DIVISION OF CANCER PREVENTION

ORAL HISTORY PROJECT

INTERVIEW WITH

Dr. Lori Minasian

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Biographical Statement

Dr. Lori M. Minasian currently serves as the Chief of the Community Oncology and Prevention Trials Research Group at the Division of Cancer Prevention, National Cancer Institute, National Health Institutes. In 1983 Dr. Minasian received a Bachelor of Arts Degree in Mathematics. She later received a medical degree from The George Washington University School of Medicine in 1987. During the early to mid-1990s, Dr. Minasian served as an instructor and Assistant Professor at Cornell University Medical College, the Memorial Sloan-Kettering Cancer Center, the Memorial Hospital for Cancer and Allied Disease, and the Medical College of Georgia. In 1996 she joined the Community Oncology and Rehabilitation Branch and served as the Program Director and Branch Chief from 1996 to 1999. In conjunction with her work with the Warren G. Magnuson Clinical Center, Dr. Minasian became the Chief of the Community Oncology and Prevention Trials Research Group at the Division of Cancer Prevention in 2000.

This interview covers Dr. Minasian's contributions to the Division of Cancer Prevention and her role in the community oncology and prevention trial programs. In particular, she discusses the process of deciding which types of cancer or agents should be targeted and the need to reframe the next generation of prevention trials.

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Interview with Lori Minasian
Conducted on December 9, 2008, by Philip L. Cantelon

PC: I'm speaking with Dr. Lori, that's L-O-R-I, Minasian, M-I-N-A-S-I-A-N, on December 9th, 2008. And I have permission to record the call?

LM: Yes.

PC: Thank you. I would like to start out some background a bit. It struck me as a bit unusual, perhaps, for a math major to wind up in oncology.

LM: Yes. [Laughter] That is true. I think – well, I mean I enjoyed math, but I was also very much interested in working with and for people. And math can be a very – a job that's very sort of isolated. I mean, you can – the options for working with people end up being more applied math, either, you know, as a professor or in an engineering field or something along those lines. And when I was at – when I was getting my math major, most of my friends in the math world were joining, you know – joining companies that contract with the Defense Department. And I was – I was less interested in that, and I was always interested in medicine. So where it crosses, where my math background has served me the best is in the clinical trials perspective.

PC: Uh-huh. In terms of statistics, in terms of –

LM: Well, I think somewhat in terms of statistics, but more really fundamental in terms of logic. I guess the rationale in the design of studies and things of that sort.

PC: You mean, in a – I was going to say natural order, but it's giving it an order, formal order?

LM: Yes. Trying to bring order out of chaos. Yes.

PC: [Laughter]. Is that theoretical math or applied math?

LM: That's applied math. Bringing chaos – bringing order to chaos is applied math, very clearly.

PC: Chaos out of order is something else.

LM: Right. And requires a lot of psycho-social support [laughter], which oncology requires too.

PC: And after you graduated from UCLA, you went on to a medical degree?

LM: Yes.

PC: But you then went in internal medicine, and you –

LM: Oh, you have to.

PC: Oh, okay.

LM: Training in the broad world of medicine and then you sort of choose your area, your general area be it pediatrics, surgery, internal medicine, GYN. You choose a broad area. And then from that, if you have an interest in cancer, then there is further training in that broad area in oncology. So if you're interested in peds oncology, you do your pediatric training first, and then you do pediatric oncology training.

PC: Uh-huh.

LM: So I was – I like general internal medicine, and then oncology as a subspecialty from that.

PC: And is that what attracted you to GW?

LM: Oh, no. I mean, what attracted me to GW was the fact that, at that time, there were lots of people applying to medical school, and there weren't that many spots. And most of the California places were pretty locked up. So, you know, there was a good 20 to 30 percent of GW's class were California State residents.

PC: And the reason you picked GW was?

LM: It picked me.

PC: Because it picked you. Well, that's often the case with graduate school [laughter]. And then tell me the progression from there into oncology. Because initially, you were into treatment, reading your CV.

