

Discovery & Challenge: The State of Prostate Cancer Research

The National Press Club
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*Transcript of a Roundtable Discussion
Sponsored by
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Prostate
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INTRODUCTION

On Thursday, April 23, 2009, the Prostate Cancer Foundation (PCF) hosted a roundtable discussion on the state of prostate cancer research. It was held at the National Press Club in Washington, D.C. and simulcast via a telephone conference. The discussion featured nine of the nation's leading experts and scientists working in the field of prostate cancer research and advocacy. The forum was frank and open, exploring various areas including progress and roadblocks, funding, regulation and the effectiveness of both public and private efforts. Planned long before the PSA debate that began in the media during the month of March, the forum also provided an opportunity to weigh-in on the two studies that were published earlier in the New England Journal of Medicine.

This document provides the full transcript of the discussion. For more information on prostate cancer and the latest advances in research, please visit www.pcf.org.

THE PANELISTS

S. Ward (Trip) Casscells, MD

*Assistant Secretary of Defense for Health Affairs
U.S. Department of Defense*

Alvin Chin

*Prostate Cancer Survivor & Advocate
Virginia Prostate Cancer Coalition*

Donald Coffey, PhD

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*Deputy Vice President of Communications and Public Affairs
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Capt. Melissa Kaime, MD, FACP

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*Professor of Medicine and Oncology
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Padmanee Sharma, MD, PhD

Assistant Professor, Genitourinary Medical Oncology and Immunology
The University of Texas M. D. Anderson Cancer Center

Jonathan Simons, MD

President, CEO and David H. Koch Chair
Prostate Cancer Foundation

Program Moderator:

Josh Wolfe

Co-Founder and Managing Partner, Lux Capital
Editor, Forbes/Wolfe Emerging Technology Report

The Roundtable Discussion

ZENKA: Good morning, everyone. Welcome to the National Press Club. My name is Dan Zenka. I'm the vice president of communications for the Prostate Cancer Foundation. We're very pleased that you could join us for our roundtable discussion — *Discovery & Challenge: The State of Prostate Cancer Research*. I'd like to welcome some members (of the audience) that we work with often. Zero — The Project to End Prostate Cancer, the Men's Health Network, the Virginia Prostate Cancer Coalition, as well as the numerous parties we have listening on the phone today.

At the end of the program, there will be a Q&A session. Those listening online can submit questions to dzenka@pcf.org. At this point, I'd like to hand over the conversation to Josh Wolfe, our moderator. He is a founding partner of Lux Capital, and editor of the Forbes/Wolfe Emerging Technology Report. Thank you, Josh.



WOLFE: Thank you, Dan. We're going to keep things moving pretty fast-paced and pretty lively. I'll make some quick introductions, and then turn it over to Dr. Jonathan Simons for some opening remarks.

◀ **Josh Wolfe, Discussion Moderator**
Lux Capital

Starting from my immediate right, we've got Mark Grayson. Mark Grayson is deputy vice president of communications and public affairs for PhRMA. Followed by Peter Nelson. Dr. Nelson is professor of medicine and oncology at The Fred Hutchinson Cancer Center. Followed by Captain Melissa Kaime — director, Department of Defense, Congressionally Directed

Medical Research Programs. Followed by Dr. Coffey. Dr. Donald Coffey, professor of urology, oncology and pharmacology and molecular sciences at Johns Hopkins.

To my left, Dr. Ward “Trip” Casscells. He is assistant secretary of defense for health affairs of the U.S. Department of Defense. Dr. Jonathan Simons — president, CEO and David H. Koch Chair of the Prostate Cancer Foundation. Followed by Pam Sharma. Dr. Sharma is an assistant professor of genitourinary medical oncology and immunology at the University of Texas, M. D. Anderson Cancer Center. Followed by Dr. Howard Scher. Dr. Scher is chief of genitourinary oncology, Memorial Sloan-Kettering Cancer Center. Followed by Alvin Chin — a prostate cancer survivor and advocate with the Virginia Prostate Cancer Coalition.

With that, let me turn it to Dr. Simons, for some opening remarks.

Opening Comments

SIMONS: Thank you, Josh. Good morning. We're so very delighted to have such a panel of distinguished experts that represent a total commitment to the end of prostate cancer as a source of death and suffering. Since 1993, when Michael Milken created the Prostate Cancer Foundation, the Foundation has been working toward a day where prostate cancer is no longer a problem for any family on the planet.



▲ *Jonathan W. Simons, MD*
Prostate Cancer Foundation

The disease affects a man in the United States, who is diagnosed, approximately every 9 minutes around the clock. There's a death from prostate cancer — currently — about every 18 minutes around the clock.

Fortunately, over the past 10 years, we've seen an overall 30 percent reduction in the death rate in the United States. In the last 6 years, we've actually seen a 4 percent per year decrease in the total number of deaths each year in the United States, using American Cancer Society statistics for prostate cancer.

The Prostate Cancer Foundation, over its lifespan, has raised over \$370 million for research. It has supported globally over 1,500 investigators, scientists and doctors throughout 200 research institutions working on prostate cancer. The Foundation has been active with two great partners. The National Cancer Institute — in trying to push scientific frontiers to a point with venture philanthropy, where NCI dollars can leverage and continue to drive new treatment and diagnostics. Another essential partner — which you'll hear about today — has been the Department of Defense prostate cancer research effort. Over the last decade, it's had an enormous impact on our ability to start to translate science into the lives of prostate cancer patients.

The last thing I want to do before I turn it to Josh, is to express my appreciation to Josh, those listening, and all that have assembled here today. We all want to leave this experience with a message of hope — but also with a very clear and pointed set of statements about what we could do to accelerate a time where prostate cancer is no longer a human burden. Thanks, Josh.

The PSA Debate

WOLFE: Thank you, Dr. Simons. It certainly is an assemblage of very powerful minds. So let's take advantage of everybody's time here. I'd like to start with an issue that's recently been in the headlines. There's been a lot of interest around PSA screening. This is as a result of some papers that were published last month — both in the *New England Journal of Medicine* — as well as articles you've seen in the *New York Times* and the *Wall Street Journal*. Let me start with some opinions. I'd like to start with Dr. Howard Scher of Memorial Sloan-Kettering.



▲ **Howard Scher, MD**
Memorial Sloan-Kettering Cancer Center

SCHER: Thank you. Certainly, there's no area that's been more controversial than screening. We all know that early diagnosis of cancer is really critical, in order to increase cure rates. The controversy around screening stems from the fact that the disease is so prevalent, and there are many men whose cancers really don't require immediate treatment.

While the results of these trials may be seemingly conflicting, I would try to reframe the question as, "What do we do, going forward?" I think the results of these trials really give us an opportunity to help identify which men have cancers that need more immediate treatment, and which ones do not. This will be a focus of the research effort, going forward.

I'm a true believer in information and using information intelligently. Obviously, we don't have all of the answers. But I think with the recent efforts in genetics, understanding family history and everything that contributes to the development of a prostate cancer, we'll be in a much better position, going forward — to make sure that those men who need treatment are receiving treatment early, and those who don't are not.

WOLFE: Thank you, Dr. Scher. Let's turn to Dr. Coffey of Johns Hopkins. Please weigh-in, and let's talk about the importance of PSA screening.

COFFEY: The trouble with those two reports is they came out in the *New England Journal of Medicine* and they were big studies that were being carried out in great detail and at great expense. And they came to exactly opposite conclusions. This is what the public is frequently confronted with, when reading scientific and medical information coming through on their television sets and through their media.



