Clinical Trials During Disruption: Meryl Selig Interviews Karla Childers

Meryl Selig:

Welcome to today's voices in bioethics Podcast. I'm Meryl Selig, a graduate of the Columbia University Master's in Bioethics program. I'm also a member of the Voices in Bioethics Team. Today we're delighted to speak with Karla Childers, who leads bioethics based Science and Technology at Johnson and Johnson. Karla is also a Columbia bioethics alum, as well as a lecturer in the program. Karla, we're really delighted to have you share your experience and perspectives, basically concerns research ethics, and most specifically, and it's so timely ethics during times of disruption. This topic is especially relevant now with wars, conflicts, population migration, dramatic weather events, not to mention the recent pandemic just happening worldwide and having impacts here, obviously, as well. So we'll get right into it. And the first question, which you've noted as a keen interest of yours is how do we conduct research during times of disruption?

Karla Childers:

First of all, Meryl, thank you so much. It's such a privilege to be talking with you and to be on the podcast. I mean, if I think about how we conducted and I think about how I got interested in it's exactly is you talked about we were, I think a lot of colleagues were reflecting on the fact that we kept talking about the pandemic, and then it became the conflict in Ukraine and then it was climatic events and more geopolitical events. And we really started thinking about this more holistically about this idea of disruption, regardless of what the event is. And can we think of, to your point, how do we continue conducting research if we can? And if we can't continue conducting research? How do we take very good care of the obligations we have as research

sponsors, during those times of disruption? And so when I think about conducting research during those times, it's it's definitely an act of prioritization and thinking through as we'll get into, you know, some of the considerations, and specifically I've been thinking about it very much from a bioethics perspective, and as we think about the natural tensions that come up. Also, a lot of the conversations were yes, these things keep coming up. But how do we think about future proofing? If we know disruptions are going to continue to happen? Can we please at least learn from what's happened in the past, not keep repeating the same mistakes and do better and prepare better next time?

Meryl Selig:

Yeah, I think we're gonna get into future proofing, which sounds exciting. And obviously, it's very important. And hopefully, we'll all as a society learn from our maybe not the best decisions as we look at them in hindsight. Perhaps you can describe what kinds of impacts happened to research when these different crises happen. And I imagine the responses are different depending upon the specific crisis. But if you want to get into that, you know, whether research continues, or it stops, or what happens. That's something that I don't think many of us know about what's going on.

Karla Childers:

Yeah, and it's so complex. And I think you're absolutely right, it depends on the nature of the conflict. But we can kind of maybe think about it, like the immediate impact to participants, you have individuals who are in a clinical trial, presumably, often patients, not just healthy volunteers, that can happen across the spectrum of research. So if you'd think of the most immediate impact, it's to continuity of care, and how do you, things like how do you handle appointments that get canceled? What about drug supply? And how do you make sure that patients continue to receive access? How do you have follow up visits after medical device procedures? So there's that initial immediate impact to thinking about the participants themselves, and how to mitigate the impacts on their actual care? We also saw and this comes up in across the spectrum of cases is that the site personnel and the health care providers, so yes, the participants but then the people who, how do they get to the clinical site? Was the bridge washed out was their hospital bombed on maybe they aren't even allowed to go into a site. So there was also that second level of the support structure and the people actually on the frontlines of administering the research, and even employees and resources in the countries where things are happening. And so again, thinking about those types of even just ability to conduct and do they have power, do they have water or do they have different things like that of actual infrastructure? And interestingly, from a research sponsor perspective, depending on the nature of the disruption, it can be multifactorial. So in particular, during the pandemic, it hit all of our clinical trials, so everything was impacted and even medical device clinical trials. that require people to be in an operating theater when they could no longer go in for non essential surgeries and things like that regional conflicts can be difficult because then you're looking at the number of clinical trials of the types in that region. And can you get into them, but that ability to really think first about that first impact is the participants and continuity of the

research comes into it. We can talk more about that later. But it's definitely that first level, what is going to happen to the participants? How do we maintain continuity of care? How do we keep people safe in doing that and make good decisions? And how do we look at the holistic impact across all the clinical trials and make good equitable assessments and judgments?

