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Incorporating EBM in Practice

Announcer:
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This episode of *Living Rheum*, titled "Incorporating EBM in Practice," is sponsored by Novartis US Clinical Development and Medical Affairs. The host and speaker have been compensated for their time. This program is intended for health care professionals.

Here's your host, Dr Jason Liebowitz.

Dr. Liebowitz:
The time it takes for medical knowledge to double in quantity has decreased from 50 years in 1950 to just under 4 years in 2010.[1] With so many new discoveries, how can rheumatologists keep up and practice evidence-based medicine, or EBM for short? This is ReachMD, and I'm Dr. Jason Liebowitz. Joining me to discuss the role of evidence-based medicine in rheumatology is Dr. Michael Putman, an Assistant Professor of Medicine in the Division of Rheumatology at the Medical College of Wisconsin. Dr. Putman is also the Associate Fellowship Program Director and Medical Director of the Vasculitis Program. Dr. Putman, welcome.

Dr. Putman:
Hi, thanks so much for having me. I'm excited to talk about my favorite topic.

Dr. Liebowitz:
Well, to begin, Dr. Putman, what do you think is the greatest challenge facing clinicians, when it comes to practicing evidence-based medicine?

Dr. Putman:
Oh. The greatest challenge for evidence-based medicine is the greatest challenge that I think all of us have, which is just time. I always like to say that I'm poor in time. It's hard to do all of this given all of the demands of a busy clinic, and, you know, we all have families and hobbies and things that we're trying to do, and squeezing in, you know, a high-quality critical appraisal is just one more thing that I think we struggle with.

You know, that problem is quite acute. You know, the first part of it is that there's just too many papers, and there are thousands – like you said – and thousands of papers published every month, and the papers themselves are just too long. People write really long papers, and it drives me crazy. You're saying 2 things, you spent 3,000 words on it. So, I think that trying to be efficient about how you read, and about what papers you read, is really important. And for me, that starts with searching. So, I think you really need to develop a method for efficiently finding papers.

I like to use a couple apps that help you identify papers and store them in an app on my phone, so that I have them when I need them. And I think that just building yourself a process is really important. A lot of people do this haphazardly. They kind of wait for journals to come out, and they prey on it, and try and read it when they have a little time, in between making breakfast and running out the door. And I think that you need to kind of make this into a system, so it's a part of your life.

Dr. Liebowitz:
I think that's very well said and I think many of our listeners will relate to this struggle of time to devote to even gathering and understanding the evidence. And on that note can you talk about how clinicians can make themselves able to understand and critically evaluate the medical literature, even without having in-depth training in statistics or epidemiology?

Dr. Putman:

Yeah, that's without a doubt the second biggest thing, is people feel insecure about their ability to do this, and in a lot of cases they're right. I mean, it's really hard to do this, but I think that every doctor has a responsibility to do it, and we're all capable of doing it. A lot of the really scary, complicated things in papers aren't how they fall apart. You know, the fact that they use some crazy regression model, with propensity score matching that you don't totally understand – that's not a problem with the paper. The problems with papers are often that – very straightforward. You know, they don't apply to the patient that you need to see, they have clear biases in how patients get into the paper, and they don't adequately assess the risks that are associated with a treatment, or something like that. So, you know, for me, I do think that a big part of this is deliberate practice. So, you know, just acknowledging that a lot of us, you know, still need to develop skills.

I'm constantly trying to learn new things. You know, right now, I've spent the last couple weeks trying to learn about negative controls. A friend of mine who's an epidemiologist mentioned it in passing, and I'd heard about it, and then I've spent a little while trying to really understand it. And I think that that is kind of what medicine is about. It's sort of a lifelong practice, of deliberately becoming better at something, and critical appraisal is just one of the things – like, you're deliberately becoming better at injecting joints. You should be deliberately becoming better at reading papers. And part of that is journal clubbing. I think trying to get connected to a community of people who are doing this is really important, and a lot of us do this naturally. You have to go to Journal Club and participate. And I encourage you to just take the extra step to read the paper beforehand and come with a couple of really insightful critiques that you thought of yourself, and you might be wrong but just engaging is a really good way to develop those skills.

Dr. Liebowitz:
I really like the way you're describing the process of improving our critical analysis skills in the same way we would develop other clinical skills, or clinical reasoning skills, and I agree, I think this makes it much more straightforward for people to start to approach. With this in mind, do you have any suggestions of how you'd like to provide our audience with ways to stay up-to-date on the medical literature, and to read the medical literature in an efficient way?

Dr. Putman:
I love talking about efficient reading. So, I'll try and be brief because I've given half-hour-long talks on exactly that question, but I think that people read papers wrong. I think that they start with – and, I'm not going to call anyone out, but just think about yourself. They pick it up, they read the abstract, they ruminate on it a little bit; They might skim the discussion, and then they put it down. And I don't think you should read any of those parts.

