Quick Takes
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HOSTED BY DR. DAVID GRATZER

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The new CANMAT depression update with Dr. Raymond Lam

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[Musical intro]

David Gratzer: Much has changed in eight years. In 2016, singer Olivia Rodrigo was just entering into high school. Quarterback Tom Brady seemed ageless. And hey, none of us were talking about pandemics. 2016 was also when the last depression guidelines were released. Well, it's 2024 and the update has just come out. How has depression management changed over these past eight years, and how should you change your clinical practice accordingly?

My name is Dr. David Gratzer. I'm a psychiatrist here at CAMH and welcome to *Quick Takes*. Today we're joined by Dr. Raymond Lam. Dr. Lam is a psychiatrist. He's a professor at UBC. He's the BC Leadership Chair in Depression Research, executive chair of the Canadian Network for Mood and Anxiety Treatments, or CANMAT. And he's also the first co-author of the new depression update. Welcome, Dr. Lam.

Raymond Lam: Thanks for having me here, David.

David Gratzer: So, Dr. Lam, this this isn't your first time at the rodeo, so to speak. In fact, you were the first author, as I recall, in the 2016 depression guidelines.

Raymond Lam: This is actually the fourth iteration of our depression guidelines. The first one was in 2001. And so we've been doing updates or guidelines, every, you know, 7 or 8 years. Since then, as you said, you know, progress happens. Right? And we need to update the recommendations for clinicians.

David Gratzer: What's the biggest surprise for you between this update and the 2016 guidelines?

Raymond Lam: Well, I think the surprising thing was how much literature there is, it's always amazing to me. For this particular update, we updated our literature review since 2016. And in that seven-year time, we focused only on meta-analyses and systematic reviews. That, of course, summarise all the randomised controlled trials that are out there. There were over 700 systematic reviews and meta-analyses published since 2016 on topics related to treatment of depression. And so I think it really just illustrates how hard it is for busy clinicians to keep up with this huge amount of literature, and where guidelines can help synthesize some of that and provide recommendations for that really huge amount of research that's being done.

David Gratzer: A huge amount of research, many good questions being asked by our clinician colleagues. And your approach is a little bit different. So, this is an update and actually focuses on eight highly clinically relevant questions. Right?

Raymond Lam: Yeah. We changed the format this year. Our previous formats looked at treatments, you know, medication treatments, psychotherapy treatments, neurostimulation treatments and summarized all the literature about various treatments. This time we took a different approach. Instead, we decided to look at the patient care journey. From assessment to selection of initial treatments to what do you do if people are better? And what do you do if people are not better? Because that, I think, better reflects how we deal with patients. So, this time instead of going by treatment by treatment, we look at some of these important questions that clinicians ask through that patient care journey.

David Gratzer: And we'll go into detail in a few moments. But you know, quickly some things are going to be familiar to those who have read your past guidelines, like a focus on medications and when psychotherapy is relevant. But there's some things that that haven't been included in past updates and guidelines, like measurement-based care, a discussion of antidepressant withdrawal. Digital psychiatry.

Raymond Lam: Yeah. Yes. And so there have been, I think first of all, for clinicians, it's nice to know when the evidence continues in terms of recommendations, treatments that they're using. So, they want to know, first of all, is it still a good treatment? So that's important. But also obviously, newer treatments and newer research that's out there. And particularly digital psychiatry because of course, that's the future, right? It's the present, but it's also the future. And so we did spend quite a bit of time looking at that evidence, even recognizing that of course, the evidence isn't as strong as for standard treatments like medications and psychotherapy. But we thought it was important to include what evidence that there was. Similarly with complementary and alternative medicine treatments. We focus on that as well. And things like exercise, which clearly have expanding evidence base to support its use in depression. So, measurement-based care is something we've always been a proponent of. But even more so now that it's easier and easier for clinicians and patients to track their symptoms using digital sources and others.

