



MIGRAINE WORLD SUMMIT

INTERVIEWS WITH WORLD-LEADING EXPERTS

TRANSCRIPT



REAL-WORLD DATA ON TREATMENTS, TRIGGERS & WEATHER

**FRANCOIS CADIOU
FOUNDER
MIGRAINE BUDDY**



Introduction (00:04): There is a sort of 20 to 30% responder rate, meaning that when starting to record and becoming more and more conscious about what is happening, seems to be reducing the frequency of headaches for 20 to 30% of users, even without any treatment.

Carl Cincinnato (00:32): Today we're speaking with someone who has an online platform that's literally recorded tens of millions of migraine attacks from hundreds of thousands of people. Just this in itself is an incredible feat, and a lot of information to process, but what can we learn from it all? Perhaps one of the most exciting areas is in treatment. Which treatments perform best? Which don't? And how close are we to identifying super responders to certain treatments? We're also going to cover the most common migraine triggers and discuss the weather in the context of migraine. And to help us do that is Francois Cadiou. Welcome back to the Migraine World Summit.

Francois Cadiou (01:13): Thank you. Thank you for having me. It has been a long time, so a lot happened since the last interview, so let's go.

Carl Cincinnato (01:24): Fantastic. It has been a long time and you have grown significantly. In fact, Migraine Buddy has become the biggest application in the world for migraine. Tell us how many people are using the platform?

Francois Cadiou (01:36): So, we have 3.3 million, today, registered users: First in the U.S., and then Europe, and then Japan. Today, Japan — Japanese is actually the second most common language on the platform.

Carl Cincinnato (01:52): Fantastic. So, it's really an international application, and you're collecting a lot of data and information. What are you doing with the data?

Francois Cadiou (02:00): So, the first part is we continuously work with users to make it more convenient. That's one. And being able to discuss while observing the data helps us in making it more intelligent. And the other part is for all of the users who have decided that they want to contribute to research. We are actually working with some of the top researchers to publish and to help the research advance. We've worked — we've published on COVID-19 and some of the first observed impact on migraine. We're having research on triggers, we're having research on weather, we're having research on the actual impact. And now we have a very significant paper coming based on more than 10 million attacks about the efficacy of the treatments.

Carl Cincinnato (02:58): Yeah, so it sounds like you're doing quite a bit of work with clinicians and publishing research to share some of the findings. Should people be worried about their privacy at all in the research that you're publishing?

Francois Cadiou (03:10): In the research, no. For the research, we have some simple rules which are really, really important. Unique aspects, unique records, like the notes and so on, that's never included in research. So you will never see anything which is unique to you go outside. It's your data. It will never reach a researcher or anybody else.

Carl Cincinnato (03:36): Right. So, when data is shared with the research scientists, it's anonymized and it's added up — like it's added all together. So it's aggregated data. So no personal information is going outside. Moving now to treatment performance: We mentioned in the introduction that there is a huge number, tens of millions, of migraine attacks that have been tracked. Which treatments do people self-report to be the most helpful?



Francois Cadiou (04:01): So today we have — we started with a very simple scale. It's a three-point scale, basically: [not] helpful, somewhat helpful, and helpful. On purpose we made it very, very, very simple. And what we're observing is that it's mostly advantaging treatments which are very strong and which are fast. Naturally, what is happening is that the triptans are coming first. Sumatriptan is in the middle of the six to seven triptans which are on the market. It's also the most common by far. And then after, you will see other types of treatments going down. So, the triptans first; they are fast. When they kick in, you really can feel it — not necessarily in a nice way sometimes by the way — but you know that it's acting. And then after you will have the DHE, you will have ... some of the opioids and going down, you will see, you will arrive to the NSAIDs — so ibuprofen, naproxen, all of those. And finally weaker things such as paracetamol, aspirin.

Carl Cincinnato (05:36): Just to clarify, so paracetamol is in the U.S. as acetaminophen, and these are regarding acute treatments for migraine.

Francois Cadiou (05:44): In that case, we're talking about acute treatment, absolutely. Knowing that there is a concept which is very important to keep in mind is the concept of responder. So, we don't always respond to a treatment, and it's not necessarily on/off. So the difficulty here when doing a ranking like that is that the ranking for people who are actually super responders on a treatment is not necessarily the same for somebody who is only partially responding to it. And so that's the next part we are working on, which is: What is the predictability of the treatment for you when you take it? Or what is the predictability for you that it will even work once? If I take an example of triptans: Some people will react to one triptan, not to another one. And they may also remark that only for some of their migraines, they're reacting to, let's say eletriptan or rizatriptan. And they may remark that after some time it stops working for them and they need to change.