▲ **Donald Coffey, PhD**
Johns Hopkins University
School of Medicine

One that came out of Europe was a larger study. It was twice as large as the American study. They concluded that PSA definitely helped reduce the death rates of cancer. Whereas, the American study — which was half the size — said it did not. The one in Europe was run between seven countries. It's the place where screening came in

a little later, so they didn't have everybody being contaminated with screening and not knowing they'd been screened. In fact, 42 percent of all the people in the American study had been screened at least once before they came in. Secondly, the European study followed it for 14 years, whereas the American study followed it for six to seven years.

Well, in six to seven years, you wouldn't expect to see much of a difference. So what happened in the European study, it seems to me, was a much better study. Much clearer. It wasn't contaminated with people having been previously screened. And it had a lower level of using PSA at three nanograms per milliliter, whereas the American had raised it to four.

If you go through this, things came out exactly as you would expect. If you looked way up front in the disease, you wouldn't see much effect. That's the American study. If you go out 14 years, you'd begin to see this effect. Now, what was the effect? It was about a 20 percent decrease in mortality in the European study, and none in the American. But even in the European study, 85 percent of the screened people were not screened. So if you correct for that, it's about a 27 percent reduction.

That's about what we see with mammograms. It's about a 33 percent reduction. And with colorectal testing, about a 30 percent reduction. There are all sorts of other ways to analyze this that I won't waste your time on. Like how many new cases were seen?

Well, if you use their system, you'd expect to find less. And we found less with the ones we used. You'd expect to have less advanced disease. All of these things worked out in logic. So I think the European study was superior to the American study, and it was a tremendously expensive study in America. These are the things we have to guard against in the future for the patients and the public.

WOLFE: Thank you, Dr. Coffey. Let's turn to Dr. Simons. I'd like you to also weigh-in on this.

SIMONS: I think Howard did a great job. The future for everyone is to talk about how we end a debate with something every patient can know what to do with. The future's actually in research.

The idea would be — in an accelerated way — to push forward tests that are simply better than the PSA test. Although right now, PSA and talking to a doctor are the two things — along with the digital rectal exam — that we should be doing. The American Cancer Society and everybody agrees.

The conversation between patient and physician around prostate cancer screening has not been lost by these two *New England Journal [of Medicine]* papers. The American people, in particular, have been very ingenious. Whale oil's been replaced by gas. It's been replaced by the incandescent light bulb. What we need is an incandescent light bulb that's cancer-specific and that you could detect either in your urine or in your blood. It would say, "A — *you have prostate cancer.*" Maybe a decade or two earlier than even the PSA could even catch it. "And B — *you have a cancer that could kill you, in your lifetime. It's potentially lethal.*"

The Prostate Cancer Foundation and the Department of Defense are actually funding five different projects around prostate cancer-specific markers. There'll be no quiz, but these are

cancer-specific because of research from the Department of Research and the Prostate Cancer Foundation and the NCI: changes in the DNA — chromosomal fusions — from the University of Michigan, which you can detect in the urine, in pilot studies. Circulating tumor cells — one in 10 billion that's actually a real cancer cell and where nanotechnology can lift it out. Actually, the probability of finding one prostate cancer cell in the blood would be about the same as actually finding one person on the planet earth in a tube of 6 teaspoons of blood. But that technology is under development. It's work from Johns Hopkins, using a piece of protein from cancer cells — not normal cells — called EPC2A. Actually seeing it in the blood that's coming from a prostate cancer.

In the end, as Don Coffey and others have said, PSA has always been a smoke detector — not a fire detector. PSA could be prostatitis. It could be BPH. It could be prostate cancer. It's better to have a fire detector rather than a smoke detector.

Our real future jobs for the next five years is to push forward the real testing of these, and get these out into the community, where they can be tested and validated.

Advances From the Past Five to Ten Years

WOLFE: That's very helpful. So that's the next five years. Let's turn now for a moment to what we've accomplished over the past five years. The past ten years. I'd like to actually start with Dr. Kaime.

KAIME: Thank you, Josh. I represent the Department of Defense — the Congressionally Directed Medical Research Program. I think what we've done in the last ten years has helped shape the culture of biomedical science.



▲ **Capt. Melissa Kaime, MD**
U.S. Department of Defense
CDMRP

One of the things that we do differently is, we're very patient-focused. We understand it's survivors with a disease and patient advocates that go to Congress and influence and inform Congress on the need for additional research dollars. Those dollars get appropriated and assigned to us to manage. We then incorporate in our advisory panels, patients with disease and survivors with a disease to help answer the questions, "What are the greatest needs?" We bring them together with senior scientists and clinicians and other researchers to ask those questions — and formulate the call for proposals that ask those questions that are most important for patients.

One of the things that we've answered in the last couple of years is the need for more rapid clinical trials — Phase I and II clinical trials in prostate cancer. We awarded, in FY'05, a prostate cancer clinical consortiums award. That brought together what we call a "forced marriage" of institutions that might normally have competed against each other. We brought them together to work together to solve a common problem. Out of that, they've done 51 different clinical trials — Phase I and II clinical trials — and enrolled almost 1,400 patients in a very short period of time. In about three years.

In FY'08, we extended that through another open competition, and added three more sites to those ten original sites, to again propel these clinical trials forward. That's just one of the things — the call to the need for more clinical trials. Meaningful tools for patients with prostate cancer. That's just one of many examples.

WOLFE: Thank you, Captain Kaime. Let's hear from Dr. Sharma from M. D. Anderson. Tell us in the past five or ten years — where have we seen progress made?

SHARMA: Thank you, Josh. I think there are actually three areas that we can talk about, where we've made a lot of progress. One has certainly been in early detection. I think the ability to detect the cancers earlier has certainly helped us to provide treatment to men in an earlier stage, so they have curable disease. We're definitely seeing a decrease in mortality from prostate cancer because of this. I also think another area is addressing certain quality of life issues associated with treatment. Surgery has certainly come far in the last five to ten years. We're now doing nerve-sparing surgery, so men can maintain quality of life.



▲ *Padmanee Sharma, MD, PhD*
M. D. Anderson Cancer Center

The other area, I think, is that of scientific research. We recognize there's heterogeneity that is diseased. We need to start identifying subsets of patients that, one, we know have aggressive disease. They then can be treated earlier with aggressive therapies. And two, those that may have indolent disease — where we don't need to intervene immediately.

WOLFE: Thank you, Dr. Sharma. Let's hear from Dr. Peter Nelson of Fred Hutchinson.



▲ *Peter Nelson, MD*
Fred Hutchinson Cancer
Research Center

NELSON: I'll just expand on those a little bit, I think. In the last five to ten years, the major advances have been in applying the tools of the genome project. For example, to really understand the molecular underpinnings of why prostate cancer develops in the first place. As was alluded to earlier, there's been a gene fusion — a juxtaposition of an oncogene with a gene that's regulated by testosterone. A very fascinating finding that will probably give us some insights as to how prostate cancer develops and progresses.

A second area is that, after doing literally hundreds of studies, we now have pharmacological agents or chemotherapy drugs that do prolong survival in men with advanced prostate cancer.

This took about 30 years of research to finally hit upon the key drugs that would actually do this. They clearly also attenuate side effects of prostate cancer, such as bone pain, et cetera.

Then, the third major area is alleviating the side effects of the cancer itself. For example, there are applications of medications that can prevent bone fractures and painful symptoms due to prostate cancer. I think those are three important translational areas and clinical areas that have seen big advances.

SIMONS: I'd just say a word about intricate androgens — which is also not going to be quizzed, today.

NELSON: What Jonathan is alluding to is that one of the first handles for treating prostate cancer was discovered more than 50 years ago. A Nobel Prize-winning discovery showed that prostate cancer was exquisitely sensitive to testosterone. That's been our main therapy for decades. We've now re-realized that prostate cancer — even at advanced stages — when we thought we had adequately targeted this pathway... is actually developing ways to circumvent it by possibly producing its own androgen receptors and producing more testosterone. This has opened up another pathway for therapeutics. There are several very promising drugs in late-phase clinical trials, now.

