INTERVIEWEE: Elizabeth DeLong
INTERVIEWER: Jessica Roseberry
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PLACE: Dr. DeLong's Office, Hock Plaza

DELONG INTERVIEW NO. 1

JESSICA ROSEBERRY: This is Jessica Roseberry. I'm here with Dr. Elizabeth DeLong. She is chair of the Department of Biostatistics and Bioinformatics here at Duke. It's October 21, 2010, and we're here in her office in Hock Plaza. And I want to thank you so much, Dr. DeLong, for agreeing to be interviewed, I really appreciate that.

ELIZABETH DELONG: Oh, I think this is a great opportunity.

ROSEBERRY: Great. Well, I wanted to ask you since you've worked at both Quintiles and the DCRI [Duke Clinical Research Institute], I wanted to ask you some similarities and differences between the CRO, the clinical research organization, and academic research organizations.

DELONG: Well, it's been a while since I was at Quintiles. I was there until the early nineties, I think, so we're talking about a long time ago. But my sense of the difference between an ARO and a CRO is that, number one, as a faculty member in an ARO there's a lot more flexibility in terms of what I choose to work on as director of biostatistics. At Quintiles I was primarily directing people who were working on projects that came to us, and I was finding people who could work on those projects. That's more similar to the job I have now as department chair. There are needs in the university, and I'm trying to match the needs with the appropriate people. But in terms of the flexibility and the academic nature of the work I would say the DCRI and the Duke school of medicine in

general takes a much—much more of a thought leadership role in what they do. There are usually clinical and statistical investigators who help shape a project, we don't just take it and work on it. But as I say, it's been a long time since I was at Quintiles, so I wouldn't want this to imply that they don't do that also.

ROSEBERRY: Okay. What are some of the—well, tell me some about some of those projects that maybe Duke and Biostatistics work on together.

DELONG: Well, actually our faculty are involved in a number of projects at the DCRI. We have altogether about forty-five or forty-six faculty members, seventeen of them are affiliated with the DCRI, and that's their primary work. Now, most of our faculty members have sort of the day job and the night job, which means that they do a lot of work on different projects that come into Duke. They might be a clinical trial studying difference in mortality among—between two drugs or it might be an observational study where they're looking to find predictors of mortality after surgery. So there's a wide range of the type of projects we work at, but our faculty also, as a function—as a byproduct of working on these projects, see statistical issues that come up that may not have obvious solutions. So there's a lot of methodology that also has to get developed, and we publish in statistical journals. We publish the methodology, so that's what I meant by the night job. They have—we try to guarantee them some protected time to work on these problems because it benefits not only them in their careers but the whole Duke profile to have methodologists who are solving problems, but it's difficult to get a lot of time to work on what we consider our own research.

ROSEBERRY: Is—

DELONG: But the DCRI is very supportive of that. Go ahead.

ROSEBERRY: Is the DCRI the main partner? Are there other partners?

DELONG: It's our biggest partner, but I guess I'd hesitate to call anybody a main partner. They have seventeen. The Cancer Center has fourteen faculty members who are in our department. Then we have—the Aging Center has two and the VA has three, and then there are individual faculty members spread out across the school of medicine.

ROSEBERRY: So why are biostatistics important in medical practice? What are they—to a lay person such as myself, what do I need to know about how that works?

DELONG: Okay. Well, you've touched on a translational component of biostatistics when you say medical practice. So for example a practicing physician, why would there have to be an appreciation for biostatistics? But we could go back to, Why is biostatistics important to medical research? And it's important because whenever you do medical research you're trying to make comparisons, and in order to make comparisons you've got to have—there's a lot of randomness, especially with individual patients. I mean, one patient to another there's a lot of variability. It's not like being in an industry where you're—the things you're studying are all alike. And as a matter of fact sometimes the basic scientists work on mice that are presumably all alike, so we have to convince them that there's still randomness and variability in what they do and to account for that randomness and variability we use statistics. So for example, you might put a number of people on—randomize a number of people to Drug A versus Drug B, and you want to know which one is better. Well, some of the folks on Drug B will do as well as some of the folks on Drug A, and some of them won't, and what are the chances that we would see that if there really was no difference between Drug A and Drug B? So that's where statistics comes in. It's really in making—making predictions that incorporate variability