Francois Cadiou (07:02): So the next part of the research for us ... is to change from ranking — which is saying how well is it working for us, the users, the patient, the population-level analysis — to a personalized-level analysis. And we have the gepants for that. We may come to it a bit later, the gepants, which are the new class of drugs, which are also very interesting here, because they are not necessarily the fastest. So they don't necessarily arrive highest with this very simple scale, but they can be very predictable for people when they're at work. And they also [let] you work without any side effects, faster than the others. So we are really at the beginning, and we can see that personalization really, really is where we need to go. Knowing also that with 10 million attacks for this analysis, we really get very strong results, very clear, statistically extremely solid. But then immediately, what we observe is that combinations, for example, are coming up. What we've seen very clearly is that people who take naproxen plus sumatriptan have a higher outcome than sumatriptan alone, or sumatriptan plus ibuprofen.

Carl Cincinnato (08:38): Interesting. Yes, so there's a lot to unpack there, but it sounds like you are able to confirm what doctors have long been telling us, which is if we don't respond to one type of triptan, it's still worth trying another type, because you may well respond really well ... to that other type.

Francois Cadiou (08:56): Yes.

Carl Cincinnato (08:57): We know that triptans are performing the best in terms of the overall performance. Which treatments sort of stand out towards the bottom that are being used by



people with migraine that don't seem to be as effective, or as sort of some of the least effective?

Francois Cadiou (09:12): Let's say triptans are the fastest, and with the scale we use, they get the best results. They are not necessarily the ones which are the best at removing all the symptoms. Just

Carl Cincinnato (09:25): OK.

Francois Cadiou (09:25): Important to keep in mind. So compared to gepants, we've been publishing other studies where, for example, if your objective is to be able to go back to work and have your cognition to the maximum, the triptans may not be ... the best choice. In that case, gepants may be working better for you.

Carl Cincinnato (09:46): That's very interesting. So even though triptans are showing up as being some of the most helpful in the way that you measure it on the platform, if we are working through a migraine attack, or if we need to take a treatment whilst we're at work for migraine, perhaps some of the data is suggesting that gepants — whilst they may not work as quickly as triptans — they may be more effective. Well, I'll be careful how I word it. They may perform better.

Francois Cadiou (10:11): Effective is a dangerous word, yes.

Carl Cincinnato (10:14): They may perform better for you at work because they bring less symptoms or less side effects than the triptans.

Francois Cadiou (10:20): Less nausea ... and better, faster at getting back your cognition.

Carl Cincinnato (10:26): That's great. I mean, it's great for us to be able to hear some of the findings. So just coming back to that question about the sort of the less helpful treatments that sort of came in. So, we spoke about acetaminophen, ibuprofen, [and] aspirin. These are often first-line treatments that doctors prescribe or will suggest a patient try first, yet they're some of the least performing ones. Why do you think we're getting prescribed this if they're not performing as well as most of the others?

Francois Cadiou (10:57): They have an objective: Which is to remove the pain; work against the headache. They work for that, or partially, and they're safe in some way. I know that like everything you can really, really take too much of it, and have terrible side effects. But the first thing is that they have a lot less side effects than a triptan, basically. They're cheap; they're well known.

Carl Cincinnato (11:32): They've said in the past that the first-line recommendations are those types of treatments because they're cheap, they're widely available, you don't require a prescription, and so you don't have to go back to the doctor if they work to keep getting refills. And so, I think that that's probably part of it. So, we've spoken about some of the medications. What about devices? Do you have sort of much global data about what devices are doing from an acute migraine perspective?

Francois Cadiou (11:58): So today there's only one device for which we have ... we consider we have enough data to make a statistical model. We're not publishing on it today; it was not



included in the publication we are publishing. But the one which is used enough is Cefaly. We don't have any support from Cefaly, to be clear. But it seems to be used enough. And roughly the efficacy reported ... so [in] regard to the helpful scale and the expectations that people put in it, it's a bit — it's at the same level as opioids or THC. So it's a bit lower than gepants; it's a bit lower than triptans, probably also because it's not that fast. So that's why it's part of what we need to adjust for the future scales. But it's clearly at a quite decent level, especially considering the side effects: the low side effect profile you can get from that. And it's clearly above most of the NSAIDs or nearly all, if not all, of the OTC drugs — the drugs you can get at your pharmacy freely without prescription.

Carl Cincinnato (13:31): So it sounds like devices could also be a very legitimate treatment then for acute migraine.

Francois Cadiou (13:37): Yeah, and we can hope that others will appear in our statistics when we will see more users. We've been discussing, exchanging with users who were really telling us it's good. Today we cannot really pronounce ourselves on the others just because of the lack of volume. There is one though, [where] you need to be careful — is that there are some devices called TENS that you can buy for very, very cheap prices. We're not even sure they're properly built, they're properly checked, properly checked for safety. So I would say in those cases, go for the brand.

Carl Cincinnato (14:29): Are there any complementary or alternative therapies that are standing out as being particularly helpful?

