

Podcast Transcript:

Race and Regulation Podcast

Presented by the Penn Program on Regulation

Episode 6: Race, Social Inequalities, and Clinical Drug Trials with Jill A. Fisher

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Music: Joy Ike's "The Fall Song"

Jill Fisher: There is generally a lack of recognition that people of color are enrolling in these clinical trials. And there aren't good data about it.

Cary Coglianese: That's Jill Fisher, a leading expert on the social aspects of medicine, delivering a lecture organized by the Penn Program on Regulation at the University of Pennsylvania. I'm Cary Coglianese, the director of the Penn Program on Regulation and a professor at the University of Pennsylvania. Welcome to our podcast, "Race and Regulation." In this series, we are talking about the most fundamental responsibility of every society: ensuring equal justice, and dignity and respect, to all people. Advancing racial justice calls for all of us to understand better the racial dimensions of regulatory systems and institutions. We're glad you can join us as we hear from Jill Fisher, who is a professor of social medicine at the University of North Carolina's medical school. This podcast episode focuses on inequities within the process required by federal regulations for testing the safety of investigational drugs.

JF: If we think about the history of drug development and drug regulation, the first major regulation that was passed was in 1938 with the Food, Drug, and Cosmetic Act, and that required that drugs be shown to be safe prior to coming on the market. But in 1962, the Kefauver Harris Amendment to that law was the turning point. That was when drugs had to not only show that they were safe to come to the market, but also show that they were effective or efficacious.

CC: To determine that a drug is both safe and effective, the U.S. Food and Drug Administration, or FDA, requires a multi-phase sequence of drug testing.

JF: Generally speaking, you are going to have basic research that happens. Then, when something is seen as promising as a therapeutic, then usually there is going to be some kind of pre-clinical animal research on that. Then, after that, if it is shown to be safe enough and potentially efficacious enough, it will move into human clinical trials.

This idea of having phased drug development is really part of the regulatory structure and it's set up to create a system where safety is emphasized first. Phase I trials are really designed to show that a new product is both safe and tolerable. It's to help establish doses that can be given to both participants in later clinical trials, but eventually to patients if that drug were approved. What's really interesting about Phase I trials is that they largely depend on healthy volunteers to populate them as participants.

Phase II trials are those that are designed both to continue to look at safety but also to start looking at some metrics of efficacy. These are generally smaller-scale trials; they enroll patients. I think of these as “proof of concept” trials to see whether or not there is enough promise and enough safety that the drug can move into the larger-scale trials.

And Phase III trials are probably the ones that most of us think about when we think about clinical trials. These are the large-scale randomized control trials that often recruit hundreds if not thousands of patients to look at whether or not a drug works. I should say that the FDA regulation does not actually require the drugs be tested against a comparative product or the standard of care, but it could be a placebo. That is another function of the regulatory system that is probably worth pointing out.

CC: Professor Fisher's research has focused on the first of these three phases—the first time new drugs are tested on humans.

JF: Rather than seeing it as one specific trial, it's actually multiple studies to establish tolerability of the investigational drug. And there is usually a dose escalation design where you might start with a small group of people, giving them a very minute dose of a drug. The next group gets a larger dose, et cetera.

But these Phase I trials are much more complex and they take place throughout this whole drug development process. That's one of the interesting things that the drug development process, despite having these stages, is not necessarily as linear as it appears. There are lots of other types of studies like metabolism studies. So, if you pick up a prescription from the pharmacy and it says to take it on an empty stomach or to take it after food, all of this has usually been done by testing these products on healthy volunteers by feeding them and not feeding them before giving them the prescription drug. Also, there are drug interaction studies that are done. All of these are actually later in the development process, usually if a pharmaceutical company feels that it's likely their drug is going to get to the market. These all require healthy volunteers as participants.

Another huge part of the regulation that increases the need for healthy volunteers is the generic market. For a generic to get on the market, a company has to conduct what are called "bioequivalence trials." These trials are very quick studies to show that the generic drug that the company wants to put forth is metabolized, distributed, and excreted the same way that the brand-name drug is. Again, these trials largely use healthy volunteers to do this.

I'm emphasizing this just to show that it's the moniker of Phase I trials that include lots of things, but there is also a very significant need for healthy volunteers in drug development.