WOLFE: Thank you Dr. Nelson. It certainly seems like the pace of innovation in the area is increasing and building upon itself. Dr. Coffey, would you agree with that? Could you share some of the things that you've seen over the past five or ten years in progress?

COFFEY: Yes. The most important one for the patient, right now, is that we've been looking at a snapshot of what the PSA level is. What's important is to get a moving picture of what it is. That is called the "Velocity of PSA Rise." Looking at the total smoke in the building — from the smoke alarm of PSA — is one thing. Seeing how rapidly that smoke is building up is a totally different thing. Now that's become very popular, and that's going to make all the difference in the world. That's called PSA velocity and PSA doubling time.

Study after study is showing that this separates what we call the kitty cats from the tigers. The great majority of prostate cancer will not kill you in your lifetime. Some of them will. This is very serious, taking out 28,000 American people (each year). That 28,000 it's taking out, in general, have an increase in the velocity speed of the PSA. Now, how you measure it and how frequently you do it, we're still working out. But in a longitudinal study, it was shown several years ago in patients followed over years — with the same sample taken every six months of PSA. This shows those people who will progress with bad disease. That's desperately what we need.

Then the other one, and I'll be quiet. Dr. Scher and his group are looking at circulating tumor cells. So, first, we're looking at what the tumor cell puts out — the PSA. Now they're looking at the circulating tumor cells that are in your blood, that are spreading. That will almost surely become a major detection thing in the future.

The Roadblocks to Progress and the Importance of Clinical Trials

WOLFE: That sounds very fascinating. I actually don't want you to be quiet. I want you to keep going. I want you to tell me what are the roadblocks you see to continued progress.

COFFEY: Oh, gee. Well, the roadblocks of continuous progress are that there's a tremendous drop in funding. Let me just read you a few numbers, here. This is a little startling.

In 2005, there was \$373 million put in by the National Cancer Institute to follow prostate cancer, from their data and their research portfolio. The next year it fell from \$373 to \$348 million. Then it fell to \$345 and to \$295. Now it's down to \$290. In other words, in five years, we've gone from \$373 million to \$290 million.

Now, at the same time, here is an absolute explosion of new discoveries coming over the horizon. But it's not only that explosion. The young investigators see that they're not being funded. This not being funded is really causing great numbers of them to have to leave the field. They don't want to.

But when you think about it, they've been in school, now — 12 years through high school. Four years through college. Four years through medical school and six years through advanced training. Their children are ready to go on to high school and things. And here, they're not making salaries and they can't get funded. They're being funded at less than 20 percent. In our field, less than or about 30 percent are being funded.

The rest of them — which are approved — are not being funded. This is the biggest danger we face, if we're going to lose the capital of our young people. Everybody has seen that other major cancers have increased over the same period of time. So this is a serious problem for prostate cancer.

WOLFE: Thank you, Dr. Coffey. Let's actually go ahead and turn for a moment to Dr. Trip Casscells. I'd like you to also speak, not only about the roadblocks to continued progress, but I'd like you to loop in the importance of clinical trials.

CASSCELLS: Josh, thank you. Speaking as a cancer patient, and not as the assistant secretary of defense... let me just say that the first time Dr. Chris Logothetis at M. D. Anderson asked me to participate in a clinical trial, I have to say, it gave me a little pause. But I'm so glad I did. I've been in a series of them, now. I'm so honored. The latest medication I've been on... I got to meet one of the developers of it, Dr. Nelson, just this morning. I appreciate the basic research that made that possible.



▲ *S. Ward (Trip) Casscells, MD*
Assist. Secretary of Defense for Health Affairs
U.S. Department of Defense

Were it not for participating in clinical trials, I really don't think I'd be here. Whether that's a good thing or not for the Department of Defense, that's for others to judge. But I'm glad I'm here. I got a chance to serve in Iraq and elsewhere.

We do still have too many patients that are a little reluctant to enter clinical trials. Doctors sometimes don't think about the wealth of trials that are available. The wonderful work of the Prostate Cancer Foundation—as great as Jonathan Simons and Mike Milken are — they can't do everything. Congress can step up here and help. And they did. Congressman Murtha —

Chairman Jack Murtha — a former Marine — got involved and started this Congressionally Directed Research Program with \$80 million. It hasn't gone up, though.

A lot of soldiers like me — and former soldiers and marines — have gotten this disease that affects us middle-aged and older males. We need that help. That kind of nudge from Congress has proven critical. In this area, we appreciate the congressional oversight. And we appreciate the advocacy of people like Dr. Simons and Dr. Coffey. Clinical trials are absolutely critical. There are hundreds of compounds in development that are just for leukemia. Just for breast cancer. They might well work in prostate cancer, but they haven't been tested. So we need that impetus. Thank you.

WOLFE: Thank you. I'm stunned by the connection here. I'd like to hear from Dr. Nelson... Peter, weigh-in on this. Talk about some of the impediments to progress.

NELSON: I think those statements are absolutely right on. Still, one of our major impediments is convincing or providing opportunities for men to go on clinical trials. It's a distinct juxtaposition to, for example, childhood cancers, and for example, brain tumors... Almost every child with a brain tumor is on a clinical trial. It's the only way we will understand exactly what drugs work and what drugs will not work, in the context of both early and advanced prostate cancer.

One of the main impediments is simply being able to offer the trials in locations around the country where adequate monitoring, et cetera, can be done. The second is just convincing men that it's really not and shouldn't be viewed as an experiment. It should really be viewed as a therapy. The connotation of an experiment is oftentimes distasteful to patients. We need to change that attitude.

I also think, to be on the soapbox for just a moment... One of the problems with the way that we currently run clinical trials is, we don't really design them with the intent to understand why they might fail. It's a fact that most clinical trials fail to meet their endpoints, despite excellent pre-clinical work and early indications that the therapy should work... But we don't design them with that in mind. It's very different than a typical laboratory experiment. Trying to understand how a drug may not work as you expect would then allow us to build the next study and the next trial, to improve upon that.

WOLFE: Dr. Scher. Tell me about some of the impediments to progress.

SCHER: You can have the greatest product in the world and the greatest idea. But if you don't have a place to produce it, you have a problem. It really was the foresight of the Prostate Cancer Foundation and the Department of Defense to actually support the infrastructure to collaborate.

The clinical trial network that we've developed really, in many ways, operates very similarly to pharma (companies). In contrast to what people think, the time, effort and thought that goes into developing a concept... We are entreating physicians that are trying to help patients. That's the primary objective of all of the trials that we do.

I can still remember about two years ago when a colleague of mine, Dr. Sawyers, had developed a new compound. It specifically targeted one of the molecular defects that was identified in late-stage prostate cancer. That is that in addition to the tumor making its own testosterone, it actually makes more of the receptor for testosterone which further stimulates it.

He had developed a compound specifically for that molecular defect. I had a patient that was progressing on treatment, and I was actually agonizing with myself, "*Should I offer him this opportunity?*" We felt that the drug would be safe — non-toxic. He was the first patient to receive it. He is still on treatment, two and a half years later.

We've actually had a discussion. I said, "*What made you go on that trial?*" He said, "*Well, I was very encouraged the way it was presented. It seemed to be rationally designed and it seemed to be safe.*" So we do have the safeguards, to make sure that what we do is not doing harm — and also has a high chance of success.

Just to build on Dr. Coffey's comments earlier... We've known clinically that the prostate cancer that a urologist removes is very different from the cancer that's growing in somebody's bones, and the setting of a low-testosterone and hormones. So it was imperative for us to learn how to understand what makes that particular cancer tick.