LM: I was interested in – actually, at the time that I finished my medical school, I was unsure that I was going to go into oncology. I mean, I had an interest in it, but I wasn't really sure that that's where I was going to end up. And then I did internal medicine because – well, because I liked sort of the whole perspective, the logic that went into thinking about and taking care of patients, as well as the psycho-social piece to it. And then when I was in my internal medicine training, it became clear that my interest in cancer grew, and that was the area that I wanted to make my specialty. And so from there, then I applied to a variety of oncology fellowship training programs. I got into Memorial Sloan Kettering Cancer Center. I was very interested in the program they had there. My then-boyfriend, soon-to-be husband, was already at Yale, and so it made perfect sense. My training at Sloan Kettering was phenomenal. I couldn't have had the training that I got there, elsewhere. The training spanned the care of patients, research and oncology research. Some in drug development, some in clinical trials, but also training in clinical trials methodology, which was really not something people were getting elsewhere in the early 1990s.

PC: And the math background, I take it, helped in that as well.

LM: Oh, yeah. Oh, yeah.

PC: Yeah. And in looking at – because I know some of the earlier papers you did were on Interleukin-2 and Interferon, which –

LM: A lot of things happen because you happen to be in the right place at the right time. Let me ask you a question, though, before. Are we doing this on me, or are we doing this on the division?

PC: Both.

LM: Oh, okay. Fair enough.

PC: The answer is yes.

LM: [Laughter]. Okay. Go on.

PC: And which was all – this was early cancer treatment drugs, I guess.

LM: Oh, yeah.

PC: And I'm curious what took you away from that and then into cancer prevention rather than treatment.

LM: Oh, a lot of things are very serendipitous, and this was classic. I did my fellowship training with – in two different areas. I did it in melanoma, and worked with somebody who spent his whole life in kidney cancer. And immunotherapy and Interleukin were the hallmark methods for treating both melanoma and kidney cancer at that time. Then I went down to the Medical College of Georgia. So I had done some work at Memorial in melanoma and kidney cancer, and then I find myself at the Medical College of Georgia with very limited resources. I went from someplace that had huge amounts of support for their young investigators, for their clinical investigators, to a place that had expectations that the clinicians were, basically, there as a service function. And research happened if you got your funding. If you got NIH grants, that was wonderful, but you know, your function as a physician was clinical service. There were some clinical research activities there, and I did work with a couple of different investigators down there. But the truth of the matter is the opportunities were relatively limited. For a variety of reasons, I came up to NIH and, again, sort of found myself in the Division of Cancer Prevention, and that's sort of how it all happened.

PC: The Community Oncology and Rehabilitation Branch.

LM: That is the old name, yeah.

PC: — was the old name for DCP.

LM: Uh-huh. It was the old name for the branch that housed my program in DCP. The old name for DCP was the Division of Cancer Prevention and Control –

PC: Correct, yes.

LM: And then in DCPC, the branch that the CCOP program was in was the Community Oncology and Rehabilitation Branch.

PC: Okay.

LM: Okay. But when they restructured the division and turned it into the Division of Cancer Prevention and the Division of Cancer Control and Population Sciences, that's when all of the branches were redone. And the branch that I was in became the Community Oncology and Prevention Trials Research Group. The name changed but the function remained the same.

PC: Where did the rehabilitation part come in?

LM: The rehabilitation part was really a research focus. We called it rehabilitation, but really what it was, was the pieces of supportive care that accompany some of the work that was done in the CCOP program. The CCOPs participate in Cooperative Group treatment trials ,which are reviewed and approved by CTEP (Cancer Therapy and Evaluation

Program) in DCTD (Division of Cancer Treatment and Diagnosis). The CCOP program funds and oversees the prevention trails in the Division of Cancer Prevention. But the CCOP program also has a focus on supportive care, end of life, symptom management, and quality of life, which was what the rehabilitation part was supposed to encompass. Rehabilitation was never the best descriptor because it wasn't really rehab. Rehab suggests that you are less functional, and you're going to actively do something to regain your function. The supportive care focus is on providing amelioration of short and long term toxicities of treatment.

PC: Correct. I think of that in terms of polio, for example.

LM: Right. While there is functional loss in cancer patients during chemotherapy and there is research to try and regain function, it is not really the same as, say, cardiac rehab or stroke rehab. Both cardiac and stroke rehab have this connotation of building back strength. There's never been an oncology rehab program that is the same type of thing. So rehab was not ever really the best descriptor. The reason why I think rehab was used, because it was a single term that encompassed many different pieces, but it was a sub-optimal term. The issues in supportive care need to address side effects from treatment during more than just chemotherapy. It could be radiation or surgery. The research focus should be on things done either before, after, or during treatment in an attempt to either prevent loss of function or regain function once it's been lost. But that is different from what is fully encompassed as either cardiac or stroke rehab. Because cancer treatments

are so varied and the potential loss of function depends on the type of cancer and the type of treatment, there's no standard way to "rehabilitate" cancer patients.