David Gratzer: In terms of the approach, you have multiple co-authors — I think here would be appropriate for me to make mention that I am one of the co-authors and thank you very much for this opportunity — which includes psychiatrists, but you also have somebody with lived experience who's advised the process.

Raymond Lam: Yeah. So, our guidelines, the CANMAT guidelines have always been different than other established clinical guidelines in that we start with the evidence. So we use a systematic review of the literature. We grade the quality of the evidence, but we also explicitly layer on expert opinions. And the reason for that, of course, is that, you know, evidence is evidence. But randomised controlled trials really don't reflect general clinical practice. You know, the real-world patient sitting in front of us. And that's where we really believe it's important for experts to be able to use this evidence and formulate recommendations. That's not always the case with many other guidelines, which is, I think, one reason why the CANMAT guidelines are so widely used, not just here in Canada, but internationally. They're I think they really are the most widely used guidelines in the world because they're more practical and they do deal with things where the evidence could be fuzzy, but clinicians want to know "What should we be doing?" And so we provide those recommendations alongside, of course, the quality of the evidence that goes along with those recommendations.

And so that's why it's important that we have a good diversity of expertise. We have over 45 experts, Canadian experts, represented in our author group, but also involving people with lived experience, which we've done in these guidelines now from the beginning. They're members of our author group. As well we have a panel of people with lived experience review all the draft recommendations to make sure that it aligns with patient-centred care. And we do focus on shared decision making and collaborative decision making with the patient. One of the ways to do that, of course, is to make sure they know what recommendations, treatments, are recommended. And that's why we've prepared a patient and family guide to the guidelines for our previous depression guidelines. And we will update that for the new guidelines. Available free, for free download from our website, so that patients know what treatments are recommended as well.

David Gratzer: So, there is an update for us clinicians, but also families and patients can have an update as well? Fair enough.

Why don't we dig in? There's a lot of good stuff here. And obviously in a podcast we're not going to cover everything, but maybe we'll run through these different questions that you've asked, and your co-authors have asked and some highlights in terms of those eight questions.

Question number one: what are important issues for assessment and diagnosis?

Raymond Lam: Okay. So, I think the key important update in that section is the recognition now that childhood maltreatment – physical, emotional, sexual trauma – maltreatment in childhood is a big risk factor for development of depressive disorders. And it's very important for us to recognise because it has some clinical relevance in terms of the treatments that will want to use, but also in terms of, you know, that the response isn't as good, right? They're more difficult to treat when people have this history of childhood maltreatment. So very important aspect to recognizing and assessing depression.

David Gratzer: I noted as well in this section, you did talk about screening tools, and there was mention of the PHQ-2 and other screening tools. I mean, that's a thread throughout. Again, a recognition of not only the importance of measurement-based care, but relevance.

Raymond Lam: Yes. And, you know, I think it is expanding the use of measurement-based care. In other words, using a validated scale to measure outcomes when we're treating people for depression. It's still a tough sell for psychiatrists. You know family physicians are actually more likely to use a scale like a PHQ-9 because they can see where it saves them time. Psychiatrists think they have time, but realistically, if you're really looking for things like remission of symptoms, it's very hard to do that unless you're asking about all the symptoms. I don't think most psychiatrists ask about all the symptoms. So, it's a good shorthand way of at least assessing the various symptoms that are seen to see what degree of improvement that there is. And it really just supplements clinical decision making and clinical judgement. So, we're not telling people to replace clinical judgement just to use it alongside of clinical judgement and clinical assessment to really be able to, you know, look at treatment options because there are some treatment options that we recommend based on severity and the degree of response that people have based on a rating scale.

David Gratzer: And here the recommendation is, and we should move on in a moment, but the recommendation is maybe start with PHQ-2 two questions and then move on to the PHQ-9. And again, you know, clinical judgement is obviously important as well but the note that is made specifically here is particularly in primary care, certainly not only in primary care, much depression is missed. And as a result, screening might be particularly relevant. Is that a fair summary?