or making comparisons that incorporate variability. And that's why there has to be an appreciation for statistics in medical research. Now, when you get to the medical practitioner, as these people get out from medical school they presumably are keeping up their skills but they're also reading the literature and they're developing their practice patterns based on what they're reading in the literature. Well, if the literature has been—if a manuscript has been produced that doesn't have adequate statistics, then they need to understand how much of that manuscript is reasonable, and they need to have some intuition as to what questions might underlie that manuscript that might not make the results quite so profound or believable. So I think statistics plays a role all the way across, from the nude mice that the basic scientists work with, the genetics that they work with, the human populations that are in clinical trials and observational research, and also the practicing physician, and then there's also how to disseminate practice into the community. You might have research that demonstrates that Drug A is better than Drug B, it demonstrates it to a high level of significance or what you might think of as reliability, everybody's convinced, but then getting it out into the community and getting people to use Drug A versus Drug B and to use it appropriately usually needs to be monitored and disseminated in a way that it happens. So sometimes we do studies in the community of trying to teach people how to use Drug A or the appropriate circumstances to use Drug A versus Drug B, and we do community trials, and we test whether these teaching mechanisms were effective, so statistics goes all the way through medical research.

ROSEBERRY: Do you think that people in those various places are receptive to the idea that statistics should and can play a vital role?

DELONG: Yes, to some extent. Of course, we're in an academic institution where there's a fair amount of recognition that statistics is important. Unfortunately, it's one of the very few professions I think that everybody can do. As a matter of fact, I was talking to a medical student the other day who wanted to do some statistics on her own. And I said, "I don't think you have the background to do that." And she said, "Well I know how to run SAS, do I really need to know statistics?" SAS is a package that people use to generate their statistics. So what we have are a lot of investigators who are relatively naïve to the necessary background and who do their own statistics, because you can go out on the Web and find power calculations or sample size estimates that you might need for your study. Everybody can be a statistician with no background at all. So we have to—we have to do a lot more education. We—one of our problems, and this is a relatively distressing problem, is that because anybody can do statistics and because there's a lot of pressure to publish—that's how you get promoted and recognized—when a statistician does an analysis and does the appropriate adjustments and whatever and doesn't find a result that the investigator really wanted to find, usually that investigator can get somebody who can (*laughing*) find it. So that's a real problem for us, because we are now sort of looked upon as police, and some people don't really want us interfering in their work because we might not find some of the things they want to find.

ROSEBERRY: How complicated or—is the process to do statistics well, do what needs to be done?

DELONG: Well, most—all of our faculty have PhD's in statistics, or biostatistics. That means taking at least two years of coursework, taking exams, doing a comprehensive exam. All programs have a comprehensive exam so that you know the theory underlying

all the statistics you're using, and then a dissertation that applies some of that theory and that's—those are the credentials. Now, we have master's statisticians who don't have that much training but who work with faculty statisticians until—we have, at the DCRI in particular, some master's statisticians who've been doing this so long that they almost function as faculty statisticians, but it takes a fair amount of background to do it correctly and to recognize all the potential pitfalls.

ROSEBERRY: Now, has—I know that DCRI does have a long history with using these—

DELONG: DCRI has been, I would say, one of the premier institutes in the US for recognizing the collaborative nature of research and for building teams that include medical investigators and statisticians, and they've been very successful doing that.

ROSEBERRY: And how—again, just as a lay person to help me understand, but how is it done? Are there—someone can go on the Web and find these programs that are fairly simple, but how is it done to someone who has a PhD? Is it through—are there programs that will—they will be able to utilize well? Is it computer work, is it—?

DELONG: Sometimes they have to write their own programs and their own simulations, depending on the project.

ROSEBERRY: Okay.

DELONG: There are packages that we all use, but you have to understand the underlying construct of the data and what the question is and what the best statistic is to answer the underlying question—for example the underlying question of drug A versus drug B in terms of mortality. You might do a survival analysis, and you need to account for patients who drop out along the way and patients who might cross over from one group to

another. So there are a lot of considerations that go into calculating the sample size you need for a study that you're going to mount. Now, the best way to do this is to have a team start working on it before the study starts and for the statistician to be involved and to say, Yes, we can do that; No, that won't work; et cetera. As I say, sometimes we're considered the police. (*laughter*)

ROSEBERRY: Well, do you also work with the Translational Medicine Institute as well?