PC: And in – why did you – how did you get recruited to come up here? Let me put it that way.

LM: Oh, I knew somebody who knew that there was a job opening. He said, "Well, you should come up and interview for this job." I asked, "Well, what does the job entail?" "Well, you should come up and interview for this job." [Laughter]. That's how it all happened.

PC: And who did you interview with?

LM: Leslie. I interviewed with Leslie Ford. I didn't know her at the time, but I interviewed with her.

PC: And what were they looking for?

LM: They were looking for a medical oncologist that knew clinical trials and knew something about the care of patients. They wanted somebody who had some practical hands-on experience, as well as understood clinical trials who could really speak to the investigators in the program.

PC: And this was an intramural or extramural program –

LM: Extramural program.

PC: — that you were running? Extramural.

LM: Uh-huh.

PC: And how did you – or how did the division set the agenda for that program?

LM: Clarify that.

PC: Well, usually – did they come to you with what they want to do, or did you set an agenda for the kind of clinical trials that you thought would –

LM: Oh, it was a combination. When I came to the program, both the breast cancer and the prostate cancer prevention trials were up and running. So that agenda was already set. There was some work in developing other kinds of trials to engage in. Do we want to have a colon cancer prevention trial? There was already a division-level set agenda with respect to sort of the high-profile prevention trials. Then with respect to some of the trials that would be under the rubric of the rehab, the supportive care or the quality of life, or the symptom management, that was not considered to have the same priority level. It

took a considerable amount of time to get a feel for what the level of interest was in the investigator community, as well as the capacity and the feasibility of the network.

PC: Were there a number of people – well, let me put it this way, a critical mass of people working in cancer prevention?

LM: There's a significant community now that has grown over the past thirty years in size and scope in the cancer treatment and the therapeutic world. There is a much smaller community in cancer prevention. There is a small core group of investigators in cancer prevention research. I think some of it stems from the fact that it takes so long for prevention trials to run. Some of it stems from the fact that you really need a good handle on the biology of carcinogenesis. We're really just now getting to the point where the targeted agents may have a significant hypothesis for how to prevent cancer. The question is which agents to choose, how to sequence them, how to think about using them for prevention. There are potential mechanisms for carcinogenesis; potential agents to target those mechanisms, and now you have investigators coming from the therapeutic world that are trying to understand the earliest steps in carcinogenesis that are thinking about how early can we start this. There's this tension about what's earliest treatment versus what's true prevention. And the FDA doesn't even call it prevention. The FDA says "risk reduction." You know, the indications that we have for Tamoxifen, Raloxifene and Celebrex are all risk-reduction indications, they're not prevention indications.

PC: Uh-huh. And how has the long view of prevention versus treatment at NIH? –

LM: Tension.

PC: Yes, [laughter], the tension between that and the tradition of being disease-treatment oriented rather than preventive oriented, I guess, prevention oriented, in NCI. How has that had an impact on the division?

LM: Well, let's – I'm going to take that question from a different perspective, okay?

PC: Uh-huh.

LM: Because there's all kinds of politics that have gone on between the NCI and the division level that I'm not going to go into. However, I think we can look to something that's been happening in cardiology for a while. Certainly, oncologists look to cardiology because they've used bio markers in their disease trials. But more importantly and more fundamental about this tension between treatment and prevention is what is happening in terms of clinical practice for the prevention and treatment for cardiovascular disease. Certainly, the cardiologists are at the forefront and remain at the forefront of treating active cardiac disease or cardiovascular disease. Nothing's changed that. That being said, there's been a huge amount of work in cardiovascular disease prevention, in terms of controlling hypertension, controlling lipid levels, lifestyle interventions. This is done by

internists who are extremely well trained in both the prevention and early treatment of cardiovascular disease.