Raymond Lam: Yes. Yes, it is. And we recognise there's a bit of controversy about whether screening is effective or not. But we do feel that in the presence of risk factors that there should be screening for depression in primary and secondary settings.

David Gratzer: Question number two: what are the principles for depression management?

Raymond Lam: Well, again, the principles remain similar, right? In terms of comprehensive assessment, educating, using psychoeducation with patients, selecting evidence-based treatments, and then using measurement-based care. I think that's the important component of it; being able to track symptoms, over time, with measurement-based care.

David Gratzer: Big role for exercise in terms of recommendations back in 2016. Nothing's changed here. It's a first line recommendation. I see for people who have mild severity and adjunctive for moderate, as a second line recommendation.

Raymond Lam: Yes. I mean, the evidence base is greatly expanded, with randomised controlled trials and meta-analyses all showing good benefits of moderate exercise. So basically the Health Canada recommended exercise levels are actually helpful for depression. Of course the issue is, along with some types of psychotherapy, is that there needs to be some motivation, right, for people to do exercise. And so, usually supervised exercise programs are more helpful. And we do have a toolkit to help clinicians use exercise and to prescribe exercise in their everyday practice. Also available on our website, developed by exercise specialists, to be able to incorporate exercise into a treatment regimen for depression.

David Gratzer: What might you say to a patient who you think has a mild or moderate depression and is not doing regular exercise?

Raymond Lam: You can always, like everything else, start off small. So just increasing activity of any kind is helpful. And then, you know, starting to increase the amount of exercise whether that's even starting with daily walks for example. Getting something that's doable in. And of course, you know, looking for programs that are available in the community and many programs are available through things like community centres. In terms of a regular kind of exercise program appropriate to the type of person that they are. So, you know, like behavioural activation, starting off with small steps and moving up is often helpful.

David Gratzer: Question number three is a big one. How are treatments selected?

Raymond Lam: We do go over the principles, in terms of selecting treatments and some of the things to look at, which include things like patient preference, but also previous treatments that patients have had, availability of treatments, the cost of waiting for a particular treatment if there's a wait time involved, etc. But one of the key factors is really severity of the depression. And so, we do break it down into recommended treatments for mild, moderate and severe depressions. And so, for mild you mentioned that exercise for example could be a monotherapy. We know that pharmacotherapy and psychotherapy are both equally effective for mild severity. But on the basis of risk benefit we recommend psychotherapy if available. Because of the lower risks involved with psychotherapy for mild depression. Whereas for moderate depression it could be either psychotherapy or pharmacotherapy again, depending on accessibility. And then looking at the combination of using both together because using both together does result in better outcomes than either monotherapy by itself.

And then for severe depressions of course we say start with pharmacotherapy because that's immediately accessible. Plus, people can't access or use psychotherapy effectively if they're severely depressed. And then sequence; add psychotherapy once people are feeling a bit better with the pharmacotherapy. But you should be using the combination for people with more severe depression. And of course, always consider things like electroconvulsive therapy for severe depression when there are safety risks involved.

David Gratzer: Next question is: what is the role of digital health interventions? Again, a very different sort of question than had been asked. Very active area of research. Takeaway messages here?

Raymond Lam: Yeah. So for digital health interventions, we're really talking about online and mobile apps. Even some of the newer, you know, chat bots and things like that. And the issue is, is that unfortunately, the evidence for many of these interventions is still slim. And we are always trying to balance the evidence versus what people are actually using and what might be helpful for them. And it was a controversial area in terms of our experts not always agreeing in terms of what the evidence was. But in the end, we recommended guided digital health interventions. So those are things like online, cognitive behaviour therapy type of programs that are guided by either a coach or a therapist, because when they're unguided or self-directed, hardly anybody ever does them, right? That's the problem. They're kind of effective. But the retention rates are very low in terms of people who actually go through a program. So, the guidance really helps people to get through the program and get the benefits of that online or mobile app. So that's our recommendation is for digital health: guided digital health interventions for mild depressions. And as adjunctive treatment for more moderate to severe depressions.