We're learning that there are common defects that occur among many cancers that are not unique to prostate cancer. What typically happens is that a pharmaceutical sponsor will identify one particular tumor type, where they believe the drug will have the greatest likelihood of success. They will focus on that area. But we know that there are subsets of prostate cancer patients, for whom that same drug can work. Part of the circulating tumor cell effort is to be able to do a blood test — what we call a liquid biopsy — to match the defect in that person's cancer to the drug. That increases the likelihood of success.

Very few people like to pay for that effort. It's very, very expensive. There is frequently little support.

But, as Dr. Nelson was mentioning, it's critical that the trials we design learn as much as possible from our successes, as well as from our failures. Make sure we're not continuing to develop things that don't work. At the same time, moving drugs that are promising forward, as rapidly as possible.

In the shortly over three years that we've been working in the consortium, there are now five products that are in Phase III — including one that started with its first patient in July of 2007, and will be in Phase III by July of 2009.... having enrolled over 140 patients at seven dose levels.

This is the type of capability that we need in order to make sure that we're developing the promising drugs as quickly as possible. And making sure that we have the evidence to show that they work. So we as physicians can tell patients what these drugs can do for them — relative to what might be the side effects of those agents.

WOLFE: Thanks very much. Let's hear from Dr. Sharma. Please give us the perspective from M. D. Anderson.

SHARMA: First of all, I'm going to echo what Dr. Coffey said. I think one of the roadblocks, definitely, would be the young investigators, and supporting the young investigator. I was very lucky as a young investigator to actually be supported by the Prostate Cancer Foundation. I think that was very important. I think the young investigators bring to the field a new molecular biology. A new translational research. A new understanding in immunology that's not out there

already. We can now take the work we've learned about in all those years in school and that Dr. Coffey mentioned, and put it into the clinic.

I think this type of research from the young investigators is very important. To bring new perspective and new ideas. The support for young investigators is important. I think the Prostate Cancer Foundation has been doing a phenomenal job to try to help us.

At M. D. Anderson, I have to say Chris Logothetis has made it all a priority, actually, in trying to keep young investigators in translational research, developing new therapies for prostate cancer. For me, in particular, immunotherapy — with an agent [anti-C-Tel-A4]. Actually, developed by [Germeil] — sitting in the audience. So we can see and try to figure out the biomarkers that predict people who will respond to this therapy.

Again, echoing what Dr. Nelson said... I think it's important to develop biomarkers and rationally designed clinical trials that will help us to understand why the therapy works and why it doesn't work.

Progress and Regulatory Issues

WOLFE: Let's turn now to the topic of regulatory issues. Are regulatory issues impeding progress? Let me start with you, Mark.

GRAYSON: Well, first, before we go there... I just want to say in representing PhRMA that when we do a survey of what our companies are doing, there are more than 108 medicines in development from the pharmaceutical industry for prostate cancer. That's actually up from 88, just two years ago. So there are more in development. But what happens there is, obviously, you need more people in clinical trials. It slows up.



▲ **Mark Grayson**
PhRMA

We've had some talks with people in the audience. We do need to look at biomarkers differently. Also, Congress is debating healthcare reform. When you're looking at it, you can't just look at this in a vacuum. You have to look at, *"What are the incentives that are out there?"* With healthcare reform — and I would even say even before healthcare reform... you have to look into when you need people in research and to look at this. I'm also a prostate cancer survivor. When I heard that I had prostate cancer, I went to two different doctors. Neither one of them talked about clinical trials. They talked about, *"Here... you can do radiation or you can do surgery."* Neither one of them, even though I'm in the industry, said *"You know... there might be something else."* And my cancer was actually at a very early stage.

I think part of what we have to do is not just to look at the regulatory area. You have to talk to the urologists that are out there. When they diagnose. To say, "What do you need? What should patients do?"

In most other areas, when you talk about clinical trials, you're talking about an experiment. Regardless of what we do now, you can find ways to design clinical trials. People will get treatment on one hand, but it will be a different kind of treatment. So that you're not saying, "Well, you're either going to get a placebo or you're going to get treatment." I think we need to look into that.

But part of that, then, goes back to the regulatory area. The FDA and Congress and other places are looked at as, "What is the right way to go? And can they really change how they regulate clinical trials?" It's the difference between placebo-control trials and non-placebo-control trials.

Also, the idea that some things are not necessarily just drugs. Do they regulate something that is either a device or a drug or between it, and they're not sure where to go? So while you have the young researchers that might not be getting their grants, you also need to get additional expertise in places like the FDA. To figure out how we do approvals of medicines that might either be a biologic [better], or that they might be something that's not quite a drug, but yet could need some additional evaluation and a better way to do the evaluation.

WOLFE: Thank you for that. Let's turn to another prostate cancer survivor. Alvin Chin with the Virginia Prostate Cancer Coalition. Talk to me about the regulatory side.

CHIN: Yes. I was giving some thought to this. I do believe one of the unwritten definitions of "regulations" is that they do impede. But they are, of course, a benefit. They do make sure that we get safe drugs out there. We're not selling pharmaceuticals out of the back of a wagon.

What comes to my mind was a few years ago, in the case of Provenge, which was immunotherapy — we had the chance with the FDA to approve that drug two years ago. Here we are, two years later, and the word is out that they have met certain endpoints. They've shown that it does prolong life. We could've shortened that period of time had we acted back then. Back then, it was on a fast track, I understand. But it was taken off that fast track for probably a good reason. Nonetheless, it was something that impeded the delivery of that immunotherapy to the public.

The other thing I'm thinking about — in terms of impeding progress — are HIPAA regulations. I understand that privacy is a good thing. A lot of information need not be out there. But it also impedes the research.

WOLFE: That's a great point.

SIMONS: I wanted to add one thing...

WOLFE: Please.

SIMONS: Pete Nelson or Alvin alluded to the nice amplification of the idea. In children with lethal leukemia, we find it immoral and unacceptable that fewer than nine out of ten children get access to the latest science and go on to clinical trial. Right now, it's about three in 100 — or say



▲ Alvin Chin
Virginia Prostate Cancer Coalition

four in 100. That means that any idea for prostate cancer would have to go 25-times slower, just in terms of bringing people into clinical trials.

It's the same society, right? It has somehow... sorry, that's how strongly I feel about it... It somehow has differentiated the urgency. So what if these are grandfathers or fathers with kids playing Little League? We've disconnected completely the urgency that's underlying. Then we've disconnected all the scientific ideas that have emerged.

One way around it is to say that you'd create more doors for children in the 1960s. Everywhere in the country, if you had a child with leukemia, they could get access. Now we have, through a sort of public/private partnership, where the American people are paying through the Department of Defense, 13 centers around the United States to get into these clinical trials. The Prostate Cancer Foundation has provided philanthropic support there.

But we're still not asking the question correctly, *"How could we actually have more men getting to Dendreon [Provenge] in every clinical trial?"* If the accrual rate is that slow, you're just predicting this slowness to getting to the answer. Probably the most important message this year — I think — is that urgency around science for prostate cancer. The urgency around getting the science to the patients ought to be now equivalent to that for children with leukemia. We look at every child with leukemia with curative intention.

WOLFE: That's a very powerful statement.

SIMONS: The other thing that just amplifies that even further is, now we have this great science around human prostate cancer to monitor earlier whether drugs are working or not. It's not a dream. It's a reality. You can actually try to match in each patient, as opposed to using a microscope. Using technology to match in a clinical trial, the best research idea or drug to the patient.



The only way to do that is to have a healthy sense of procurement and project management. A lot of the culture of the DoD program actually has infiltrated, wouldn't you say? Infiltrated in a

positive sense... into the academic community. That's actually how the military approaches solving problems for people in harm's way.

WOLFE: Let's hear from Dr. Scher and let's also hear from Dr. Casscells on that.

