

Jenn McNary

Mother to Austin(20), Max(17), James(11) and Norah(8)

Austin & Max have Duchenne Muscular Dystrophy & James has Primary Immune Deficiency

1	<p>TITLE: <i>Clinical Trials: A mom on assessing risk when her child has a treatable disease.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-on-assessing-risk-when-her-child-has-a-treatable-disease/</p> <p>Description: In this video, a mother of two sons, Austin and Max with Duchenne Muscular Dystrophy and a son, James with a Primary Immune Deficiency, talks about evaluating her risk tolerance in finding a curative treatment for James. She talks about the barriers and biases when your child's disease is considered a chronic, manageable condition and the limitations on the quality of her son's life.</p> <p>Transcript:</p> <p>Jen: No, they are only natural history because it's considered a treated disease because you can get these plasma products even though there is no -- it's not curative. They do have a new gene therapy for severe combined immune deficiency, but the risks of what you have to do to do a gene therapy, you know, SCID is considered terminal whereas primary immune deficiency is not considered terminal. And so they're not trying out anything on the boys like James because it's a chronic illness. Yeah, so the risk benefit assessment although I would venture to say that I would do it, you know, I would try a gene therapy or a stem cell replacement or something on James because he's very, very sick most of the time.</p> <p>Jen: So it starts when James was in the hospital and he was diagnosed. The first thing that I asked the doctor, the immunologist, was what's going on in the clinical trial world for primary immune deficiency. I did some Googling, I found out that there were blood plasma products that you could use weekly or monthly. Some people even use them daily to help build up your immune system with other people's blood plasma. But they also have -- you can get aseptic meningitis, you get migraines, you can get severely dehydrated, it's terrible for your kidneys. Like, these people are very sick, all the people that have the disease.</p> <p>And so I said, what's going on in clinical trials because clearly there is this treatment, but it's not a cure. And the doctor looked at me and she was baffled because she was like there is a treatment, he can live a fairly</p>
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	<p>normal life, he's sicker than most, you have to use lot of hand sanitizers, he's got to wear mask, like, just all of this stuff, like, he's got to rest. We'll get him a 504 plan at school. So I was realising that, you know, even with this treatment that has all of these side effects, horrible side effects, he was not going to live a normal life. And I was really pushing her because -- for the more severe type of the disease there are some clinical trials and stem cells, some radical stuff, some gene therapy, but James is not considered sick enough for those kinds of things.</p> <p>And honestly I have a pretty high risk tolerance in that I want to push for normalcy and I do believe that for the most part clinical trials are fairly safe.</p> <p>You're never going to move forward with treatments and cures for chronic, manageable, seemingly non-emergency conditions unless you have a population of people that are saying what we have now is not good enough and are saying that we are willing to take some risk that the outcome is not better or even worse in order to see if we can get a cure. So the benefit is obviously to science. You know, I believe that it should be easy enough to cure an immune system problem. They know what the problem is. He's missing B cells. It's primary humoral deficiency, missing B cells. There has got to be a way to put these cells back permanently.</p> <p>And then the other thing for James is that I don't want to give up on him and say, okay, well, here it is, you're going to get needles in your legs for two hours every Sunday for the rest of your life, you're going to have to wear a mask on a plane, you're going to have to be careful and be scared all the time that you're going to catch something, you're going to have to drink 20 gallons of water in order to not have kidney failure. I mean, all of these things, I really do feel like his quality of life could be so much better and he's so young. This is not a 60 or 70 or 80 year old person that's looking at living out the rest of their lives quietly.</p> <p>He has a lot to do and he would like to be a chef. You know, that means that he's got to be around a lot of people and touching people's plates and foods and he's going to be exposed to things. And he's already deaf in one ear from the tumours because the radical infections caused the tumours to keep coming back. I just feel like he has a whole life to live. And I think that science is good and so the benefit could be that he doesn't have to deal with this at some point in his life.</p>
2	<p>TITLE: <i>Two sons, a spontaneous mutation and two diagnosis of Duchenne Muscular Dystrophy</i></p>

<https://courageousparentsnetwork.org/videos/two-sons-a-spontaneous-mutation-and-two-diagnosis-of-duchenne-muscular-dystrophy/>

Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about her oldest son, Austin's diagnosis and how instinctually she knew he had an issue. She describes the unlikely occurrence of a spontaneous mutation and her son Max's subsequent diagnosis via the thoughtful evaluation of a P.T.

Transcript:

Jen: So generally Duchenne is diagnosed not at birth because there is no new-born screening. And so Austin was -- you know, I started seeing symptoms of something being wrong when he was about two. And he was just not meeting his milestones. I was running a home daycare -- a licensed home day care, so I had a lot of children his age. And so I could see that he wasn't walking upstairs, he was falling a lot. He was really whiny, always wanted me to carry him. And I was pregnant with his little brother. And so I kept bringing him back to the doctor. And the doctor just said, he was sort of lazy, and you know, accused me of carrying him around too much and he had a big head and he would grow into it and everything else.

But he was diagnosed when he was three and Max was a newborn. Actually they were diagnosed really quickly because the physical therapist that was sent to my house -- the processes for a motor delay or gross motor delay, which is what the doctor thought it was, is that a physical therapist would come out and do an evaluation of the child to see basically I thought -- I was trying to see if we were gonna get services. I thought, okay, am I going to get a PT to work with my son, cool. You know, so I was 21, Austin was 3, Max was a newborn.

And the physical therapist put Austin on the floor, laid him on his back and watched him get up. And he did what I always saw him do where it was like he crawled up his legs to stand up. Then she brought him -- we lived in a raised ranch house, so stairs to go up, stairs to go down, no landing. She brought him all the way down and she told him to go up. And first of all, he fought it, and I knew he would. I said, he doesn't do stairs. And she said, what do you mean, he's three, he does stairs. And he took the stairs one at a time, never alternated feet, just pulled himself up on the railing.

