ORAL HISTORY INTERVIEW WITH ROBERT CALIFF
Duke University Libraries and Archives
Submitted November 12, 2019
Researcher: Josephine McRobbie

COLLECTION SUMMARY
This collection features an oral history I conducted with Robert Califf on October 18, 2019, several weeks before Dr. Califf left Duke for a position at Google parent company Alphabet, serving as head of strategy and policy for Google Health and Verily Life Sciences. The 110-minute interview was conducted in Dr. Califf's office at the Davison Building at Duke School of Medicine. Our conversation explored Dr. Califf's upbringing in South Carolina, his formation as a cardiologist, his work as a clinician, researcher, and administrator at Duke, and his 2016-2017 tenure as Commissioner of the Food and Drug Administration. The themes of these interviews include advances in cardiology, developments in clinical trial research, and leadership and mentorship.

This document contains the following:
- Short biography of Dr. Califf (pg. 2)
- Timecoded topic logs of the interview recordings (pgs. 3-4)
- Transcripts of the interview (pgs. 5-32)

The materials I am submitting also include the following separate files:
- Audio files of the interview
- Scan of a signed consent form

*I recorded the interviews as a two-track recording, with one voice in the left and the other in the right. For production purposes, I recommend approaching each channel of this stereo recording as a single mono track.

BIOGRAPHY

Prior to his November 2019 hire at Alphabet, Robert Califf, MD MACC, spent the majority of his career at Duke University. Most recently, he was Vice Chancellor for Health Data Science; Donald F. Fortin, MD Professor of Cardiology; and Director, Duke Forge. Under the Obama administration, he served as Deputy Commissioner for Medical Products and Tobacco at the Food and Drug Administration (FDA) from 2015-2016, and was Commissioner of Food and Drugs from 2016-2017.

Califf was born in Anderson, South Carolina, and spent his early years in Clemson, South Carolina. After moving to Columbia, South Carolina, as a young boy, Califf went on to be captain of the 1969 AAAA South Carolina Championship basketball team. After attending Duke University to study psychology, Califf switched his focus to medicine, enrolling for a Doctor of Medicine at Duke University School of Medicine. In the year before beginning medical school, Califf worked as an orderly at a hospital in Greensboro, an experience he calls “amazing.” He assisted patients with basic care, noting “These kind of things still play out today, in terms of the gaps we have in healthcare, which are less related to use of high-end technology and much, much more related to very fundamental things that people need that, they're having trouble getting.”

Califf went on to complete his residency in internal medicine at University of California-San Francisco and a fellowship at Duke in cardiology. His early faculty appointments at Duke corresponded with his time as Director of the Cardiac Care Unit. Califf is a prolific researcher in the areas of improving health outcomes, cardiovascular medicine, quality of care, and the clinical research enterprise. Califf is also pioneer of clinical trial research methods, and solidified infrastructure for clinical trials at Duke by founding the Duke Clinical Research Institute. From mentors like Dr. Eugene Stead, Califf learned the value of critique and intellectual exchange in medicine, and this served him in later administrative appointments at Duke. “Sometimes it can get emotional and tough,” he said. “But if you don't have differences of opinion, first of all, there's no reason to have a meeting. And if you do have differences, you ought to really express them.”

INTERVIEW TOPIC LOGS

Interview (October 18, 2019)
File: CaliffInterview.WAV

00:00 Introduction
00:24 Upbringing; family focus on education
01:29 Father's WW2 experience, family settling in South Carolina
04:04 Early personality and interests
06:46 Experiences with classmate Lee Atwater
08:54 Summer jobs in college
09:32 Family experiences with Baptist and Methodist Churches
10:50 Playing high school basketball during integration in South Carolina
13:24 Draft numbers and college enrollment
14:36 Choosing to enroll at Duke
15:34 Majoring in psychology at Duke
15:59 Work release program in state prisons and switch to medicine
17:50 Peers in prison
19:11 Inclination towards medicine fields
19:36 Enrolling at Duke for medical school and marriage
20:15 Experience as an orderly
23:04 Taking medical prerequisites summer after senior year
24:01 Duke's curriculum and memories of New Orleans' Charity Hospital
26:33 Clinical research on Holter monitors; mentorship by Dr. Galen Wagner
31:25 First experience of seeing defibrillation
32:53 UCSF residency; mentorship by Dr. Eugene Stead
36:20 Short-tracking of residency
37:00 Early experiences with computers in medical research; early conference presentations; left ventricular ejection fraction research
42:47 First faculty position and Coronary Care Unit; treating heart attacks effectively; importance of interactions with patients as part of research method
47:55 Memory of 8th grade presentation and development of personal confidence
50:53 Importance of critique by colleagues; FDA Commissioner nomination process
54:39 Early experiences with FDA under George H.W. Bush and George W. Bush administrations; Peggy Hamburg recruitment of Califf for Deputy Commissioner for Medical Products and Tobacco
57:21 Serving as civil servant in Deputy role
58:46 Working with tobacco-related policy as cardiologist; impact of Sir Richard Doll smoking study
1:01:31 Nomination process for FDA Commissioner
1:04:29 Experiences interacting with President Barack Obama and administration
1:07:17 Interactions with Senator Bernie Sanders
1:07:55 Technology regulation during Obama administration
1:09:10 Food safety issues; Serepta case
1:15:37 Opioid epidemic and the FDA; experiences with Senators Joe Manchin, Ed Markey, and

Angus King
1:16:34 Navigating opioid abuse policy
1:19:42 Listening tours; later experiences researching prescription drug abuse in Durham, NC
1:23:06 2016 election and transition out of FDA role
1:25:44 Leaving Washington, DC, on January 20th, 2017
1:27:11 Experiences in administration at Duke; work with Wanda Bride and Mary Ann Peter related to CCU; helicopter program; Genentech and clinical trials; developing Duke Clinical Research Institute
1:33:18 TAMI-1 multi-center trial; congressional investigation and experiences with Congressman John Dingell
1:36:58 Approach to ethics in clinical trial research; experiences with Senator Elizabeth Warren
1:41:12 Establishment of clinicaltrials.gov and industry versus academy approaches to data science and clinical research
1:43:00 Experiences with President Obama and Vice President Joe Biden; bonds with colleagues from FDA tenure; Duke leadership over the years
1:48:07 Relationship with Dr. Stead; bonds with Jim Wyngaarden and Holly Smith

TRANSCRIPTION
DATE: October 18, 2019
LOCATION: Robert Califf's office, Davison Building, Duke School of Medicine
CITY, STATE: Durham, North Carolina
AUDIO FILE: CaliffInterview.wav

Josephine McRobbie 00:00
Alright, so we are recording and this is Josephine McRobbie and it is the 18th of October 2019. I am at the Duke University Medical Center, Davison Building and I'm speaking today with Dr. Robert Califf. Dr. Califf, thank you for taking the time to speak with me today about your life and career.

Dr. Robert Califf 00:22
Good to be here.

JM 00:24
Great. So I thought we would start with where you were born, and what your upbringing was like. So I understand that though your your mother was a teacher and your father was an architect, you and some of your siblings have ended up in the medical field.

RC 00:40
That's right. I have a brother who's an orthopedic surgeon and my sister does computer programming for medical centers and operating rooms.

JM 00:50
Okay. And so where do you think that interest came from?

RC 00:54
Well, medicine is such a big part of all that goes on. And our parents were, I guess you'd say, very focused on education. And as you sort of got educated about what was going on, what was interesting and important, medicine rose to the front. I can't say that they were particularly focused on our going into medicine, though, as opposed to maybe some parents who want their kids to be doctors. That was definitely not the case with us.

JM 01:29
So you were born in South Carolina? Where abouts?

RC 01:32
Yeah, my dad was at Clemson and his class was picked up in 1944 and sent en masse over to Belgium for the Battle of the Bulge. At the time they were told the war was over, the Germans are ready to surrender, and they just needed to show up and everything would be fine. And literally within 24 hours, at the time that they got there, they heard all the noise on the other side of the line of tanks. They were told not to worry about it. Then the next day they woke up on the wrong side of enemy lines. And so literally his whole class had been picked up, was put in an impossible situation. He spent a few days behind enemy lines, and then was recaptured by

Americans, thankfully, but a lot of his classmates didn't have such a good fate. So when the war ended, he went back to school at Clemson and had just graduated when my parents got married and started a family. And he was working in teaching there, at Clemson, at the time. So I was born in Anderson, South Carolina. There was no hospital in Clemson.

JM 02:54
Okay. And what was your upbringing like?