David Gratzer: In some ways the successful digital interventions are laced with humanity.

Raymond Lam: Yeah. Yeah! We also actually go over how clinicians can assess or evaluate a mobile app or a digital health intervention, because it's so rapidly changing that it's hard for us to make recommendations specifically because, you know the apps change every day. And so, it's important that clinicians know how to tell if an app seems reasonable in terms of using it with their patients. And we do put some effort into helping guide their evaluation.

David Gratzer: And there are some recommendations. Again, the evidence here is lighter. But people who are familiar with apps and so on will recognise names like Headspace and of course moodgym. But again, a framework for evaluation in a very evolving field.

Raymond Lam: Yes.

David Gratzer: Okay. How was treatment monitored?

Raymond Lam: Again, we've kind of talked a bit about that in terms of measurement-based care. Using rating scales, some tips in terms of incorporating measurement-based care into your practice. Nowadays, though, I mean Apple iOS now includes the PHQ-9 and the GAD-7 in its Health app. Patients can use it now and track their results over time in the same way they can monitor their steps. It's, you know, it's the way to go.

David Gratzer: Next question: what should be done when a patient is better?

Raymond Lam: Well, this is when we talk about maintenance treatments. People are better with pharmacotherapy or psychotherapy. You know, what should be done? How long should they stay on the medication? How should they come off of the medication? And clinical issues like that are covered in this. There are not many changes to this because we know that, for example, maintenance pharmacotherapy is better than stopping it too soon. The evidence before our recommendation was 6 to 9 months for everyone after remission of symptoms with a medication. Now the evidence is more in the 6 to 12 months is the recommendation. And of course, with people with risk factors they need to have longer term maintenance, for two years or more. And that hasn't really changed. A couple of changes in terms of the risk factors. For example, childhood maltreatment is one of the risk factors now, right, for longer term treatment. We do talk about discontinuation effects and, how best to reduce medications, because that's an important consideration when you're starting someone on an antidepressant you also want to be thinking about: what about stopping? Are there some medications that are harder to stop than others? And I think that's where we're pretty clear that medications like paroxetine or venlafaxine are more have more discontinuation effects than other medications.

David Gratzer: Patients often talk about discontinuing their antidepressant trial when they're doing well, perhaps not surprisingly. What's a way you might speak to a patient who has, to be blunt, a complicated history. Perhaps many past episodes, maybe childhood maltreatment, but at the same time wishes to be medication free?

Raymond Lam: It's shared decision making. Making sure they have the information. Right? Because not everybody relapses. And even if people stay on their medication, there's still a relapse rate. So, we're playing percentages here. And so the percentages are often, you know 15 to 20% more relapse with stopping the medication too early, which translates, into 1 in 3 or 1 in 4 people, right? So, of every four people who stop one will relapse if they stop too soon compared to stopping. So you know, that's not everyone, but it's a sizeable number of people. And so people have to understand their risk in terms of stopping the medication. So, I think that's the important thing. There are mitigating things that help though. And psychotherapy is one of those. People who do CBT, when they're well, do better when they stop their antidepressant because it gives them some tools to help regulate their moods and prevent another depressive episode from occurring.

David Gratzer: Next question. What should be done when a patient is not better?

Raymond Lam: Okay. And this is the meat of the section for psychiatrists in particularly since that's who we see, right? People who are treatment resistant, who are not getting better with standard treatments. And that's where we go over some of the particular medication treatments that are available. Options from switching to adjunctive treatments and some of the newer recommendations for adjunctive treatments. What is clear now from the evidence is that switching to monotherapy antidepressants time and time again is not a good strategy. There are diminishing returns after the first switch. And so, we are not looking at saying you should be constantly switching medications. Instead, we're moving adjunctive treatments earlier into the treatment algorithm. Maybe as soon as the first treatment if they've, for example, had a partial response, because you don't want to lose that response by switching to a different antidepressant. You're better off adding an adjunctive treatment to boost the effect of that initial treatment. And similarly, after the second kind of failed antidepressant, that's where we'd really be thinking about for sure about adjunctive treatment rather than switching to a different medication.