And when things become either very complicated, or even somewhat complicated, the referrals to cardiologists are relatively quick and relatively – I can't say seamless, (because nothing's seamless in the current system). The cardiologists get involved in the design of the early cardiovascular disease prevention trials, but they're also actively involved in treatment trials. There seems to be a sense that the internists need to be on the first line of cardiovascular disease prevention, and possibly even the very first lines of treatment, but there is this interplay between referrals and discussion of what is involved in prevention of cardiovascular disease, and what is involved in treatment. Can we get oncology to that point? Right now, once a patient is diagnosed with cancer, immediately everybody suddenly takes a step back. Your internist, your non-oncologist takes a step back and says, "It's now time for the cancer specialist." Boom, that's it. As opposed to the oncologist will take care of the cancer, and we'll take care of everything else. Or we'll do some supportive care involved, no, it's like now the oncologist becomes a primary care physician for the cancer patient.

PC: In cancer prevention, it seems that there are a couple of levels here. One is a public health issue.

LM: Yes.

PC: And the other is more specific clinical towards specific cancers. Do I read that correctly, or –

LM: One of the public health issues is the concept that cancer is one disease. Many in the public see cancer as one disease entity. However, not all cancers are the same. The carcinogenesis process for breast cancer may be substantially different from colon cancer, may be different from head and neck cancer. Carcinogenesis is not one process that applies absolutely the same to all the different cell lines in the body. It appears to be quite different. Cervical cancer, head and neck cancer may be virally mediated. Hepatomas may be virally mediated. And then you have other cancers that may not be virally mediated. If you're thinking that cancer prevention is going to be the interruption of the cancer process, then you got to know the cancer process, and you've got to figure out what's the pivotal place to interrupt that process and return back to normal. And it may not be that the same process to prevent cancer in every cell line. It may be that there are a couple of different processes. And just like we vaccinate against multiple different types of infectious agents, we might have to consider a couple of different strategies for reducing the highest prevalence cancers, or we may have to move from a concept of treating everybody, thinking of population cancer prevention to thinking about targeted cancer prevention.

PC: And where will genomic, advances in genomic research fit into that?

LM: Well, advances in genomic research would feed very much into the idea of targeted cancer prevention, so that if you know that you're at risk for these three cancers or this one cancer, perhaps your cancer-prevention strategy is different from someone who is baseline risk.

PC: And what's the impact of that on community trials?

LM: Well, there's potentially a huge impact, depending upon where the prevention trials go. The last four large prevention trials have basically been recruiting the general population, or in the case of breast cancer, the higher risk population, but from a general population. There hasn't been a requirement to date of requiring some sort of a screening blood test before you could be considered eligible for a prevention trial, and we may be moving towards that. But other diseases may be moving towards that as well. There's going to be a need to think about disease somewhat differently as we understand and unfold what the genome is trying to tell us. From my perspective, just understanding what the genome says is like finding the alphabet or like finding a dictionary. Even with a dictionary you don't have the tools to understand the language. You can understand the words, possibly, you can translate the words, but you don't really get the meaning that you do from a sentence based upon the context, the idioms, the culture, all of that falls into understanding the language. And we're quite a ways from understanding the language of how to translate the genome into practical medicine.

PC: No Rosetta Stone yet.

LM: No Rosetta Stone yet.

PC: Could you describe for me the changes in the community oncology program over the, let's say, the last two decades?

LM: Oh, there's been considerable change. One of the most apparent changes is the complexity in the level of the clinical trials. When the trials started 20 years ago, they were rather thin. The trials were simple and the protocol documents were thin. It was very specific. There were a lot of regulatory issues involved. You had your IRB, and you had oversight. But the amount of regulatory barriers or hurdles was much smaller. The consent forms were much simpler, and the design of the trials were much simpler. Twenty years ago, we were looking to see if any chemotherapy agent reduced a recurrence rate. Now, we have several different successful regimens and we have lengthened the time from diagnosis to death. We have a growing number of cancer survivors and we are looking to make more improvements.

Most of the treatment clinical trials that were started in the 1980s had few survivors. Now, twenty-plus years from now, thirty years now, we have a growing number of survivors. So we have had success. But now the trials, to show even more success, have to be larger, somewhat more complicated, and the regulatory oversight is more complicated as well. The trials are larger because what we're looking for is incremental

benefit over the already-successful regimen. So we're trying to take a successful regimen and make it more successful by adding additional things to it.

PC: And these different regimens, have they changed as well?

LM: Over time, yeah.

PC: For example?

