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Introduction: [00:00:01] Hey, this is Adrian Hernandez and welcome to the NIH Collaboratory Grand Rounds Podcast. We're here to give you some extra time with our speaker and ask them the tough and interesting questions you want to hear most. If you haven't already, we hope you'll watch the full Grand Rounds webinar recording to learn more. All of our grand rounds content can be found at rethinkingclinicaltrails.org. Thanks for joining.

Adrian Hernandez: [00:00:25] Hi, this is Adrian Hernandez. And I want to welcome you to today's collaboratory podcast, and we're here with Harlan Krumholz who just gave a fascinating presentation on Preprints: What, Why not and How. Harlan's been leading the discussion around this nationally from Yale and really has some great thoughts about what this could look like. Harlan welcome. Let's get started. So what is preprints and the concepts behind it.

Harlan Krumholz: [00:00:54] Thanks Adrian. The idea around preprints which exist and are highly used in a lot of other areas of science, like physical sciences, physics, astronomy and economics and a lot of other areas, is simply a means by which scientists can post pre peer reviewed content on a server and know that it will be preserved, archived, searchable, findable, downloadable to others in the scientific community. So when this work preprints, I suppose, was meant to convey the idea that it was pre official publication, pre peer reviewed publication and it sort of took on this moniker is called a pre-print.

Adrian Hernandez: [00:01:40] It sounds great. Everything has benefits and risks. I wonder if you could comment about the benefits.

Harlan Krumholz: [00:01:46] Well I think a lot of what we thought about in clinical research is the dissemination of our work to non-experts. You know we do our work to have impact and that impact we see ultimately as sort of the end results of the clinical research. We want practitioners to learn about our work and think about how it change practice and want guideline committees to take it into account. And we want, actually as consumerism moves forward, we look forward to the public and patients being able to understand what advances mean for them and how they may be able to change behaviors or engage in conversations with health care professionals. And we thought a lot about that avenue of dissemination. What we've neglected I think is the notion and importance of ensuring that scientists working across the country and across the world are rapidly communicating their work such that it can help influence the work of others so that they can be aware of the kind of progress that's being made, that they can think about how that might change the kind of studies that they're conducting, the kind of grants that they're submitting, the progress of their thinking about what problems are most important and pressing and what kind of progress other people are making. And so for those people, for the scientists who are trying to make progress, the peer review process is adding a length of time to dissemination that may not be necessary. By recognizing that work and sharing it we're able to learn from each other and move faster. And even if you've done something that influences me I can as I'm writing it cite it as a preprint and it can influence me positively so I don't maybe completely overlap with you. If I would have only had access to the peer review publication, I might not even be aware of it for a year until it finally comes out, and then I would have maybe done a lot of things that I didn't need to do because I could have learned from what you did.

Adrian Hernandez: [00:03:46] You've been an editor for a major journal and I'll just say from my personal experience I've sometimes thought that we had the greatest data from a research study and really we're promoting our findings, yet when we went through peer review we got a little humbled in terms of the interpretation here, so what are the risks about this.

Harlan Krumholz: [00:04:09] I think the concern about the harms, which is what you're raising, derives from this sort of mixing of purposes. If the preprint server is understood improperly as being ready for prime time information that people should be acting on, then there is the possibility that people are posting something that hasn't been filtered or commented on and people are prematurely acting on something they shouldn't. Now we know even when you publish something through the peer review press it's hard enough to get people to change behavior, so I'm not sure it's a big concern that all of a sudden something comes out on something which we're going to label as preliminary science for scientists, this is about fostering discussion not about influencing practice. With those caveats on top it seems unlikely that the next day the entire practice is going to change or even some patients are going to change practice, but that is something we have to think about. I mean we have to make sure we're were properly framing what this is. I mean in the same way when we go to the national meetings we are presenting often preliminary data, even sometimes a reporter may report on it and it's important that we tell them that this is not done yet. You know this is something we're in the midst of.

Adrian Hernandez: [00:05:26] You raise an interesting concept there in terms of the reflections on scientific meetings. Years ago scientific meetings were so-called less bait and actually people were sharing preliminary data and debating it. Do you see this as kind of a 21st century venue for getting back to that discussion and debate?

