Dr. Vincent DeVita, Jr., Perspective on the War on Cancer November 8, 2009Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Foss is a Professor of Medical Oncology and Dermatology specializing in the treatment of lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening, Ed and Francine welcome Dr. Vincent DeVita. Dr. DeVita is the Amy and Joseph Perella Professor of Medicine at Yale University, and he is the former Director of the National Cancer Institute and Yale Cancer Center. Chu We are going to be talking about the 'War on Cancer,' and obviously you were there at the National Cancer Institute when all of this started. It was back in the early 1970s when President Nixon formally declared war on cancer and signed into law the National Cancer Act.DeVita There was a very famous philanthropist, Mary Lasker, who was responsible for getting many health initiatives through Congress, and in 1969 when chemotherapy was shown to be able to cure some people with cancer, she became convinced that we had found the missing link and she convinced many of her friends in Congress to put together a commission for the eradication of cancer, a senatorial commission. They then presented an act to Richard Nixon that was rather a radical departure in many ways, and Nixon signed it on December 23, 1971 as a Christmas present to the nation. Since then, we have invested about $55 billion, tax dollars, probably more like $60 billion in cancer research, and it was during the time of the Vietnam War so it was referred to as the 'War on Cancer,' not always a wonderful appellation, but that's how it got going and it has been going for a long time.Foss Can you talk about the money? How is that money actually invested? Was it primarily through the National Cancer Institute, or was it invested in a broad range of programs?DeVita This is an interesting question because Jim Watson just wrote an editorial about this and I wrote something in response. It is often mistakenly thought that all that money went into clinical trials and drug development, things of that sort, 85% of it went into the support of basic research through the ordinary grant program of the NIH, and 15% went into the application of the results of the research. The mandate written into the act, by the way, was a very specific mandate, it said "to support research and the application of the results of research to reduce the incidence, morbidity and mortality from cancer." 85% went to support research and 15% to the application results and we are seeing the impact of the 15% now, and the basic stuff is just coming along and the investment in basic research is really responsible for all the targeted therapies that we are seeing and for molecular diagnostics and so forth. It was heavily skewered towards supporting basic research contrary to Jim Watson's opinion that "they went clinical." I thought it would be worth mentioning that to people.3:24 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3Foss Vince, I think it's important for people to realize how long it actually takes to do the basic research. How long does it take to go literally from a bench discovery, to a bedside treatment of the cancer?DeVita It depends Francine, I mean it's not uncommon for ten years

to lapse. Take a cancer drug, its not uncommon for ten years to lapse from when you find that you have an interesting drug until the time that you get it marketed; that's just one example, many other examples take longer. The treatment for chronic myelogenous leukemia with Gleevec took, if you go all the way back to when they began to talk about using Gleevec to treat the disease, ten years. It was only a few years when they got really excited to get it approved, but people forget that there were eight or nine years of slugging along in the laboratory trying to show that they had a compound that was effective and so forth, so it's a long time. I think one of the mistakes that Mary Lasker made, bless her heart she was referred to as the angel of mercy, was that when the cancer act was passed in 1971, she wanted cancer eradicated by the bicentennial, and once the press realized what was going on they became very angry and felt they were hoodwinked a bit, and by 1974 they were asking how come people were still dying of cancer? That's the kind of criticism that has dogged the 'War on Cancer.' If you look at what's happened, the cancer war has fulfilled the mandate actually very nicely. Mortality rates are coming down, incidence rates are coming down, and cancer therapy is much less morbid if you look back 20-30 years ago, but people still die of cancer and I think if your definition of success is you have to eradicate cancer entirely, then the 'War on Cancer' probably will never succeed because I don't think we will ever be totally free of cancer. But they have fulfilled the mandate very well.Chu It's really quite remarkable, because just within the last about six to eight months, these hundreds of billions of dollars, trillions of dollars, are being spent to save the car industry, and the banking financial industry, and health care, when you talk about an investment of 60 to 70 billion dollars, is a pretty remarkable investment truthfully. DeVita Absolutely, and if you look at the figures, there are some economists from the University of Chicago that have written a paper, it's a wonderful paper and they are not related in any way to the cancer institute, they are just looking at health issues and what a healthy populous means to the economy, and when they got around to cancer they calculated that a 20% reduction in cancer mortality was worth 10 trillion dollars to the economy over a decade. We have seen a 10% decrease in mortality rates from 1990 to the year 2000, probably like 16% now. So, if you look at the investment of $60 billion and the return of $10 trillion in economic terms for a healthier economy, it has a big impact on the issue of healthcare and what you pay for healthcare because this is really an investment in a healthier population, it6:37 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 was a very-very good investment. My daughter is a writer and she is doing this book with me, but she points out that you know bad news sells, good news doesn't, unfortunately, and every time that somebody writes about the 'War on Cancer' in order for you to pay attention to the article they have to start by saying it was a failure and then they talk about how things could be changed to make it better. But it was a quite a success with a lot of blips along the way like the one saying we can get rid of cancer by the bicentennial, but nobody but Mary Lasker believed that, but it caused a lot of grief.Foss So one of the major ways to save money in the 'War on Cancer' is to prevent cancer.DeVita

