Brigham H.

Hey Ed, since you are "Digital" and I am "Real World Data", can you explain something to me? Why do people always conflate the two? Isn't Digital just apps and stuff (kidding)? I mean, I guess anything generating data points about patients is technically real-world data, and I guess anything built on the binary world of 1's and 0's is technically digital. Wait now, I'm confused again. Why don't you take a swing at defining "Digital" and I will consult my nondigital abacus on an RWD definition. Go.

Ed C.

Ha Ha. Awesome. This is going to be a blast.

Brigham, yep, those get conflated constantly. I've got a couple theories why (some more conspiratorial than others). Mostly I think it's just a combination of jargon assault + general inexperience + terms that are still themselves fluid and being defined.

If you couple that with the fact that half of these things are acronyms I'm amazed anybody can even carry on a coherent conversation about this.

Brigham H.

So true! I'm interested in your conspiracy theories, but first I want to hear your definition.

Ed C.

At its core I think life science and healthcare see a digital invasion coming and we're beginning to use phrases like Digital Therapeutics and RWE as shorthand for that inevitable (and ominous) transition. I think for most people these are not yet actual things as much as abstract concepts that they're trying to put a name to.

Hope that's a workable answer.

Brigham H.

That makes a lot of sense and I see it manifesting across the industry as innovation continues to pick up pace.

Sun., Mar 1, 2020, 3:33 PM

Ed C.

So now I'm going to ask a dumb question that I think a lot of people would like to ask, but aren't brave enough. Is there a difference between Real-World Data (RWD) and Real-World Evidence (RWE) or do they mean the exact same thing and people just debate the acronyms?

The analog for my sector is the difference between Digital Therapeutics (DTx) and Digital Medicine and to some degree Digital Health. Ugh. Let me come back to that.

GO!!

Brigham H.

Ah yes, the GIF(JIFF) vs. GIF(GIF) debate of health tech. Let me parry at least a glancing blow at this debate of bad words. In my world, Real-World Data is patient-level data that can be clinically validated against the current gold standard "controlled clinical trials." I won't give an oral history of the evolution of the FDA, but there is substantial research about the importance of data collection methodologies and statistical approaches to clinical trials. RWD definitions require careful analysis through this lens. I also think there is an important element of auditability, currently governed by 21 CFR Part 11 compliance in clinical trials that drives much of the evidence validation in healthcare.

Ed C.

I'm tracking! Keep going.

Brigham H.

So for me, RWD has to be A) auditable; B) validated against Control Trials; and C) statistically valid and appropriate. Today the RWD that meets that measure includes "Regulatory grade EMR (electronic medical record)" registries, and increasingly digitally-captured biometrics captured on 510k validated devices (Apple Watch, etc.). I think the unfortunate thing about my definition is it tends to leave out the voice of the patient experience which could be so well captured by other digital means. But I do think it helps us draw a distinction between "digitally collected patient data" (that may or may not be RWD depending on the above) and "digital interventions or therapeutics."

Ed C.

As a patient focused organization, I understand your dilemma about the patient voice. There are many ways I can include this in my work.

Brigham H.

You will notice I have a pretty strict definition of RWD. This sort of implies that there is other health data that might not meet my definition of RWD. As this relates to real-world evidence, I view it as something you can use RWD, or non-RWD, to create. The term evidence implies measurement and comparison. The survival curve, the cox regression, the hospitalization rate, the cost of care, the summary table of model feature importance, these to me are all RWE. RWE is essentially aggregation and analysis of RWD and non-RWD health data.

Ed C.

If I'm understanding you correctly, RWD has defined sources and everything else is non-RWD.

Brigham H.

I think there can be a whole range of "evidence" and inherently there will be weak and strong evidence. In some ways that is the caveat emptor of RWE and healthcare evidence in general. In terms of grades: Prospective double-blind randomized control trials in humans is Grade A RWE / RWE based on Regulatory grade EMR is Grade B (and perhaps rising) / RWE based on non-RWD Health data Grade C / Grade F, I guess, would be yoga studio Instagram likes or something.