DELONG: Sure, yes.

ROSEBERRY: Yeah?

DELONG: I mean, we're—as far as I know everything is pretty much in the DTMI, and we're spread out all over the place. We don't work as much with basic scientists as we do with the clinical studies, but it's moving in that direction.

ROSEBERRY: Okay. And I know that you were involved in the Outcomes Research and Assessment Group. Can you tell me a little bit about that?

DELONG: Sure. Outcomes research is one of those terms that—like bioinformatics, that doesn't have a uniform definition. Some people consider outcomes research as basically a counterpart to clinical trials. Clinical trials are randomized controlled experiments, outcomes research is more observational. So some people would definite it that way. Some people define observation—outcomes research as incorporating far more types of outcomes than clinical trials do. For example, clinical trials might be—have a primary endpoint of mortality whereas observational and outcomes research might be looking at quality of life and readmissions and a number of other issues that are harder to deal with. But I don't think either one of those definitions is exactly right. My view of outcomes

research is that it's observational analyses that incorporate a number of different outcomes, and it could just incorporate mortality just as a clinical trial does on observational data, or it could add to that data other things that are sometimes harder to collect, like quality of life. The new buzzword right now is *comparative effectiveness research,* and I see that as sort of a combination of taking—well, I should back up and say the proponents of outcomes research maintain that clinical trials are too rigid. They only include certain types of patients, for example. They usually exclude pregnant women, they exclude people over a certain age. They want to make sure they're capturing a pure population that will—could possibly benefit from the intervention, and they want to see an effect. So if they target the clinical trial to patients who are more likely to have an effect if the drug works, for example, then they have a more conclusive result but they narrow the population quite a bit. So the critics of—the observational people who are critics of clinical trials say that the inclusion criteria are much too strict and that they follow a very strict protocol. For example, the patient has to come in every two weeks to get blood work, et cetera, et cetera, et cetera, and there's a mechanism to make sure that happens. So it's not real-world experience but it's a rigid experiment that's controlled. On the other hand, clinical trialists will say observational data are riddled with all sorts of problems, selection bias. For example, if you have a new surgical procedure and you want to show that it's fine, you might—if you're not in a trial for it, you might recruit mostly younger, healthier patients for that new procedure, but younger, healthier patients are going to have a better outcome than the older, frail patients. So if the people on the new procedure do better than the other—the standard procedure, you can't really make a conclusion there, because you don't know if it's due

to the new procedure or it's due to those patients having a better prognosis to begin with. So in outcomes research we do a lot of what we call risk adjustment. We try to adjust for the age of the patient and the health of the patient, the comorbidities and whatever, so that we can make valid comparisons. But the trialists will still say, That's observational data, how do you know you've captured all of the bias that goes into selection for a certain treatment? So what comparative effectiveness research tries to do is to take the best of both worlds and try to, among all of the studies that are done in this area, try to figure out what is really the right answer. For example, the clinical trial that showed great results in optimal patients under optimal care has to be—has to be only considered for those optimal patients, and the protocol has to be followed exactly, because when you get out into the community if patients aren't being followed the way they were in the trial, they're not going to do well, that sort of thing. So it's a wide—wild field.

ROSEBERRY: Do you feel comfortable that you're able to kind of walk those lines and be able to—?

DELONG: Well, that's part of our training. We have to try to eliminate bias and to try to keep investigators—. It's very difficult for the investigators. I mean, they're invested in certain things. And that's another thing. Trials are done on the basis of equipoise. Equipoise means that you don't really feel that one option is better than the other. You want to know the right answer. If you don't have equipoise going into a study, for example the physician recruiting patients, it's possible that if a physician feels that this patient wouldn't do well on drug B and I've got to randomize this patient to drug A or drug B, maybe I won't recruit this patient into the trial. So it's important to maintain equipoise. And some studies have failed because they can't get enough recruitment

because physicians just don't want to put people in these trials. So I don't know how I got off on that, do you remember?

ROSEBERRY: I had asked you—you were talking about the outcome versus the trialists and talking about kind of balancing those two perspectives, and I had asked if you felt comfortable in being able to balance those two perspectives.