Francois Cadiou (14:35): There we also have a little bit of the same problem as the TENS versus the branded devices, which is that we don't know yet if all of the complements actually have the active ingredient they claim they have. And today, for now, the problem is that we see big, big, big differences. That's one. The other part is that complements are more — really taking a long time to work. By definition, they are less heavy on the body, so less efficacy usually comes with less side effects, but it also means that it takes a long time. So we will see them coming up progressively. We need a bit more, we will need a bit more digging in and probably making differences between the producers.

Carl Cincinnato (15:32): Let's talk about super responders. So, we've had some people respond fantastically well to some of the newer treatments that have been made available. And a super responder is described as someone who has an 80% or higher reduction in migraine frequency or migraine burden. How close are you towards predicting who might be a certain responder to certain treatments?

Francois Cadiou (15:55): I don't know. Today this is really the fundamental research on the prophylactic, so preventative treatment, responding. I cannot tell you if it'll take one year, two years, three years — how many millions of records it will take us — to be able to really be able to predict who is a super responder. I could give you a random figure, but behind, after the question, is for what proportion of the patients, or what proportion of the cases, would we be right in predicting that somebody will be a super responder?

Francois Cadiou (16:37): Today our focus is more on another aspect, which is to be able to see which treatment you should take or what you can do potentially when you are anticipating that an attack is coming. So, we have a first patent there, and we are running models. Because for years we've had people asking us, "So can you help us in predicting the migraine?" The problem



we were having is that predicting it without having any way to help was not really satisfactory. But now we are seeing more and more possibilities to help even before the pain is there.

Carl Cincinnato (17:22): That's exciting. So you get a little notification, or a little opportunity, to intervene and prevent before it's too late.

Francois Cadiou (17:31): Yes. As long as it's not stressing you [out], and making you think that truck will be running [over] you tomorrow, and that it's making you stress and get a migraine.

Carl Cincinnato (17:41): Yes, you don't want it to be a self-fulfilling prophecy if you get an alert saying you're at risk of a migraine. It could be that thing that could trigger the migraine. Yes, so it's a balance.

Francois Cadiou (17:50): Yes. It needs to be something practical that you can do, and you're confident that it'll avoid it. It will really work in a high proportion of cases.

Carl Cincinnato (18:01): Let's switch now to the ER — so visiting the emergency room, you know, hospitals. How many people used the ER last year as a percentage of users of Migraine Buddy?

Francois Cadiou (18:16): So that's a figure we don't necessarily ... we don't continuously check. What we know is that 40% of the users have used the ER at least once. And that's in line with other studies which have been published. So, I was very, very surprised that my neighbor was actually working at the ER, and I went to ask him and said, "Do you see many migraine patients?" He said, "Oh, yes." So yes, that's actually a lot more common than people think. The thing is that though, it's not necessarily recorded as migraine in the systems there. So, if I had to guess based on the latest figures I've seen, I would say that 5 to 10% of the users have had a case last year where they could not find something else, anything else to do, other than going to the ER.

Carl Cincinnato (19:19): Looking at the number of people that get better, I mean, I'm sure that there are people that are getting better who are using Migraine Buddy. What kind of patterns do you see in those individuals?

Francois Cadiou (19:31): We've been observing for years that people after four months get better. And we've been wondering, we've been asking, checking, discussing about that with other researchers. And the first thing has been: better understanding. Better understanding of their migraine; better understanding of what is happening. The second has been discussion with the — better exchange with the doctor, access to better treatments. And so, the figure we've reached at which was that being able to, reach this better understanding, and to some extent it can be done with paper, also. There is a sort of 20 to 30% responder rate, meaning that when starting to record and take becoming more and more conscious about what is happening, seems to be reducing the frequency of attacks for 20 to 30% of users, even without any treatment.

Carl Cincinnato (20:47): So just the pure act of keeping a regular diary can be almost therapeutic for some; can have a positive impact?

Francois Cadiou (20:56): Yes. It's not necessarily just in the head, it's also in the relation with other people. It's also in the management of the stress because you depend on ... if you understand better what is happening to you, if you're able to better compare it with other



people to better explain it, it's also reducing the stress. And as we know, stress is one of the top triggers, and it's a loop. So anything that helps in reducing, blocking this loop is actually meant to be quite positive. [Also], we have many other patients, users, who actually get better because they get access to better treatments, not necessarily drugs, but it can be also support, it can be also better handling of comorbidities such as depression. Depression and anxiety are extremely common together with migraine.

Carl Cincinnato (21:56): Are there any patterns about sort of lifestyle behavior that you notice in people that are getting better, or even those who are getting worse?