CC: But why *healthy* volunteers and not individuals with the diseases or conditions the drug is aiming to address? Fisher offers four reasons for drug testing with healthy participants.

JF: First, it's this idea of separating the signal from the noise. If patients have diseases and symptoms that you could potentially get confused about whether or not a drug is causing a side effect or if it is a symptom of the disease itself. The idea with healthy volunteers is that it's a cleaner model where you would be more able to assess whether or not a symptom is really a cause of taking the drug.

Another idea is that there is less risk to participants. That if people are healthy and they have normal kidneys and liver function, that by exposing them to these investigational drugs, they are much more likely to be able to bounce back quickly than patients might be able to.

The third rationale, which I would argue is probably the most important one is availability of participants. That it is much quicker and easier to recruit healthy people to participate in clinical

trials than it is to find appropriate patients for these clinical trials, particularly when you think about the inclusion/exclusion criteria that a company might have for exactly who they are looking for the clinical trials. It is definitely faster to do clinical trials with healthy volunteers than it could ever be with patients.

There is also an ethical rationale that is given for why you might want to use healthy volunteers instead of patients. Patients might misunderstand the purpose of a clinical trial like this that is designed just to study safety. This is called a “therapeutic misconception.” Healthy volunteers are not going to have that same kind of sense that they are going to have some medical benefit from being in the study because they don’t have an underlying illness. Additionally, patients are seen as a scarce resource in medical research. There is also this kind of ethical idea that if patients are so scarce, it might be better to recruit them for the clinical trials that there might actually be a medical benefit as opposed to a safety trial that doesn’t have that kind of benefit.

CC: Professor Fisher also explains that drug trials occur through what she refers to as “inpatient confinement.” That is, the participants in these trials check into a facility staying overnight for days, or even perhaps weeks, as they take investigational drugs and are monitored for any ill effects.

JF: In order to incentivize people to do this, not only to take investigational drugs but to stay in these research facilities, of course, they have to be paid. There would be very little reason to do it otherwise. The going rate in the U.S. is between two-hundred and two-hundred-fifty dollars per day spent in a study. Depending on the length of the study, this could add up. The median clinical trial compensation is about three thousand dollars. In the work that I have done, I found that some studies pay very, very little, less than a thousand dollars, sometimes just a few hundred dollars. The highest paying study that I have seen paid thirteen thousand dollars. Although each clinical trial appears to pay handsomely, it is difficult to earn much more annually participating full time than one would in a minimum wage job, so even though it looks like it might be lucrative, data from my own research shows that it is not as lucrative as it might appear on first glance. In fact, fewer than eight percent of the participants that I tracked in a later longitudinal study earned more than twenty thousand dollars in a single year. To do so, to earn at least twenty thousand dollars, they had to participate in five or more clinical trials in that year to get to that level.

Music: Joy Ike’s “Home Stereo”

CC: The participants in these clinical trials are assuming a risk. Let's not forget they are taking investigational drugs that have yet to be shown to be safe in humans—that is, after all, the question a Phase I drug trial seeks to answer.

JF: At least sixty-five percent of all healthy volunteers are going to experience at least one adverse event when they are in a clinical trial of this type. But generally speaking, these kinds of adverse events are not particularly harmful or all that serious. It's a meta-analysis of hundreds of clinical trials worldwide found that between one and four percent of all adverse events are serious. Of course, there have been some catastrophic things that have happened. I'm not going to go into details of these things — there are cases where healthy volunteers have died or have been harmed long-term from their participation in clinical trials. Fortunately, it is quite rare.

CC: The United States is the site for about three-quarters of all clinical trials worldwide. Many of the U.S. facilities for Phase I drug trials are located in the Midwest.

JF: In fact, in the Northeast, in places like Philadelphia, there was a closure of a lot of the Phase I clinics, with companies deciding to relocate to the Midwest in particular. What was striking about this was not just that there was money being funneled into it, but also that the scale of the Phase I units was changing pretty dramatically. Historically, academic medical centers may have twelve-bed, maybe eighteen-bed units where they can house participants. None of the newer facilities had fewer than 50 beds, but some had hundreds of beds. In fact, the one in Fargo, North Dakota, is a 540-bed facility that almost exclusively does research for the generics industry. Again, using healthy volunteers to help generics get on the market.

CC: In her study of clinical trials, Professor Fisher visited testing facilities. She interviewed the study participants and the research staff. And she engaged in standard sociological methods of observational study at these facilities.