SCHER: The trials that we've tried to design in the consortium are asking relevant questions, looking for definitive answers. In our experience, a key problem in many of the products that have come to the FDA, has been flaws within the specific trial design. While we've seen some very promising early results, we've also seen where the more definitive results have shown a worsening of survival in patients who are receiving the experimental drug. That's part of the reason we have data safety monitoring boards. To make sure that if there are any signs that a particular product may be harmful, the trials are immediately stopped.

In 2004, the FDA and Medicare ACO-ASCO issued a challenge to the prostate cancer community. They basically said, "*If you don't like the way we're conducting trials, get together and propose alternatives.*" So a group of 20 of our colleagues, over a period of several years, did work to develop a new set of endpoints, which were published last year. They were presented formally at an ODAC [Oncology Drug Advisory Committee]. Now through the consortium, we are prospectively using those guidelines to really see if they make a difference in how we conduct trials.

One of the key factors of the whole program was to really focus less on whether a drug met a specific criteria, but to focus on whether or not the drug was actually working. Focusing on what the clinician does day-to-day. If the drug's working by whatever means you want to assess it, by all means, continue assuming that it's safe. If it's not, you want to obviously discontinue that therapy.

With the effort that we're doing in biomarkers, we're really trying to focus on, "*Can we prove what's called an intermediate endpoint, or an early result?*" — which would actually predict that a drug is going to prolong life. So we do not have to do complete survival-based studies.

A very close collaboration now exists between the biomarker group at the FDA and the foundation of the NIH Biomarker Consortium, who's supporting this effort intensely. The Prostate Cancer Foundation — the drug division at FDA... To really collaborate. They invite you to come in and discuss your results as they're ongoing. Prospectively go over the design of your study. Engage in the conversation. So that if, in fact, you do satisfy the endpoints, you can really bring drugs to patients faster.

WOLFE: Thank you, Dr. Scher. Trip?

CASSELLS: Josh, I agree with Dr Scher. Let me just issue a caveat, if I may, because of conflict-of-interest. The Defense Department's prostate cancer research program began before I arrived there. It was really a congressional brainchild of Congressman Murtha. The funding has remained flat.

I have to be particularly careful, of course, not to advocate for it. We stick with the President's budget. The fact that I've had this disease for eight years is not relevant.

But I would like to share with you what I think is good news for people in the biomedical research community. That is that the secretary Bob Gates announced recently that while we

were having to make some cutbacks in some of the big iron projects—some of the ships and planes—but he does not want to cut back on biomedical research. He wants to increase that focus. That doesn't apply specifically to prostate cancer, but it's an across-the-board statement, and those of us on the health side of the Pentagon welcome that.

Let me mention also that President Obama sounds determined, from his public statements, to increase the funding for the FDA to cut into the backlog. To try to streamline procedures to get to a "yes" or a "no."



We used to have a sign in my laboratory, "*We may not have been right, but at least we were wrong.*" It's important to have enough information to cut something out if it doesn't work. That applies to clinical trials, too, and patients who enter into them. I know I've been on several trials that have failed. But as the doctor monitors your PSA and other useful markers and how you feel and everything else, you can get yanked out of the trial. I've been yanked out of a couple of trials that failed, and I've had a couple that succeeded. My gosh, I hate to think where I would be without that. So I think that's important.

If there's a message that the journalists can help us convey, it is that people ought not fear clinical trials. For most of us, they're the best hope. And to our congressional colleagues — some of whom are here — do whatever you can do to remove barriers. And as Mr. Chin mentioned, let's not let privacy and the so-called HIPAA rules become factors that intimidate doctors from getting patients involved in clinical trials.

This is absolutely critical. That's where the bottleneck is.

WOLFE: Thank you very much. Dr. Nelson, would you like to add anything?

NELSON: I think most of those points were well covered.

Prostate Cancer and Research Funding Levels

WOLFE: Let's turn then to the funding levels. The topic of funding levels. Are they sufficient? Are they sufficient today? Let's start with you, Dr. Coffey.

COFFEY: Well, first of all, let's start off with what we just heard in the funding. There is no doubt that what you just heard about the clinical trials is at the heart of the difficulty with this disease. Let's just take a look. When Dr. Scher put together this group of really the best young drug development research, with the best clinical interactions — and that goes all the way from radiotherapy to pharmacology to pathology — they set up 13 different groups.

Let's look at the cost of that: \$4.9 million of that comes from the DoD; \$3.2 million of that comes from the Prostate Cancer Foundation; zero comes from the NCI. So without NCI, that's \$8.1 million. That supports about 13 sites, with about 500 patients. This is desperately needed. Sometimes I'm a little amazed as to how the funding works out.

Why does it work out so well with the ones that are funded? Because the people that are doing it are up close to the science and what's being developed. It's not filtered through great layers. Dr. Scher's a great authority on this. I am a scientist. I am not a physician. I have never taken care of a patient. But I spent 50 years in this. What you're talking about is the roadblock — one of the big ones. Somehow, we have to get those clinical trials up from 3 percent to a more reasonable level.

Then on the other side, you look at what's happening to the aspect of new discoveries. Obviously, we don't have a cure. If we had a good cure, everybody would run to the thing.



Well, they've talked about looking at our failures. We also have to look at our successes. Let's just take one example. This has, once again, a little conflict. It's something that I'm very much interested in. We asked the question, *"How did Lance Armstrong win seven Tour de Frances, when he had metastatic lesions in his body, his brain, his lungs and everywhere?"* That's not just Lance Armstrong.

About 80 percent of patients with testicular cancer — which is one of the major things that used to kill young men — are now cured. Even when they have lung metastases and are just wiped out. They can be treated and be playing golf 20 years later.

How do we cure childhood leukemia? What is the mechanism by which these small children are really cured? We don't know why they work. So we decided to take an effort looking at why they work. Now comes the funding part.

If you put some of the ideas we came up with into a study section, it sounds like old-timey stuff. Hyperthermia. That's been tried and discarded for years and years. But we have ways of specifically taking it to those sites and doing things. How do we get it funded?

In that case, Safeway. You put your money at the cash register, and all those people out there... It turned out they took a look at it through the Prostate Cancer Foundation's review and others, and decided toward a study to do that.

Ted DeWeese and Robert Getzenberg at Hopkins are the PIs on that. That's just one. We need more new ideas. We need to know why things, as we say, failed. That's just as important. And to find out why they succeeded on some of these. To bring that up, and let it be quickly run through experts who know how to evaluate it. So it's not sitting there eight or ten years. I was shocked at how long it takes some of this to come up.

Prostate kinetics. That came up about 1992 in the *New England Journal of Medicine*. It's just now falling on the street in a big way. We have to speed it up. We don't have enough urgency. I'd like to say that Prostate Cancer Foundation and DoD and NCI... All these people that fund research... These are people that are trying. But sometimes we just get too bogged down. I love this ability to get things rapidly on the board through DoD. I'm not receiving DoD funding, so I can say this pretty openly.

The second thing is, that's the first time I ever saw patients — advocates — at the review table. My goodness, that changed my whole attitude. Once you really see the patients, it's a different story. They have input. They don't know science, but they bring the urgency to us, and they ask the right questions.

I think that the funding level has to be increased at all levels. I think the NCI has to put more into this. I think the DoD, which is now running at 80 [percent]... and they can tell you more about this with the 30 percent funding of these grants... You say, "*Well, what should it be?*" Well, it should be higher than that. That's for sure. I've seen a lot of excellent things lying on the table. It looks like what may be \$200 million would be [appropriate].

That would be in a reasonable range for what other cancers get in this area. That's why I'm very excited about the public's input. People in private industry. I'm just using Safeway as an example, because they stepped up and said, "*Listen. Collect here from people coming through the line. Would you like to give something for this or that?*"

I have often wondered, does that ever make it out into the field? Well, it sure did. It came our way. We were stunned that these people were very serious about helping out. Just as the DoD is. This is the type of urgency we need.