Francois Cadiou (22:04): What we see — and what we saw with COVID — every year, when comes the 20th, roughly around the 20th of December, when people start going on holiday, we see people have a reduction in stress-related migraines. It takes three days — so don't expect that every weekend. Usually we have to wait at least three days before seeing that people are at home. And then stress-related migraines are going down. We've seen that also with COVID. So it seems that work from home for some people — not everybody, for some people — work from home helped. That's one. After, there's no magic solution. One thing which seems to be coming again, and again, and again, and again is regularity. We still need to do more research on that, but regularity in the sleep time, when you wake up, when you go to bed, seems to be even more important in many cases than just how long you sleep. Variability in the wake-up time seems to be impacting more than sleeping six, or eight, or 12 hours.

Francois Cadiou (23:37): So we have some research ongoing on that matter. But it's not just about that: It's about regularity in life, it's in the food situation. So you should not be eating always the same. But there are elements related to regularity which are pushing us [to] believe that regularity helps a lot. Why? Again — and that's only a hypothesis at this point — it's because we're facing brains which are hypersensitive. And to avoid our brains to go up to the threshold where everything goes into migraine, regularity helps in keeping us under the threshold.

Carl Cincinnato (24:31): You've spoken about a couple of triggers there: sleep; we've spoken about stress; and then you're just speaking about the importance of routine, and how the migraine brain, particularly one that's vulnerable with lots of attacks, doesn't like changes to that routine. What are you seeing to be some of the most common triggers across the platform?

Francois Cadiou (24:53): So, I will share with you the fuller list, but stress, super common; weather changes, obviously; a lot related to different elements of food. So many of us are searching in the food. You don't really have “magic food” which is making you react, like an allergy. So, it will be how much; it will be potentially combined with others. You will have everything which is really testing your body, like alcohol, coffee, all of those. And after, it can be related to your environment and things that you don't necessarily control. Jet lag will be one, typically. The weather as mentioned, the change in seasons — which could be related to pollen. We are doing research now on pollution. Also, for some of us, small particles, ozone, that could also be. Again, it's a combination. And what is very, very, very difficult and needs to be kept in mind is that sometimes triggers can be mixed up with prodrome. You can have a case where you think that taking those potato chips was your trigger — junk food. But actually, the fact that you were craving was more of a prodrome; a sign that you get before your migraine.



Carl Cincinnato (26:53): Right. So it's a bit of a puzzle to untangle as to when you binge or you have a sudden craving for potato chips, and then you eat them. Was it the potato chips or was it just the prodrome? The migraine was already underway, and you were just, you know...

Francois Cadiou (27:06): And the fact that you were waking up in the night suddenly, or the fact that you woke up extra exhausted, or that you felt fatigue, that can be something which would be a prodrome. So, but the key point — because knowing the trigger, avoiding it is one. But we should never feel guilty because you try to avoid everything — we try to avoid everything, and we still get the migraine. And that's when it's important to [remember] that what we thought was a trigger was actually maybe just a prodrome.

Carl Cincinnato (27:43): What do you see about how weather influences migraine?

Francois Cadiou (27:48): That it's not the same model for everybody; that's one thing. Until now, a lot [has] been said about pressure drop, which is happening just before it's raining. But nobody to date, including us, managed to find a model where we could say: "Just with that level of pressure drop or that slope of pressure drop, we get most people triggered at that point." So first, our sensitivity is changing, that seems to be clear. And then it's not necessarily just that. Some people can be potentially related to the temperature, to the direction of the wind, to some specific types of winds in some places, to other elements that we're searching for. So that's why, for example, now we've added UV tracking, we've added the temperature, we've added pressure. We already had the pressure, the humidity, all of that, and we're continuously observing. And we know that not everybody will be sensitive at the same level. There are places that it may even be — depending on the latitude — you may be more or less sensitive to elements depending on the season, also.

Carl Cincinnato (29:15): So it's a lot more complicated than just, "Yeah, the weather's a trigger." There are multiple aspects to it.

Carl Cincinnato (29:21): Francois, thank you so much for sharing so many insights from Migraine Buddy. Before we let you go, can you tell us a little bit more about what Migraine Buddy is, specifically, and how does it help people?

Francois Cadiou (29:34): So, Migraine Buddy, first: is an app; you can download it. It was conceived as a free migraine diary to let you document in an easy way with your doctor; everything you may want to document for your doctor. And over time with the community, it became a community. You can find other users with whom you can, if you want, exchange with. And we also have more and more intelligent tools that we're developing in it, such as weather sensitivity, analysis of your potential triggers, and suggestions of where to start. And it's a massive, massive tool to be able to push research by the patient, for the patient, all over the world. You can find it — you just search Migraine Buddy on any app store, Google Play — you will find it very easily, no worries.

Carl Cincinnato (30:36): Fantastic. Well thank you very much Francois for joining us again on the Migraine World Summit.

Francois Cadiou (30:41): Thank you. Have a great day.