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Digital Therapeutics Clinical Trials: From Design to Data Interpretation

Announcer:
Welcome to ReachMD. This medical industry feature, titled "*Digital Therapeutics Clinical Trials: From Design to Data Interpretation*," is sponsored by Otsuka. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck.

Digital therapeutics are a rapidly developing type of treatment option across several therapeutic areas, including mental health. Joining us to discuss this evolution and its implications for treatment is Dr. Sarah Shizuko Morimoto, who's a Licensed Clinical Neuropsychologist, Director of Cognitive Remediation and Psychiatry, and an Associate Professor in Psychiatry at the University of Utah in Salt Lake City. Dr. Morimoto, welcome to the program.

Dr. Morimoto:
Thanks for having me.

Dr. Turck:
Let's start with some basics; what exactly are digital therapeutics, and how does the FDA evaluate and classify them?

Dr. Morimoto:
Digital therapeutics can be described as a software-based intervention, which can be prescription or non-prescription, that's designed to help treat or alleviate a specific disease or disorder. Every digital therapeutic requires an FDA authorization, which means that the FDA has evaluated the evidence supporting the technology's use as a therapy for a specific clinical indication.[1,2]

So keep in mind that while technology advances rapidly, the science behind it really needs time to catch up. So, when you or your patients are considering a digital therapeutic, it's important to evaluate the supporting evidence yourself. Do your own research and make sure that what the intervention is claiming to do is really supported by the data.[3]

There are many health and wellness apps available over the counter that claim to improve sleep, or help with relaxation, or even longevity. And while they sound great, these are likely not be held to the same standards of evidence that an FDA-authorized digital therapeutic requires. So if you're treating depression, attention deficit disorder, a substance use disorder, you really need to differentiate for yourself and your patients between a wellness app which does not have FDA authorization and therefore likely maybe not so much data and a digital therapeutic that does.[1]

Dr. Turck:
Now most of us have some understanding of how pharmaceuticals and devices get approved by the FDA. So, Dr. Morimoto, what does that process look like for digital therapeutics?

Dr. Morimoto:
So for a digital therapeutic to be FDA authorized, the FDA looks at two main factors: the efficacy or effectiveness of the digital therapeutic in achieving its goals and the risks associated with its use.[4–7]This evidence is typically gathered from clinical trials designed to assess how well the digital intervention works and what potential risks it might pose.[1]

In terms of risks, digital therapeutics are generally non-invasive, so they may appear to pose fewer physical risks compared to

traditional medical devices, such as an implanted defibrillator. But they can still have unintended outcomes related to how users interact with the software, which is why FDA evaluates their safety.[4–8]

So data safety and monitoring boards are often involving in keeping track of all adverse events during a clinical trial, even those that might seem unrelated. This meticulous approach helps ensure that any potential risks are identified and addressed. The FDA will then re-evaluate the findings to confirm that no adverse events have been missed and no bias has been introduced into the data. It's also common for companies developing digital therapeutics to consult with the FDA's before or during the trial design phase to align with regulatory expectations. More company are moving toward this collaborative approach to ensure that their products meet FDA standards.[4,5,7]

Dr. Turck:
So thinking about trial design, what are some of the key considerations when setting up a clinical trial for digital therapeutics, especially in terms of choosing the appropriate control arm?

Dr. Morimoto:
Yeah this is a great question and one that's answer is evolving. Digital therapeutics are what I like to think of as the third pillar of treatment, alongside pharmaceuticals and behavioral interventions. The pandemic has really highlighted for us the potential, making high-quality, evidence-based care much more accessible to a broader population, assuming internet access is available to them.[8–10]

But to answer your question, choosing the right control condition is critical in a clinical trial for safety and efficacy. If the goal is to compare the digital therapeutic to no intervention, a waitlist control might be appropriate. But if we want to understand its effectiveness compared to other treatments, more specific controls are needed. For example, if the therapeutic uses a type of psychotherapy that's effective in-person, it would be better to compare outcomes between in-person psychotherapy and the digital version. So for digital cognitive interventions, comparing them to a regular video game rather than no intervention could help isolate what makes that digital therapeutic effective.[11]

One thing I'd like to point out is that often what we call placebos are actually a form of treatment. For example, most of us who work with patients know that attention and care from a provider is a treatment in and of itself, although that type of care may be used as a placebo in some clinical trials. So, I think it's important to also keep that in mind when you're evaluating the evidence, that even interacting with study staff or a provider, or having people ask how you're doing each week, is a treatment within itself and an important one, which can all impact how the data are interpreted overall, since in a digital therapeutic that's not being done to the same degree.[11]

Dr. Turck:
For those just tuning in, you're listening to ReachMD.

I'm Dr. Charles Turck, and today I'm speaking with Dr. Sarah Shizuko Morimoto on understanding and evaluating digital therapeutics in clinical practice.