Meryl Selig:

I just can't imagine how challenging that is, in dealing with the impact of whichever crisis it is obviously, again, the pandemic affected all of us, right, and the complexity of coordinating, as you said, with both the site whether it's a hospital or an academic institution, you know, what our pharmaceutical company, contacting patients, calming people down, I used to have you continuity really is key, but it's word but then making that happen. And then dealing with such a really complicated network of partners and engaged people. Can you talk at all about who coordinates that maybe from the perspective of a pharmaceutical company, but one might apply who's calling the shots and then sending out the orders to, if you will, the instructions to all the engaged parties?

Karla Childers:

Yeah. And so one thing we did a lot was during disruptions talk in a non competitive way to other companies to try to figure out how they were doing things. And so most companies have a typical business continuity plan, there's some kind of crisis management team put in place. So there's internal infrastructure in a company that pulls in the right stakeholders who can take care of that. In general, it's going to be colleagues typically in things like clinical trial operations, who are the individuals that can actually contact the local sites, make sure the sites have the appropriate information. So really leveraging those contacts and connections, a lot of emphasis on supply chain, how are supplies being distributed, are they getting safely into the region. So there's a lot of supply chain implications and security questions about making sure that products aren't diverted inappropriately during these times of disruption, making sure that supplies get where they need, as you can imagine, on these teams, there's a heavy emphasis on compliance, quality, following legal requirements. So there's also that element of as we do all these things, making sure that we're still adhering to the good practices, we know we should for good clinical practice safe execution of clinical trials. So there's a lot of that oversight and advising from that perspective, as well, from a bioethics perspective get pulled in, to really help teams think through those as we get into these gray spaces of making decisions and making trade offs and thinking about how we continue to conduct research ethically, in these times. There's also an advisory component, so that all get pulled in as well. But it's really a constellation of internal stakeholders that are working very closely. And then you've got all the on the ground personnel where that research is actually happening, that you're communicating with and talking with. And you can imagine, from their perspective, we've heard a lot of this feedback, they're doing clinical trials for many different companies. So one thing we thought a lot about ways as companies was can we at least be better about trying to be more consistent as we work with clinical sites so that we're not all asking them to do six different things to achieve the same goal. So that was an interesting learning as well. And kind of taking that

perspective from the other side, in addition to our side as manufacturer.

Meryl Selig:

I mean, if we take this apart, and just imagine what is going on with the complexity seems almost overwhelming. And from, let's say, the hospital side, and the researchers, the odd the site investigators, so many staff, like during the recent pandemic are repurposed. And so you know, you may be engaged in XYZ project, but if there's a heavy demand and emergency and one might imagine it could happen in a natural disaster as well, where staff diverted just sitting back and imagining your the complexity actually is huge. I'm just curious though, if that study, let's say a research program is disrupted and stopped. Are there examples of how that starts up again? Or I guess it's a one off kind of thing, depending upon the protocol. If things are so disruptive, or they're partway through and things have to stop? Is there some general rule of thumb where you have to start all over? I don't know. I'm just wondering, is it start at the beginning, rewind. Do you know what happens then?