RC 02:57
It was a wonderful upbringing, in many ways, I mean, the first five years we lived in Clemson. I'm, uh, like it or not, I'm just still a diehard Clemson football fan because as a little kid, we would sit in the end zone at Death Valley, which was a remarkable place and, you know, just tremendous fan support there. And our parents, as I said, were very focused on education, very politically interested. So there were always a lot of political discussions going on in the family. And then my dad decided to go into the private practice of architecture and move down to Columbia, which is the state capital in South Carolina, and just had a great time in a typical suburban neighborhood. We lived right behind the elementary school and could walk to high school, played a lot of sports. It was a good time. A lot of friends.

JM 04:04
And what kind of kid were you?

RC 04:09
I was a relatively shy kid who.. I sort of gravitated between playing sports, watching and listening to sports, and reading a lot. My mom was a musician, in a way, she and a lot of the family members that played music, so I was forced to play the piano, which I couldn't stand. I could actually hear the basketball bouncing in the court behind my music teacher's house. And ended up playing high school basketball, and was captain of a state championship team in 1969. And that forged, some very deep friendships and bonding, like goes on in sports. But it was also a very tumultuous time. The South was being integrated. I started out in all white schools, and our basketball team was sort of the tip of the spear in South Carolina for integration because it was mostly the athletes that came across the lines to start with, and, and we had a super team that was mixed race at the time. And I'm still convinced one reason we won the state championship was the summer before, we went around the state playing the all black teams, because we still had two sets of high schools at the time. But it was it was intense because all these changes were occurring. And of course, 1969 was the peak of the Vietnam War. So, the Kennedys had been assassinated. Martin Luther King had been assassinated. And friends and family were going off to a war that a lot of people didn't believe in. So, we had quite a bonding of our high school class.

Another notable thing about the high school is one of my classmates was Lee Atwater, who is well known posthumously for being the architect of the Southern strategy of the Republican Party. And I spent a lot of time with Lee, we were sort of frenemies, I guess you would say, we had very different views of the world. But he really put together the way of thinking, which is still playing out today in the Trump administration.

JM 06:46
So what was your impression of him at the time?

RC 06:49
Well, in junior high and high school, he was the life of the party. He literally spent Saturday nights at Township Auditorium in Columbia, which is where all star wrestling takes place. And his goal growing up, we would talk about it on Sunday nights because we were in the same church youth group, his goal was to be a promoter of all star wrestling, you know, the fella with the microphone that introduces the wrestlers and manages the wrestlers. And then his, uh, he was not a great student, but a lot of fun to be around. And then his freshman year, he went to Newberry, I came to Duke, and we spent the whole summer after that together working in a gravel quarry that a friend's dad owned. We were painting the tressles that the trains go under that the [inaudible] when the gravel was dumped into the tressle, and then it goes down into the train cars. And over that freshman year at Newberry Lee had been to a barnstorming speech by Strom Thurmond, and they just immediately hit it off. And Lee literally told me that summer that managing politicians was the same as managing wrestlers, just can make a lot more money, and have a lot bigger impact. He had read The Art of War, and really that was his sort of sacred... I mean, a lot of people talk about it now, but it was scoping out the weaknesses of your enemies. So you know, like all people Lee was complicated, he had many good things about him, but maybe sort of like J.B. Duke he also, at least in my view, promoted a philosophy which has caused a lot of destructive things to happen.

JM 08:48
And you said that you worked together at a gravel pourery?

RB 08:52
Quarry.

JM 08:54
Quarry! Oh, okay, great. So it sounds like you had a work ethic from when you were a teen, is that correct?

RC 08:59
Well, we weren't wealthy, being an architect is, for most architects is, you don't make a huge amount of money. But we lived comfortably but my parents always encouraged that I work, which I did. I worked in a grocery store, I delivered eggs door-to-door, worked in a lumber yard. And this was just a summer's work, after freshman year of college. Yeah, so the work ethic was definitely part of it.

JM 09:32
And you said that your mother played music? Was she a music teacher?

RC 09:36

No, really she had grown up, her dad was a Baptist minister. So she had grown up in the church, and played the piano, and like to sing, for better or worse. And so, she just thought it was the right thing to do, that children should learn music. I just wasn't very good at it.

JM 10:00
Did you grew up in the Baptist Church as well?

RC 10:03
No, we ended up growing up in the Methodist Church. It was a definite significant part of life. My dad designed the church that we grew up in. And in the latter part of his career, he mostly designed churches, and did historical reconstruction of plantations, which was a fascinating thing to watch. He would scope out what had happened at the plantation, do the reconstruction part of it, and then write the history of the people who had been involved on, all sides of the equation. He was really, at heart, a history buff and loved historical architecture.

JM 10:50
And and you mentioned that, did you say the basketball team became integrated while you were playing?

RC 10:59
Right.

JM 11:00
So that was which year of your high school years?

RC 11:02
That would have been about sophomore year, 1967 is when all this happened. Some members of our class were featured in Time Magazine at the time because of all the tension that was in play. It really wasn't an issue in basketball. It was all about the team jelling to win but, there's much history wrapped up and concentrated in that short period of time. You know, one of the most revealing things to me about remembering the moments, I spent a decade doing interviews of famous cardiologists. Just about the person, what had motivated them, much like you're doing.

JM 11:53
Oh, amazing.

RC 11:56
And there's a gentleman named Clyde Yancy, who's a very prominent heart failure specialist who is the Chief of Cardiology at Northwestern. And he had grown up in Louisiana, on the other side of the tracks. And he had been the one coming across at the time of integration at exactly the same time, also played sports. So we had an amazing, to me it was an amazing discussion, of what it was like to be on one side or the other. If I remember correctly, he told me that he was the first student at LSU to take the chemistry class as an African American, which, you know, hard to imagine what that was like, on the other side.

JM 12:40
And so you felt that on the team itself, that it wasn't an issue, or it was more about the forces surrounding that. So what were some of your experiences like?

RC 12:53
Well, the most vivid experience I have related to integration was, when I was younger I used to play basketball at the YMCA in downtown Columbia. And I would just take the bus down there. And I remember when I was about 10. It was a typical day, I just jumped on the bus, and ran to the back, and sat down. And the bus driver stopped and said "You don't sit back there." So, quite an experience.

JM 13:24
So, you're in high school, what do you think you're going to do with your life? What were your hopes, or thoughts, at that point?

RC 13:30
I had no idea. It was such a tumultuous time. In that year, we had the draft coming up. And it was early in the freshman year, as I remember, the draft numbers came out. Mine was a high number, it was over 300, which meant I wasn't going to be drafted. But that was just the luck of the draw that determined the fate of so many people. It was also a crazy time at Duke, because a lot of classes just didn't occur, because there was so much turmoil and upset on campus about the Vietnam War, and all the things that were related to it. 1968, the year before Brenda Armstrong and her collaborators had occupied the Allen Building, which was a very momentous time in the history of Duke. And you know, that there were things like that just happening, as a routine.

JM 14:36
So what inspired you to apply to apply to Duke, and did you know what you wanted to study at that time?

RC 14:43
I really didn't know. My older brother had matriculated to Duke two years before. So it seemed like a reasonable thing to do. And my parents were happy that we were going to a, you know, a prestigious school that wasn't so easy to get into. And tuition at that time I think was like 2000 bucks. Which was a lot in 1969, but obviously pales in comparison to what students are paying today. But I didn't know what I wanted to do. I majored in Psychology and spent the first three years sort of just learning, and being a little bit confused about the future. Which I don't think it's a bad thing when you're a student.

JM 15:34
And so what drew you to psychology at the time?

RC 15:38
I was fascinated by what made people tick. And we had some great professors at the time, who were really good at making you think about what you were doing. Very formative teachers, at the time.

JM 15:59
And then at some point you made the decision to go to medical school. How did that unfold?

RC 16:05
Yeah, that one was pretty clear. I ended up working in the work release program in the state prisons in South Carolina after sophomore and junior years, and that cured me of wanting to be a clinical psychologist. I felt like it was just too... for me it was too ambiguous, and hard to tell when you were helping people, and making progress. Seeing the complexity of that. So, medicine seemed like a good option. You know, I don't know if it still happens, but at the time kids like me were subjected to multiple tests that were designed to tell you what your profession should be. And I don't remember all the details, but mine kept saying "medicine", and I wanted to be a psychologist. So, I finally gave in when I realized that being a psychologist was not what I wanted to do. But yeah, it was it was actually quite an experience in the work release program, because more than a couple of the inmates had been basketball competitors, on schools that I played against. So we put together a prison team, which was a darn good team. Went around playing during the summers. But, it was another lesson in how complicated people's lives are. And very sad to see how things ended up for some people.

JM 17:50
So there were some people who were your peers, or at least you knew them from playing against them.

RC 17:55
Yeah.