LM: Well, we can start – using the breast cancer analogy. We, in the early 90s, had treated most women with early-stage breast cancer with Adriamycin and Cytoxan (AC). Then we found that adding Taxol decreased the rate of recurrence and improved survival. Then we found out that Herceptin could improve survival if you were HER2 positive. Now you have a much more complicated regimen that involved three chemotherapy agents, a targeted agent, and possibly also hormonal therapy depending on whether or not the patient is hormone responsive. We have gone from a time when very few things worked to a time when we have several effective agents and we're adding them on top, and potentially, lengthening the time of treatment. But the numbers of survivors is also increasing.

PC: So in this case, we're preventing a return –

LM: Right.

PC: As opposed for prevention from the beginning.

LM: Right. And that's where the bulk of our success has been, and that's considered adjuvant therapy in cancer, and that's not considered prevention. That's actually treatment. As opposed to, in the cardiovascular disease world, they would consider that prevention. They'd consider that secondary prevention.

PC: But in cancer, this is just called treatment.

LM: Right.

PC: So in the prevention programs, the community oncology program is primarily in the secondary treatments or –

LM: Well, the community clinical oncology program sort of spans both treatment and prevention and cancer control. So under the treatment side of things, everything that I've explained has occurred. And so at the local level, the oncologists have become more sophisticated. The trials, all of the trials have become somewhat more complicated with more regulatory burden. The care that the local oncologists deliver is more complicated and more multi-disciplinary. And that certainly has evolved over time. You're now seeing multi-disciplinary clinics in more rural areas than there ever used to be. So that as trials have changed, cancer care has also changed in order to reflect the results of the

trials. While cancer care doesn't always change with the results of the trials, we do know that those physicians that participate in the trials readily adopt the results. In the same context, the same infrastructure that's been working on the treatment trials has also been focused on symptom management and cancer prevention trials.

We had second generation prevention trials with STAR and the SELECT studies. Those are now winding down and there's been little support for moving forward with the third set of large cancer prevention trials. There is concern about how to understand and approach the prevention trials. Are there agents ready to move forward with quickly, or do we need to take a pause, so to speak, and get a better understanding of what's happening in terms of targeted therapies and reframe some of our prevention questions.

PC: And who are raising these questions, within DCP, or NCI or a larger medical community?

LM: I think within NCI and the larger medical community, as well as within the division. I think the issues are somewhat broader than just the division. So there's been discussion inside the division and discussion inside NCI as well as in the broader community about how to think about agents to bring forward, what information do we need in order to think about how to frame the next generation of trials. But consider also that this has happened within the context of larger trials across NIH too. I mean other disease prevention areas where interventions that have been considered to be low toxicity have been studied across different diseases, and I think people are now beginning to sort of

say, "Okay, it's important to have these large trials, but maybe we need to think about what goes into them, and think about having a strategy for how to bring them forward, and what to move into it so that what we bring in has the highest chance of being successful."

PC: Uh-huh. Is this – is there an old engineering adage that we don't – we learn more from our failures than our successes that has ever come to play here or not?

LM: I think the first thing that we can learn from clinical trials is to expect the unexpected. The Women's Health Initiative was the perfect example. Initially the thought was that it's unethical not to give women estrogen [laughter]. Then you find out, oops, it turns out that estrogen is not as good as everybody thinks it is.

PC: Uh-huh. That comes true with a lot of trials, doesn't it?

LM: It does. But, I mean, that's also part of the strength and the need and the importance of doing the trials.

PC: And in these, has – in setting them up, when I say – well, let me ask this question. How would you define community for me?

LM: Ah, yes. We are defining it in this program as the local level of oncology care. So, essentially, it's local regional. It's where patients actually get the bulk of their oncology

care- the private practices, the community hospitals. There is an interplay with the academic centers where the academic centers are, essentially, the niduses for the scientific, for the scientific design, etcetera, but not the only. We have the community physicians sitting on the scientific committees to develop the study so that there is a good interplay between those that are practicing cancer care in the community, and those that are practicing cancer were in an academic setting. And there's more fluidity now than there ever used to be. Twenty years ago, you went into private practice, or you joined an academic institution, and you were there for the long haul. Now people are moving five, ten years, and there's not just one place they practice their entire lives.

PC: What about – is the nursing community part of this as well?

LM: Oh, absolutely. It really is thought to be at the team level with the physicians and the nurses and, potentially, other support people there as well.