DELONG: Okay, so I think the equipoise has to come in when we're doing clinical trials. Now, when you're doing observational studies, it's very difficult to maintain equipoise because you have certain suspicions and you're just working with data that usually aren't prospectively collected, but even if they are, they're for a certain purpose, to demonstrate a certain effect or something. It's very difficult to go at any of this with equipoise. And then we have the issue of clinical judgment. For example, one of the—one of the paradoxical findings in a lot of observational data is that high cholesterol is beneficial, and there are a lot of—there's a lot of clinical and logistical background to that. It used to be that these kinds of findings would show up in administrative data, and administrative data are data that are collected for billing purposes so they don't have a lot of detail. And we used to think, Well, it's because they're only limited to a few diagnoses and if somebody has high cholesterol chances are there wasn't enough—they didn't have enough other comorbidities that trump high cholesterol so high cholesterol got coded and therefore it came out as beneficial, mostly it was marking that the patient was relatively healthy. But that finding is still there; we're still finding high cholesterol to be—and it depend—a lot depends on how the question is asked when it's filled in, because it could mean does this patient have a history of hypercholesterolemia, which means the patient is being treated and therefore is doing better. So there are a lot of

clinical intuition and coding rules that come into play in the background here. So once you get the clinicians involved they could say, This doesn't make any sense. There's no rationale for that, so why are we finding this result? And usually if we find something like that it's—(*laughs*) it's difficult to say whether—I guess the worst situation is when we have something that plays a big role but we can't explain it, but it eliminates the effect we were looking at—looking for, so if we leave it in what we call our model we don't have any evidence that our effect is there, but if we take it out and it doesn't make clinical sense to be in there, our effect is there. That's where we really have trouble reconciling.

ROSEBERRY: It sounds like there are so many variables to consider.

DELONG: Yes. Yes. And we talk about unmeasured confounders—those are the things that mess us up and possibly account for selection bias, but we don't know what they are. For example, I think experienced clinicians can take a look at you and decide whether you're healthy enough to undergo this or not, whereas all of your data might not demonstrate exactly that picture. So I think there's a subjective component to data that we collect—well, that we don't collect.

ROSEBERRY: So is—would the subjective data—would the data be more accurate than the subjective data?

DELONG: Well, actually years ago some people at Duke did a study where they asked clinicians—I mean, this is a very narrow study—I think they asked clinicians for—to write down for each patient they saw their estimated survival after surgery or something like that—what's the probability this patient will survive, and then they used a statistical model to estimate that probability. And they found that the statistical model was more

valid than the physician's suspicions, although that's a very narrow study, and it's only linked to one particular outcome. I'm not sure you could say that in general.

ROSEBERRY: Well, I wanted to—I was looking at your website, and I noticed a statement on it, and I wanted to read it to you and kind of see—get some feedback on it. It says, "Both risk factor assessment and the prediction of response to treatment rely on statistical and computational models to provide estimates as to who will likely get certain diseases and which treatments will be effective when they do." And I wonder if you could kind of elaborate that—on that?

DELONG: Okay. That's sort of what we've been talking about, that the risk factors are comorbidity and family history, things like that, and what we do is we build models, statistical models, that will predict, for example, what—whether a patient will benefit from a treatment. Usually we're predicting whether the patient will survive surgery or will get a certain disease. Lately they've been predicting and trying to use genetic information to predict who will benefit from one treatment versus another. Some people just don't respond to certain treatments, even though clinical trials may have demonstrated that those treatments are beneficial in the population they studied. And this gets us to the realm of personalized medicine. I think most people acknowledge that even though a clinical trial might have a positive result, it doesn't mean that everybody will benefit the same way from the treatment that was supposedly better. And we're now moving beyond, Is this treatment better than this treatment? to, Who is this treatment better for? Is there a genetic component there? Is there a lifestyle component? Who are the people who actually will respond positively to this treatment? So I think that's what our website meant.

ROSEBERRY: So personalized medicine is aimed at kind of a group of people that look alike or somewhat alike?

DELONG: Yeah, you have to have groups of people that are sort of alike in order to be able to make those conclusions. I mean, you have to have a lot of data.

ROSEBERRY: Yeah. (*laughs*)

DELONG: Some investigators don't like to hear that. (*laughs*)

ROSEBERRY: Do you find these predictions to be accurate and—I mean, have they—have they followed through? Have they—?

