there's definitely a lot more work to be done.

**Amy Mowbray (28:44):** Are there any final thoughts that you'd like to leave with the audience?

**Dr. Cohen (28:48):** I guess what I've been harping on the whole time: If you yourself feel that, "Hey, my migraine's not being adequately treated," seek proper treatment. I always tell people: See headache specialists. I never knew — a headache ... someone trained specifically for headache existed — that was a thing until I was in residency, and it was very life-changing. I can't tell you how many people are like, "Oh yeah, my friend, someone I know ... Oh, I get this bad headache and I just have to go to a quiet, dark place." Like, hey, tell your friend, "I think you might have migraine. That sounds pretty bad. There are doctors for this; go see someone." It's all about getting word out and improving, you know ... people knowing what this is ... being a better advocate.

**Amy Mowbray (29:34):** Where can we learn more about what you're doing or follow your work?

**Dr. Cohen (29:37):** So, to know more about migraine, there's a lot of societies out there: The American Headache Society, the American Migraine Foundation, Miles for Migraine is a major advocacy group — they do walks and runs to promote and increase awareness. Me, myself, I'm



an assistant professor of neurology at Mount Sinai. I am continually doing epidemiology work there, and looking for more trends and patterns we see in migraine. My Mount Sinai profile — my work is displayed there. There are, like I said, there are a lot of societies and advocacy groups that are working to improve the awareness of migraine.

**Amy Mowbray (30:20):** This has been a fascinating insight into the progression of migraine. Here at the Migraine World Summit, we remain hopeful that the increase in education and awareness around migraine, paired with the huge advances in migraine research and treatment options, will help reduce the burden of migraine disease over time. Dr. Cohen, thank you for joining us today at the Migraine World Summit.

**Dr. Cohen (30:40):** Thank you. It's been a pleasure and privilege to be here.