Yeah.Foss Do you think that screening for cancer really got its start with this act?DeVita Yeah, I started the first cancer prevention programs at the Cancer Institute, and I hired Peter Greenwald who became the head of the Cancer Prevention Program. One of our problems was very early on we didn't know how to prevent cancer, and critics used to say, well your scientists said, and there were two British scientists Doll and Peto who said this, that two thirds of cancers are caused by environmental factors, then we should invest two thirds of our money into cancer prevention, but you could waste a lot of money doing that and it was in the early 1980s that we began to get a handle on a way of prospectively preventing cancer. Unfortunately, Francine, in the long run you do save money by preventing cancer, in the short run its not something that, if you are talking about healthcare proposals, you are going to see on the balance sheet for the next ten years, but we can now actually prevent some cancers, colorectal cancer, you can do a lot to prevent colorectal cancer with drugs that prohibit polyp formation, for example, right now.Chu Where are we with respect to early detection screening of major cancers?DeVita Again, one of the problems with early detection in screening is that you have to be sure that when you find something, you have something you can do for it. It's a little bit like looking at prognostic factors or genes that make you susceptible to a disease. The ability to look and find things like that now is really quite terrific, but the ability to do something about it is not quite as terrific. You can identify women who are at risk for breast cancer, but you are left with taking the breast off rather than giving them something that can prevent breast cancer, at least that's the more effective way of doing it now. We have many-many tools now that can identify abnormalities in people that may lead to cancer that can be used for preventive purposes as soon as we find better ways of preventing it. Still, the major culprit in terms of9:27 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 cancer etiology is cigarette smoke. It has been estimated that something like 40% of all cancers would disappear and mortality rate would drop by about 40% if we could stop everybody from smoking tomorrow. By ten years from now, you would have a 40% decrease in mortality rates from cancer. We have nothing else that's even close to that.Chu That's an important point you raised, because probably the listeners out there think, well cigarette smoking causes lung cancer, but really as you suggest, cigarette smoking has significant implications for a whole host of other cancers.DeVita Cervical cancer is caused by cigarette smoking, and so is bladder cancer. People ask how that can be, but when you inhale, you inhale about a thousand different chemicals and those chemicals get into your blood stream and they circulate and bathe every organ in the body, so there are really quite a few cancers that would diminish significantly, or go away, if it wasn't for exposure of cigarette smoke. There is a lot of data now accumulating that in cities where smoking is banned in bars and restaurants, first of all, the heart attack rate drops very quickly and mortality rates from cancer come down because sidestream smoking is a very potent exposure to tobacco smoke. Again, people ask how can that be, and the answer is that when you inhale a cigarette the person inhaling the cigarette is inhaling through a filter, the person sitting next to you is inhaling sidestream

smoke without any filters at all and all the chemicals are sitting right there, only a smaller dose. So, smoking is still a big culprit and we have done extremely well. Almost 50% of the population smoked three decades ago, and we are now down to something like 20%, it is still a big chunk, but people have gotten the message. When we started at the NIH you would go into a medical meeting and there would be a cloud of smoke over all the doctors.Foss Exactly.DeVita Now, if you pulled a cigarette out, you would be ousted into the street.Foss Vince, people don't really know what to worry about with respect to risk for cancer. People talk about radiation and exposure from CAT scans, and diagnostic radiation, and then they are also worried about environmental pollution and the role that may play in cancer. Can you put this into perspective a little bit for people?DeVita It's interesting because obviously a lot depends upon your exposure, but if you could draw a scale sitting here at the table and then put a bar for the risk from each of those things, environmental pollution probably accounts for 5% of all cancers. Then if you put a bar for cigarette smoking, it would go through the ceiling of this building. Except for a worker who works with aniline dyes, then there may be higher exposure and a risk of bladder cancer. For12:10 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 the average person in the population, the risk of getting cancer from chemical exposure from smoke and from auto exhaust is relatively small. Smoking is still number one on the list. We know diet plays a role in cancer, but we do not really know how to pick apart all the things in diet that might do it. So, generally speaking, the healthy diet, the diet high in foods that are relative low in fat, lots of fruits and