JM 17:57
What was that experience like, interacting with those with those former colleagues?

RC 18:03
Well, when you're in a state prison system, particularly back then, it felt like when you were at work, your main goal was just to survive, and make it through the day. I mean, it was a relatively forward program, because here you had people that were serving prison sentences, and they lived in what was like a barracks, and then they would go to work during the day, and report in, spend the night in prisons. But they did all the things that you would expect, like sneaking out at night, and I even had my wallet picked when I was coaching the basketball team by my own players on the team. So it was a good lesson in the complexity of life.

JM 18:58
So you had that experience. You were also taking these tests somewhere along the way that said that you might be inclined to work in medicine. Do you know what it would have been, that you would have been writing down, that would have said that?

RC 19:11

I really don't know. It's a good question. You know, it's most likely I just like to try to solve problems. And I might have thought that an engineer might have been a better pick. But I have no idea how those things were done back then.

JM 19:36
And I read that you were planning to go to Tulane, and decided somewhat last minute to go to Duke instead for medical school.

RC 19:46
Yeah, I had a great experience at Duke, but it was also, it was a complicated time because of all the tumultuous nature of things. And I really never expected to come back to Duke after I left. Right after graduation, I married my high school sweetheart. We're still married 46 years later.

JM 20:14
What's her name?

RC 20:15
Lydia. And she was in the last year of nursing school at Greensboro. And, you know, interestingly, she had started at UNC Greensboro, and then decided to transfer, and had been accepted at Duke [sound of Code Blue alarm in building]. But the costs were just too high for our family to pay. Another lesson there. But I worked as an orderly in one of the local hospitals in Greensboro for a year, while she finished nursing school. That was an amazing experience. And years later I had a mentor named Eugene Stead who was one of the grand old mentors of Duke Medicine. And Dr. Stead was famous for starting the PA program and was really one of the amazing leaders of American medicine. One of his beliefs, that he espoused greatly in his last several decades, is that everyone that goes into medicine should started out working as an orderly. Rather than starting out at a high faluting academic institution, and work their way up, and then differentiate from there. And I have to say, there's a lot to it, because you learn a lot about people by emptying their bedpans, and putting in Foley catheters, and doing all the things that have to be done for people to get through the day when they're sick.

JM 21:50
Yes, talk more about that. What did you get out of that personally?

RC 21:56
I learned a lot about people's basic needs and the importance of taking care of them. I learned a lot about teamwork. If you want to see a team, things have changed a lot since then, but at that time you basically had doctors and nurses and orderlies. And the orderlies just that everything that needed to be done, that the doctors and nurses didn't do. And so there was a squad led by a fellow we called Big Al. And we would get deployed to take care of things that people needed throughout the day. And it was meaningful work at a different level, that most doctors I think had just no understanding of. And these kind of things still play out today, in terms of the gaps we have in healthcare, which are less related to use of high-end technology and much, much more related to very fundamental things that people need that, they're having trouble getting.

JM 23:04
A sort of user-centered approach. maybe. So you spent a year doing that, before going to medical school?

RC 23:14
Right. Because I decided late to go, so I had to take all my science classes in the senior year. And including another unforgettable experience that relates to this continuum of politics that I've always been a little bit involved in. The summer after my senior year, I was taking organic chemistry down at University of South Carolina, and that was the Watergate summer. So, I spent most of that summer studying chemistry and watching Watergate, kind of reminiscent of what's going on this year.

JM 23:56
So those things are connected in your mind in a way?

RC 23:59
Absolutely.

JM 24:01
Okay. What was your experience like at Duke for Medical School? I read that you were interested in Duke's program because it was set up sort of uniquely in terms of how much time you got to spend doing research?

RC 24:12
Right. I really wanted to go to University of Virginia because they just had a few years where they had started a program where essentially you enrolled and then you did whatever you wanted to do for four years. Because I really, at the time, I really didn't think that structured classes would be the best way to learn. But Duke was the next best thing. I didn't get into university of Virginia, and I think it worked out well. Duke had this -- still has this -- curriculum where all the basic sciences are packed in the first year. And then you go out, and deal with patients, and learn from that in the second year. Then you have a third year of freedom to do research. And that was very attractive. But I didn't get into Duke until relatively late. So I'd already accepted and paid the the startup fee at Tulane before that happened, and still when I go down to Tulane, I was just there, the old Charity Hospital I still think is one of the most amazing relics of American medical history. At the time I think it had 2,500 beds. They were all in wards. It was just medicine in the raw, almost all indigent patients. Really, really sick. Now it's been decommissioned, and was just bought by a bunch of commercial real estate people. And it's going to be mixed-use residential and clinic. So it's fascinating to see how these buildings can be repurposed for good use. And speaking of that, we're sitting on the fourth floor of Davison, which is where the entire first year of medical school took place, except for the lectures. So it's sort of a weird, full circle thing that my office now is back where I spent the whole first year of medical school, for all practical purposes.

JM 26:33

So you're taking courses that first year, seeing patients the second year. And your third year, what what did you decide to do with that freedom and space?

RC 26:43
Well, I had decided that dealing with patients or people was the main thing that I wanted to do. And most of the students were -- not most but all -- were all encouraged to do basic science research because the Flexnerian model of medicine was developed at Hopkins and Duke's initial faculty all came from Hopkins and very much focused on the basic sciences. But there was an option to do clinical research and that's what I really wanted to do. And so I'm linked up with a faculty member named Jim Margolis, who, those were the very early days of cardiac catheterization. And he was a person who did that really well, and had been working with computers. And that made a lot of sense. But what happened was, I finished the second year. And I still have a very vivid memory of walking in to Dr. Margolis' office to get started, and the whole office was full of boxes. He was packing to leave. That was a kind of a sinking feeling. And we had a good talk and basically what he said was, "This is an amazing time for cardiology, Miami is starting a big heart institute, and it's gonna be a big thing, that's what I'm gonna do." But he said, there's this other fellow named Galen Wagner and he's willing to take you on. And I had no idea who Galen Wagner was, so I march down to see Dr. Wagner. And he did take me on, and became a lifelong friend and mentor.

So I spent that whole third year hanging out with cardiologists, learning about computers. And it's a really serious time for cardiology, because we didn't know that much about the risks of smoking. Most men smoked. And at the time, things have changed, but at the time women were much less likely to smoke. And our intensive care units were full of men with heart attacks at a young age, or having had sudden death. So, bad events were very common. And I think the Holter monitor had come on the market. And that was, for the first time, a device that you could put on people and you could measure the heart rhythm over time, even while they were at home. So my project was to put Holter monitors on 350 or so people, who had documented coronary artery disease, blocked up arteries. This this week, I can say "the Bernie Sanders problem". And the idea was, what would predict who was likely to die in the upcoming year? I think a sign of the times, we didn't angioplasty or stents. We didn't have statins. We didn't know that aspirin prevented recurrent events. We basically sort of had bypass surgery, prayer, a few other drugs that weren't highly effective. So a lot of people died, and it only took 350 people to get some very meaningful results.

So it was an amazing year. That was also the year that a fellow named Mel Scheinman had come from the University of California to learn how to do cardiac ablation, which these days you'd say "Well, that's a common procedure for people with heart rhythm disturbances." But there was a cardiologist here named John Gallagher, who was a pioneer of doing that. Duke was a place that really did that first. And I sort of got to be there as this new technology developed. It was just amazing, the idea that you could put catheters into people's bodies and in a very micro, circuitry way, do surgery through catheters. Just amazing. And way ahead of its time. So I learned a lot and saw a lot.

JM 31:25

Did you think of that time "Okay, this is the area of medicine I'm going to stay in", or was it just so exciting because of the developments happening?

RC 31:34
Yeah, I didn't mention that as an orderly we got to see everything including autopsies, which I'll never forget. But the event that really crystallized things for me was walking into the emergency department and seeing someone defibrillated. That was amazing. You have someone who is dead. Then if you get there early enough, and defibrillate, you have someone who's alive. You compare that to the complexity of psychology, that was very instantly gratifying where you know you're doing good.

JM 32:11
Did you understand what that was at the time? When you when you saw it unfolding?

RC 32:16
I did, but when you actually understand what it is, you can get very metaphysical about what does it mean to be dead and alive, and what are all the implications of that technology. And many things evolved from that, of course, including the development of ICDs, the ability to implant defibrillators, so you don't have to be shocked externally. We did a lot of the work on that, later in my career here at Duke.

JM 32:53
When you were in medical school, thinking about what you were going to do next, you ended up at UC San Francisco to do your residency, and what did you plan to do at that point?