Karla Childers:

And I think and so if I stay, I'll give you a little bit of an operations flare even though that's not my primary expertise. But I can give you some of my experience from that. And then I can tell you that what we think about is this was especially relevant. And I kind of want to go back to your prior observation about the disruption. And how that happens in the repurposing, because that was a real big impact. During the pandemic, of course, when you had frontline health care workers diverted to critical COVID treatments, you had hospitals shutting down to only those life threatening surgeries, which might not have been clinical trials for certain medical devices. So you had, we had people waiting for months to have a knee replacement, because that wasn't deemed life threatening. And so there were there were real impacts. And you raise an interesting question, and the second part of that, and then what happens? Can you how do you continue it? Can you pause it? Or do you have to stop it? And like you said, almost start over. So I think we saw a range of different things happening. First of all, is can you continue safely? And that was the first one of like, instead of stopping or slowing down or impacting the ability to conduct it? Can you continue it? Can you continue it a little bit more slowly? But still continuing? Can you find other ways to do follow up visits? Can you use telehealth to have a follow up appointment? Interestingly, in medical devices, that was difficult, because like, if you have an implanted knee or a replacement, you might need to actually palpate the limb to see how things are going. You can't do that through telehealth. So in thinking about the decisions, though, in general, it usually would depend, I think, on the extent to the disruption. So you can imagine that the pandemic where we have global disruptions, you might have had to stop studies, and most protocols have built in scenarios that are going to consider what happens if something can't continue. And if something so disrupted or you can't get all the data and follow up visits, but in general, you're going to see if you can continue, maybe you can pause it where it's a little bit more challenging is when you have something like the conflict in Ukraine or when there's such climatic devastation that you have really significant impacts to infrastructure, and you you don't even have a hospital to go to so then we go into you do a lot of

triaging can you get the participants do at different clinical site, can they we had patients who were transitioning and fleeing to Poland and then finding clinical research sites in Poland that we helped facilitate even just moving away from Kyiv to another city help for a while. So I think we go through a lot of steps to try to help participants remain in the study. If we can keep it open before we would then start assessing if they need to discontinue as an individual or if the study is just not possible to continue. To my knowledge. We didn't have an I won't quote numbers. But my recollection is that we didn't have as much stoppages we did more slowing down, not meeting timelines finding other options for that

Meryl Selig:

I was picking up on again, the complexity is mind boggling. And you're realizing we're dealing with individuals, right, the

Karla Childers:

right

Meryl Selig:

The tail end of all the people engaged, you've got someone who's also perhaps well traumatized by, you know, whatever the cause causes incredible trauma. And I just was wondering that if research protocol trial is stopped, and yet the participants seem to be gaining benefits from the trial, and it has to stop. Is there a general rule for providing access, if possible, to the next best option?

Karla Childers:

That it's a great question. And I think it's even so maybe I'll take a step back and answer it from the even non disruptive time. So let's say it will then probably depend on why it's been stopped. So let's say we have a clinical trial that is stopped, because let's do an easy one. There is a safety signal, something's wrong. It's not safe to take the medicine, the benefit risk. It's not favorable. That one's easier, because then yes, you look to transition them to local standard of care, they exit the trial that drugs not moving on. It's trickier, though, to your point that you made about, let's say, when people are in the clinical trial, they're benefiting and now the trial can't continue or they can't continue. Yes, you're right. There is that assessment of if they can't continue in the trials and individual is that product that's being studied, available in the market where they are. So let's say it's already on the market. For one thing, they're in a trial to study something else, can we transition them to that local commercial supply so that they then have a more stable access to a commercially available product? If it's not even on the market for anything, it's still investigational, then yes. And the trial cannot continue and there's no legal way no legal pathway to get them investigational medicine, then are there are local treatments that they could be transitioned to.

Meryl Selig:

Okay, well, thank you. It sounds like a lot of care has been given and on an international basis. Are there other organizations that companies like yours work with you didn't mention that there's this sense of this cooperation agreement, if you will, between companies to streamline things, make them, you know, cooperate in times of external stress. So what are their global organizations that help at all?