Harlan Krumholz: [00:05:46] In these days, first of all, many people are quite busy. They're traveling a lot. The meetings have become quite frenetic and I think that provided less of an opportunity for real reflection and in-depth discussion of preliminary work, or work in progress, and it's become more of either people presenting fully cooked stuff that gets published simultaneously or sort of just rapid interchanges, not really in-depth. What do we need today? Well we need something that's continuous. It's sort of like a platform for collaboration that's open 24/7 that enables people to communicate with each other when they need to, and if I've got something that I'm working on that I think is ready to share broadly with colleagues, I mean I can shared at a local conference in my own institution, I can send it around to some friends, but it may be better to post it on a preprint server, let it be sort of an enduring place, and then you can invite people to comment and you know help improve it, create the conversation. And like I said we've accelerated the entire scientific enterprise because we're more aware of what other people are doing. And what I said, and what I see in the presentation, and what I've said before is that in some of these areas that we're doing work right now like machine learning or AI, if we were just leveraging the peer review publications, we'd be way behind the field because the only way to keep up with that rapidly moving field is by tracking the preprint servers. You can be skeptical of whether what they're finding is real or not, or you can be engaging in conversations about it, but it's pushing forward the way people are thinking about the research. And I'm just noticing in that area how effective it can be. I think that we can iterate faster and keep that excitement level higher than we are when we're you know kind of hit this period where we're going to peer review and sometimes you can be as much as a year or more and you've moved so far past that paper by the time it comes out in the peer review press. I know you've has that experience, I have. Where by the time it's published it's like gosh that's ancient history for our research group. We finished that a long time ago.

Adrian Hernandez: [00:07:55] You're exactly right. I want to ask you about economics. So both behavioral economics for individuals to embraces this, what's needed say for a young investigator to embrace and to use it, and actually groups and large groups of people to do this. And then on the related issues, and some ways as the economics for journals.

Harlan Krumholz: [00:08:19] A couple of things need to happen. People need to get feedback. We senior people need to engage with junior people so that they feel they get feedback and they're being made better. They can even incorporate that into revisions they make in peer review. And I

think we need to work on the journal that people aren't penalized by using preprint servers in a way that because they say that they consider prior publication. Even though they'll allow it at meetings, right now some journals are saying that if you put it on preprint server then they consider that prior publication. So we have to work on diminishing the penalties and we have to make it a vibrant community. This is an experiment right. If the experiment works, the scientific enterprise will be better off because we are learning about what our colleagues are doing and their learning what we're doing, and we're having to make their work better and they're having to make our work better. And we all see our common mission of making the world better. So Harlan, this is great to hear the benefits and also addressing what's the risk, how do we make this happen now?

Harlan Krumholz: [00:09:23] I will say that you know our team with a Yale Open Data Access Project, the YODA Project, a group that has been primarily focused on fostering data sharing and open science and trying to get the opportunity for people to take advantage of existing data sets, we sort of turned our attention to say another area of importance is this notion of creating a platform on a preprint server, and so we've committed ourselves trying to figure out if we can move this forward. We're in discussions with people of bioRxiv, the life science preprint server that's been very successful over the last several years, really has promoted a lot of great communication collaboration in life sciences. And so we were intent on seeing whether or not we can in working with people like you, in the NIH Collaboratory, and with institutions like Duke, seeing whether or not we can bring together a group of like-minded people who want to give this a try. We created this email at Medarrxiv@yale.edu, and if anyone's got any questions or ideas or you know we're trying to foster community discussion around this to see whether or not we can push this forward. But our hope is you know maybe the next three or four months we can pull our community together, have talked to stakeholders and see whether or not we can make a run at this, and then evaluate whether or not it actually is making things better.

Adrian Hernandez: [00:10:42] That's great to hear Harlan. And so let's see if we can get things going quickly over the next few months and then learn from each other. So Harlan, thanks again for a great Grand Rounds and discussion on this podcast. I just want to remind people our next podcast will be with Karen DeSalvo, and she will discuss health as more than health care and really highlight her experiences during the Obama administration.

Closing: [00:11:10] Thanks for joining today's NIH Collaboratory Grand Rounds podcast. Let us know what you think by rating this interview on our website. And we hope to see you again on our next Grand Rounds, Fridays at 1:00 p.m. Eastern Time.