I think that when you read a paper, you're answering 3 questions. You're asking, does this apply to my patient? And you're going to find that information in the methods. You're asking, what is the risk of bias? Because that will influence how much you should believe the results. And you're going to find that in the methods as well. And then you're asking how great the benefits are, which you're going to find in the results section, and you're going to ask how great are the harms, which are mostly in the results section. And so, I think you should spend most of your time reading the methods and results, looking at the tables and figures, and I think you should not read abstracts, because they're a waste of time. So that's my biggest piece of advice. People think I'm a little bit crazy here, but I feel strongly about this.

Dr. Liebowitz:
Well, I'm certainly going to have to revise my own strategy of how to read papers. But it is very helpful and very important, I think, as you've outlined, thinking about what are the questions we're trying to answer and get out of these papers, really namely, how does it apply to our patients? Is there a reason to question the way in which the study was conducted, or question the results that were yielded? And really help to translate that into clinical practice.

Dr. Putman:
Well, let me jump in briefly. So, and this goes to what I was saying about deliberate practice. Like if you want to become a better scientist, you should read what better scientists than you do. And you're never going to find that in the abstract, or the introduction, or the discussion. You're going to find it when you read the results, and they tell you how they came about answering the question that they posed. And so that's why I think it's just so important to spend a lot of time in the methods. It's part of becoming better at reading papers and becoming better at critical appraisal.

Dr. Liebowitz:
Now, one criticism of EBM is that it can be used blindly and can cause clinicians to generalize when treating their patients. With that in mind, how can clinicians practice evidence-based medicine without resorting to a cookie cutter approach to patient care?

Dr. Putman:
Oh, man. So, you absolutely nailed one of the major critiques people have of evidence-based medicine. And this is one of those things where I think the truth is the exact opposite. I think that evidence-based medicine is incredibly liberating because if you don't do

evidence-based medicine, you know, you wind up having a lot of faith in things that don't work very well, and you wind up relying on a lot of received wisdom, and a lot of guidelines.

And so, I feel like you wind up practicing cookie cutter medicine, where you just do the thing that you feel like you have to do. So, evidence-based medicine is liberating, because you discover that a lot of the things that are received wisdom, as terribly helpful and important, are actually not true at all. And you can stop doing said things. So, for instance, today I saw a patient with gout, and one of my fellows recommended not starting allopurinol during an acute flare, and I said, "Well, that's actually not true. We can start allopurinol during an acute flare, given certain conditions, and if you talk to the patient." And there's a specific part there. Fellow also recommended that we have discussion about the standard recommendations for, you know, dietary modifications, and I said, "Well, those don't really work very well." You know, tart cherry juice, for instance, failed spectacularly in a randomized trial. I don't talk about tart cherry juice anymore, and that is very liberating, because I can tell the patient about the things that are really going to improve his quality of life. And so, I think that that's very individualized, if anything. So, I think that this is a bad rap that it has gotten, and misapplied, I can see that. I think if the business majors get their hands in it, you know, they'll build algorithms that we're all stuck following. But on a personal level, I think EBM is very liberating.

Dr. Liebowitz:
That's very well said. You know, treat the patient in front of you, and use guidelines as just that– as guidance, but not the final word on any particular decision.

If you're just joining us, I'm Dr. Jason Liebowitz, and this is a special episode of *Living Rheum.* Joining me for this discussion about innovations in rheumatology is Dr. Michael Putman.

And on that subject, what role do you think clinical guidelines from organizations, such as the American College of Rheumatology should play in guiding the practice of evidence-based medicine?

Dr. Putman:
Yeah, so I love guidelines. I think they're really interesting, and I've actually devoted a substantial amount of my research agenda in the past year or two, to guidelines. So, you know, the ACR and EULAR and BSR generate really good guidelines. They spend a lot of time thinking about them, and I think they're very, very well done. And part of that is that they've formalized the process of critical appraisal, and evidence-based medicine. They generate pico questions – they say this is a question that is worth answering, and then they perform a literature review, and then they grade the quality of evidence, which is really one of the most important things to do – say how confident are we of this? And you know, when you look at guidelines, a really fascinating outcome from this is that you discover that about half of them are based on extremely low quality of evidence, which again, is liberating, because it means that there's a lot of opportunity for you to tailor your approach to specific problems. Now the downside of guidelines is that for one – we treat classification criteria as if they are diagnostic criteria, and they're not. And there's a big difference between classification and diagnosis. Classification is where you try to define a homogenous group of patients, to put them into a clinical trial.[2] And, it winds up excluding a lot of atypical presentations, and it winds up being somewhat unwieldy in a lot of cases. If you look at the 2017 guidelines, for instance, for the diagnosis of myositis, it's a total mess. I mean, no one has ever used that in clinical practice, because it was designed to be put into a calculator by some poor research assistant, you know?