And she said, you know, I actually just took a class and I think he has Duchenne muscular dystrophy. This is not the usual diagnosis, but just because this woman, her name was Diana, she had just taken a class. And she said, I think he needs to get a blood test to rule it out. And so

	<p>she called the pediatrician who said, there is no way this kid has muscular dystrophy, I'm a paediatrician, I would have noticed. But low and behold, he had a CK test and he had Duchenne . And the neurologist they referred me to told me that genetically -- because he was the first in our family, we'd never had it, that probably he was a spontaneous mutation, but they wanted to test me too. And they said, if you don't have it then -- you know, if you don't have it in your blood, if you're not a carrier then your baby is fine. So they tested me and I was not a carrier.</p> <p>And so I -- you know, I did some reading and, you know, it was early in the Internet years. I didn't have Internet at home, but I was at the library. And I was doing some searching at the library, some record searching and I read something about mosaicism and that you could not be a carrier and still have more than one child with an x-linked disease. And so I asked for him to be tested. The neurologist yelled at me and told me I was wasting resources. But he called me back five days later and said, well, I've had to call in some experts and it turns out that your baby also has this disease, I'm sorry, I've never heard of such a thing. And he was the local expert at the local biggest medical centre around. And so they both were diagnosed with Duchenne.</p>
3	<p>TITLE: <i>"I actually think that it was an advantage to be young and not have any preconceived notions about the diagnosis."</i></p> <p>https://courageousparentsnetwork.org/videos/two-sons-with-duchenne-muscular-dystrophy-and-no-preconceived-notions-about-the-diagnosis/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about how she felt it was an advantage to be young and have no preconceived notions about her son's diagnosis.</p> <p>Transcript:</p> <p>Jen: I actually think that it was an advantage to be young and not have any preconceived notions. I mean, my life was already in shambles when I found out that the boys had Duchenne. I was not with their father. So I was a single mom. I think my mother actually took it much harder than I did when the boys were diagnosed. I was just sort of like, okay, so I just got to figure out where to take them to the doctor because we went to this first doctor and, you know, this neurologist that had told me the kids were -- you know, the baby was fine then told me, well, I'm really sorry that you have this early diagnosis especially for the baby because there is absolutely nothing we can do. Like, there is nothing, you could put him on steroids, but that's evil. You know, there is nothing we could do, come back when they start really needing</p>

	<p>a wheelchair in, you know, maybe 5, 10 years. And so he didn't even want to face it. You know, they should have their heart tested when they're older, you know, no big deal.</p> <p>I also started interviewing doctors. I realised that I didn't have to see the first doctor that talked to me and he was really rude. And so we found a doctor we liked, but unfortunately it was like across the country, so then I had had to fight Medicaid and prove that there were no doctors that were specialists around me and I did that. So we started seeing -- going to conferences. And you know, we went to my first conference when the boys were like two-and-a-half and five-and-a-half and those evil steroids turned out to be standard of care.</p> <p>And so we started ordering the steroid from outside of the country because it wasn't available in the U.S. Prednisone was what people in the U.S. were supposed to be using, we ordered Deflazacort, which was not even a drug in the U.S. And so I put them on steroids which greatly reduced the inflammation and they gained skills like crazy, it was really great. I wish I had started earlier. And I just -- you know, I just started learning about the disease. But ultimately these kids looked pretty normal. You know, they appear like normal little boys. You know, one of the things about the boys and I is that, you know, we never really grieve about the diagnosis, it just is kind of just is. And we all grew up together. So it's never really bothered me. It's just been part of our lives. And I know people get these diagnoses all the time and they cry and it's horrible and, you know, it's scary and everything else, but it's not been a scary thing for me. It's been our life.</p> <p>So there is this really great book by Mary-Lou Weisman. And I actually recommend it to every rare disease mom or caregiver. And it's called Intensive Care. And it's about the life of a boy with Duchenne back in the day where there was nothing you could do and really nothing you could do, and I know Mary-Lou personally now, I met her at a conference. But she had all of her chapters very aptly titled. And the last one was called The End. So just to show you sort of what my personality is, I read The End first. So I was like, alright, so that's where we're going when they're 20, now we'll just work backwards and we'll see what we can do between now and then because that's what we, we have 20 years. And so you know, we just -- life evolved.</p>
4	<p>TITLE: <i>Clinical Trials: Excitement to participate can blind you to the details (BTW the trial failed).</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-excitement-to-participate-can-blind-you-to-the-details/</p>

Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about the excitement and pressure families feel when there is the possibility of participating in a clinical trial and how that excitement can blind you to the important things like attending to the informed consent.

Transcript:

Jen: They were curing a lot of mice when the boys were little. So I went to conferences and I saw mouse models that were living longer. Just heard at a conference this week that it's a really great time to be a sick mouse because we can cure them all, but there weren't any clinical trials in boys. Then we had a couple of clinical trials in boys that failed miserably. I took a few years off from conferences because my boys were getting older. And then I heard about this type of medication. It was no longer a medication, it was an RNA alternating therapy. And there were two drug companies that were going to be working on it. And it was called exon skipping.

And I actually met the man who invented exon skipping in Perth, Australia, Dr. Steve Wilton. I met him at a conference at a bar. And he took this cocktail napkin and he was showing me what exon skipping was. And I said, well, my boys are missing exon 52. And he says, I have great news, the first one I've developed is to skip exon 51 and that will bridge the gap and so this drug is going to be available soon for clinical trials. And the boys were six and nine. And I was like, oh my God, seriously? And he said, you've got to go to London because both these companies are going to be presenting at a conference in London, you've got to go find out your boys -- you know, your oldest boy is coming to the end of his walking days, they're not going to let kids in that aren't walking, you got to get there.

And so I had never really flown very far, but I got on a plane and went to London with my mother and met with both the companies. And I said, who's going to be first, because I want my kids in the study. They argued, they argued about who was going to be first, but it turned out that there was a three-year delay, so neither one of them was first. Everything just slowed down to a snail's pace. There were some patent wars. There were just a lot of details that don't matter. But basically we went home with a lot of hope and then we sat and we waited. And Austin stopped walking. And so I got really kind of annoyed and jaded. And you know, I stopped going to conferences, I stopped talking to other parents.