vegetables, is a safe way to go because the cultures that have that diet tend to have lower cancer rates. If you don't smoke, and you eat a reasonably healthy diet, then you are doing the best you can now-a-days to prevent cancer and you will live a lot longer.Chu What's your sense of how well we have done in terms of communicating that message, educating the public about the do's and don'ts?DeVita You know, it's very difficult to educate the public, especially in cancer treatment. Everybody wants to prevent cancer and they are willing to listen to almost anybody. There are a lot of nostrums out there and people selling stuff, but for cancer treatment they are not interested unless they get cancer, and so we're broadcasting to an audience of people who don't have cancer, some of them anyhow, many of them, they are not going to be interested in cancer treatment until the day that they are diagnosed with cancer, and then their interest is hyperacute. But since the majority of people in the country don't have cancer, and wont get it, then its very hard to transmit the messages, you have to play it over and over again or have different avenues of distribution. It's just not something that's very easy to do, we think it is, but it's not, you have to keep repeating the messages and have doctors. For example, it has been shown very clearly that any doctor, any specialty, who spend 15 seconds with a patient reminding them that they shouldn't smoke, if they do that repeatedly on visits, patients will eventually quit smoking, and that's a way to get at patients, to have a general physician, a primary care physician, say to a patient, hey by the way stop smoking, you will live longer. They have the contact, but your audience

will be interested but maybe not as much because they are going to be healthy, hopefully.Foss We are going to pause for a minute, please stay tuned and learn more about the history of cancer from Dr. Vincent DeVita from Yale Cancer Center.15:02 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3lifestyle are the most important factors in defeating breast cancer. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make new treatments not yet approved by the Food and Drug Administration available to the patients. This has been a medical minute and you will find more information at yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut Public Radio.Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu and Dr. Vincent DeVita of Yale Cancer Center. Dr. DeVita, could you tell our listeners what you think the role of the National Cancer Institute has been over the past 30 or 40 years in the war against cancer?DeVita They have been the main drivers, the money comes in to the NIH, the Cancer Institute is part of the National Institutes of Health, the NIH, and they are the major distributors of the research fund. They are the overwhelming distributors of the research fund. While there is a lot of money spent in industry, they are very focused on products that are related and it is very important in research, but they are focused on their products. The money that supports most medical schools and keeps them in the research business all comes from the Cancer Institute. That 85% of money that went into basic research went to medical schools like Yale. Yale has a very large grant program from the Cancer Institute and it plays a very-very important role.Chu Certainly from the 60s through the late 80s, I would say that the NCI has certainly played the key-leading role in terms of developing the clinical trials and has led to a number of treatments for cancer.DeVita Are you referring to the Intramural Program of the NCI, or to the NCI as a role in the country?Foss I think a lot of people out there hear the word NCI and they don't really appreciate what it is, what the institution is.DeVita It is the largest institute at the National Institutes of Health. It's about 23% of the entire NIH and the whole NIH has an intramural complex like a great big university and there is quite a lot of work that goes on there. As Dr. Chu pointed out, in the early periods in the 60s and 70s, a lot of the curative therapies were developed at the clinical center, and that's where I did all of my work, and you guys were there at the time. A major part of the NCI then is also to set up what's called the peer review system to allow people to submit grants to be reviewed and then get money distributed around to the university. The NCI was responsible for a lot17:37 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 of clinical trials and still is, and also for that period from say the 60s until the early 1980s, they were largely the cancer drug development program for the nation. It wasn't until around then that pharmaceutical companies felt they could make money developing cancer drugs and they began to do it, and now the industry has taken over. By the way, this is what the role of the drug development program was, to get it started; now it is totally dwarfed by the industry. And another myth about the cancer war is that it was

dominated by cancer drug development. When I left in 1988, we were spending $68 million a year on cancer drug development. Now it's less, it is miniscule compared to the billions that are being spent around the world on cancer drug development. It has succeeded famously, and it has really been a wonderful investment by the federal government.Chu And one thing our listeners may not be aware of is that Vince, you were really responsible for developing the cure for both Hodgkin's and non-Hodgkin's lymphoma when you were at the National Cancer Institute.DeVita Yeah, that was great. We enjoyed that. That was seeing miracles happen. We have to think back to those days, it was when you had advanced cancer and nobody thought you could cure any of them. When we put people into remission and they stayed there, it was quite a buzz, I used to have fun training young doctors like you guys coming in and trying to convince you that you could really do this and we trained a bunch of people who went out and