Now beyond trial design, Dr. Morimoto, are there any other special considerations we should keep in mind when it comes to evaluating digital therapeutics?

Dr. Morimoto:
Yeah, one major concern that often comes up is data privacy and security. Patients are understandably worried about how their personal health data is being handled. As technology advances, so could the risks associated with data breaches.[12]

Data coming from the apps are in some instances considered protected health information so it's important for investigators, developers, companies to comply with regulations like HIPAA and implement strong security measures, such as encryption, to protect sensitive health information that's being collected by the apps.[12] Now on the positive side, digital therapeutics can remove some of the barriers that have traditionally limited access to quality healthcare, such as cost, geographic location, or availability of specialists.[8]

They're noninvasive, they don't interact with medications, and largely have few side effects related to technology use itself.[8] So providers can maybe feel safer prescribing these to patients knowing that they don't pose as many risks.

Still, something that I struggle with as someone who designs and helps execute these trials is that the typical clinical trials needed for a drug to be approved by the FDA can take five or more years to collect the necessary data to establish safety and efficacy or effectiveness. But unlike a fixed molecule in a drug form or a regimen like a behavioral treatment, digital interventions continue to evolve, and they need to because technology is always evolving. Just think about how often you have to update your phone or your apps on your smartphone. So to be effective, these interventions need to remain engaging and relevant to the patients that we are

trying to target. If they don't, there's a risk that people won't want to use them, and they won't get the active dose that that the studies have – have investigated.

So, one thing that digital intervention developers must contend with is balancing the need to innovate with requirements for clinical validation.

Dr. Turck:
You've brought up some important points, Dr. Morimoto. And when it comes to evaluating the data from these trials, what should healthcare providers focus on?

Dr. Morimoto:
Yeah so I really believe that patients are experts in their disorder and the doctors, especially those that have long term relationships with these patients and in long term treatment settings, also know their patients really well and what sort of barriers are preventing their patients from accessing treatments or reaching their goals.

So, I'd like people to keep in mind that there are several positive things about digital therapeutics that they may offer to you and your patients that other treatment modalities do not.[3] For some apps, the clinicians and patients can track what's happening while they're using the intervention. And so instead of just prescribing something to someone, either a medication or a behavioral treatment, and having to rely on them being accurate reporters, sometimes over a month in between sessions, some digital-age therapeutics can provide ongoing data to both the patient and the clinician for tracking their progress in real-time.[8]

Going back to the other aspects clinicians should evaluate in these therapeutics, again, the type of control used in the trial is critical to interpreting the results. We need to understand what the digital therapeutic was compared against, whether it was a waitlist control, a digital sham, or a comparison with a traditional treatment and what non-specific factors are introduced with each of those.[11]

Also consider the scales used to measure the outcomes. Are they commonly used in clinical practice; do they provide meaningful insights into the patient's experiences? Translating trial data into real-world clinical benefits is crucial for making these informed decisions. Ultimately, healthcare providers and patients must determine if the trial results align with that specific patient's treatment goals, weighing the potential risks and benefits.[3]

Dr. Turck:
Now let's talk about clinical meaningfulness. How does the FDA define this concept, and why is it important for digital therapeutics?

Dr. Morimoto:
So the FDA defines clinical meaningfulness as any improvements or deteriorations that occured from the individual patient's experience.[13] It's important to note that traditional between-group differences that we usually think of as demonstrating the product's impact don't always signify a meaningful impact on the individual patient. So while the typical between-arm comparison is very important, it's also important to think about how the intervention changed each patient's experience of their disease or condition. To that end, the FDA recommends obtaining meaningful patient experience data alongside the regular between group data and they're interested in what constitutes a meaningful within-patient change in scores and between-group differences.[13]

For example, when we're treating depression, we look at more than just symptom reduction. We consider whether patients feel better about their overall progress and if these small improvements can lead to broader positive change.[3,14]

Dr. Turck:
Now, with all this in mind, Dr. Morimoto, how should clinicians and patients approach using digital therapeutics?

Dr. Morimoto:
The approach to digital therapeutics should be centered around understanding both efficacy and meaningfulness. Clinicians can use trial data to set realistic expectations for what a therapeutic can achieve. And by identifying how digital therapeutics can impact their patient experiences, we might see greater patient utilization of the therapeutic because patients are looking for that meaningful clinical change.[5]

Let me also add that these interventions may also allow more patients the opportunity to engage in evidence-based care, so I see that a digital therapeutic can be a great tool for clinicians and patients to focus on the goals that matter to that patient.

Dr. Turck:
Well, you've certainly given us a lot to consider. And I want to thank my guest, Dr. Sarah Shizuko Morimoto, for sharing her insight into the evidence-based evaluation and the practical application of digital therapeutics. Dr. Morimoto, it was great speaking with you today.

Dr. Morimoto:
Thanks for having me.

Announcer Close
This medical industry feature was sponsored by Otsuka. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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