PC: And when you – what about the funding for this? Is this funded both out of the division and at the local level or the matching funds? How –

LM: There's no requirement for matching funds, but it is very clear that the majority of CCOPs, and minority-based CCOPs, bring institutional support to the activity. And it is felt that institutional support is something that is in everybody's best interest, not just from the monetary or financial perspective, but more from a perspective of really integrating the whole program into that community setting—for instance, a community

hospital may be the grantee organization, and may actually be the recipient of the grant, but that grant then provides an umbrella, and a means by which the community hospital, in conjunction with its cancer program then will galvanize to offer research. Potentially, there will be offshoots from that, not just the clinical trials but also, they'll start to develop programs internal to that community that will feed one another, so it becomes much bigger than just the grant itself.

PC: And what – how do you guarantee that this will continue over the length of time needed to make the – I suppose, the statistical results valid?

LM: Well, I mean part of the reason for funding them through a grant is to make the funding commitment over time. So that it's not just a year-to-year, such that if they don't get money that year, well, they have no ability to continue that activity. It's meant to be an ongoing research activity that the institution and the community invests in. That's part of the reason for having the institutional support. It's an investment. We're going to start this project. It's going to take some time to get started, but it's a long-term commitment, it's not a short-term thing.

PC: And they are – and in that long-term commitment, they have to reciprocate with one of their own, I take it.

LM: Yes.

PC: And when you say when people move –

LM: Oh –

PC: Does that mean the PI's will move too?

LM: Oh, potentially, yes. But the program is such that even if the PI moves, he or she can still be involved in the trials. It is possible to move and still maintain your interest and your involvement in the whole program because it's a national program, it's not a regional or a local program. We've actually had patients be able to move as a result. When Katrina hit, patients went all over the country. And those patients that were on clinical trials that knew which trials they were on were able to continue their clinical trial participation because there were sites across the country.

PC: Doing the same –

LM: Yes. Yes.

PC: Uh-huh. How is the Community Oncology Program integrated into the other aspects of the Division of Cancer Protection – or Prevention, I'm sorry.

LM: Prevention. This program is integrated into the cooperative groups. And to the extent that the rest of the division is involved in the cooperative groups, it's fully integrated.

But most of the division is not involved in the cooperative groups. And so we use expertise in the division, we try and share, you know, expertise across the programs. It's not always clear that all the other programs in the division are applicable to the Community Clinical Oncology Program. But in some cases, in the drug development side, in the Phase I/Phase II side, there are some CCOPs that participate in the Phase II consortium for the development of prevention agents.

PC: And it strikes me, for so many years, Peter has been the leader of this group, and – does he still set the tone for what the Division of Cancer Prevention is doing?

LM: Yes.

PC: Could you explain that to an outsider?

LM: Well, you know, he – well, from a structural and an organizational perspective, we have meetings on a fairly regular basis. Usually, it's a couple times a month with all the branch chiefs, and we talk about issues of scientific importance, issues of administrative importance. It's a meeting where we do, basically, the work of the division. There are some administrative things that have to be done, but there's also a fair amount of science, an attempt to share across the division what's going on. We've had retreats over the years where we present to one another some of the interesting findings from the studies, some of the interesting research activities in an effort to try and bridge the different programs in the division according to the priorities that are set by the division and set by Peter as

well. So we've had scientific retreats where we'll talk about what things are going on in the different programs, where the science seems to be moving and prioritize the areas for all of us to think about and foster amongst our investigators.

PC: And how is it determined which funding goes where within the division?

LM: It's a combination of where the grants are, and how well they compete in peer review, that's one piece of it. In fact, that's the biggest piece of it, I think. One of the issues in prevention is that so many of the initiatives that have been started are very, very long-term initiatives. There needs to be a balance between maintaining the commitment to the long-term commitments, as well as identifying new opportunities to tap into. So the PLCO was started, the screening trial for Prostate, Lung, Colorectal and Ovarian Cancer was started in the 1980s with early screening technology and early in the 2000s, the whole issue of CT scan screening came up. Through the PLCO network of investigators, they were able to get up and running rather quickly a randomized control CT scan screening study for lung cancer. That was an opportunity built on an existing infrastructure to answer a very pertinent timely question, and the answer will be coming within the next 18 months, I think. The CT scan screening study (NLST) could not have been initiated as effectively or efficiently if the PLCO network did not exist.

PC: Indeed, the announcement was about, I guess, two weeks ago now that the cancer rates have been dropping.

LM: Right.