JF: I wanted to have some distribution across the country, so I went to two in the Northeast, two in the Midwest, two in the Southwest, and I also had some variation in the kinds of organizations, so academic, pharmaceutical company, contract research organization, independent commercial sites.

CC: Now who are the participants who show up at these facilities? That turns out to be the surprising, yet troubling, finding from Professor Fisher's research.

JF: One of the things that I think is most surprising when thinking about Phase I healthy volunteers is that they are not students. I find that those of us who work in universities tend to think students are the primary participants in research studies. With the Phase I clinical trials, this just really isn't the case.

CC: Who are the volunteers, then?

JF: They are mostly male. There is a disproportionate number of minority participants. Most participants are between 20 and 45, and most cluster in the thirties and early forties. Most are lower-income, low educational attainment, and have an unstable employment history. Many have a history of incarceration, and many are immigrants, some of whom are not legally permitted to work in the U.S. Particularly for these last two groups, I think what is important is that the Phase I centers don't discriminate against people either because they have a record or because they don't have a work visa. So, it does create a really important economic opportunity for groups that do face employment discrimination in the normal, regular sectors of work.

CC: Professor Fisher discovered that the people participating in these most risky of clinical drug trials are disproportionately drawn from racial minorities and lower-income communities. And she found that the racial differences varied by region.

JF: On the East Coast, it was a disproportionate number of Black, mostly men, as I said, but Black individuals who were participating in clinical trials. One clinic, I would say it was about eighty percent Black and twenty percent everybody else. The second clinic was more—sixty-five or seventy percent Black. In the Midwest, there was one facility that was almost evenly split between Black and white healthy volunteers with maybe about fifty-five percent Black. The second clinic in the Midwest was overwhelmingly white. It was probably—I don't have these numbers in front of me, I should, but I think it was like seventy-five or eighty percent white. On the West Coast, it was mostly Hispanic participants or Latinx participants.

My argument in the book is that racial and economic inequalities in the U.S. create a market of healthy volunteers for Phase I trials.

CC: Drug safety trials, in other words, exploit inequality. The driving force of inequality came through to Fisher when interviewing volunteers. She starts with one example from her interviews:

JF: This is a quote from Lewis, a multiracial man in his late fifties. He said, “I wanted to make some money. It’s definitely not because I want to save the world. Let’s get that on the record right now. No, I don’t want to save the world. No. I need to make money.”

CC: The need to make money, of course, is felt differently across different economic classes in society. Race and class constitute overlapping social forces, or what Fisher refers to as “imbricated stigma.” These overlapping or imbricated social forces come to affect individual decisions to participate in FDA-required clinical trials.

JF: Imbrication typically refers to overlapping patterns dictating how tiles or shingles, bricks, are laid to create a surface that is stronger, more impenetrable, and more durable for its staggered structure. Thinking about that as an analogy or as a metaphor to use for stigma, I define imbricated stigma as the myriad combined stigmas that individuals face by virtue of how they look, the activities in which they engage, or the identities they inhabit.

When imbricated, the component stigmas retain their own social disadvantages for the individual but taken together, they also reveal the broader pattern of profound tenacious inequalities through which material resources are distributed unevenly throughout society. Individuals are subject to different patterns of imbrication based on their social address and life experiences. Some individuals are subject to numerous stigmas whereas others are relatively privileged being white or educated, maybe even if they are unemployed or poor. Thus, healthy volunteers as a group experience a range of stigmatized identities with some of the component imbricated parts being more intractable and others more malleable.

But importantly, the effects of imbricated stigma are not solely repressive. While individuals themselves might face greater obstacles when fettered with multiple stigmas, they are not necessarily captive to these imposed stigmatized identities. Indeed, the more deeply imbricated the stigma, the more emboldened individuals might become to attempt creative solutions to combat their social disadvantage. This is where Phase I trials enter into the scene.

Music: Joy Ike's "Home Stereo"

The decision to engage in another stigmatized activity, such as medical research, participating in clinical trials for money, could become an important way to deal with these other kinds of stigmas.