RC 33:15
Well, part of what had happened.. I became very close to the old Dr. Stead. And by the way, one of my most vivid memories of first year of medical school was right at the beginning of the year. They used to have these things called clinical pathologic conferences, which was really just a chance to talk about a case. And then the faculty would have a discussion. And I still remember the Head of Neurology was presenting the case. And right in the middle of his presentation, Dr. Stead stood up and just started berating the guy. So much so that he actually walked out, and it was over. None of us knew what to make of it at the time. But what I learned later was a slightly toned-down Dr. Stead, I think is a really good thing. [sound of Code Blue alarm in building] That is, people actually really say what they mean when they're in meetings. And sometimes it can get emotional and tough. But I've always believed, since then, it was better. If you're going to have a meeting, if you don't have differences of opinion, first of all, there's no reason to have a meeting. And if you do have differences, you ought to really express them.

But Dr. Stead was my mentor, and he had encouraged me to think about going other places. It turned out that Jim Wyngaarden was a Chair of Medicine. He was another impressive mentor. He went on to become head of the National Institutes of Health before he finished his career. And so, I had loved San Francisco as a place, and when we went around and interviewed, it was sort of Seattle or San Francisco. But at the time, Seattle had a surplus of nurses and Lydia said "the only jobs I'd have for me would be the midnight shift." And so, I ranked San Francisco first.

Well, in the meanwhile, Lydia got pregnant, and when the match came out, I was ecstatic because UCSF was like, one of the top three or four places you could go. She was not too excited. You know, deeply pregnant at the time. We had grown up in the Carolinas, San Francisco's a long way away. But that was the time of short tracking, so you could do a residency in two years. And Dr. Wagner and Dr. Stead arranged that I could solidify my fellowship back here at Duke in Cardiology after doing two years of [inaudible]. So I already knew I was going to come back as a fellow after two years out there.

JM 36:20
Was that unusual to have an appointment set up already?

RC 36:23
That was unusual. The short tracking was fairly common, because typically it's internship and two years of residency, but you could cut off that last year if you're going to go into a fellowship. So that was the plan. Of course, after we arrived, we loved it in San Francisco, and neither of us really wanted to come back because it was such a fascinating place, but we were committed so we came back.

JM 37:00
You mentioned that you were working with with computers very early on. So you saw the potential of them to transform medicine, you found them interesting. What was your interaction [with them]?

RC 37:12
Well, one of the funny things about it is I'm basically hapless with.. I'm just a user of computers. But I've always for some reason, been able to work well with people who are the deepest computer-type people. And what Dr. Stead taught me right away, very early on, one of his things was, there's no way a human being can integrate all the information that's needed to make the best decisions about health. Particularly because many health decisions, you have to understand the importance of time, that decisions that may look better immediately actually turn out to be worse, and vice versa. That's just too complicated a problem for the human brain to comprehend. And some of the famous doctors of the past like Paul Wood and Paul Dudley White, they just wrote things down on note cards to categorize people, and kept them in stacks. And that's basically what the simplest form of computing does. It sorts things.

So he took me to a Cath Conference. At the time, as I had mentioned, there were no stents or percutaneous procedures. It was either bypass surgery or medical treatment. What he said was, "They're going to look at a case, and they're going to conclude that medical treatment is best because the last three people that went to surgery died in the hospital." And he said, "But here on the computer, I can show you what happened three to five years later with people like this. And you're much more likely to be alive three to five years later, if you're treated surgically." So it's a case where there's this early hazard with a procedure. And of course, people remember what happens proximally when things are done. Sure enough, they recommended medical treatment. At the time it was such a big deal that the cardiologists and surgeons would meet together and look at the cases. Of course, now it's just routine. It just happens. And I asked them, I said, "Why

don't you show them the data?" And he said, "Because they won't believe it, it's coming from a computer." So that was a real lesson.

And then what happened, when my research project came to fruition, I worked very closely with a gentleman named Kerry Lee, who was the first Biostatistician here at Duke. He had been working at Bell Labs, and gotten a Ph.D. at UNC, and was brought over by Dr. Stead and Frank Starmer, who was a Computer Scientist that worked with us. And was brought over, and Kerry taught me all about analyzing data. And what happened was that we were trying to predict who was going to have sudden death. Because obviously, despite defibrillators, we didn't have ICDs at the time. So if you dropped over dead at home, you were dead. So if you could predict who would be likely to do that, you might be able to intervene earlier. And the idea was that the more extra heartbeats you had, the more arrhythmias that were on your monitor, the greater likelihood that you would drop over dead in the future. And that turned out to be true, but it turned out a much bigger predictor was the functioning of the heart muscle. The so-called left ventricular ejection fraction, and that was a dominant factor compared to the heart rhythm. So we analyzed the data, it was surprising. Our conclusion was that if you could develop a treatment, you would oriented more towards people with damaged heart muscle than just the people with arrhythmias. And so I went off to do my internship. The American Heart Meetings that year were in Miami and, I got the day off to come present my data. It was really, you know, fly to Miami, do the presentation, and leave. And it turned out it was a big arena full of people, and they made fun of me. They said, "This is just ridiculous, it's not right." But Dr. Stead, and Kerry Lee and others said, "We did the analysis, it's right, even if it's not popular, and it's not what people believe before, you should stick with it." And we wrote a couple of papers. And of course, it turns out today, what's the indication for implanting an ICD? It's an ejection fraction less than 35. So it was the right answer. It just wasn't what people expected. So, a big lesson there. You could fast forward to deep learning today and say, when it comes to artificial intelligence, the whole purpose is to unearth attributes that are not visible to the eye. And then develop ways of assuring that your integration of information is yielding something that's truthful and predictive. So big lesson at the time.

JM 42:47
And as somebody has come to be so associated with data science, you also continued to see patients up until 2013ish, is that correct?

RC 42:57
Yeah. For me, that was crucial. And I think I was really lucky. What happened was, I was working away as a fellow, I'd done a short track as a resident, and then in the middle of my fellowship, the Director of the Coronary Care Unit went into private practice. And Joe Greenfield was the Chief of Cardiology at the time. Joe is not the most.. how should I say it? He doesn't spend a lot of time waxing on in his speech. So he basically said, "Look we need someone to run this CCU. Why don't you do it? And you can get credit for your fellowship while you're on the faculty, too." So I said, "That's great." He said, "You get a big raise all the way up to $35,000 bucks a year. And for that you get to be on call 12 out of 14 nights." So it was pretty exciting.

But it was later that year the first angiogram of someone with a heart attack was done. Up until then, we didn't know what caused heart attacks. And it's obvious now that it was blood clots. But what happens when you die is that you have endogenous fibrinolysis, your blood clots dissolve. So when autopsies were done, the pathologist didn't see blood clots in the coronary arteries. But some enterprising cardiologists did acute angiograms. And sure enough, there were big blood clots in the arteries. And so, because we had the best computing capabilities and medicine here at Duke, and one of my interns at UCSF, Eric Topol had the drive and the intuition to know where to go, we formed an alliance. And did a lot of the research with collaborators around the world that enabled us to figure out how to treat heart attacks effectively.

And that really worked well, because the research was being done on the patients that we were seeing, and you could relate the research directly to the care of people. It was all integrated. And I was really lucky because Dr. Stead had all these insights that people still talk about, what we now call the learning health system, he built it here. Because what he had set up that I benefited from, is if you came to Duke and had a cardiac procedure, your data was entered into a computer, which no one else in medicine was doing. And then you were followed for life. We had a phone bank of people that we'd call and ask how you were doing, so that we could measure how people did over time. And then apply algorithms, which at the time were just developing, to understand what was happening with people. And so, literally your job, if you were a cardiologist was to see the patients and enter the data. Make sure it was right. It was just part of your job.

This led me to believe.. and the derivative of it was that as a senior medical student, I could sit down with a patient and say, "We're thinking that you may need bypass surgery. Here is what you can expect if you have surgery, or if you don't." Doing that in real time. So stupidly, I wrote an article, one of my first publications, that said within the next few years we'll be doing this for every disease, because it was obviously the right thing to do. What I didn't understand was the deep resistance in the culture of medicine to this. And the fact that computing just simply wasn't scalable. It just could not be scaled to the degree to... we had a whole team of people that were paid by research dollars to make this happen. And you just couldn't do that for the 10,000 different diseases that exist. So, I spent most of the rest of my career trying to figure out how to make that happen. But without seeing the patients as part of the job... I don't I don't think all members of the team need to be that way. But having a few team members who really understand what the experience of people with the problem is, I think is really a critical element. And Dr. Stead just knew that and made it happen.

JM 47:55
And so you mentioned very early in our conversation, that you were a shy kid. And you've also mentioned a few occasions where at conferences, people were having very excitable dialogue. So when you were first presenting as a researcher, what was that experience like for you? And knowing there was some resistance to the things that you were interested in.