And some of the newer adjunctive treatments are – brexpiprazole is now a first line adjunctive treatment along with aripiprazole. Those two atypical antipsychotics, clearly have efficacy and tolerability and are first line recommended adjuncts.

The second line adjuncts include some of the other antidepressants like mirtazapine, adding bupropion to SSRI, for example. Some of the other atypical antipsychotics like olanzapine, quetiapine and risperidone, which have good evidence for efficacy, but because of their side effect profiles, you know, have been downgraded to second line, because they have more side effects than aripiprazole or brexpiprazole.

And then a newer adjunctive treatment, the atypical cariprazine, which has some data now to support its efficacy as an add on strategy. And, of course, the interest now in ketamine, both the intranasal s-ketamine as well as intravenous ketamine, which now has sufficient evidence to recommend it as a second line treatment for people with treatment resistant depression.

David Gratzer: A significant shake up of recommendations over the last couple of guidelines. So traditional meds like bupropion, lithium lower on the list, ketamine, and of course the atypical antipsychotics having a bigger role. Is that maybe the biggest change in the guidelines overall perhaps?

Raymond Lam: I think so because of the focus on our monotherapies are not that good for a lot of people. The antidepressants. And so, we really are looking at, you know, combination and novel treatment approaches. But we also looked at, of course, psychedelics. There's been some really interesting new studies but they're pretty preliminary still. And so, we really do regard psychedelics right now, with psilocybin and MDMA for example, as still being investigational treatments. Not good enough evidence yet to include them in our recommendation list.

David Gratzer: Is that one of the big research questions that you have having completed this update, thinking about the next update?

Raymond Lam: Oh, absolutely. Because there's some pretty interesting data coming out about psychedelics. And, you know, the only question is the expectancy factors, the placebo factors because it's so hard to do blind studies with these medications and that that's a key consideration. We're going to have to kind of look hard at that evidence and see how it expands out.

David Gratzer: And the last question on the list is: When should neuromodulation treatments be used?

Raymond Lam: And again, we separated this out a bit because, unfortunately, most of the newer neuromodulation treatments are not widely accessible. Certainly, here in Vancouver for example, it's very hard to get transcranial magnetic stimulation, even though the evidence is very good that it's a useful treatment in people

with treatment resistant depression. So that's very unfortunate. But that is the case. ECT, electroconvulsive therapy, of course is still very helpful and effective, particularly when everything else has failed. But it's really the transcranial magnetic stimulation and some of the newer protocols like theta burst stimulation where you can reduce the time it takes in a session. Still need to use the five days a week, unfortunately, but you can get the session time down to 15 minutes. So certainly the protocol, some of the recommended protocols, have changed for transcranial magnetic stimulation but probably the major issue, particularly here in Canada, is availability of some of these treatments.

Transcranial direct stimulation treatments have very interesting evidence but unfortunately, we think, still not to the level where we can recommend it as a first- or second-line monotherapy. You know, we really think that more research needs to be done on tDCS before it's ready for prime time.

David Gratzer: But this section, which has a similar section in 2016, is evolving, right? Mention not just of rTMS, but theta wave and so on. I mean it seems that neuromodulation has really changed over the last eight years in terms of the research and what's clinically relevant.