For example, a young Black man who is unemployed, never finished high school, and has a history of incarceration, experiences imbricated stigma in the sense that each of these types of stigma can operate singly or in combination as he navigates his world. Like imbricated materials, the imbricated stigmas he experiences are obdurate with race relations and economic opportunities highly resistant to change. In this context, the stigma of research participation can add one more form of judgment for him to face, perhaps from his family or friends, but a clinical trial can also relieve the stress of his other forms of stigma by providing an unparalleled economic opportunity that his history of incarceration, educational background, and skin color might routinely foreclose.

CC: The people who sign up for Phase I trials are disproportionately individuals who face multiple forms of stigma or have been marginalized in different ways. Drug trials offer them an opportunity to make money.

JF: As I look at people's narratives about how they use their money and why they use the money that they get from clinical trials in particular ways, I was struck at how they were oftentimes using the money they were getting from clinical trials to manage these stigmatized identities. Especially, I think, this comes into play when we're looking at differences between different types of participants. For instance, there is a different level of financial desperation that I was getting from participants who had a history of incarceration or were not permitted to work in the U.S. that I think came across.

CC: Professor Fisher illustrates by referring to a Native American man in his twenties named Manny.

JF: He found out about clinical trials from a flyer at his parole hearing. When he was trying to explain to me why he ended up participating, he said, “Well, where else am I going to get it?” meaning some income. “Car is broke down, what are we going to do? If I don’t pay my parole, I am going to go back to prison. That’s pretty much how I see it. It’s income. That’s for real and anything else is maybe helping out, you know, seeing what the medicine does, too.” For him it was really important just to be able to earn some kind of money to be able to manage not only being able to stay out of prison—he lived in a state where he did have to pay his parole fees—but also that it’s a situation where it was unclear how he was going to be able to get a job and quickly.

Music: Joy Ike’s “Home Stereo”

CC: Fisher asked another participant, a Latina woman in her twenties named Marisol, why she signed up. Fisher recounts Marisol’s answer:

JF: “Truthfully, hardship. The people that go to these clinics, very often—well, they are people who, how can I explain it? They are people that because of lack of work, we take part in many studies consecutively. And there are people who do not go to places like this because they have a stable job. Like years ago, when there was steady work like that, we would not even go near studies. They would offer them to us, and we would not go near them.”

Music: Joy Ike’s “Home Stereo”

CC: And there is a racial dimension as well to the repeat participation that Marisol refers to in her explanation.

JF: I think this is telling in the sense that these participants are not only talking about a catalyst to participating, but in at least Marisol’s case, that it becomes a thing that they do over and over again as something that they end up really counting on.

This, I think, was a striking difference to some of the white participants in the study who did see it as a temporary stopgap measure. For instance, Ted was somebody who had recently been laid

off from an IT job. He had found out about clinical trials through a friend, and both he and his wife decided to screen for a study to keep up with their mortgage. He had told me, “I suppose if I don’t find work right away, yeah, I’d be open to it.” Meaning, to participating in a subsequent clinical trial. “But I probably won’t do many of these because I’ll get working again and won’t have time.” I think what was interesting to me was that a lot of the white participants did have a very strong belief that unemployment was going to be temporary. That this was going to be a story they were going to be able to tell at dinner parties, and they were going to move on from it.

I think this is quite different than when we think about this kind of persistent precarity that many people of color experience. Wesley, a Black man in his thirties, illustrates this really well. He said, “I think I’ll keep doing them,” meaning studies, “until I get old. Until like I can’t do no more. I mean, I am going to always do studies, you know, because I know I can always count on the cash because sometimes you can get a big chunk of money and you can get out of your debt for a little bit of time, you know. But you’re going to always be in debt, you know, unless you hit the lottery because the bills keep coming back. As fast as you pay them, they come back.”

Music: Joy Ike’s “Home Stereo”

Of course, these are the kind of cases of participants who perhaps they would rather do other things than participate in studies, but nonetheless, they find themselves doing studies. There are also the participants who end up being the so-called professional guinea pigs, or they typically refer to themselves as ‘lab rats,’ who are choosing to do clinical trials full time. It’s sort of a way of life for them. When I was interviewing Bennett, a Black man in his twenties, he explained to me why he decided to choose this particular lifestyle. He said, “Probably the biggest gain I have ever had is that the money comes in a large lump sum. I have made more in a month than most people make in half a year. The longest study I ever did was like 36 days. It was like seventy-three hundred dollars. Never have I had that much money in my possession at one time. It’s not a lot of money, but it’s enough to really do something, you know. It’s enough to have somewhat of a free life, you know. I don’t consider this a career, but at the same time, busting my hump at McDonald’s for eight or nine dollars an hour and bringing home nine hundred to a thousand dollars in a month when I can make that in a week, just doesn’t seem feasible to me, you know. Like doing the lab rat thing, I have grown accustomed to a certain kind of lifestyle, having lump sums of money whenever I need it, you know, and being able to do whatever I want.”