RC 48:16
There were a couple of memorable things. This is kind of funny, but it's been written up before. I believe deeply on the importance of leaders, and having the courage to set examples. And I was

very shy, and in the eighth grade we had to do presentations, and my presentation was on National Geographic, and they had those articles they used to have about Jane Goodall and apes. And I had a teacher named Mrs. Belias, and I just.. for some reason, it just hit just right that she basically said, "You gotta remember, if you've studied this thing, you know more than anybody else in the room. So just get up and talk about it, it'll be fine." And she sort of gave me the courage to do that. She was also, you know, this sounds weird now, but eighth grade boys, she was a really good looking young teacher. And it was meaningful. But it wasn't her looks that made the difference, it was that she really encouraged and stood behind the effort. Well, we fast forward to being a Fellow where you do make these presentations, and we had these amazing sessions, where you would present and the real purpose was to have the audience tear you apart. This turned out to be really important later, as I'll mention, but I still remember it was really fascinating. Joe Greenfield who is still alive, at the time was a very powerful but very gruff man. Drove a pickup truck, had a shotgun in the back, real prototype of a person like that. And he took me aside again, and said, the most important thing to remember when you're presenting your work is that no one else in the room knows more about your work than you do. So it's important to listen to the question and answer it, but don't be intimidated when people attack. And it was almost exactly the same advice that I had gotten in eighth grade.

JM 50:47
And you said the goal is to have people tear you apart.

RC 50:51
Yeah.

JM 50:53
Can you talk more about that?

RC 50:54
I think the best way to test out your ideas is to have people attack them from every angle. And I worry that in our educational system, and specifically medical education, it's considered offensive if you disagree with somebody. And I think we might have gone too far in that regard. Because no one knows everything, and you learn from having people disagree. And you really learn how to articulate what it is you're really saying if people attack what you're saying, because then you have to defend it. This became critical when I was nominated for FDA Commissioner, because the exercise in and of itself is making your entire life exposed to the public for attack. And there's a thing that happens for nominees called "murder boards". Which is exactly the same thing as what I did as a Fellow. Basically you sit in a room, and people imitate the people who are going to attack you. And they take on that persona. And you have to defend yourself as if you were in the real room.

JM 52:19
So they were taking on personas of people who are going to be on the committee.

RC 52:24
That's right.

JM 52:25
Okay. Interesting. [laugh] And how did you feel that you fared in the in the murder board situation?

RC 52:32
I think I did well, because I was had been prepared through life to deal with it. And so it didn't really didn't bother me, at all. It was very revealing about the people I would encounter in politics, and the motivations for sometimes why people do what they do.

JM 52:55
And so that preparation you did feel like it translated to when you were going through the nomination process.

RC 53:02
Yes. And I wish more leaders had the kind of experience that I was exposed to, as part of their training and education. But I worry we don't. We're too genteel with each other now.

JM 53:19
It sounds like you view the process of critique of your work as part of the testing of the hypothesis, almost. Part of the process of research.

RC 53:31
Yeah, I think part of it is getting perspective on whether the findings are correct. And the questions are correct. But another big part of it is being able to explain it, because I think in, particularly in clinical research, if you can't explain it, it won't have an impact. And it's hard to justify doing things like human experiments if it doesn't lead to some benefit for people and in the future. So I think it's a great way to fine-tune your arguments. You know, when you when you're at the hearing as a presidential nominee, especially when it's already been publicly said that there would be no more nominees for the President who nominated you that would be allowed to be confirmed. You're sitting there with no notes. You're there on your own, you're on TV. And people go after you. It's just the way it is.

JM 54:39
So, seeing as we're already talking about this, let's maybe move into the FDA Commissioner period of your life and then go back later to more of your time at Duke. So you were first nominated in Medical Devices [note: Products, not Devices] and Tobacco, is that right?

RC 54:58
Well, what happened was, I had been interviewed twice before for FDA Commissioner because part of the just natural flow of my work and our work at the Clinical Research Institute involved clinical trials of products that were going to be up for review by the FDA for whether they should be put on the market. And so I had a long history of working with the FDA. And in both the older Bush and the younger Bush [administrations], I'd been brought in to interview. But the problem is, I'd not donated money to either, and I'm not really a donor to any political party. But

there I think there was a strong preference for people who are in sync with the Republican party line at the time. So when Obama came in, he nominated Peggy Hamburg, who I didn't know at the time, but we got to know each other because of all my interactions with the FDA. And after six years, she had decided to step down. That's a pretty long term in a job like that, with all the stress. So she had been there a long time. And she came, she actually called me and then came down to visit, and basically said something to the effect of, "We're looking for a Deputy Commissioner, and there's a high likelihood that if you take that job that," she said, "I'll be leaving and the commissioner job will be open." But the problem is you have to be nominated by the President. It's not a thing where the FDA decides who its Commissioner is going to be. It was just the right time for me to do something else. So I actually went as a civil servant. The Deputy Commissioner for Medical Products and Tobacco is a civil service job. And that was an amazingly good year.

JM 57:18
What were you working on at that time?

RC 57:21
Well, the way it works is, the FDA has centers. So there's a center for drugs, a center for devices, a center for biologics, center for tobacco, center for animal health and products. And the Deputy Commissioner job, basically, was to oversee medical products and tobacco. And I say oversee lightly, because it's not a command and control position. The center directors are very strong, kind of like department chairs and academic centers. But it was a great.. I learned about everything, and I had influence on policies and new programs, and all the things that happened in government. So I was protected from the politics because I was civil servant. I wasn't a political appointee. So I learned so much, and it was a chance to serve, as I mentioned I had a high draft number, so I didn't serve in the Vietnam War. And I think it would be good if we had a way for every American to serve in some way. So I gained a lot of respect for civil servants in that year.

JM 58:46
And as a cardiologist working in the field of tobacco policy, was that common that someone with your background would end up in that kind of position? And how did you approach it with your medical background?

RC 59:01
Well, I'd say people in leadership positions and the FDA come from, some are from public health backgrounds, some are veterinarians. It's a lot of different kinds of people. I was highly motivated from my early experience, as I described, as seeing all these people die from tobacco-related illnesses. I'd also had this very meaningful experience. I've gotten to be friends with the people in Oxford, where there's another big clinical trial center. And they invited me over, for reasons I still don't understand, for the last big celebration for Sir Richard Doll. And Sir Richard Doll was the man who really did the definitive study about tobacco and cancer and death. And I still love the study. I'm just writing a blog about it now. But basically he took a sample of British doctors, asked them whether they smoked and if so how much, and then followed them all until they all died. So he had complete 100% follow-up on the entire population. And there are many important findings like 18 different kinds of cancer were directly

related to tobacco use. But the simple way to summarize it, is there was a 10 year difference in life expectancy between doctors who smoked significantly and those who didn't. And at the time, there were advertisements and magazines where doctors were recommending Camel cigarettes. And the military was giving out cigarettes as a way to deal with the stress of being in the military. So Sir Richard had a huge effect. I got set at the head table with him. He was 92 years old at the time, and still working every day. So I was very aware of the data and the human toll. But I knew nothing about the regulation of tobacco. And that was.. I spent a lot of time with the Center for Tobacco Products, and the people involved, and it's sort of a combination of horrifying and interesting.

JM 1:01:19
So this year ends, and and then your predecessor decides to leave her appointment. And she was in it for quite a long time, it sounds like.

RC 1:01:20
Six years.

JM 1:01:31
So what was the process from there?

RC 1:01:34
Well again, it sort of relates to what's happening as we're sitting here today. But it turns out that she stepped down. There were two years to go. The nomination process itself is very complicated, and it's very, very political. There are all sorts of people who want to have a voice in who a presidential nominee is. And so they appointed Steve Ostroff, who is a long-serving civil servant, just a great public servant guy, and he was appointed as Deputy.. I mean, as Acting Commissioner. And that turns out that, I think the administration was unsure what to do. And I had this weird set of experiences where people will drop by and say, you know, "When are they going to ask you to be Commissioner?" And my answer was, "Well, it's kind of like being a member of Augusta National Golf Course, The Masters. If you ask to be a member, then you can't be." So there's no way to promote yourself for that job. And eventually, as I got to know more and more people.. what happened was, I was preparing a briefing for President Obama on whole genome sequencing. A big issue of technology development and regulation. And I got a call at four in the afternoon and it said, "You know that briefing you're preparing? You're going to give it. And it's tomorrow at noon. And you've got five minutes to convince the President that the FDA is not the problem." Because a lot of technology people were complaining that the FDA was holding up technology. And that was kind of an amazing experience. I'd never been in the White House. So I went into the Roosevelt Room and it was quite interesting, because I later learned in the many meetings I was part of, the President read everything the night before. So you didn't have to go over the material that you had. He already knew it. And it seemed to go well, and as I was walking out, they said, "Why don't you come to the oval office tomorrow?"