DELONG: In some cases. I wouldn't say all cases, but some cases, certainly. Yeah, I think there's a lot of promise out there. It's a combination of the appropriate methods and the right data and the right attitude, making sure that everything is clean. There's a—it's so easy to overlook something when you're doing a very complicated analysis and to plow on and then realize there was a problem, and then you go back and you fix something but then something else breaks and—(*laughs*) after you've built this enormous machinery it really—it needs a lot of testing; for example when we do our programming and trying to create these data analysis models. There's a lot that goes into it, and every step of the way needs to be carefully done so that when you get to the end result, you have confidence. So I think there are a lot of—there's a lot of effort now by statisticians in particular to make sure that the process is well documented and the data are well documented so that the results can be replicated by others.

ROSEBERRY: We talked about the informatics piece, the bioinformatics. How does that fit in?

DELONG: That's exactly where that fits in—

ROSEBERRY: Okay.

DELONG: —because we need—the bioinformatics piece, as I said at the beginning, it's very difficult to define bioinformatics. And some people actually include medical informatics in bioinformatics, medical informatics being—well, the way I look at it is it's the data that are collected in the process of patient care. And medical informaticists design systems that talk to each other and that I think used to concentrate on the patient so that any doctor can look at the patient and have all the information they need going backward on that patient. For example, a patient who comes into Ophthalmology might have been seeing somebody else for high blood pressure and is on high blood pressure meds and coordination of services for the individual patient. We're moving beyond that in medical informatics to trying to create systems so that we can learn from our patients, we can have groups of patients that are alike and see how they perform. That's what I consider medical informatics. Bioinformatics has two more bins, one of which sort of connects to the medical informatics in terms of the data that are gathered and tries to organize that data in a way that can be used by statisticians. And the organization of some of the complex data that are collected—for example, imaging and genetics and genomics and proteomics and metabolomics, that's huge. So there's a lot of structure that needs—and standardization that are needed for that component. And then there's another bin for bioinformatics that I see, which is actually an alternative approach to statistics, where models are being built, but they're being built differently. They emphasize more computational aspect rather than accounting for variability and they—they're more connected to the underlying biology. So bioinformatics is sort of an amalgam of computational methods along with biology background, and I think a lot of

people in bioinformatics either come to it with a computer background or a biology background or biochemistry, so—whereas statisticians usually are introduced to the biology and biochemistry but are more concentrating on adjusting for variability.

ROSEBERRY: Okay. Well—so we had talked a little bit earlier about kind of how these things fit in with the larger picture and maybe that you were—the department was seen as a little bit of the police. Do you feel like there are places where you can fit in that maybe need your services, that need the department services that could use it that maybe don't use those services?

DELONG: Yeah. We have a lot of education to do. I think part of the education, unfortunately, comes from external sources. For example, grant review committees are—there are statisticians on grant review committees, and they're looking at the statistical methods and the statistical write-up on grants. So people who are submitting clinical grants at least recognize that they need to be working with a statistician. Some manuscripts, some journals, require statistical review. And those journals, the people who submit to those journals, recognize the need for statistics. But there are a lot of areas where the grant review and the manuscript review doesn't really emphasize much in the line of statistics. And so it's our job to educate these people, that even though their grant reviews and their manuscript reviews are overlooking statistics, we could help them do a better job and possibly get funded or get manuscripts published. So it's a matter of our being able to persuade them that we can help them.

ROSEBERRY: Are you in a small number of collaborations at Duke or a large number?

DELONG: We're in a large number, mostly clinical departments. And there's a growing need. I mean, I hear it every day, people are saying, I need more statistical help. There's

a growing recognition and a growing need, and I'm just scared to death about keeping up, (*laughs*) because we're going to have to start hiring.

ROSEBERRY: I see. So you have an opportunity there for lots of growth, maybe.

DELONG: Oh, yes. Yeah.

ROSEBERRY: Well, have I kind of gotten a—?

DELONG: Yeah, you've done a—

ROSEBERRY: —a bird's eye view of what you do?

DELONG: Yeah, you've done a great job of asking questions. You seem to have understood most of—.