Karla Childers:

Exactly, there really are. And so the pharma industry in general, we have trade associations where we come together and talk about different aligned priorities and objectives in a non competitive way. They're also for example, in the bioethics space, there are a handful of different places where people can get together. So there's a forum that was created years ago by Lilly that is still around that brings together people who have roles like mine to talk about, again, in a non competitive way, the ethical challenges that we're facing in r&d. And a lot of really fruitful discussions come from that. And there can be knowledge sharing. One of the things that happened both during the pandemic and the conflict in Ukraine was multi stakeholder conversations in an organization called the Drug Information Association, or DIA. It's a nonprofit organization that brings people together in a non competitive way across all different regulators, scientists industry, and a colleague of mine, Lindsey McNair, and I founded a bioethics committee with dia. So we feel that a lot of multi stakeholder multi function kinds of conversations around Ukraine and the pandemic. There are also other organizations like the bioethics collaborative at Harvard Multi Regional Clinical Trials Center that supports needs. So there are communities and groups where a lot of different stakeholders and companies can come together and talk about how are you responding to this where the challenges you're seeing, and especially with this particular topic, we found those incredibly useful because of the reason I mentioned also with the pandemic and Ukraine, can we as manufacturers try to do a better job of engaging with sites in a more consistent way during those times of disruption. So it's not so difficult. And I would be remiss if I didn't mention the health authorities, of course, we talk a lot, especially in the some of the disruptions of Regulatory Flexibility and different things like that.

Meryl Selig:

I think it's so important that you just outline these things. Pharma tends to, you know, it's the big beast, and it gets attacked first. And it seems like it's, you know, they're easy to attack. And yet, I'm so glad you brought this up, because there's so much work going on behind the scenes, like you're talking about these organizations, where people or companies are cooperating amongst themselves with each other for the benefit really, and truly, people patients.

Karla Childers:

Yes

Meryl Selig:

I truly, that's the first I've learned of it. And I'd certainly there's more sunlight being shined on it, because there's so many good things that happen in farms, so many. And this is certainly one where work is clearly being done. People have good intention, good intellect, ethically straight people who want good outcomes, and making progress in benefiting people. So I'm so glad you mentioned that, Karla.

Karla Childers:

Thank you for asking. And I don't ever want to be an apologist for industry and all institutions can benefit from scrutiny and critique. But I do appreciate the opportunity to highlight some of the things we actually do get right and do well. And that is really what we're thinking of when we're making choices.

Meryl Selig:

Great. It's really enlightening, actually. Now, here comes the big question, future proofing. Could you tell us what that is about? And maybe give us some examples?

Karla Childers:

Sure. And this is when I think we continue to wrestle with so when we talk about future proofing, how we had been discussing it in these various different groups was, what were the lessons we learned from the various disruptions? What were the pain points, we felt, and were there ways to change things to make them different the next time a disruption happened? So for example, one thing and this is where I think bringing ethics into it directly as well as thinking about the informed consent form there are, well, first of all, they're incredibly long and complicated. But there are some key provisions that talk about things like what happens if you can't get in for a visit? Or what might we tell you are some of the really good questions you raised about what happens if it stops and things? And do we have to amend the protocol or amend the ICF for these things. And so giving a little bit of flexibility to operate during times of disruption, which without having to go through an administrative amendment because that takes a lot of time. So what were those things that we could maybe contemplate like telemedicine visits, direct shipping products to patients at their homes? Could we build those things in so if that happened, we wouldn't have to do an amendment to be able to ship drugs to someone's home. So those types of very simple things that we could build in upfront could save weeks if not months of changing those and then having to slow down or stop until we could do that. That's one particular example. J&J, has Bolsa, an innovative medicines and med tech business. And some of the big pain points from the medical device perspective, what we're what I alluded to earlier, let's say you'd have a clinical site where a patient had gone to their procedure, but then due to the disruption, they weren't able to get back there. But there might be a doctor in their hometown that they could go to see. And we actually talked about this with the FDA a little bit, could we be flexible around some of the site qualifications in the case of a

disruptions so that they could have a follow up visit at an appropriate provider near them if the disruption prevented them from getting back? And that goes, again, to your question about continuity of research, if they can maintain those follow up visits with sufficient rigor and quality, that will keep them in the trial that will keep them compliant with the protocol. So a lot of things like little bits of flexibility from getting places, getting drugs to people thinking about engaging with them for follow up visits was where we were really looking for that operational flexibility, and really trying to be disciplined about not making it so broad and flexible, that somebody wouldn't understand what was going to happen. But those types of things were the things we were really thinking about with future proofing.