This sounds maybe pretty good. It maybe sounds like Bennett has stumbled upon something that is definitely more rewarding than—and he literally had worked at McDonald’s prior to doing this. But it’s not so rosy. The more Bennett talked, he was able to articulate some serious downsides of being a professional lab rat. He said, “The thing that the lab rat thing lacks is

consistency. You know, if my rent is due and I get into a study and the study gets canceled, my rent gets canceled. If something happens, like my muscle enzymes are up or something is off and I don't get into the study, I'm screwed. It has its pros and it has its cons, and that's probably the biggest con for me is just that, you know, it's not guaranteed. Not only are you competing with yourself, your own body, you're competing with other people, you know."

Music: Joy Ike's "Home Stereo"

CC: The lack of consistency means that drug trials can't guarantee anyone a steady source of income. Even when people want to join in a study, that doesn't mean they'll be selected.

JF: One thing that is striking is that for a lot of these participants, the main risk that they focused on when I spoke to them was not the risk of the studies themselves, but the risk of not qualifying, the risk of not being able to get into a study when they really needed the money, and they were counting on this as a source of income. Bennett's narrative about this I think shows that. That not only is it not guaranteed because you have to qualify, your body has to be ready for it, but there are also other people that want to get into the studies and there are usually fewer spots available than there are individuals who want to do the studies.

CC: In the end, Fisher sees a drug safety regulatory system that is based on neutral, non-racial principles, specifically safety and efficacy. But the way these neutral principles are applied taps into and perpetuates racial inequalities.

JF: The regulatory system governing drug development has established this industry that requires healthy volunteers and needs healthy volunteers. Healthy volunteers are those who are incentivized by the financial compensation, and they have the time and the ability to be confined for long periods of time. It's not just, again, that you need to be somebody who is motivated by the money, you also need to have the time that allows you to be locked up in a research clinic potentially for days or weeks at a time. It's already shifting the segment of the population who might be eligible to smaller and smaller numbers of people.

To look at this, then, reveals that the U.S. context of social and economic inequalities funnels people of color into these clinical trials because they do not often have better options to earn

income, often are unemployed, and, therefore, do have the time to become this market of healthy volunteers for the pharmaceutical industry.

Music: Joy Ike's "Home Stereo"

CC: Where do we go from here? Is there a way to move to a better system? How might pharmaceutical companies and regulators develop a system that better respects the agency of drug trial participants and eliminates their exploitation? Professor Fisher shares her ideas.

JF: I do think we should pay people more. There's often concern that by paying them more, are you making it an offer that they really can't refuse. I think, in this context, the bigger concern is exploiting individuals and that we shouldn't be concerned about trying to artificially keep these stipends low.

But I think there is a larger question about the value of the science and how much are these clinical trials benefitting our knowledge about how safe drugs are. But nonetheless, I think that what's really at stake here is questioning whether or not this is a system that makes sense for the kinds of data and the kinds of science we want to have when we have new drugs coming into the market. I am not necessarily saying we need to entirely do away with healthy volunteer trials, but I think there is a much larger reliance on them than perhaps is in the interest of the public health.

Music: Joy Ike's "Walk"

CC: Thank you for listening to this episode of "Race and Regulation." We hope you have learned more about the racial dimensions of drug safety regulation and its implementation. This podcast has been adapted from a lecture delivered by Professor Jill Fisher in 2021. She spoke as part of the Penn Program on Regulation's lecture series on race and regulation, co-sponsored by the Office of Equity and Inclusion at the University of Pennsylvania Carey Law School.

I'm Cary Coglianese, the director of the Penn Program on Regulation. For more about our program and free public events, visit us at pennreg.org. You can also find other episodes in our "Race and Regulation" series wherever you get your podcasts. This podcast was produced by

Patty McMahon, with help from Andy Coopersmith, our program's managing director. Our music is by Philadelphia-based artist, Joy Ike.