And so, I think that you need to take guidelines for classification with a grain of salt, because they aren't designed for you to be diagnosing patients with them. And so, again, I mean, guidelines I think are very helpful for teaching, but you need to, you know, approach them from a personalized perspective. And that's really where I think they're really helpful, is for fellows. I mean, I spend a lot of time with fellows, reviewing guidelines, I talked about the gout guidelines for that patient today, because I think it's very valuable for fellows to know what good, smart groups of people, applying a rigorous methodology, decide about a problem. But you have to take them with a grain of salt.

Dr. Liebowitz:
And actually, on that subject, I think Dr. Sharon Chung has done a great job. I've heard her at a number of venues discussing the new ACR vasculitis foundation guidelines and discussing a few things – one that one of the reasons for developing these guidelines was it was requested by rheumatologists, to better understand how to think about treatment of patients with rare conditions, vasculidities and that guidelines – the process of developing them – really brings together some of the best and brightest experts in a field, to help them cull the research literature and dissect things in a way that would be very hard, I think, for each individual clinician, and – and ultimately arrive, like you said, at guidance to help give a grading of the evidence, but to still allow the final decisions for patient care to be left in the hands of clinical rheumatologists.

Dr. Putman:

I had the to do a little podcast and an article with her about those guidelines, and she is very, very smart. It was just a really fun experience talking to her. And I think that is exactly what you're saying– it kind of helps all these people get together and, you know, perform a rigorous appraisal of the evidence. Now, a flipside of those guidelines that she mentioned, I think, is really interesting – is that it's very empowering for patients, because patients have the opportunity to say, you know, this is what all these smart folks thought about this disease. And if they're receiving care that is not guideline-directed, that's very appropriate, but the rheumatologists should be capable of explaining why, and so I think that there's a lot of value to empowering patients to be participants in their care from guidelines.

Dr. Liebowitz:
Absolutely. In what ways do you think evidence-based medicine will interface with personalized medicine in the future?

Dr. Putman:
That's a great question. I love talking about personalized medicine. So, you know, the first answer is that I think that personalized medicine is still a long ways off. I mean, at the end of the day, we diagnose people with rheumatoid arthritis, and then we all give them methotrexate. You know, there's a lot of information we can glean about their care, and their various antibody profiles, and their involvement, and all this stuff, and then we give them methotrexate. And I think that that's going to continue for quite some time. But I think that there's some risks to personalized medicine that we need to be aware of. You know, one is that there's a lot of, you know, personalized antibody panels and such, that have truthfully relatively poor performance characteristics. And understanding how limited they are, I think, is going to be very important.

Now, the second thing is that there's going to be a lot of new diagnoses popping down the pipeline. I think on a prior episode, we talked about DADA2 and the VEXAS syndrome, and a big barrier in rheumatology to personalize medicine is that we don't have adequate phenotyping of our diseases. And I think as this progresses, and we learn more about these subsets of diseases that may be better typified, like VEXAS, or like DADA2, I think we will have more opportunity to provide personalized treatments to people. And maybe not personalized on a personal level, but more specific to their particular disease pathology. We haven't decided on this. You know, another really neat paper that came down the pipeline recently was about cytokine hubs, and I think this is where personalized medicine may ultimately be coming from, where we identify the cytokines that are actually driving people's diseases, and then target those cytokines specifically. But if you read the papers about those right now critically, you'll notice that there's really not that much that's worth changing your practice. Some people with lupus express interferons, but that doesn't really influence very much whether or not they're going to respond to hydroxychloroquine or not. And you need to be very cautious when you hear these recommendations for personal therapies.

Dr. Liebowitz:
And on that subject, do you think developing a better understanding of genetics and epigenetics will allow us to better interpret why certain research studies are successes or failures, and better understand subgroups of patients when we apply this to clinical research?

Dr. Putman:
No. If you're talking about genetics, I think no. I think the well of genetics, if you're talking about germline mutations and, you know, the genes that you were born with, I think that well has run dry for rheumatology. I don't use any of that in my daily practice, and I don't think that we ultimately will find much more that will be of use.

I do think that the next phase of genetics is going to be quite interesting, where we actually talk about sequencing people's RNA, we start searching for somatic mutations, and we start looking past the genome to the cytokines that immune cells are actually expressing. So, I think if you mean genetics 2.0, as in what the genes have created, I think yes, that will be very influential. If we're talking about genetics in the conventional sense, I think that that ship has sailed.

Dr. Liebowitz:
I appreciate your honesty, and this has really been a wonderful discussion. I want to thank my guest, Dr. Michael Putman, for helping us better understand the ways in which clinicians can incorporate evidence-based medicine into their practice. Thank you so much, Dr. Putman.

Dr. Putman:
Thanks. That was a lot of fun, Jason, and I really appreciate being here with you.

Announcer:
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