And then Austin's doctor contacted me and said, actually one of these companies is doing a safety study and they're only accepting

	<p>non-ambulatory patients. And I have to say in hindsight that should have been a red flag to me that they were doing a safety study in only non-ambulatory patients. This is not the drug they're currently on. But I was desperate for anything. So I was very pregnant with my daughter and we flew to Columbus, Ohio and we stayed for three weeks to be part of the safety study where he received injections in the stomach to see if the drug was safe. He received placebo I now know. And we signed paperwork that said that if the drug was safe that he would then be allowed in the study.</p> <p>And the company never honoured that. He was never allowed in the study. So we went home. It was a horrible trial experience. I've learned to read consents a lot more carefully about extensions and whether or not your child is going to be able to continue receiving the trial medication and what happens if he is on placebo, will he roll over to drug and all of those things I had no idea. I was just so excited to be invited to a study.</p>
5	<p>TITLE: <i>Clinical Trials: Mom finds out about a trial on facebook, learns about the trial design & the screening process.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-mom-finds-out-about-a-trial-on-facebook-learns-about-the-trial-design-the-screening-process/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about finding out about a trial on Facebook, taking her son to be screened. She speaks about gaining an understanding of trial design and why it is important to enroll the right candidates in trial. She also discusses the misconception that you can “train” your child to meet the inclusion criteria, in this case a walk test.</p> <p>Transcript: Jen: And the interesting part is that, you know, everybody thinks you can follow clinicaltrials.gov or you can wait for your doctor to call you. I found out about this study that was only accepting 12 patients from across the country on Facebook. I had a friend who posted that she was flying from California to Columbus to screen for a study, happened to know that her son had the same mutation as mine and was the same age range. And so I messaged her and she said, oh, yes, the doctor is pre-screening. The company is not even screening yet. The doctor is pre-screening by invite only.</p> <p>And so I happened to be at the same site that Austin had been in and I called the nurses and I said, you owe me, I want Max screened for this study. And they said, we've already screened our 12. And I said, I don't</p>

care, I'll be there on Monday. And we screened him and he failed because he was too fast. He had walked 20 meters faster than he should have in the six minute walk test.

We got a call back in three months. And they said, so the children in the original 12 that got screened, one of them couldn't walk the full six minutes when he came back, let's screen Max again because we know these kids get worse over time. And they said, Max was almost there, let's see. And in those three months he had lost 25 meters and he got into the study.

So I did not understand clinical trial designs at all. And so at that time point I had no idea what they meant by Max is too good. I said, great, you'll have better results, you know, I mean, he looks great. And I also -- the second thing I thought was, gee, I wish they would post these parameters before hand, so I could train him, so I could make him walk slower. But they don't let you walk with your children. So there is -- let me just put this out there, in case anybody wants to try training their children to walk a certain amount of meters in six minutes, it's impossible, even really smart kids because you just can't do it, so let me get that out there because people have tried.

I understand now that, you know, having been through the regulatory process, they have to be so particular with their trial guidelines because they've got to get -- they only had 12 kids. They had to make them as similar as humanly possible in their disease progression. And interestingly our trial had a really -- our trial had a very near miss because the doctor had included a set of identical twins that were really on the cusp of not walking anymore. But he was really interested in seeing what happened with identical twins, so they were included and they stopped walking before the drug took effect, so 2 out of 12 kids stopped walking. So those are the kinds of things where making exceptions. I mean, they met the criteria, but barely. And you know, they were my good friend's twins. But that was really hard for them and it was hard for all of us because they were a little bit more progressed than the rest of the group.

So we got lucky, we are incredibly lucky. We call those kids the Columbus 12. I mean, they were the kids that travelled for two-and-a-half years. Well, we had to go to Columbus every week for our infusions. So we drove from Vermont to Hartford, Connecticut, flew to Columbus every Tuesday, had infusion on Wednesday and did the reverse on Thursdays. And I brought the baby with me. Sometimes I brought all the kids with me. But yeah, we took a couple of years off of our lives to do it and we're incredibly lucky.

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TITLE: *Clinical Trials: My son participated in double-blind placebo study...I did not anticipate the extended trial timeline.*

<https://courageousparentsnetwork.org/videos/clinical-trials-my-son-participated-in-double-blind-placebo-study-i-did-not-anticipate-the-extended-trial-timeline/>

Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about only one of her sons meeting the inclusion criteria and qualifying for the study as well as her naivety about how often timelines in studies change. She explains a double-blind placebo study and how in her son's study, all the participants began receiving the drug once evidenced proved safety and efficacy. She talks about the FDA process and the importance of knowing the sponsors plan for the period of time between study completion and approval of the treatment.

Transcript:

Jen: So I knew that all Duchenne studies were based on the only approved standardised method of testing efficacy and that was a six-minute walk test. And people have been priming me for that for years that if your child stopped walking, you're not getting in a clinical trial. So I knew when we went to the study that Max had a chance of getting in, but Austin never would, we couldn't even screen.

And Austin was actually fine with that. It was such a horrific experience being in a clinical trial that he was like, hey, Max, you go try this thing, I'll see if it works and if it works, I'll get it too. Like, he was very fine with not getting weekly infusions. At time I was fine too because I didn't understand, you know, I thought, okay, if this drug works, Austin will get it, I had no idea how long it took to get through a clinical trial. You know, the original study was only 24 weeks. I'm like, cool, 24 weeks, we find out if it works then everybody gets it.

The drug approval process even as fast as it's possible, even the fastest pathway Max started when he was 9-and-a-half and the drug wasn't approved until he was 15-and-a-half.

I knew that after 24 weeks -- so there is 24 weeks of a double-blinded placebo controlled study. We didn't know what was happening for 24 weeks. We didn't know [00:33:57:23] if Max was on drug, we didn't know if he was on the high dose or the low dose. We didn't know anything. These 12 kids were randomised. Twenty-four weeks it was un-blinded. They had another muscle biopsy, so they had -- by then each had two muscle biopsies. And then all the kids at 24 weeks were