Meryl Selig:

Yeah, it's a lot of

Karla Childers:

Complexity.

Meryl Selig:

Yes, it sounds simple. But again, sitting back and thinking, this is lots of people and many places. I don't know if you'd like to answer this question. But would you like to share any travel experience related to your work? I don't know if you've ever had to go to places that were experiencing stresses at all, any kind of specific experience?

Karla Childers:

Yeah, that's an interesting one. I don't necessarily traveled to clinical sites. But I do have there was an instance that sticks out to me. One of the things I have the privilege of doing that I'm grateful, j&j supports, as I sit on the board of directors of an organization called FASB Fellowship at Auschwitz for the Study of Professional Ethics. And they do they teach ethical leadership through the lens of the Holocaust, and the perpetrators of the Holocaust. So they do a lot of travel to Germany and Poland. And I was on a one week study abroad trip with them in Poland, the second or third week after the initial invasion in Ukraine. And it was very interesting, we got to speak with Ukrainian refugees, in particular Poland and talking with them and talking with the Polish people. And it was it really brought to life because prior to that, I'd been on some of our business continuity planning, crisis management team discussions, but actually being in the region, talking to people actually affected by the conflict, talking to somebody who was running clinical trials there, who had brought patients into her home so that they could continue their participation. It wasn't a J&J trial, it was a different company. But that type of commitment, that type of compassion, just really brought to life and reminded me of the humanity and the human side of this, which it's one thing to say in your principles, the first thing we think about is patient safety and people. But then it's another thing to actually be on the ground and meet those people. So it was a really special and important moment that I

hang on to so whenever we're thinking about impacts on people, just to have that humanity about it, and humanity about thinking and remembering

Meryl Selig:

That is quite significant. And I can imagine it would be impactful for most people, but someone with your background, your focus in bioethics to experience that is really bringing studies, you know, the studies that you've had and coursework, you've had life experience, and you're bringing it all together and had to be exceptionally touching and provocative.

Karla Childers:

Yes.

Meryl Selig:

So thank you for sharing that.

Karla Childers:

Oh, absolutely.

Meryl Selig:

When I asked the question I really didn't expect to profound answer to all of our listeners will appreciate that.

Karla Childers:

I think you make a good point. And, and even during the pandemic, I mean, I was finishing the degree, my degree program at Columbia during the pandemic, and it was both a blessing to be actually practicing bioethics in real time and a pandemic. And at the same time, I felt the responsibility I had family calling me go Karla, you're an ethicist. Why should we be doing so anytime I think you ethicist and can be in touch with the actual real application of the decisions and the advice you make is a really powerful way of reminding yourself of the implications of the advice we provide.

Meryl Selig:

That was so beautifully stated, I actually do not have any other questions for this interview, and I think you wrapped it up so poignantly that if you have anything else you'd like to discuss, please feel free to do so or other I was going to thank you very much. This was very enlightening, and I hope other people feel so as well.

Karla Childers:

I would just say that I am grateful for the Voices in Bioethics podcast and the work that is done because I just appreciate the opportunity. I think it's a great forum to allow those of us who are in this space and doing this work and opportunity to share their stories and I'm just grateful for the opportunity to talk with you Meryl. This was a lot of fun, and I really appreciate it.

Meryl Selig:

I feel the same. And I'm gonna sign off it's Meryl Selig, and I've been speaking with very wonderful Karla Childers, head of Bioethics Based Science and Technology Policy at Johnson and Johnson. Thank you so much, and I wish you well and your continued work.

Karla Childers:

Thank you Meryl it's been a pleasure.

Meryl Selig:

Bye bye,

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