ROSEBERRY: Good. (*laughs*) So let me shift directions if that's all right, if we've got a good picture, but I wanted to ask about being a female department chair and if that has felt—if it's felt any different or kind of unusual to be a woman in science or medicine or mathematics, or if that has not really been—?

DELONG: You know, that's never been an issue for me. I'm not—I can certainly identify with the difficulties some people have had. I'm not sure why I've never had any. I grew up in a small town in Maine. My father was an immigrant. He came here at age fourteen and got put in the first grade, and I don't think he finished high school. He was a farmer, and we lived in this small town, and it was a small mill town. and I was one of the brightest kids in the town, and people were just very, very supportive and proud of anything I did. And I don't think anybody considered that I was a female rather than a male. I was just brought up to do the best I could, to work hard, and I've just never encountered any what I consider discrimination, and especially not at Duke.

ROSEBERRY: That's wonderful.

DELONG: Yeah. I've been very fortunate.

ROSEBERRY: Good. Have there been any mentors, male or female, that you would like to talk about in your development and in your career path?

DELONG: Um, well, my first mentor was probably my thesis advisor who's a wonderful person, and he was just—he's this Indian statistician who is just very, very welcoming to anybody. He helps everybody. And I guess maybe in terms of the mentoring I—he helped me figure out how to do my thesis, but he also helped me see that it's a good idea to help (*laughs*) people. I mean, he was just so magnanimous with his time. He's really an excellent guy. Since I've been at Duke I would say that I've had a number of mentors or role models I guess who have been both men and women who I look at as performing at a high level but being honest and good people, and I hope I've learned from them.

ROSEBERRY: Well, can you tell me about Dean Andrews's leadership style?

DELONG: You know, that is one thing I was thinking about. I don't think men and women are interchangeable. I think they have different skills and different intuitions maybe. And Nancy's wonderful. I mean, I never—we were discussing this at lunch the other day with some of the other chairs, that you send Nancy an e-mail, and she answers it within a day, and she listens, she understands. But she's not soft. She's firm in what—how she thinks things should go forward, and she's not afraid to—I don't think she could be manipulated. I think she's very strong but nurturing and gentle or something like that. I don't know how to describe it, but she's terrific.

ROSEBERRY: Do you think you bring different things as a female department chair to the table?

DELONG: Um-hm, yeah. I think—I actually think that sometimes you need a male and sometimes you need a female. I think at this point in our faculty's development we need—and you know, this is a generalization. I think probably there are males who would take this role and do a better job, but I think that being a female I have more—I can identify with people's angst or psychological needs possibly more than I think a male might. So I think that our department really needed to pull together, we need to work as a team, and I'm hoping that I'm doing some of what I need to be doing to have that happen. I think a male in this position might be a little less intuitive but maybe a little more ambitious and might work out just as well, but I think it would be a different approach.

ROSEBERRY: What are some directions that you see for the future of the department?

DELONG: Well, we have a master's program that's been approved. I certainly want to see that develop into a PhD program, and I think we have—we have great faculty here who I think are underrecognized, and I think as we get a PhD program up and running it will help the stature of the department. Another avenue that I really want to see develop is that we feel like a department. We've been—we have people scattered all over the university but we've got a hub here of seventeen faculty members, and I want people to feel as though they have a departmental home. Another thing is that I think our younger faculty are now starting to think in terms of submitting more grants, all of our faculty I think are, and I think our department has—I guess I'm thinking that for some reason our—many of our faculty haven't been encouraged or motivated to be the leaders that they could, to be independent investigators, and I think we have some work to do there.

ROSEBERRY: How will that—what would that take to happen?

DELONG: Well, part of the problem is that they get so consumed with everybody else's work, so we're trying to figure out mechanisms to protect their time, and we've had a fair amount of support for that. The DCRI's been very supportive, as I said earlier. Another thing we're doing is we're going to develop sort of a support group that's going to meet regularly and talk about issues that they want to investigate, statistical issues that might lead to a grant proposal or a manuscript so that we can all help each other get these things out the door.

ROSEBERRY: Well, what have I not asked you today that I should have asked you, or anything you'd like to cover or add?

DELONG: I think you've been pretty thorough. I can't think of anything right now.

ROSEBERRY: Okay. Well, I thank you very much, Dr. DeLong.

DELONG: You're very welcome.

ROSEBERRY: I appreciate it.

(*end of interview*)