	<p>rolled onto drug because there were no significant safety concerns. And they actually saw improved dystrophin protein in the boys' muscles. So they saw some efficacy, early efficacy, and they -- so they kept all the kids on drug. And then at 48 weeks, it should have ended, but they were still -- they ended up -- the FDA wanted to see more dystrophin, so everybody had to go for a third and then a fourth muscle biopsy.</p> <p>We were lucky that while the FDA was screwing around, the company committed to providing drugs to all 12 participants. And actually we don't need to keep on this, but it's interesting -- you know, I was fighting really hard for Austin to get access because I did see benefit during the study about 24 weeks in and between 24 and 48 weeks, Max was doing tremendously well. He stopped using his wheelchair at the airport. I mean, he was doing really well. And I was fighting really hard for access. I was fighting against the company, I was fighting with the company, I was on the news. I was really a horrific human being at that point because I was really pissed off about the process. But I was able to talk the FDA and the company into allowing an older child study. And so Austin got on drug when he was 15-and-a-half because I helped to design and implement a study across the country for 24 non-ambulant patients. And so Austin did get on drug too.</p> <p>So the company also started a study for five to seven year olds because under seven wasn't allowed in the study either because they can't take accurate six minute walk test in the five to seven population. And so we had 24 kids in the five to seven year olds, 12 kids in Max's study and then 24 kids in the non-ambulant study. So it was a really nice process to get these studies going. So they were only safety trials. They didn't do efficacy and endpoints, which they should have, but it got everybody on drug. So that's why I say it's like the best possible scenario, the FDA and the company were both very flexible and transparent and listened to us. You know, they didn't take kids off drug.</p> <p>There have been studies and I tell patients this all the time, one of the first questions you ask is what is your plan between study and approval, commercialisation, because there are plenty of companies that take all their patients off drug and wait for it to get approved. And that would have been horrible for Max. So Max has been on uninterrupted dosing of the drug despite a long regulatory process, despite no insurance coverage after commercialisation. The company has continued to provide drug for eight years.</p>
7	<p>TITLE: <i>Clinical Trials: Deciding if this is the right trial – Are you looking for curative or something that mitigates? What if there is a placebo?</i></p>

<https://courageousparentsnetwork.org/videos/clinical-trials-deciding-if-this-is-the-right-trial-are-you-looking-for-curative-or-something-that-mitigates-what-if-there-is-a-placebo/>

Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy offers guidance on deciding to participate in a clinical trial. She asks, “what are you looking for- curative treatments vs mitigating symptoms?”; “What can your children stand – can they tolerate the tests required?”; “Can your family/marriage survive the lifestyle changes you may need to make to participate?”; “What if it is a trial with a placebo arm – can you handle your child being getting the placebo?” She encourages asking lots of questions of the trial sponsor, doctors and the disease community.

Transcript:

Jen: We're really lucky in rare disease that many disease states -- I mean, I think that's why we're talking about this, right -- many disease states have options. And I get messages every day from the Duchenne community and others, how do I choose. So the first thing is you choose. If you've got a five-year-old with Duchenne right now, you've got at least 10 choices for clinical trials, incredibly overwhelming. So how do you choose? You know, you first have to decide are you looking for something that's pie in the sky, are you looking for something curative, are you looking for something that either works or doesn't, you know, that's your gene therapies, you know, eventually your CRISPRs. You can also say, I'm not ready to alter the DNA, but I would like to get rid of some of the fibrosis. Like, what are the symptoms that matter most to you and then you have to read the data, like, you have to. You cannot let anybody else make this decision for you. You have to read it, you have to understand it.

Luckily, companies are really good as a whole at giving you access. They'll give you their corporate slides, they'll explain their corporate slides, they'll talk you through what the benefit, risks are. You know, they'll talk you through projected side effects. They have to disclose all of these things. So do research, ask everybody. I mean, Facebook is an incredible resource because also, you know, for example, there is a family in New Zealand that's trying to decide between a study for the drug that my kids are on, that's approved in the U.S., it's now in open label will study there or a new drug that only have some safety data. And so she was asking what should you do. In my mind, always pick the approved drug, we know it works, right. So ask people's opinion.

She had no idea that it was approved in the U.S. and that there were hundreds of kids already on it and she could get that much information.

So first you have to pick, what are you willing to risk. You know, the higher benefits are going to have the higher side effect risks, right. So what can your kid stand, what are the criteria? Can they do four muscle biopsies? Can they be in an MRI machine? Is that something that they can handle? Can you and your family travel weekly across the country? Are they providing financial reimbursement for that travel? Not everybody is.

However, I will say that if finances are the problem, there are lots of places that will cover your travel. So don't make a decision based on finances. But can you take time off work? I was lucky, I was married at the time. Could I do it now? Probably not. And then you have to ask some really tough questions of your doctor and the principal investigator for the study. You have to ask what's this company's track record. You know, there was a company that I was talking to from another country who left all of the kids in their original trial in another country without drug when they came. They did the original study for six months, came to the U.S., all those kids were off drug. Nobody had asked them that question, what happened to your original kids. Their policy is to take kids off drug.

Now, also those things are not inflexible. So you asked about tenacity and fight. If you make a big stink out of something and say, this protocol sucks and you tell everybody that's thinking about being in the study, we want to see an extension study written into the protocol because you can't just put a kid on -- you know, if the drug works, we want to see an extension. If it's safe, we want to see an extension. If there is a rollover, we want to see them off placebo. But that's the other question, placebo versus no placebo. You can get no placebo now probably for a drug that's not going to be that effective. Any drug that's expected to have a big effect has a placebo because the FDA requires it. So one of our drugs in study has a three-year placebo.

Think about that, can you handle the chance that you put your child in a three year placebo because the worst possible thing you can do is drop out of a study. You know, if you can't make a commitment to stay in a study no matter what happens, don't do it. You can also find out at what points is the company willing to share data so that you can make other decisions. You know, if you are in a three-year placebo study and you're pretty sure your kid is on placebo and they've seen no benefit from any of the kids, you know, and they're evaluating a year-and-a-half in, well, then maybe you do drop out for your child's own personal gain, you know, if you say the drugs aren't working. But some companies won't give any data. So you just have to ask a lot of questions and any decision in the end that you make is the right one.