JM 1:04:23
So was that, you think that was sort of him getting a sense of you as a person?

RC 1:04:29
It seemed that way. I think what was striking, in the room, I think Obama's ambiance.. It's sort of professorly, but it also has an element that's sort of like being in a locker room at an athletic event. I think we were very at home together. So when I came into the Oval Office, of course, during that short period of time, the handlers gotten a hold of me because when you become a presidential nominee, there are people whose careers are made based on the proportion of nominees that get through the nomination process and get confirmed. And they said, "We noticed that you were captain of your high school basketball team, President Obama was also captain of his high school basketball team. And he's very competitive, so you can expect he's going to give you a hard time." Sure enough, we had a half an hour. The first 10 minutes were spent on the fact that he loves UNC basketball. And there's a story behind that. His personal manager, early years in the White House, was Reggie Love, who had been a Duke basketball player, and football player. And they had quite a rivalry. So, and Obama has always picked UNC to win the National Championship in the lottery. So, we had a good back and forth about that. And then he got into the serious issue of technology regulation, and what needed to be done. And, given my history, I felt like I was pretty well prepared to deal with that. And he offered me the job. A problem with that is, as I walked out, the handlers showed up, and just reminded me, they said, "You don't have the job until the Senate confirms." So the President can offer you the job, but can't actually give you the job. And this is going to be hard because they it's not good between the Senate and the White House. This is going into the last year of the Obama administration. So it turned out that Richard Burr was a big help. And Tim Scott from South Carolina, my place of birth, really backed it up. So it ended up I had really more Republican support than Democrat support, even though I was an Obama appointee. So we got through it.

JM 1:07:17
So were they represented as part of the murder boards, their personalities.

RC 1:07:22
The biggest one was Bernie Sanders. Bernie hated me. I don't think it was personal, just because I've done a lot of work with the medical products industry. He seemed to think I was a bad person. We never really had a decent conversation. And that was different than even senators that I had significant differences with. But there were there were others.

JM 1:07:55
And you expressed that..So President Obama express to you that technology regulation was a big issue for the next Commissioner. So is that thinking about how to make sure that new innovations are able to come into the market quickly while also proving their safety? Was that what he was talking about?

RC 1:08:18
Yeah. I mean, basically, he had become convinced that the tech.. the fourth industrial revolution was happening. Getting that right was the most important thing [for] the future, the American economy, and its health. He knew that the current FDA paradigm was not suited. And something different had to be done. But he also strongly believed that regulation was essential. Because a lot of technology people were arguing at the time that regulation was just an impediment to

innovation, and was unnecessary, and everything would work out fine. So, those are also beliefs that I shared. So it worked out pretty well.

JM 1:09:10
So what were some of the other big issues that you worked on during your year in that position?

RC 1:09:15
Almost every day in that job, there's a big issue, because you're regulating something like 20% of the economy. And people don't think about it as much, but food is half of the work of the FDA, and I was certainly not an expert in food. But we had multiple things with food poisoning, which were politically tough issues. The Chipotle food poisoning episode happened during my tenure. But the most substantive issue related to food was genetic engineering, which is still not solved. But I learned a lot. And I think there's a pretty good understanding in the scientific world about the likely correct way to go with genetic engineering. It's just not popularly accepted right now. It's going to take a while to get there. We developed a framework for software as a medical device which has played out, which directly related to what the President had wanted. The most controversial issue was the Sarepta case, of accelerated approval of a drug for muscular dystrophy, where the review group at the FDA thought it shouldn't be approved, but the center director overruled them. And they protested for one of the first times in history in an adjudication process that I had to adjudicate. That was a very public controversial issue. I can go on and on.

JM 1:11:08
Was that about efficacy versus safety?

RC 1:11:14
The specific concern about the drug was it was developed on a very small number of people. And people, in this case, means boys who have this dominant mutation, which typically causes progressive deterioration and death at a young age. And so the question is, how do you study a drug in a situation like that? The company that developed a drug had done some things clearly wrong, but they had data that suggested that the protein that you need to have in place to not lose your muscle strength was increased by this drug. And so there's a law that had been passed about accelerated approval for situations like this. Basically, when there's no effective treatment, and it's a serious disease, in this case, a hundred percent lethal at a young age, the drug could be approved without definitive outcome based clinical trials. And then the law says it's up to the FDA to exert judgment as to where the evidence is enough, that it's reasonably likely that the drug will be effective. So it's really a judgment call. But it was hyper controversial because mostly the mothers of these boys, had a very loud patient advocacy group. And by loud I mean, just highly effective. And the advisory panel meetings, related to this had been public spectacles, and some members of the advisory panels had been physically threatened. And it was just a very high tension situation, that played out publicly.

It turned out, as a CCU director, and as a clinician I'd always regarded dealing with lawyers is, like, the worst thing that could happen. It always meant something terrible was going on. But I gained a tremendous respect for the way the law plays out related to things like the Food Drug and Cosmetic Act. And it turned out the the issue was relatively easy for me, because there had

only been one other case in history where a political appointee had intervened above the level of a center director at the FDA on a specific product. And that was the Plan B birth control issue. And setting a precedent of political appointees overruling full-time civil servants should only be done when the center director, which is the ultimate authority, it's deemed to be not functioning, not being rational. And I couldn't argue that Janet Woodcock was not being rational. She'd been evaluating drugs much longer than me, and had her reasons. They were arguable, there was reason to have different opinion, on different sides of this. And so for me, it was basically one of those things where you say "It's not my call, calls been made." Because once a political appointee starts intervening.. right now the FDA gets deference from the courts. Because it's regarded as a scientific organization, not a political organization, and if a political appointee makes decisions, then why shouldn't a judge be able to intervene and make decisions about specific policies. So there's a really interesting division of labor, where the political and legal system evaluates principles and policies, and decisions about individual products based on the balance of risk and benefit is a scientific judgment made by full time civil servants with no conflict of interest.

JM 1:15:37
You were also in this position when the opioid epidemic was starting to become more public as an issue that people were thinking about. And I understand that as part of your role, you ended up doing a lot of listening events in regions affected by opioid abuse. Can you talk a little bit about that?

RC 1:15:56
Sure. And, in fact, I described walking out of the Oval Office office, and that afternoon I saw three Senators -- Manchin, Markey, and Angus King. And all three were just livid about opioids, and I was not prepared for the degree of upsetted-ness.

JM 1:16:21
And that was the day you were confirmed?

RC 1:16:22
No, the day I was nominated. The day the president said he was going to nominate me. Because what you do is you go see the senators on the committee, and others that are interested.

JM 1:16:31
That's their first chance to let you know what their..

RC 1:16:34
What their priorities are, to get to know you, and all that. But when I think about the opioid problem, basically I go back to my grandfather, who was a Southern Baptist minister, who told me that we are all sinners. And this is definitely a case where we're all sinners. But there's a tendency to blame the FDA for things that happen, in political circles. And so all three were very upset. And they knew the devastation that was occurring in their electorate. And it was fascinating to me because they seemed to blame me, although I had not been setting the policy. And my point was, if you want something different, you should vote for me because I'll be

different. If you don't, no one else is going to get nominated. So you'll have the FDA that you had before. Now, of course, that's a tricky thing to navigate, because I didn't think the FDA was the sole culprit in all the problems that were in play.

But that was a signal right away that I had to really pay attention to this. And in the year before, as a civil servant, I had been to a lot of meetings, and tried to help shape policy in a very complicated set of circumstances out there. So we took it seriously. But there are a lot of very deep issues, partly because there's... FDA has a major role to play. But also the DEA handles the distribution of opioids. There's a Drugs Czar are in the federal government. The NIH has a research portfolio. The industry is advertising and selling and hadn't been investing in alternative treatments for pain. So.. just very complicated. But at the base of it was an important thing to do, when you're in a public position, is to visit with the people who are being affected by whatever the problem is. So yeah, I made the rounds of.. particularly in Eastern Kentucky and West Virginia. I should also mentioned that at the DCRI, we had been the coordinating center for NIDA's, the National Institute of Drug Abuse's, clinical trials network, which did a lot of the early work in medication-assisted treatment for opioid addiction. So, I was not naive about the problem. It's just understanding the politics of it was a whole different level of dealing with things.

JM 1:19:42
And then I imagined being on the ground and seeing the impact in those communities was interesting too, do you want to talk a little bit about that?