PC: That should've given the division some kind of positive –

LM: Well, some of it happened serendipitously. When you look at the ACS graphs and you can see what's happening with the incidence and the mortality, I mean it's not like anybody ever implemented a public policy to reduce stomach cancer. And yet, stomach cancer has plummeted over the last century. And there's speculation, but colon cancer in men has dropped and, you know, that was probably – and in women has dropped, and that was probably a combination of the availability of NSAIDs and of polypectomy and colonoscopies. Yet nobody implemented a national health policy in those regards. So there's a combination of things going on in terms of what actually impacts your cancer incidence rate. And there are certainly some things that we could do. Part of the reason why we think the breast cancer incidence are dropping is because, after the Women's Health Initiative, women were tossing out estrogen. You can actually correlate the drop in the prescription rates for estrogen. There are clearly some things linked, and then there are other things that it's not clear. So everybody's happy that both the mortality and the incidences are dropping, but not all of it is fully explainable, or the direct result of a cohesive policy.

PC: This gets me back to the public health issues. That is, especially when you're doing community studies, as these get announced, it goes into the – I guess the realm of public

health an announcement about how important it is to get the colonoscopies, which I think in my father's generation probably wasn't a – at least I never heard it was very common.

LM: Right.

PC: But certainly in the last thirty years has been, twenty-five years maybe.

LM: Yeah. The – okay, so I guess I missed the question. Maybe I'm spacing.

PC: Well, I guess I'm wondering does this automatically spill over, especially when you're doing these studies at the local level and you say working with the local medical community, that's really the seed of getting this out, as it was, you mentioned for cardiovascular diseases. So it seemed to me it's also happening with cancer, with advanced diagnoses early on, and then saying that, "Well, you shouldn't – you should be doing this. More mammograms, more –" well, even though – I guess that one's now come up, there was some question the last time.

LM: Well I think the part of this really also is, yes, we are working with the community, and there are some things that translate very quickly. Most of what translates relatively quickly is on the treatment side because the investigators at the community level that are involved are, for the most part, oncologists, whether they're medical oncologists, pediatric, gyn, they're all oncologists. So the treatment pieces seem to translate relatively – relatively quickly, at least the investigators within the community adopt the research

findings into their practices so that they're – they're practice-wide benefits from the fact that they've been participating in the research and not just the patients that are on the studies. So that's a fairly profound amount of dissemination about the research findings and the improvement in cancer care at the community level. That being said, beyond that in terms of prevention is a little harder because the oncology community isn't as engaged in the delivery of what would be considered prevention modalities. The people that come to the oncologists have cancer. We are beginning to see more family members of at-risk women come to the oncologists for a discussion about risk because the internists, at this point in time, are not as adept in discussing the risk for cancer as the oncologists are. And for the most part, this is now, right at this point in time, pretty much limited to what we know about hereditary cancer. So BRCA1 and 2. What we are seeing is breast oncologists delivering some counseling recommendations to family members of BRCA1 and 2 mutation carriers. We're not necessarily seeing that in non-oncology practices. We also are not necessarily seeing the discussion about at-risk women for BRCA1 and 2 at the family practice, the internists level. We're seeing much more of that occurring at the level of the oncologists. And, not all oncologists. So it's a little harder to bring the prevention constructs out of oncology and back into internal medicine.

PC: Why do you think that's the case?

LM: I think it's because all of the research that is happening in risk is happening in oncology. And at the practical level, what happens in terms of the identification of these at-risk people is coming through family members. So you'll have the family come to the

oncologist because one member has cancer. They'll do a family history and they start counseling in the context of – they take care of the patient, but they also start counseling the rest of the individuals as to what, because then that becomes the discussion of, "Well, what is my risk?" The quintessential scenario is the woman with breast cancer who's a BRCA1 or 2 mutation carrier who comes in to the oncologist with her sister and her daughter. You talk to the patient, but you also end up counseling the sister and daughter about what they should be doing as well. And it's not something that is a discussion that they're having with their internist.

PC: Uh-huh. I understand. Which of the programs would you highlight as your – as you think being most successful out of the community programs since you've been running them.

LM: You mean in terms of across the country the different programs?

PC: Yeah.

LM: We have – actually, we have several. There's one in Wichita, in Wichita, Kansas, there's on in Delaware, there's one in the south that encompasses multiple states. But those are the ones that are high accruers, high data, data quality. Those are the big guns successes. I would also say we have small successes because we do have communities that have steadily been involved in cancer research for two decades that do a wonderful consistent high-quality job in smaller communities as well, in Iowa, in parts of rural Illinois, parts of

South Dakota. The Midwest and the South have been tremendously good for smaller communities. I mean this program is wonderful for smaller communities because it galvanizes the whole community around the idea of contributing and helping out for cancer and cancer research.