	<p>Because I did all of my research and I knew all of the risks and I knew all of the potential benefits and it was what was available to him. You know, I chose the other drug because it looked safer to me. But if the only choice I had, it was between I know that Duchenne is going to kill him, this drug might kill him, but it might benefit him, that was my decision. It's a terminal illness versus a potentially beneficial drug. I mean, it's a no-brainer for me when it's a terminal illness. You know what's going to happen to your kid.</p>
8	<p>TITLE: <i>Clinical Trials: Assent to Participate: My son is old enough to decide for himself.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-assent-to-participate-my-son-is-old-enough-to-decide-for-himself/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about the Assent to Participate, a document that children over nine, with developmental capability must sign to receive a treatment or procedure. She also talks about being honest with her boys and asking them questions about procedures and trials. She discusses the altruistic nature of participating in research.</p> <p>Transcript:</p> <p>Jen: If the kid is old enough, ask them. I mean, my kids will say that I ask them, but I probably would have made them do it anyway. But I always ask them because at this stage in the game, they're 17, almost 18 and 20. I don't get to make their decisions anymore. If gene therapy pops up for them, I don't get to decide that. And I have one that would do it and one that said he wouldn't. So educating the kids, they're going to have to be compliant, so you got to know if they're going to be able to do it or not.</p> <p>This is important, kids over nine have to sign an assent to participate. So I had to sign consent, but every time they were going to do something Max, every time the trial was extended, Max had to sign his own paperwork. Talk about sweating and bribery. And if at any point he said, no stop, during any procedure, they had to stop. He was considered an autonomous human being.</p> <p>In no other context, my 20-year-old, still not autonomous human being, they're still looking at my financials for college. But for a clinical trial, he has to sign before every surgery and say, yeah, I consent to this.</p> <p>I think I presented to the boys that there was this thing that we were going to do. And then I sort of went backwards from there and said, you know, this is going to happen, how do you feel. Do you have any</p>

	<p>questions? What are you going to say when they ask to take a piece of your muscle? Do you understand why they need to take a piece of your muscle?</p> <p>But I think to the extent that you can be honest with your kids too. My kids knew they were terminal. It's a decision I made. But if they don't know that they're getting worse, are they going to up for a drug that might make them better, no, they feel fine. If they know, well, Max watched his brother stop walking. He really didn't want that to happen. It ended up happening anyway. But to the extent that you can be really honest and say, you're going to take this medication and we are really hoping that it prevent some of the disease -- the bad things happening from this disease and we don't know and you talk about being altruistic, you know, this may not help you, but it may help new babies born with this disease. My kids were well aware of all of those things.</p> <p>And again, it depends on your kid's cognitive ability, what you say to them. But if you ask -- if you watch interviews of both the boys from when they were younger, they both say, it may not help me, but we're doing this for everybody. And if you really believe it -- you have to believe in it. You can't be wishy-washy. If you really believe it, I mean, they're pretty impressive brave humans. They've done some things I don't know if I could do honestly.</p>
9	<p><i>TITLE: We are a medically complex family – It is the fabric of who we are.</i></p> <p>https://courageousparentsnetwork.org/videos/we-are-a-medically-complex-family-it-is-the-fabric-of-who-we-are/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy and one with a primary immune deficiency talks about her sons Austin and Max understanding their own life-limiting diagnosis, normalizing it within their family and the impact it has had on both boys.</p> <p>Transcript: Jen: They started knowing about the terminal nature of their disease on day one. I mean, Austin was three. I mean, you talk about it in an age appropriate way. But we started familiarising them with wheelchairs, having them around kids with vents. I mean, I remember Austin -- I sent him to summer camp when he was seven and there were adults at this camp with ventilators. And he came home and said, they have Duchenne, I have Duchenne. And I said, yep, aren't they awesome human beings and one day you'll have some special mechanics to help you breathe. So I mean, we talked about it from day one. And the last</p>

thing you want is your kids Googling what happens when you have Duchenne.

I mean, I've seen this -- and Austin says it now, it's nice to hear that he likes the way he was raised because you now could any way, right. But he will say things -- he was just on a panel not too long ago and he was like, you know, I have a shortened lifespan and I've known that my whole life and I think that that made me live my life way differently than I would have, like, everybody should live that way. And so we started talking about it -- I mean, I never sat them down. But you just -- you make it normal, it's just this normalisation.

Interesting fact, James thought he was going to get a wheelchair at some point. And I remember he was probably two or three and he asked when his chair was coming. And so to him, he thought you reached a certain age and you got a wheelchair. And so I just remember that being like -- I never told him he wouldn't.

And so I think if you put that combination together, I love my children, but everything is finite, you know, everything, the whole world is finite, you never know what's going to happen. And so if you put that hat on where you're like I'm just going to go forward full steam ahead. I'm going to hope that really smart people who are smarter than I am figure things out and I'm going to do my best to support them. I think that there are certainly periods of time, you know, sometimes I look at Austin and go, I'm really going to miss this kid. But I'm also like he's kind of a pain in the ass and -- you know, we live our lives. Like, I don't just look at him and stare at him all the time and think he's dying.

You know, I've raised my kids to just be so normal that we don't really -- it doesn't really affect us so much anymore. I mean, it's the same thing just coming back to like sort of this medical family, it's so normal for us to be in this medical world at this point that we take for granted that other people understand it. For example, Nora's first -- one of her first words other than mama, dada was vitals. And so she was standing, holding onto an IV pole because that's how she learned to walk is with an IV pole up and down the research hallway. I mean, she was raised in clinical trial. She's eight, Max has been on drug eight years.

She was six months old when she started going on these trips to Columbus. So the nurses practically raised her. She can hang out with anybody at this point. But she's running up and down the hall and the nurse said, time for vitals, Max, and Nora goes vitals. And we were like, alrighty then first word, it's great. So we just kind of do our thing. And it's interesting that when James was diagnosed with immune deficiency,