WOLFE: That model of public and private, I want to turn to in a moment. But first I want to hear from Captain Kaime. What level is sufficient for funding?

KAIME: Thank you, Josh, for the question.

It needs to be clear that within the DoD and the CDMRP, we are happy to follow whatever the direction of Congress is that gives us to enact. We will follow along the choice of Congress. But I can provide data on the state of the science that we see. For example, for FY'08, we received over 1,300 proposals. That number keeps going up and up, year after year after year.

Of those proposals, one of our major awards is called an Idea Development Award. That's kind of our bread-and-butter award. It takes very fresh, new ideas and gives them a chance for life. Of all the Idea awards we got in, we funded only 7 percent. So our funding rate on that, our bread-and-butter awards, was only 7 percent. That means that we leave a lot of good research on the table. How much do we leave on the table? Of all the idea awards we got in, about 30 percent were in the highly fundable, highly meritorious. Scoring outstanding or excellent or thereabouts in our scoring system. So, very meritorious proposals.

30 percent were in that range. Again, we only funded 7 percent. So if you just kind of multiply that out, you can see that we leave a lot of good research on the table that goes unfunded.

It's usually almost two-thirds of the merit-based ideas that are being unfunded.

SIMONS: So as an American citizen who was the recipient of a very large DoD grant at Emory, and a very enabling grant at Johns Hopkins before... But as an American citizen, what I think I heard was that you fund 7 percent and when you add all that up, and you could've funded 30 percent. Seven goes into 30 a little bit more than four times.

So you could easily justify the American people that were saying, "*Is this an idea that could save a life?*" You could actually have put out about \$180 to \$220 million worth of highly meritorious scientists agreeing, "*That should be tested.*" Is that a fair arithmetic?



KAIME: The math is as you say. Yes. The other thing is, when people see that our funding rate on these awards is only 7 percent, there may be good researchers that say, *"It's not worth my time to even put in for these awards."*

So we may not be even seeing the best science come forward, because our funding rates are so low. We don't measure who doesn't apply. We have not assessed that population out there. But I'm sure there are some that are out there.

One last comment. As an American citizen, people in uniform — including when they're actually not in uniform — are simply serving the American people. So they can't lobby. They can't advocate. It's a great paradox.

SIMONS: Cancer advocacy — one of the great programs — is in the DoD, which cannot advocate.

WOLFE: Mark, what's your take? Adequate levels of funding?

GRAYSON: Well, obviously, the industry does put a lot of money into cancer research. I don't know the exact numbers for prostate cancer research. Someone had asked me, *"Well, what about basic research?"* The more money that's put into research — no matter where it comes from — industry thinks it's great. We need continually more money into research. Basic research is very important. I, again, don't have the exact figures of the uptake. But I do know that very little is from the NCI and the NIH. Very few of the projects that are put out there are utilized by private industry.

There is a lot of debate around the world, as well as in Congress and [with] others about what kind of funding there should be, and who should pay for that funding. And, should private industry even be able to take advantage of the funding from government? Obviously, our take is that even though there is a lot of money that's put into basic research and there are great things, you still do need to have the profit motive. It does cost a lot of money to bring things through clinical trial and development, and all the other things, and all the great ideas that do get developed. Without having incentives, it will make it that much harder.



Having many people question whether private industry should be able to take and utilize the basic research that comes out of government, I think that as an American, we're wasting all the money that we're doing on research.

WOLFE: Peter Nelson, what's your take on the issue?

NELSON: I think a simple answer is [that] you could easily double the amount of funding going into cancer research, and still be funding the top five. That would be catalytic, in terms of translational into patients. I think another thing to recognize is the message you're sending to the next generation, in terms of getting the best and brightest people into medical research.

You want to know that the careers that [represent] both altruistic individuals as well as those that just have a passion for the science are directed into this field, if we want to continue to improve our healthcare outcome.

WOLFE: Let's hear Alvin Chin, please.

CHIN: One thing that's not been mentioned, I think, is the budget that Captain Kaime is working with. It's stagnant, at \$80 million a year. It's been that way since 2001. She has a budget of \$80 million that's given to her by Congress. But it has not grown. In fact, it has gone down by \$5 million in the 8-year period. On the other hand, we have inflation. That continues to increase every year. It may be 3 or 4 percent. But nonetheless, it's an increase. And we haven't even been able to address the inflation factor in our research. Costs increase. But yet the budget that we have to address those increases is not there. That certainly is something that Congress — at a minimum — should address.

WOLFE: Dr. Scher?

SCHER: There's no question that the funding levels could increase. But I'd also add then, when you're applying for a grant and submitting an application, you need preliminary data. One of the things that's been extremely helpful has been philanthropic support. That's enabling us to essentially turn on a dime. If you don't have the funding to start along the path of an idea, it's very hard to develop it so you're even competitive to apply for funding.

We look very closely at how we can actually leverage these funds. It was really the Prostate Cancer Foundation that was instrumental in changing the philosophy. To say, "*Don't spend 20 pages telling me about the problem. Just focus on the solution.*" They put a system in place that allowed turnaround for promising ideas in a matter of a few months, as opposed to over a year. There was a very nice picture, I remember, of Jonathan — when he was first working on a biological project for prostate cancer. The regulatory documents that he needed to file, which took probably close to two years of his life, were actually larger than he was.

Whereas, when you submit an application — a model actually emulated by the DoD, I think to their credit — the applications are five pages. "*Tell me the answer that you think you wish to pursue. Tell me what your question is. We'll see if we can get you the funding as quickly as possible.*"

Public and Private Partnerships

WOLFE: You mentioned the philanthropies, Dr. Scher. But talk to me now about public and private partnerships. Are you getting a sense that there is a most-efficient model on how this should proceed.

SCHER: I think there are going to be many models. There's no one answer. I think the key is being able to be flexible.

Again, another advantage of the [clinical therapy] consortium is that we have people that are experts on handling legal aspects. We're trying to run all of the processes that might impede the development of a trial, in parallel. My expertise is on trial design. It's on translating scientific discovery. I spend considerable time with my laboratory collaborators, trying to understand what they're doing. That helps me design a trial that's more informative. I'm not very good at reading contracts. I have no interest in doing that. But I'm fortunate that I do have people that can handle that. There's nothing more frustrating than when you have a protocol approved and it's waiting for some signature to start... Until all of the regulatory documents are complete, nothing can happen.

Again, we are now trying to develop a business model in our consortium. One of the charges from the DoD was that we have to be financially independent at the end of the five-year period — because there's no guarantee that this program will be renewed. This is a totally new area. I did not learn about it in medical school. But we've been fortunate to be in a position to explore ways to address the issue.

I would argue that if we can show, for example, that we can take a drug from Phase I to Phase III in a very short period of time, that adds value to a sponsor. The expertise that we can bring to the table in terms of trial design, biomarkers, understanding the biology, going to the sponsor with an idea... That has to have value. How do you create that metric? Again, I'm happy to listen. I'm really seeking help on how to design it, because I think this is a unique opportunity.

WOLFE: I think that's very open-minded. Let's hear from you, Don.

COFFEY: Well, I just think when you're talking about the level of funding, I'd like to remind you of one thing that I think helps me put it into focus. We've used this before... In two and a half hours, that's just about as long as we're going to be here this morning before lunch and everything... two and a half hours, seven people will be murdered in the United States — *seven* in two and a half hours. *11* will die of AIDS. *163* will die of cancer. Let me repeat that — *163* will die of cancer. *Seven* for murder and *11* from AIDS.

This is a serious, serious thing. One out of three people get it. One out of four people die from it. So I think that when we say, "*What level should we support here?*" you have to put that in that type of focus.