PC: And do they come to you – for example, there was a – I've forgotten the name of it. Is it Anniston in Alabama where they had all the chemical plants, and there was a high incidence of cancer? Would a place like that come in as a community, or is that too, is that –

LM: That's too –

PC: It's an anomaly and not what you'd want to take.

LM: Right, right.

PC: The anomaly then.

LM: It's more the anomaly.

PC: You'd rather do something –

LM: Well, we do best by working through the oncologists, as opposed by working directly with the community. It's the community oncologist that we form the relationship with. And the community oncologists work within their community to develop the program.

PC: And this is a group that has been growing over the past twenty years.

LM: It has grown over the past twenty years. It's been really hard the last, I'd say, six years with the budget kind of, you know, being fixed for multiple years now, it's been a little hard, it's been much harder to grow the program. We've done well by sort of consolidating – consolidating is not the right word. We've done better by identifying which are the success – you know, which programs are keeping their infrastructure in place, which ones have a weak infrastructure and maybe need to rethink the program. So we have new CCOPs and we have lost old CCOPs. We haven't had a huge influx to be able to support significant further growth. But I would say at the same token, it's not just the dollars that NIH provides. It's also the dollars at the local level. And we're hearing much more these days about difficulties at the local level because of reduced reimbursements for medical care, and I'm very concerned that the financial situation in the country, the economic situation in the country is going to have a bigger impact on the program in general than, potentially, the funding that NIH can or cannot provide.

PC: Has there been any tradition of outside funding by outside private groups?

LM: Not outside funding to NIH or NCI to –

PC: No, no, into the communities, I mean.

LM: Oh, well, yeah.

PC: That would tie into the –

LM: Well, yes, they are, there are. I mean, depending on the community, there is fundraising done at the local level. As I said, I mean what happens is the grant provides a platform for a program. That program involves fundraising at the local level to help support those things that are not covered in the NIH grant.

PC: And would they go to other medical funding or foundations like Johnson –

LM: Well, they already do.

PC: — Hughes?

LM: So some of the CCOPs get an Avon grant. Some – they can't go to Hughes because Hughes is science based, you know. Where they do the best is go to those – there are research, there are foundations that provide the support for the research to happen. So the Komen Foundation, Avon, other things like that where they're raising money and they

provide additional money. Whereas Howard Hughes is basically funding specific investigators to do specific science.

PC: Right.

LM: That's not applicable to the community.

PC: Okay. Uh-huh. And that would be the same as the Johnson Foundation or anything like that.

LM: Yeah.

PC: What haven't we – what have I missed that we – that is important to get in here?

LM: Well, I mean, I think we've been fortunate in oncology that we have had so many oncologists participate in the program that we really do see a translation of the research results into practice across the country. I think cancer care has improved because so many physicians are involved, and there is – by being involved, they take ownership in the research themselves, and by taking ownership then, want to be at the forefront of providing the best-quality care. And I think, honestly, the physicians engaged and involved in this program believe that and that is their prime motivation. They want to give their patients the best possible care. They feel that participating in science keeps them in the leading edge, and they can do that as a result of offering the studies, and then

offering the regimens, once they're successfully reviewed, to their patients. That's it in a nutshell.

PC: And the future for the Division of Cancer Prevention?

LM: The future for the Division of Cancer Prevention, I think it can be very bright as we get a better understanding of genomics, and a better understanding of carcinogenesis, and possibly tailor our prevention strategies a little bit more to the at-risk population. O ver the next ten years, we're going to identify better profiles for risk, and that has to happen – that almost has to happen first as we move into where we want to go in prevention.

PC: Well, thank you very much.

LM: Oh, you're welcome.

PC: I appreciate it. And if I – I just may also take the opportunity to ask if I need more information to be able to call you back.

LM: Absolutely. Call me back, e-mail me.

PC: Okay.

LM: Especially if you say, "Well, I don't understand what you said here." I'm happy to clarify.

PC: Well, that may occur [laughter]. But thank you very much, and best for the holidays.

LM: Thank you. You too.

PC: Thank you. Bye.

LM: Bye-bye.

[End of Interview]