	<p>I kind of came home and I'm just like if any family is going to deal with this, it is totally us. Like, we already have a whole closet dedicated to infusion supplies. We can make another drawer. I slapped his name on it and now we have a third.</p>
10	<p><i>TITLE: Clinical Trials: A mom: I didn't worry about disease progression then and I don't post trial.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-i-didnt-worry-about-disease-progression-then-and-i-dont-post-trial/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy, both of whom now receive drug treatments, explains how she did not really worry about the disease progression; how there were no guarantees in expected timelines pre-treatment and there are none post. She also talks about her son's peers dying and the guilt associated with participating in a trial.</p> <p>Transcript:</p> <p>Jen: I never really knew what the timeline was. I knew what the expected timeline was, but then I've watched my friends' sons die at 8, 11, 12. I mean, boys with Duchenne don't die from Duchenne, they die from chest infections, they die from severe cardiac involvement, they die unexpectedly, they die suddenly, they break a limb and get a pulmonary embolism. I mean, our guys don't just fade away in general. I mean, they die catastrophically. They wake up and somebody is gone. And so Austin's peers are dying now. So that's been one of the hardest things, but not in the way that you would think. It's not because I'm worried about Austin. It's because I'm feeling somewhat guilty that we are the family that's pulling out in front. We were all the same, right.</p> <p>But I get scared to open Facebook every day because they're dying at alarming rates. So while our kids are surviving longer, our kids are not surviving longer. I mean, statistically I think they're saying that our kids are surviving into their 30s now. It's not my personal experience, so I don't know where they get these numbers. Maybe we're just holding out these people that survive into their 30s and 40s. And that's an interesting word, survival, because most of them are bedbound on tubes and vents and can't move a finger. And I don't know that that's what I'd want. I know that's not what Austin wants. He's saying -- he's refusing a ventilator and a feeding tube. And he had said that since he was six, you know, that he won't breathe like that. He's not going to eat like that. He likes food too much.</p> <p>Max can still stand. He's 17-and-a-half. He was supposed to stop walking at the latest at 13, at the latest for natural history, anything</p>

	<p>more than that, you don't have Duchenne anymore, you have Beckers. So he essentially -- the drug did what it was supposed to, it turned Duchenne into a Beckers. Beckers can have normal life spans.</p> <p>Austin was on the 30 milligrams per kilogram and he's doing terrifically. I mean, his pulmonary function hasn't declined in over three years. He is independent as a 20-year-old. Remember, when the boys were diagnosed, I was told I had 20 years. Austin is going to be 21. And he can drink a beer on his own when he turns 21, so we've succeeded. We've succeeded to keep him alive and happy and healthy. And so this is the best case scenario for a clinical trial.</p>
11	<p><i>TITLE: Clinical Trials: A mom: Sometimes if feels like there are "Haves" and "Have Nots".</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-sometimes-if-feels-like-there-are-haves-and-have-nots/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks honestly about how often in rare disease it feels like there are "haves" and "have-nots" in the community. She talks about both the division trials can create in a community but also the support you can gain.</p> <p>Transcript:</p> <p>Jen: There is so much that makes you a "have" versus a "have not" in diseases, right. So there is, what mutation does your kid have? Does your kid have a rare mutation? That already sets you apart. My kid had one of the most common mutations, right, the most common mutation, which was why drugs were aimed at my boys first, right. So that already made me a have. Also, my kids don't have the cardiac problems. You either have cardiac problems pretty much or you don't. They have mild scarring in their hearts. So my kids are healthier than other boys with Duchenne. Then we got into a clinical trial. And now they're really healthier and were lucky we're on an approved medication and we have access to that approved medication.</p> <p>There are a lot of families who were not in the clinical trial, who do not have access because insurance was not paying for it. I fight for those people every day. But sometimes it was almost like people didn't see that I was fighting for their kids too by putting my kids out there. I mean, my kids lost years of their lives. They didn't go to school. Max lost two years of school because I'd bring him to congress, I'd bring him to the FDA. He had dinner with Janet Woodcock at the FDA because she needed to see the drug was working. My boys would go and speak on</p>

	<p>the Hill at congressional briefings. That was not fun for us. That was not fun for them.</p> <p>And so I thought a lot of times people would send me sort of nasty messages about gloating or about how lucky we are or I'd post a video and they'd say, don't tell everybody Duchenne is cured, it's not cured. And I never meant to represent it, but they would say stop promoting that there is a treatment because there is not a treatment for everybody and you should only support drug companies that are making treatments for everybody and incremental benefit didn't matter. So we've experienced a lot of hate. We've also experienced a lot of love, people that just were cheering for us, people that have lost children, but were still cheering for us, people that were grateful. I mean, when I got that trial started for Austin, there were 23 other boys that weren't going to access to drug and they got on drug, those are grateful families. So there is a lot of haves and have nots.</p> <p>So we post a lot about what the boys can do because I think for some people especially with newly diagnosed, they see Austin working at a biotech company for this summer, getting a degree in mechanical engineering, playing soccer in Fort Wayne, Indiana, he's an athlete, he's a speaker, he's a really cool guy, he's normal. And so for a lot of families, that's hope. But for a lot of families, that's bragging. And so I think it's the same situation with normal people, you know, my kid got straight A's versus my kid has learning disabilities versus I have a big house, you have a small house. Portions of our life suck too.</p> <p>So I think that it is hard the divisiveness in disease communities is really toxic. And I think the further divisiveness when you throw into it, you know, people doing better than other people and people getting lucky, it was incredibly lucky that Max got into that study, but it was also because I was motivated. And so I tell people that all the time. Nobody called me and said, hey, would you like Max to get into this study. Nobody called me and said, hey, would you like another study for Austin to get into. This was blood, sweat and tears. So not everybody has to be that kind of advocate and I understand if you're just trying to keep your head above water, but for me, for our family, surviving means that I'll push any buttons and I'll go anywhere and I'll also do it for you.</p>
12	<p>TITLE: <i>Clinical Trials: A mom: We can't ignore the economics.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-we-cant-ignore-the-economics/</p>

Description: In this video, a mother of two sons, Austin and Max with Duchenne Muscular Dystrophy and a son with a Primary Immune Deficiency talks about why we cannot ignore the economics of drug development and how individuals advocating to insurance companies can help ensure that they have accurate knowledge about your disease.

Transcript:

Jen: I just want you to know that innovation cost money and you -- years and years and years ago there was no interest in rare diseases because there was no return on investment. Companies couldn't make money. And advocates have worked very hard with Orphan Drug Act, 21st Century Cures, regulations to speed things up for FDA to give lots of perks to drug developers so that they have interest.

The reason we have three more drugs at the FDA for Duchenne right now, two approved drugs and a pipeline of 40, 50 drugs right now is because people think they can make money. Drug companies are publicly traded.

That said, most of these drugs, for example, the medication that my boys are on is not going to be profitable for at least another 5 to 10 years. So right now the drug company is charging -- I think that it's weight based, but typically 400,000 or more per year for this treatment. It's a weekly infusion. They're not going to make money for 5 to 10 more years. They have a drug pipeline that includes gene therapy, which I'm very happy about. I really want gene therapy for my kid. But if they can't get reimbursed at this high dollar amounts, they will never be able to put more money into a pipeline.