The second thing is, notice that we've talked the whole time about treatment. We haven't talked about prevention, lifestyle, diet, obesity and all the things that are big, big, big. You do *not* have to get prostate cancer as you age. It's ten or more times higher in the United States than it is in Asia. When people from Asia move to our country, [their chances of being diagnosed with prostate cancer] jumps up close to our level. There is more than just genetics here. There's a

whole aspect of lifestyle. Even on top of that, there's stuff called pain and all the psychological aspects that we're not even touching here. So we're not close to funding where this should be.

WOLFE: Those are remarkable statistics.

SIMONS: Bone health. Osteoporosis. The effects... Probably the most remarkable science we've seen in the last year is going to be about how you can improve your skeleton as you survive prostate cancer. That research just was not happening, in terms of survivorship, until Lance Armstrong said, "*Surviving cancer is just as important as being cured.*" And the DoD started actually funding a lot of early work in understanding bone biology. That was not on our radar. That came from patients. That didn't come from laboratories, first.

WOLFE: In the last few minutes that we have here — and hopefully, nobody gets murdered in those few minutes... Let's open it up to some Q&A, if there are any questions. Sir — please.

Question & Answer Session



ZENKA: One moment. We also have several.... We have nearly 65 attendees listening by phone. So I want to download some of those questions. Then we'll get to your question.

Several of those questions have to do with clinical trials reaching as far as India. I think we're going to spare our panel that discussion until the results are out and they're analyzed. So we won't address those questions. But we have had two questions regarding radiotherapy. I'm going to combine them.

First — What are your thoughts about brachytherapy followed by external beam radiation therapy versus surgical measures? A very general question. Then a second question — A recent study published in *BJU International* reports that radiotherapy following radical prostatectomy does not improve overall cancer-specific survival. This is annotated, "*Inquiring spouses want to know.*" Any comments?

SCHER: I stand on one foot. It's very difficult to extrapolate a very general question. What you're really trying to deal with is an individual and his particular cancer. I believe every man is different. They'll have different concerns about potential complications of therapy. Different things may be important to an individual. Some are more concerned about incontinence and others about potency. Others are willing to make certain sacrifices in terms of one particular complication or another, in their decision.

I think just to make categorical statements... I think there are patients for whom each therapy is appropriate. It's important to have a very careful dialogue with their physicians. Make sure you make an informed decision, and one that you won't regret, based on information.

ZENKA: Thank you Dr. Scher. Does anybody wish to add? Dr. Coffey?

COFFEY: Yes. Let's make sure that we understand the differences in this question. In other words, if you have a fire in the trash can in your basement, then you can remove the trash can with surgery. Or you can use brachytherapy. You can spray all sorts of CO2 and radiation on it to try to put it out.

But if the fire has spread to your attic — spread to your bones and to other parts of your body — then brachytherapy and radiation therapy cannot be applied, here. Neither can surgery, in general. It's time now to go to systemic therapy.

So we've been talking mostly about some systemic things. The radiation therapy locally and the surgery locally is in very good hands, I think, right now. They've got the morbidity of both of those procedures reduced, and it's much easier to do. So that's one of the great advantages of what's happened in the last few years. But it's the ones that are out in the blood and spread around that are going to come back and get you. Radiation therapy and surgery don't touch that. Is this correct, Dr. Scher?

SCHER: Yes. To keep it simple. There's a whole controversy about, "*Do you treat the local cancer, even if a few of the bad actors may have escaped?*" So there's still discussion about that area.

But it really boils down to understanding as much as you can about the risk of that individual's cancer. If it's localized or appears to be localized, is it going to cause that patient to suffer or to have a shortened survival? In which case, it needs to have something done. Has it spread very, very early? In which case you need probably both treatment locally and something systemic. Or it could be cured by one modality — directed only at the trash can.

COFFEY: They've done that with radiation therapy and hormonal therapy. The hormones will go throughout the therapy. They've combined those two, and it's been very beneficial.

SCHER: Right.

ZENKA: Okay. We'll take one more online question before we go to the floor.

Diet and exercise once was in the realm of alternative medicine. Now it's coming more to the forefront. Can we get some more comments on the effects of diet, exercise, body mass, LDL

levels, triglycerides? I think I'll hand this one to Dr. Simons, because he's got a lot of information on that.

SIMONS: In the last decade, we've learned that it wasn't a goofy idea that nutrition is important. We've learned that if you char your meat, that's a carcinogen. It's about the same as having a prostate smoke a pack of cigarettes a day. That's the work of Bill Nelson from Johns Hopkins.

We've learned in the last five years, actually, that 30 minutes a day of aerobic exercise — walking — probably will increase your outcome and survivorship.

We've learned that Vitamin D — 1,200 units a day — is very important. We've learned that lycopene and tomatoes and selenium are probably not as important as we thought. And that laboratory Petri dish work is not the same as doing large clinical trials.

We've learned that the fat in a man's body is just as much an endocrine organ as the pancreas. The pancreas makes insulin. It turns out that fat cells make factors that can allow prostate cancers to grow.

We've learned that actually the Asian diet itself is a very important thing to molecularly understand. It may be very protective, as well. And we have a new monograph that's come out, which is going to be up on our website.

Survivorship research — in the same way that Lance Armstrong's interested, as we are at the Prostate Cancer Foundation — in every aspect of life after the biopsy, there's a lot more work to do, here. But there's a whole set of dietary recommendations.

Fundamentally, we've also learned to basically take the facts and start to communicate. A lot of things that are bad for heart disease are actually probably accelerants for prostate cancer. But it's looking like it's total calories. Not fat. And processed carbohydrates. In other words, the overall energy intake that can fuel fat cells that can provide hormones that are different than testosterone, that can allow prostate cancers to grow. That's an important area as Dr. Coffey was saying, as real intervention prevention.

That was the seminal answer to a simple question. But we've got a nice monograph for anyone that just goes to our website.

ZENKA: Is there anyone who'd like to add on to those comments? Dr. Coffey?

COFFEY: Yes. One of the big breakthroughs that's occurring now is the fact that most of the genome in your body is not human genome. It's bacteria. Your intestines are loaded with 400 different kinds of bacteria, of which 80 percent we cannot even culture and cannot even identify. They process the food and do all sorts of interesting symbiosis that is helping you help them grow. They help you grow. They're sort of friendly bacteria.

For instance, when you eat soy, it's converted into a form of estrogen called a plant estrogen — phyto estrogen — based upon the bacteria in your stomach. So you eat that same soy in China and in the United States, and you may have a different product being made.

This is one of the big hot areas of science called microbiomics. That's the area of the interaction between the bacteria. It's throughout your mouth and body and eyes. There are 30 different islands of bacteria in your mouth, between the teeth and the roof and the back of the tongue. This is very complicated. We know the helio pylori, which causes ulcers and things, has lots of different functions in the body. It's going to be a very exciting area, as we work on that aspect. That's certainly affected by diet.

ZENKA: Thank you. Now we'll hear questions from the floor.

JOHNSON (in audience): What has the impact been and what is the future impact of level funding for the Prostate Cancer Research Program in terms of the decision-making process for the types of research that the program tries to fund? I am hoping that your answer will be able to talk about making tough funding decisions in certain areas of research and development such as clinical trials or the young investigator grants.

KAIME: The fact that the Prostate Cancer Research Program has had level funding for the past eight years has had significant consequences for the field of prostate cancer research. First, while funding has remained level, the costs for performing research have risen due to inflation. As a result, fewer prostate cancer research projects can be funded. Indeed, many superb prostate cancer research projects, including those designed to bring researchers from diverse fields of expertise together to more rapidly address central problems in prostate cancer, have been left without funding.