RC 1:19:51
Well, I think it's fair to say that every segment of society is affected by opioids, but the most devastating areas are the ones that are already economically in trouble. And so you would see families who were destroyed, and people who really saw no hope. And then there would be all these beliefs about them, ranging from religious beliefs that they are just sinners and there should be no treatment offered, to beliefs that they should all be in jail, to people who thought the drug should be no longer illegal to be distributed, and, you know, just all across the board. There was no consensus on what to do. And even if you went from one town to another in the areas most ravaged you'd see very different approaches to treatment. For those who are in recovery, the biggest question they had was, "How soon can I get off of medication-assisted treatment? Because I can't get a job and there's a stigma associated with it."

So it's an extraordinarily difficult set of circumstances, and people who offer simple solutions like just outlawing opioids. Well, then, part of listening was hearing from people that really have chronic pain like children with musculoskeletal problems that have had major operations or adults with orthopedic or cancer problems. Or people said, "Well, change the label on every opioid." But there are 250 opioids on the market and by law, you have to negotiate with each company. So you need an army of people to do it and even knowing exactly how to fix a label, this is an area that has a real deficit in evidence. Doing research in addicted people is really hard to do. You know, I learned in our NIDA experience, you're dealing with people who, because of concerns about the law, don't actually want to be followed. So it's hard to get the follow-up. And then you have doctors who were in hospitals that were prescribing opioids by the boatload. Just

coming back to Durham.. Before I left for the FDA, we had done a massive community engagement project in Durham about what people thought the most important health problems were, and what to do about them. And interestingly, one of the ten identified by the people who live in Durham was prescription drug use and there were more opioids being prescribed in Durham than the population.

JM 1:23:06
So, it sounds like you were setting a lot of groundwork in that year. And what were you expecting what happened from there? You couldn't predict the the election.

RC 1:23:16
Right. I think all of us were shocked by the election, because most of the planning was what to do in the next Democratic administration, with continuity of a lot of the people. I mean, I had no assurance that I would be asked, if a Democrat had been elected, to stay on. That doesn't always happen. But a lot of the policy people would have continuity. And one of the things that we had done, there's an issue, that the law tells the FDA to evaluate drugs by weighing the risks and the benefits to the individual and [for] whom it's intended to be used. And there's this other issue with opioids, which is the collateral damage of all the people for whom the drug was not intended to be used, but got ahold of it. Over half of the opioids prescribed were being diverted for illegal use. And so we had commissioned an Institute of Medicine study, which is the body convened by President Lincoln, actually, to start with, to inform the Congress on matters of policy. And so the question was, "Is there a framework by which you could take into account societal impact as well as individual impact?" So we published a very deep set of things and recommendations, policies, many of which were being implemented. Educating doctors was a part of it. And the hope was it would be continued, but then the election happened and everything was turned upside down. We had no idea who would get appointed FDA Commissioner and what would happen. The good news there that also relates to current times, in my opinion, if you look at the FDA, it's over 17,000 people, there are about a dozen that are political appointees. The rest are civil servants. And they know what their mission is. It's the well-being of the American people. And their loyalty is not to the political appointees, it's to the institutions, and the laws. And so there was a relative calmness within the FDA about this, but I was worried about it.

JM 1:25:40
Was there was there any expectation that you would continue to serve in that role?

RC 1:25:44
No. I mean, there was a slim chance. There's also a question of, even if asked would I want to do it. The answer would be no [laugh]. So January 20th, 2017, I drove out of Washington having served my term. As I like to say, looking through the rearview mirror as the barbarians came through the gates on the other side of Washington. There was one other time in Washington when barbarians came through the gates, in one of the wars, Washington was almost captured. So, anyway, in this case, it was captured. The good news was, after a lot of uncertainty, Scott Gottlieb was appointed as FDA Commissioner, and he turned out to do a really good job. So I

think the FDA has done pretty well through all the political turmoil that's been going on in Washington.

JM 1:26:56
Which would you like to take a short break before we finish up?

RC 1:26:58
I'm okay. How many more questions do you have?

JM 1:27:01
Let's see, we've got an hour and a half, maybe like 10 minutes more, or so, is that okay?

RC 1:27:08
Okay, yeah, let's just keep going.

JM 1:27:11
Excellent. We sort of skipped over a huge portion of your career. So moving on to administration at Duke. What interested you in that, in general?

RC 1:27:23
I'd say my involvement in administration was really just an evolution from my role as a clinician. As I described before, [inaudible] figure out what caused heart attacks. We had more technology and capability than almost anyone else to deal with it. North Carolina is like ground zero for tobacco-related disease. So our CCU became like a MASH unit, because there weren't many other cath labs in the state. And we were just overwhelmed with referrals. And it also turned out that we started a helicopter program, because when people had a heart attack in a small town, since all the treatments we had were brand new, there was reluctance at the local level to do what needed to be done. So literally my beeper would go off, and I would run and jump in the helicopter and fly to a small town and we'd land and deliver the blood clot thinning medicine, and shove the person on the helicopter and fly back. So I spent a lot of time doing that. And building that system involved administration. There was a lot of money involved, a lot of people.

Our of my great lessons in administration there was a tremendous nursing leader at Duke, Mary Ann Peter, whose husband just was one of the kingpins of the cath lab at Duke, just a tremendously talented cardiologist. But I was of course, excited, we were saving all these lives. But we couldn't keep nurses in the unit, because it was just too hard. And it was overwhelming, we'd often have four or five people who would die in a day. And most of these were not chronically ill people. So it was very devastating to deal with the families as they came in. And so I couldn't understand why the nurses wouldn't want to work in a MASH unit. And then she took me aside and said, "Look, you know, you're just doing this all wrong. And you got to build a system where the nurses have a reasonable life, and they work really hard because they are mission-oriented, but rather than pitching it as you can destroy your personal life by working in this place, pitch it as we're saving lives and we're going to do it in a way that's built on teamwork." And I think that's been sort of a lesson at every level that I've worked.

And then, sorry, going back to my roots. Wanda Bride was the quintessential nursing leader. At the time she didn't have a bachelor's degree, she had a two year degree in Nursing. She had started out taking care of patients, and she became like the ultimate CCU nurse manager. And everyone knew, I mean, there's a whole generation of Cardiology Fellows who learned what they know about coronary care from Wanda. And she had an amazing career, and just retired a few years ago. So we built an administrative team that was very mission-oriented. And as I look back, we were really lucky because we were dealing with a problem and a disease that for whatever reason, people decided should be well-reimbursed. So while while there was tension and it was high pressure and lives were at stake, for the most part we had a lot of backing from the system to build what needed to be built.

And so, you know, the idea of having a technology center, and then a referral network where chronic care was taken, was something that we played a large part in developing. And then on the research side, you know, we were doing this research that I described, and it seemed like "Gee, if it worked in cardiology, it ought to work in everything." And along the way, that it turned out that the world got fixated on how do you dissolve the blood clot in the coronary artery? it's life-saving, there are several ways to do it, which is better? And there was a new American biotech drug made by a company called Genentech, and an old generic drug that was already on the market, the difference in price was $2,000 versus $200. And in order to know which is better, a clinical trial needed to be done. Now, this gets a little dicey. But in the early studies that we did, it was basically a group of us who had been interns and residents together at UCSF. We spanned out across the country. I don't know why most of us went into cardiology, although we should have gone into HIV treatment. Because when I was an intern, we were seeing the first AIDS patients, but we didn't know what it was. So we had a lot of experience with the medical problems related to AIDS. San Francisco was epicenter of AIDS at the time. But I don't know why we had a big group that fell in love with cardiology.

RC 1:33:18
So we were studying this, and my friend Eric Topol called up and said he was at Hopkins and he said, "There's this new drug, made by Genentech." Genentech was formed by UCSF professors, the first real biotech company. So we got on a plane and flew out and said "We'd like to do some clinical trials with your new drug." And they said, "Well, you know, that's okay. But we've already locked up the leaders in cardiology." And we didn't know exactly what they meant by "locked up" but it turned out stock options had been given to cardiologist doing the studies. And as this played out, these were the early days and almost everyone gave their options back before it was a problem. But they did give us $100,000 and all the tPA that we wanted to do a clinical trial. And that was our first big multi-center clinical trial, called TAMI-1. And it was sort of like my experience with the first study I did. We were sure that doing an angioplasty right at the time of the heart attack was better than just giving the drug. But at the time, the technology was new, and it turned out it was the opposite. So the answer we got it was exactly the opposite of what we expected. So that was a real lesson, that there's a real value in putting things to the test and finding out.