For my loved ones I would want a decision being made or value being assessed on the basis of Grade A and Grade B. I think there are limitations to control trials, in particular the lack of diversity, coverage of women and children, overall size of the study arms, and the lack of considerations for differences in healthcare delivery. RWE based on RWD solves for a lot of these issues and standards and methodologies are maturing.

Ed C.

Nothing against yoga studios, of course, and I think your delineations are spot on!

Brigham H.

To hit it back to you I will pose this question that I have been mulling: Do Digital Therapeutics need to have their digitally collected RWD data points validated against classic clinical endpoints, or should it be enough just to have the intervention itself perform better against SOC [standard of care] in control trials? Sort of regardless of how it got there?

Ed C.

Brigham, I think that's an awesome explanation and actually very helpful.

To answer your question about what is the correct order for Digital Therapeutics – Getting them approved by preexisting endpoints (probably PRO or collected by clinician... on paper), or going out and validating the digital endpoints, which are already collected by the products themselves and then try to get DTx approved based on those evolved endpoints. I'm going to take a pretty strong position on the former.

Brigham H.

I agree with your position.

Ed C.

There are many indications where the endpoints, although not ideal, are well-established and well-accepted by the regulators and the clinicians. DTx needs to get a beachhead of approved (cleared) products before we start trying to rewrite the way everybody else measures things.

Plus sometimes a product designed to drive behavioral or biological change is driving towards a different goal than a tool designed to collect clinical data. If you're trying to build something to grab clinical data, one might forget to actually build something that actually has a therapeutic effect.

Brigham H.

I think what this comes down to is clinical validation. Could we run a trial of an app vs. a drug? What would be the standards? The methods? The labels?

Ed, your last comment about "focus" in digital health really resonated with me. It feels like some investors push digital health companies into becoming data collection engines as opposed to focusing on the technical strength of their intervention. It's sort of understandable given that the tech giants of today tend to be the ones who got engagement and data collection right. Almost as an ever spring strategic advantage. It feels like therapeutics are different, and maybe health tech in general, in that the focus needs to be on algorithmic and clinical validation. I also find most digital health companies are collecting such a narrow slice of data (disease area, behavior, experience, etc.) that it's not really a viable strategy anyway.

Phew, that was a lot but I feel like we are getting somewhere. Care to take a swing at digital health/ digital medicine buzzword definitions or should we cap off with a speed round of burning questions?

Ed C.

Well since it's clear to me this is probably going to become a recurring project, I'm going to wait on the definition of digital therapeutics and digital medicine until our next exchange. That's a rabbit trail... Or is it rabbit hole? Anyway, that's an entire conversation in itself.

Let's go straight to burning questions!

Burning question for you: Which therapeutic indication has the greatest chance to be fundamentally reshaped because of data? Go!

Brigham H.

Ed, overall pediatrics. RWD/E is desperately needed in pediatrics who are heavily underrepresented in clinical trials today. I will also throw in oncology (the tip of the spear in regulatory grade RWD), and immunology which has the biggest need to find proxies for efficacy and patient experience from the real world.

Last one for you: Which therapeutic/disease area will have the first digital intervention to surpass SOC drug intervention on efficacy?

Ed C.

Brigham, great question, but wow. As a general rule I think about this being used alongside drugs or in the absence of a drug, so trying to think of winning a head-to-head efficacy comparison is generally not the way I think about it.

But to try to sort of answer the question, I'm going to cheat a little and say Alzheimer's disease specifically and CNS generally. I personally believe the Therapeutic Area that can benefit the most from digital therapeutics is CNS and Neuro but in many ways that's because there are so few drugs and the standard of care is generally very limited.

Well this was a blast. Let's try to make this a regular thing.