If they can't get their drugs reimbursed at these rates, then we won't have a pipeline of innovation. And so it's very important to remember how much money goes into these drugs, how long it takes. Remember, you know, 8 to 10 years for a drug approval, even in the fastest pathway.

Your job as an insurance company is to pay less money, that's your whole job when you're reviewing claims. And anybody that has a child or has anybody in their family with a chronic illness of any kind knows that the first stop for anything is a denial. That said, commercial payers tend to have a really great process with an external review. And they tend to be pretty fair and they are covering our treatments. They take a lot of interaction from outside pressure. I worked very closely with a couple of them to develop positive policies. But in general commercial payers are doing their job in paying for things. It's always a battle, right.

	<p>Medicaid states are scary. Medicaid doesn't have enough funding. And even with a handful of patients with rare diseases in their state, they have a hard time approving therapies. And so the community is going to have to get together, attend regularly, attend these drug utilisation review board meetings, educate on disease states, educate on prevalence. I mean, I went to one Medicaid review board hearing and they didn't understand that our drug can only be used for 13 percent of the Duchenne population and had no off label use. So they were calculating how many people do they have with muscular dystrophy in their state. So they were thinking, oh great, we're going to have to cover 200 or 300 people, they had 3. And so it's that kind of thing where patients boots on the ground, drug companies do their best, but patients need to be in every state.</p>
13	<p>Title: <i>Clinical Trials: A mom: Don't feel rushed, don't feel desperate – read the Informed Consent.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-dont-feel-rushed-dont-feel-desperate-read-the-informed-consent/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about the consent process and how parents/patients often ignore because they feel rushed and desperate. She talks about what is included in the Informed Consent documents, the importance of asking questions, taking your time and understanding what you are signing up for.</p> <p>Transcript:</p> <p>Jen: So the consent process is something that I think a lot of participants and parents kind of ignore actually. I think that when you're given a pile of documents and you're feeling rushed and you're feeling desperate, people often just sign the document. But in fact, people don't often read them, and that's a problem for me . I think that the consents are getting better and easier to read with input from patient advocates, you know, saying, this is hard, I'm still pushing for videos or brochures or breaking them down into understandable sound bites.</p> <p>But in general, it's really hard to understand all of the things that you're signing away because if you start to read these documents, they talk about worst case scenarios, they talk about best case scenarios, they talk about what your rights are, whether or not you can pull out of a study, which you always can. A lot of people don't understand their rights. You can quit at any time. I don't advise it. Try not to sign up for it if you're not going to complete it, but you can quit. But the important</p>

	<p>parts of the consent are what's going to happen during the study. How long -- you know, people have signed up for studies and not understood that there is a placebo. Not understood that there is a surgery, not understood that after the end of the original period, like I said before, you're not going to continue to get drug. So really that's the time that you have to ask your PI every question.</p> <p>And you also have a right to have the entire consent read to you and explained. So you can take as much time as you need to understand. And then you can even take it home, you don't have to sign it then. You can take it to anybody you want to, to have it understood. But I think it's a really important process to understand, it's a legal document, it's binding. Often in the consent you're told that you can't talk about the study to anybody outside of your family. Often in the consent you're told that your child cannot be active for 24 hours before the study -- before the measurements are taken. You know, it's just important to understand what you're signing up for just like you would for any other legal document.</p>
14	<p><i>Title: Clinical Trials: A mom on weighing risk, understanding endpoints and managing expectations.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-on-weighing-risk-understanding-endpoints-and-managing-expectations/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy discusses the fact that all trials involve some measure of risk. She used her understanding of the trial's endpoints to evaluate her risk tolerance and set her expectation about outcomes. "This is being studied because we don't know if it works." She also discusses risk in relation to the phase of the trial and safety trials.</p> <p>Transcript:</p> <p>Jen: I don't think that every clinical trial is completely safe. There is always risk. I mean, you've got first in human safety studies and in general the first in human safety studies for diseases like Duchenne are in Duchenne patients. And those patients are compromised already. So I mean, we had a child die on what was a seemingly safe drug, not even a curative therapy, but a seemingly safe drug because of a hiccup during the trial, you know, just a combined medication issue. So no, you know, there is always risk.</p> <p>But I think when the disease is bad enough and it is interfering with either your quality of life or interfering with your life expectancy, like I said, I have a very high risk tolerance. And I do believe that they do</p>

	<p>adequate safety studies and get things as safe as humanly possible before it goes into humans.</p> <p>It's really hard to remember exactly what the company thought that they were going to see. But I knew what the endpoints looked like. So I knew that they wanted to see improvements on the six minute walk test and I knew that they wanted to see an increase in dystrophin production, so more protein production, basically some protein production because the boys had none. So I understood those two things as the endpoint. There were some secondary endpoints for stair climbing, grip strength. But I understood that this drug was meant to slow or stop the progression of the disease.</p> <p>And I think that the doctor did a great job. A lot of this falls on the physician. The doctor did a great job of explaining this wasn't a cure, it's not going to reverse any of the damage that was already done, it would help to protect some of the existing muscle. I think that not all doctors do a great job of explaining what could happen until a lot of people -- you know, their expectations are not met with the study because they think that it's curative and their kid is going to come out of it doing cartwheels. And that was never my expectation. But I think certainly it was some people's expectations.</p> <p>I think it's important to remember that the reason that there is a clinical trial is that they don't know what's going to happen. And so you have to go into it knowing that this is being studied because we don't know if it works.</p>
15	<p><i>TITLE: Clinical Trials: Child Life can help make the trial experience better for your child.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-child-life-can-help-make-the-trial-experience-better-for-your-child/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy describes how she made participating in a clinical trial more tolerable for her son by utilizing Child Life Specialists.</p> <p>Transcript: Jen: And then also trying to make it fun, like, we had to go to Columbus, Ohio, we have -- you know, he freaking loves Denny's. So it was like I would just -- he loved his trips to Ohio. He just had his little sister, no brothers with him, you know, and we made it fun. But it's a lot of child life. I would say when you're in a clinical trial, one of the first things you want to ask for is if the hospital has a child life specialist because a</p>