For example, the funding rate for Idea Development Awards has gone from 17 percent in FY'02 to only 7 percent in FY'08. In addition, level funding has resulted in the program's inability to fund certain types of research such as clinical trials, as these studies, while critically important in the war against prostate cancer, are very costly. Indeed, the PCRCP discontinued offering the Clinical Trial Award for FY'09. Finally, one of the most distressing consequences of continued level funding has been that established prostate cancer researchers are being forced to close their labs and leave the field due to lack of funding, diminishing the ability to continue the war against this disease. As a side note, the PCRCP has had such a strong commitment to the New Investigator Awards that, despite the level funding, we have not decreased our funding rate for these types of awards.

BURROUGHS (in audience): Thank you very much. I'm Frank Burroughs. I'm president of the Abigail Alliance for Better Access to Developmental Drugs. It's really an honor to be here today. I want to thank all of you for all of the great work you're doing. I'm not just saying this—this is one of the best panel discussions that I've ever been to.

You can tell from our name that the Abigail Alliance — the short version of our name — works on better access to investigational drugs that are showing promise in clinical trials. I have a quote here from our website: *"Every drug for cancer and other serious life-threatening illnesses that the Abigail Alliance has pushed for earlier access to in our eight-year history is now approved by the FDA."* That number is 16. We don't have the resources to track all drugs. So it's a really important issue. By the way, this issue is covered on Capitol Hill. We need more support by the Access Act. That would provide earlier access to people who cannot get into clinical trials.

It was very interesting in this meeting that Ward, you benefited from a clinical trial. Howard, you were talking about a patient. Peter, you were talking about something I'd known for a long time — about how many children are helped. Mark, it's interesting that your boss, Billy Tauzin is benefiting from having been in a clinical trial. It's really a testimony to why we need this better access.

One of the roadblocks to better access is — unfortunately — the FDA. They do a lot of good work. But they do block progress toward having better access for people that can't get into clinical trials. One point has to do with a prostate vaccine. That's Provenge. What sadly happened there is that there were shenanigans in the advisory committees regarding Provenge.

One of the many things the Abigail Alliance is working on, as small as we are, is we're communicating with the FDA on advisory committee reform. When I asked a question on an August 4th telecon, the question was, *"How can we prevent the shenanigans that happened with Provenge from happening again?"*

By the way, the host of this telecon was FDA Social Commissioner Randal Lutter. The answer was, *"It was an anomaly."* They used the phrase, *"Too generous."* That means it happened, but it's highly unlikely to happen again. Anyway, feel free to comment on anything I've said — and thank you very much.

WOLFE: Thank you. Dr. Coffey?

COFFEY: I'd like to separate the word, "Shenanigans," from "incompetence." I think they're sort of different. I don't know what the dictionary says, but... Let me go to the aspect I think we're going to have to deal with. American medicine — American Wall Street — a lot of things are broken in this country. They need to be, obviously, fixed.

One of those is, *"Should you protect me if I know I'm going to die from cancer? Should you protect me from toxicity from a drug? Or should you protect me from cancer?"* This is an age-old question that the FDA and many committees work on, and try to figure it out. How does the American government really work?

There's a series of really top-quality physicians appointed by the physicians of the country. Top scientists—best scientists. Not political. And top engineers. They're called the National Academy of Sciences... Their job is to advise the government on how to best handle science, medicine and engineering. I think at that level, they've had the Institute of Medicine address some of this. But I think it's time to look at these questions seriously. What are the patient's rights, if they want to be treated with something? What right does someone have to say, *"You cannot be treated with that,"* if I have a fatal disease, and you know that?

The second thing is — and I don't want to get into this or we'd be here all day... It's the litigation side of it. If a person comes up... Let me give you just a few numbers on prostate cancer that will help this audience. As you know, there are about 35 million PSAs [tests] run every year. Somewhere around that. We're not sure of the numbers, but it's around that. About 1.6 million of those 35 million, which is a small percent but it's still big, have to have a needle put into their prostate [a biopsy] to see if they have prostate cancer. Out of those 1.6 million, 186,000 have prostate cancer. Out of that, 28,000 die.

My goodness! So why would you keep doing something that... Well, because you would be sued if you had an elevated PSA and you didn't do a needle biopsy. If you see cancer on that biopsy and you don't do anything about it, you're going to get sued. If you come into my institution, we're going to run the same tests on you that they ran down in North Carolina on them, because we have to have that data verified by our team, so we know exactly what the quality of it is.

This thing is out of control. It's out of control on the price of medicines. It's out of control. The price of medicine is out of control. The price of drugs are out of control. We could debate it all day.

I think this is the time to have some of these things fixed. You're quite right. There are lots of injustices. I don't think it's as much people out to do you in, as people with a system being forced to do this and that. Dr. Scher and others around here are clinicians. I have to be careful, because I'm a [lab] doctor. It's a little different.

WOLFE: Thank you, Dr. Coffey. Let me turn it to Dr. Simons for some closing remarks.

ZENKA: We have one more question from the floor. Could we do that?

WOLFE: Please. Sure.

MEADE (in audience): By the way — this is wonderful. I hope this is going to be available after this program, so that many people can hear it. It's unusual to have a conversation that's as open as this one. You started out by talking about the *New England Journal of Medicine* and the confusion about the two studies, the American study and the European study.

As a patient advocate, one of my concerns is that we're approaching a period here in the United States where we're going to be looking at healthcare reform. I am very concerned that issues like these are going to enter into the debate. It's important that the research that you all are doing is out there. I think that what we need is a mechanism for early detection of prostate cancer. Then we need a way to treat the aggressive or the progressive prostate cancers without over treating them.

We may or may not have a marker — and I don't know how long it'll take. I'm interested to hear from you how long — if you were just going to give an estimate as to how long it's going to take before we have a marker or some way of doing that. In the meantime, is there a way we can work out some sort of protocol? I'm really concerned that what's going to happen is in the debate about saving money for healthcare, we're going to have problems in getting coverage for appropriate treatments for prostate cancer.

WOLFE: Thank you for that excellent question. Would somebody like to field that? Dr. Scher?

SCHER: I think what you're highlighting is the importance of the strength of evidence. This ultimately gets back to well-designed experiments that are designed to answer questions. We may have the tools now at our disposal, but we have to be able to demonstrate that they work. Unfortunately, not every therapy that's available is effective.

I think this emphasizes why it's critical that before something gets an imprimatur from an agency, it does so on solid evidence. I think that issue is separate from a patient that wishes to be treated with an experimental therapy. The two should remain distinct. But ultimately, if we are asking to fund everything or have everything available to everyone, that simply can't happen. We have choices. We have many drugs that are available. We have many tests that we can do.

As a clinician, I want to know what a test will do, to help me decide how to treat individuals. That's the same metric for a drug. What will the drug do for the person before I recommend it? The more evidence I have to support that recommendation, the more appropriately resources will be utilized, we won't be wasting money, and we'll be able to move forward.

WOLFE: Thank you, Dr. Scher.

ZENKA: Thank you. Before we go to Dr. Simons for closing remarks, I'd like to remind everyone who's listening in to the conversation that a full transcript of this discussion will be available later next week. Following that, we will have the video file available at pcf.org. Thank you for attending. Now I hand it over to Dr. Jonathan Simons.

SIMONS: I'm going to close with what Winston Churchill said — the three Bs. The closing remarks are to "Be Clear, Be Sincere, Be Seated." So, I'm seated. So thank you for being with us. The future of solving the problems are these public/private partnerships. PhRMA, academia, NCI, DoD, Prostate Cancer Foundation, Zero Patient Advocacy, Young Investigators, clinical trials — and actually, patients who really participate. Thanks for being here today.

[applause, sessions ends]

Note: *For more information on prostate cancer and the latest advances in research, visit www.pcf.org.*