But then this question came up about which drug is better. Genentech needed to do a big clinical trial and they couldn't do it themselves. They needed to basically pay somebody who was

independent to do it. So they came to us. And that enabled us to build an organization that could work in multiple countries. And in doing that we developed the first computerized pharmacy distribution system, which today sounds trivial, but at the time, you would have these stockpiles of drugs at every hospital. For expensive biotech drugs this is just an enormous cost. But we developed a system to resupply at the right time. Again, sounds trivial now, but it was the first one. And we did a 40,000 person clinical trial. That built the research organization. It also got me a congressional investigation, which is another interesting part of the history. Because the answer turned out.. this one was exactly what we expected, because we [inaudible] updated a model ahead of time, of what it ought to look like. And there were a lot of people who were unhappy with the result that we got. So there was a Congressman named John Dingell who.. fairly famous guy, and he made us a target for our investigation, which was quite an experience. Two people moved to Durham and followed me around everywhere I went after that, and many other stories to tell about it. But the university backed me to the hilt. And you know, I'd have to say the FDA backed me to the hilt. And it turned out our data were analyzed by all sorts of different people. They all got the same answer. So it worked out fine, but it was pretty harrowing. I had stories written about me in the News & Observer that I was evil because we'd done this work with industry and all sorts of things like that.

JM 1:36:58
What has been your approach, or ethics of engagement, to public-private partnerships, and working with industry, working with companies?

RC 1:37:07
Yeah, it's obviously really complicated. My general view is that, there's an element of healthcare which is human, and there's an element of healthcare which is technological. So the companies that make the technology that enables treatment or diagnosis to be more effective, if we don't work together, how are we ever going to advance the technology in the way it needs to be advanced? But I also believe it ought to be done by a set of rules about how the engagement is done. And it's still not completely worked out. But I would say the general strategy that we developed was we would contract with.. let's say, there was a new treatment that might be effective. Or a company wanted to evaluate its treatment already on the market versus something else. We would form an academic steering committee, we would manage the data, we would manage the trial. They would be able to sit on the steering committee, so they weren't ignorant about what was going on, after all, these things cost a lot of money because you're dealing with a human experiment done in the setting of clinical care. And then we would do the analysis and publish the results.

And that worked really well when we were in a dominant position in cardiology. What I learned when we tried to do this in other areas, is most other areas of medicine don't work that way. And it's sort of gone back and forth, and it's still not quite the way it ought to be right now, in my opinion. For the most part, the medical products industry controls its own trials. There's a lot more transparency now than there used to be. But the issue of how the studies are designed and sort of what questions get asked.. much more control about the medical products industry than they should [have]. On the other hand, one thing I like to point out is when we use the word industry, it's almost like the doctors and the academic systems are saying, "We're the good guys,

and they're the bad guys," and we have to interact sometimes. But if you look at it, the health delivery industry is enormous compared to the medical products industry. And while systems like the Duke Health System are not-for-profit, not realizing it's an industry, I think, is a big mistake.

Or the way I like to say it, try publishing a result of a study that would show that a big profit-making procedure done at an academic medical center is useless. It can be rough. So, it gets back to this saying that "we are all sinners," and it's really the rules of the game that turn out to be important. Now I actually had to deal with Senator Warren in great detail about this, because she started out thinking I was another bad industry person. We spent many hours together, I actually had to make a list of all the clinical trials I had led. There were 64. And what the results were, who had sponsored the study, whether result helped the sponsor or hurt them. I don't know if it's good or bad, but the majority of trials that I lead had a negative result for the sponsor. And I think as we discussed it, I think she came to realize that it's better to engage the clinical community with the industry, and do the tests, and report the results, honestly. So that's that's sort of the schema.

JM 1:41:12
And you've also done a lot of work, Duke Forge is committed to to open data practices in medical research, so I imagine that when you're also working with companies that are proprietary about what they're doing, that is an interesting mix. But [open data] has obviously been a priority of yours.

RC 1:41:32
It is. I would just point out though, one of the things that I worked on through a good part of my career is clinicaltrials.gov. And the idea here was: if you going to do a human experiment, part of the consent is that you're doing it to create generalizable knowledge. You're not doing it to help that individual. By the way, that's something that recently has gotten out of control again, the idea that a clinical trial is a way to get yourself a better treatment. It's really to learn, so that future people can get a better treatment. Because particularly with experimental drugs, 90% of them don't work. But clinicaltrials.gov was the idea that the government would run a registry into which you're required to submit your data. Very much opposed by the medical products industry to start with, but through a series of laws that were passed and requirements of the government, the last one finalized while I was Commissioner, which was really fun and interesting. What's happened now is that the industry is following the rules. They're putting their results in. It's academia that's not doing the job. So when we talk about suppressing and hoarding data, I'm sorry, I think academia makes industry look really good right now.

JM 1:43:00
Well, I have many more questions for you. But I thought I would just end with one that's a little more general. So you've talked a lot throughout this interview about the importance of honesty, teamwork, building a team around you that can hold you accountable. So, do you have another example of that that you'd like to share, and how that shaped your work?

RC 1:43:29

Yeah, that's that's a little bit... I don't think I want to say what initially comes to mind there [laugh]. What I what I would say, and this is very political, but I was surprised by the ambiance of the Obama Biden team. I felt like when I was in the White House with them, it was always the smartest people they could find on whatever the topic was. And it was an odd team because Obama was very left brain, very analytical, very mathematical, actually, which is unusual for a lawyer. Biden is almost completely right brain, he lives on stories. But the combination, creating an atmosphere where people said what they thought, and they felt like they were working on a team for a purpose. And I think if you talk to anybody that was involved in the HHS environment at the time, they felt like if we just had four more years with that team, yeah, forget all the other political stuff, just talking about health. It was an extraordinary.. I got to work very closely with Francis Collins, who's still head of the NIH, and who I admire a lot. I just saw David Shulkin, who was an Assistant Secretary, he stayed on the run the VA for a while. And we were sort of reminiscing about this. And interestingly, now in my next career at Google, it was just announced that Karen DeSalvo was the Assistant Secretary for Health and Human Services is going to be a colleague there. And Kristie Canegallo, another person I admire. And her story, I think may be a good one to recount. Kristie worked for Republican and Democrat administrations, was the administrator in the green zone in Afghanistan for a while, I mean, she's tough. She became Obama's sort of super project manager for difficult projects, particularly in health. So the Precision Medicine Initiative was her baby to work on, which we all really liked working on. It's now called All Of Us. It's the biggest NIH project. Christy's now the Head of Trust and Security at Google. So we'll be working together again.

I'd also like to come back to Joe Greenfield. There was an era at Duke that I think was quite remarkable, in terms of leadership. And I'd start with Terry Sanford who came in as president during those tumultuous times. We called him Uncle Terry. He just knew how to convince people of a direction to go that would be new and different, like, [inaudible], elementary education in the state of North Carolina, I mean, he just knew how to make things happen. And then he was succeeded by Nan Keohane, who I thought was quite an astounding leader in terms of just guiding things. But then at the local level in the medical school, we had an era with Dr. Stead, and then at the same time we had David Sabiston heading Surgery and Joe Greenfield heading Medicine, and they were people, you know, I could give long lectures about their faults, they were not perfect. They had some really significant faults. But the one thing they did, was they saw where the future was going, and they bet on young people and backed them up to be disruptive. And I think that really made a difference and enabled Duke to rise from being sort of a well-known Southern University to having the national and international reputation that it has. So through it all, I think leadership telling it like it is, even when it's painful really is something important to keep in mind.

JM 1:48:02
I read the Dr. Stead would send you an unusual Christmas card each year?

RC 1:48:07
Every Christmas I'd get a handwritten letter that would tell me all the things I'd done wrong. And also he told me how much money he was donating to Vanderbilt because he was mad at Duke. But I think honest feedback in life is one of the most valuable things that you can get. One other

leadership story that is not a Duke one, when I went to UCSF Jim Wyngaarden was our Chair of Medicine. As I say he was a distinguished gentlemen. His best friend was Holly Smith, who was the Chair of Medicine at UCSF. And Holly gave this great after dinner lecture after he retired, we kept up all the time because it turned out our daughter had congenital heart disease and had a big operation when I was an intern, I spent a lot of my internship year hanging out in the ICU at UCSF while she was recovering. So we became relatively close, Holly gave a lecture called "Academic Sex". And everybody was mystified, like "What could this possibly be?" And it turned out it was about progeny. And this point was that the amazing thing about academia is, your real purpose is to transmit the ability to learn to the next generation, and the true measure of success is not what you've done yourself. It's what all the people did, who you've trained and educated. And I think that's very much at the heart of what a university is about.

JM 1:49:53
Well, Dr. Califf, thank you so much for spending this time with me today, and congratulations on your new role.

RC 1:50:01
You bet. Thank you.