	<p>lot of times they would let me leave the room and they would deal with it.</p> <p>You know, Max is really hard to access for an IV. They have a lot of scar tissue and their veins collapse. Eventually he had to get a portacath. But sometimes on the third or fourth or fifth stick and I was losing my mind, it's okay to step out and involve child life. And Max made his own friends in the hospital. He had the nurses he liked. That was the other thing I fought for. He would walk in and tell them what nurse was drawing his blood. And sometimes oh, we could -- nope, you know, the kid gets to make the decisions. And so he was treated like a little prince. It was like a hard culture shock when he got out of his study and he wasn't that special anymore.</p>
16	<p><i>TITLE: Clinical Trials: A mom: "Eventually we are going to be looking at combination therapies.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-eventually-we-are-going-to-be-looking-at-combination-therapies/</p> <p>Description: In this video, a mother of two sons with Duchenne Muscular Dystrophy talks about how eventually science will be looking at combination therapies – “adding to the next best treatment.” She discusses washing out of standard of care treatments and warns against doing so to participate in a trial.</p> <p>Transcript:</p> <p>Jen: So the therapy that the boys are on is a weekly therapy. So theoretically you can wash out of it to try something else. For example, the boys have a mutation that's amenable to either exon 51 skip which or exon 53 skip.</p> <p>It's my understanding that medically there is no reason that they can't stop the therapy they're on, wash out they're saying three to six months, I think it should be less, I'd push for less and then try something else. However, the other thing you can think about is this is an approved therapy that the boys are on. Eventually we're going to be looking at combination therapies for Duchenne at least and pretty much every other drug. Even gene therapy is not going to be curative for Duchenne because it's a truncated form of the dystrophin protein. You're always going to need a combination. Our community needs to start looking at combination therapies.</p> <p>They're already on the first two drugs that are approved that steroid that I mentioned, plus, the drug that they're on now, which is an exon skipping drug. Now they could probably add an anti-myostatin drug or</p>

	<p>another anti-fibrotic or a circulation drug or pulmonary drugs or whatever. So I think that the way that we're moving with these therapies is that we're going to start adding to the next best treatment. Once this drug is accepted as a gold standard of treatment and standard of care, then there should be arms of clinical trials that accept the boys into them. I'm certainly pushing for that, right, although they're aging out of the acceptable -- you know, once you're over 21, you're really weren't supposed to live, so you're not really allowed to be in clinical trials anymore, but that's changing. It's starting to change.</p> <p>I'm certainly pushing the current company that's working on gene therapy to have an arm for their boys that have been participating. We're not there yet, but if you think about clinical trials, they allow patients to be on standard of care treatment. They wouldn't expect them to wash out of standard of care. So that also points to another point that I want to make is that if your child is on an approved therapy and it seems to be working for them, it's never a good idea to wash out of your approved therapy to get into a clinical trial. Seems to be a misnomer, but why take something that's standard of care and then you wash out it to be in something that doesn't have any evidence. And it's happening, so it's just not a big enough pool of patients.</p> <p>I'm Lucky, I don't have any decisions to make anymore. Isn't that interesting? Well, the boys are adults, and not only are they adults, but they're out of that window. We had our, you know, 15 seconds of fame in that lifespan that they had where they were prime age and the focus of everybody. We're benefiting from the first drug. We don't have any decisions to make right now because we've already made all of our decisions. We may have decisions later, but we don't have any choices. There is nothing for the older guys anymore, but we made it through some really had ones.</p>
17	<p><i>TITLE: Clinical Trials: A mom on dose escalation studies and gene therapy.</i></p> <p>https://courageousparentsnetwork.org/videos/clinical-trials-a-mom-on-dose-escalation-studies-and-gene-therapy/</p> <p>Description: In this video, the mother of two boys with Duchenne Muscular Dystrophy talks about putting a child in a dose escalating study. She explains the difficult decision of participating in a Phase 1 gene therapy trial at the lowest dose because currently you cannot be redosed. She briefly discusses placebo-controlled trials.</p> <p>Transcript:</p>

Jen: If I were talking to a mom friend about whether or not to put their child in a dose escalating study where there could be no benefit in the low dose and that might be the only dose their child receives, I would say make sure it's not a one-time dose only. I would never -- and I don't think there should be allowed to be a study of gene therapy where any child -- any single child is given a dose that is sub-therapeutic.

So there is -- under no circumstance would I ever tell somebody to do it if they're aware that it could be sub-therapeutic. That said, if it's a drug where you can then dose again, we have to know what the lowest threshold is because that's what the FDA is going to approve, that's what payers are going to want to know, they have to see multiple doses. Gene therapy is another animal. You can't expect children to be sacrificed, you know, they can't get treated again once you're treated for gene therapy. And I think there needs to be a whole educational series. I don't think there is enough education about gene therapy.

Gene therapy is permanent. Now, you have doctors that will tell you, it shouldn't be, we should be able to re-dose, we might be able to change the vector. You know, the sciencey people will tell you that gene therapy shouldn't be permanent. Right now everything we know about gene therapy is you can never have another dose. So first of all, it might last 10 years.

You dose a five-year-old with Duchenne with a gene therapy, in 10 years they're just starting to see the major effects. You can't redose, think about it. So there is a lot of information needed. And I am so excited for the pioneers that are doing it now. But for any type of decision that you make, if you can just really stack the cards to your advantage the best possible way, do not accept a sub-therapeutic dose because you just can't do it again.

Somebody has to do clinical trials, somebody has to. But if you -- we have three companies in the gene therapy space. They're doing it three different ways. The doses for two of them are expected to be therapeutic, choose wisely. I mean, that's really the advice that I would give because I'm not somebody that's always thinking about the bigger picture alone. These are people, these are children. And I would hate for somebody to not tell me that a dose was sub-therapeutic.

So that's a huge pain point for me. I don't think you can mess around. I also don't think you can mess around with placebo for very long in these studies because we're going to have to follow these four and five-year-olds that are given gene therapy or even the newborns for SMA, we're going to have to follow these kids for 20, 30 years to find

	out what the true benefit is. So at some point you're going to have to take a leap and get rid of placebos.
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