Raymond Lam: Yeah, absolutely. And, you know one of the things that we were really hoping would be included in this update was biomarkers. And unfortunately, they're still not near prime time. But maybe in eight years because, in particular for neuromodulation, there are some really interesting EEG studies showing potentially good biomarkers. And we're investigating one right now in our Canadian biomarker integration network. Looking at predictive use of EEG for treatment response. But particularly for neuromodulation that looks very promising. That we may be able to predict who is going to do better with the neuromodulation treatments in future using EEG. But unfortunately, at this point, no biomarker has achieved the prediction requirements to be clinically useful. And, David, that includes pharmacogenetic testing. So that was again a bit of a controversial area because there are several meta-analyses out now showing benefits of pharmacogenetic testing for treatment outcomes in depression. However, there are real major methodology issues with those studies included in those meta-analyses. And the effect sizes seem small. And so we don't recommend pharmacogenetic testing for routine clinical use before starting someone on an antidepressant. There may be utility in people who are treatment resistant or not showing standard responses or having more side effects than expected in terms of these medications. But those studies haven't been done. So, they haven't been focused on these subtypes or subgroups of patients. And so we want to see more of those studies before we recommend pharmacogenetic testing.

David Gratzer: Many of our patients do learn about these sorts of testing and are encouraged. What might you say if a patient raises it?

Raymond Lam: So, I think there's no harm certainly. It's pretty easy, right? It's a, you know, a swab that's done. And if people want to do it I think the information is helpful. It's just that the necessity of doing it before selecting an antidepressant for most people is just not there. Compared to just starting them on an antidepressant and seeing how they do. So that's where, if they have the results, then we do make some suggestions in terms of how you can use the results. It's the recommending it routinely for every patient that we don't recommend.

David Gratzer: Dr. Lam, it is a *Quick Takes* tradition that we close with some rapid-fire questions over the course of a minute. Are you ready?

Raymond Lam: I'm ready.

David Gratzer: Let's put one minute on the clock. Dr. Lam, [what's] one thing all clinicians should know about the new update?

Raymond Lam: That they're not standards of care. That these are evidence informed recommendations, not standards of care. They're suggestions or recommendations that people need to consider in a context of the patient sitting in front of you.

David Gratzer: What was one of the biggest debates of the co-authors and putting together this update?

Raymond Lam: The biggest debate was definitely around the digital health interventions, because there were some people who felt that security and privacy issues were paramount, and we shouldn't be making any recommendations unless they have been vetted that way. And others who felt that people are going to use them no matter what, so we better be prepared to give them some advice on what to use.

David Gratzer: What keeps you up at night? Thinking about this update?

Raymond Lam: What keeps me up at night are the special populations that we weren't able to deal with. Because we just can't distil things down for, you know, pediatric depression or geriatric depression and be able to give the nuances. And so we've decided not to include special populations this time. You know, I'm sorry about that, but we do have full guidelines coming out on perinatal mood disorders, on OCD and we have plans for some of these other specialty subgroups.

David Gratzer: And at the buzzer, one last question. You've been involved in depression guidelines in Canada for more than two decades now. Are you going to lead the next update?

Raymond Lam: I'm definitely not leading the next update! One of the things we did with these guidelines is to involve junior colleagues or less senior colleagues who we are sure will be able to take over the mantle of leading the new depression guidelines the next time they're needed.

David Gratzer: Fair enough. Well, you know, the update is readable, timely, relevant. I it's a great effort and you should be very pleased with the outcome.

Raymond Lam: Oh, thank you very much, David, and thanks for your participation as well. Very helpful.

David Gratzer: Well, we appreciate your efforts. The guidelines are now published. It's published in the *Canadian Journal of Psychiatry*. Of course, as you've made mention of the resources on the CANMAT web-page, including for families and patients. Are there any other resources we should be aware of?

Raymond Lam: We will be developing a pocket guide, which is a quick summary of the guidelines. We know that clinicians can't always read a full issue of a journal. And so we will be updating our pocket guides which are very popular amongst the clinicians and trainees.

David Gratzer: Dr. Lam, once again, thank you for your time.

Raymond Lam: Thanks very much, David.

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