reproduced this throughout the world. The mortality from Hodgkin's disease has dropped by about 75% in this country since we introduced that therapy. Not 100%, but 75%, there is still a ways to go.Foss Certainly it was a very exciting time for us to be there. Ed and I were both there when these therapies were being developed and what was really exciting about being a fellow then is that we were learning from people like Vince who are really pushing the envelope and going in different directions and doing things that couldn't be done at that point in time anywhere else.DeVita That's correct Francine, you are absolutely right, and I think that's actually still a problem. The cancer institute is not as flexible as it used to be, but it still is one of the very few places where you can do things and you are only limited by what's between your ears. The regulatory environment around most hospital has gotten so complex that even when you have something really exciting, it's very difficult to go out there and do it. I know Francine because I follow a number of your protocols that you must spend a third of your time filling out forms for.20:06 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3Foss At least.DeVita I am being conservative, and I know that other grantees have told me that they spend at least three to four months a year writing grants, filling out follow-up forms and so forth. It is overdone and it gets in our way and at the cancer institute in those early days we were careful, and we had to be careful that we didn't harm anybody, but we had a lot of flexibility to follow our instincts, and now you have done the same thing. You have done the same thing with cutaneous T-cell lymphoma, but it wasn't easy and as you know you have to sort of struggle to get what you want done.Foss Exactly, and the other point I wanted to make for our listeners is that the Intramural Program still does have these kinds of clinical trials ongoing, these high risk, exciting trials, in certain cancers.DeVita They do, and cancer centers are an interesting animal, so to speak. Basically the way you translate from the laboratory to the clinic is you take the best idea, no matter where it happens, and then you apply that idea so patients can get access to the best. It's often mistakenly thought that you can only apply what you develop in your cancer center. You don't, we actually interact with the clinical center here at Yale and we send patients down there and they refer patients up here, depending

on who's doing the best job, or something new in cancer. We developed a system, as you remember, called PDQ in the early days. It was for who's doing what and where because patients always want to know who is doing what and where. They want to get the best possible chance of curing their cancer and it may be that Sloan-Kettering is great in five cancers, but not in the sixth cancer, and Yale is great for cutaneous T-cell lymphoma, we are very far ahead then many places and a lot of people come here, especially for that particular cancer where they might not go some place else, or they do better off coming here.Chu The buzzword these days is translational research, but really when you think about it, the NCI back in the 60s and 70s was really the model where translational research was being developed and implemented.DeVita It was, maybe the first experiments, and we had the late Howard Skipper who was a mathematician, but he used to call himself NCI's Mouse Doctor, and he was doing some brilliant experiments in mice with leukemia, and we were watching very closely when we were developing the MOP protocol because their experiments with the biology of the growth of the bone marrow and the tumor and comparing the two, integrating them into someway of treating a mouse. In 1964, it was the first time that anybody reported the cure of a mouse with leukemia, it was Howard Skipper and we copied a lot of those things and had to make23:01 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 adjustments for humans. Humans are very different than mice, but it was the integrated approach of the laboratory and the clinic that was exciting, and it worked. It worked to cure childhood leukemia and it worked to cure Hodgkin's disease, and we did the first studies on the diffuse large B-cell lymphoma as well, which was also another curable lymphoma. It was a very exciting time.Foss Vince, with the human genome project it seems as though we are now moving in a slightly different direction, instead of moving towards killing a tumor cell, we are starting to move towards effecting a gene and a gene product because we can identify so many of these genes now. How do you think that that's going to change our approach in the 'War on Cancer?'DeVita It's a very interesting dilemma Francine; first of all, one of the principals that we developed in the 60s and 70s was that you need combination chemotherapy. Cancer cells were too smart to be able to use one drug and come out, you need combination. Now, with these molecular targets that we have identified partly because of the genome project, we still need combinations of drugs that affect more than one target in order to do it. It becomes exceedingly difficult to develop these drugs, why, because we got our wish. You develop a very specific drug for a very specific target, it tends to be very non-toxic, but it also does not work terribly well by itself. It is so specific it does not have any spillover to other pathways. So, pharmaceutical companies find themselves in this dilemma where they have something that does not do a lot of damage, but by itself doesn't do a lot good. It has to be tested with something else. Trying to get two pharmaceutical companies to do a parallel test of two different compounds owned by two different companies' turns out to be an extremely difficult thing to do in this kind of regulatory environment.Foss The NCI has this 60 cell line panel and they have done a lot of screening looking at actual cancer cells

and all kinds of natural products as well as some of these new drugs, and one thing that we have learned doing that is that some of these targets that we think would only affect a certain type of cell, actually has affects on other pathways, or other types of cells. Are we still using that approach today?DeVita It is used, but again, that's the remnant of the Cancer Drug Development Program. It originally was a program that screened 40,000 compounds a year and essentially one mouse model of the leukemia that I referred to before, and it morphed into this panel of cell lines and they are learning different kinds of things. They are not picking up the drugs themselves because the industry is doing that, but they are learning a lot about the biology of those drugs by using different tumor types. Frankly, I think what we are going to find out that an important pathway is an important pathway regardless of what cancer it occurs in, and so we may be able to find one drug that, if used intelligently, with one maybe two or three other 25:58 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 other drugs will benefit patients with a whole variety of different kinds of cancer. To use intelligently means, to me, sitting at Yale in a conference room and saying you know we have to put those drugs together this way because of the systems that we all know are important, and then after you try it in a few patients, say you know what we should change it to do this and that. To do that now requires that you go back to the NCI, that you go back to the FDA, and that you go back to Human Investigation Committee and that makes it extremely difficult to use your innate intelligence. We need a more flexible system. I have suggested, and I will suggest in writing as often as I can, that this ought to be delegated by the FDA and the NCI to cancer centers. That all phase 1 and phase 2 studies, the studies that we use to test these approaches should be delegated to the cancer centers. NCI has put a lot of money into 68 cancer centers and they were designed to do this, and I think if we did that then we would be able to sit around and use our scientific brains for what they were designed for and make changes and get there faster.Chu You played a key role when you were the Director of the NCI in developing the NCI Cancer Center's Program. Right now there is maybe 41 or 42 NCI designated comprehensive cancer center throughout the country. Can you tell us why you think that's important, because when we listen to the radio and TV talk shows here in the state of Connecticut everyone says that they have a cancer center. Truthfully, Yale is the only NCI designated comprehensive cancer center in the state of Connecticut.DeVita There is a lot of competition in medicine and cancer centers compete with one another, but there is a very strong distinction between cancer centers and the NCI comprehensive centers. I said 68, but if you talk about those that are designated as comprehensive, you are talking about 41 of them. That's not a lot for a country our size and some states don't even have a center. There isn't a treatment out there, if you count the clinical center at the Cancer Institute, that works that was not developed at a cancer center. That's where you develop new therapies, that's what you are expected to do. You are expected to put together all the resources that you get and develop new approaches to diagnosis, to treatment, and prevention of cancer. Every private hospital has a cancer center; they deliver, if they are

good, state-of- the-art treatment. So you develop state-of-the art treatment, they deliver the state-of-the-art treatment. You deliver it too when you develop it, because you have to give the patient's the very best on top of whatever new thing that you are developing. People sometimes don't understand that, but the private cancer centers are not able to do the complex kinds of studies that you need to develop new drugs. It's a very sharp distinction. Down the street we have very wonderful hospitals and doctors at their cancer centers and they are delivering the therapies that we developed 20 years ago as well as we delivered them when we developed them, and as well as we deliver them now, but what we are doing is adding something on top29:04 into mp3 file http://www.yalecancercenter.org/podcast/nov0809-war-on-cancer.mp3 of that that will improve it hopefully, and that's the big distinction between the two of them. The cancer center program issue is a very complex one, we don't have time to go into this, but it has been not as successful as we would have liked, but it has been a successful program overall.Chu In the last 30 seconds or so that we have remaining on the show, I know that you and your daughter are working on a kind of historical perspective of cancer, your own experience in cancer. Can you tell us a little bit about that?DeVita Yeah we are working on a book. The running title for it now is called The Death of Cancer, which gets people confused, which is good because they are perplexed when they hear it so hopefully they will pick it up. We are about halfway through and my daughter is the science writer and its kind of fun. We count the experiences I have had and I have boxes and boxes of files of information and she converts it into language that the average person can enjoy. You have to make these subjects something the people are interested in reading. I am learning a lot about how to write for the public from her and she is learning a lot about the cancer program.Chu We look forward to having you back on a future show to hear about how the book is coming along.DeVita That would be great.Chu Thank you again for joining us. It's always great having you on the show to talk about your perspective on cancer. Until next week, this is Ed Chu from Yale Cancer Center wishing you a safe and healthy week.If you have any questions or would like to share your comments, you can go to yalecancercenter.org where you can also subscribe to our podcast and read written transcripts of past programs. I am Bruce Barber, and you are listening to the WNPR Health Forum from Connecticut Public Radio.