Hey everybody, I'm Kerry Gross director about cancer outcomes. Copper Center and also primary care doc. And with that background, it's a particular treat to welcome Doctor Philip Castle to join us today. Doctor Cassell's work has been foundational in our understanding of the etiology and prevention of HPV, associated cancers and cancer prevention with General Electric Castle received his PhD in Biophysics, actually. A masters in public health
from Johns Hopkins, who was previously the Chief scientific officer at the American Society for Clinical Pathology. There’s been a principal investigator for more than 15 years of self initiating, conducting and reading by several large NCI sponsored electoral and clinical research studies, both in the US and abroad. Is that the party is widely appreciated. It’s contributed to virtually every major guidelines regarding cervical cancer screening and prevention, and his work really has extended globally. His papers have been cited more
than 40,000 times in aggregate.

Currently Dot the castle serves as the director of the Division of Cancer Prevention and Control at the NCI.

Working overseas.

The conduct and support our research in cancer prevention, early detection and screening.

And now is a particularly relevant and timely setting for Doctor Castle to present to us. This is the 50th anniversary of the National Cancer Act, and as we reflect on the role of science in public health and society.
in general and in the efforts against cancer in particular, the role of prevention is a means to decrease the burden of cancer. This clearly is central work, so thank you for joining us today. Doctor castle. And we look forward to your comments. Thank you so very much. It’s a real honor to be here and it’s a real honor to lead the NCIS division of cancer prevention. Today I’m going to give you sort of a broad overview, recognizing as I learned that many of my colleagues don’t actually understand
what the division of cancer prevention does, how it’s different from the other divisions, but also to. Highlight the work that we support and to engage you, hopefully in the future. In some of these cancer prevention activities. So just a few disclaimers that get started, opinions expressed or mine should not be interpreted as representing official viewpoints of EU. S. Department of Health and Human Services, the National Institutes of Health,
the National Cancer Institute, or the Division of Cancer Prevention. My comments are informal and should not be taken as a signal for funding priorities. I will speak in broad terms of what I think is important, where I would like to see the science head towards in the future and my aspirations, whether and when I or we can implement those priorities depends on many factors beyond my control. I wish that weren’t the case, but it is in fact the case I wanted to highlight the burden of cancer and I know you all know this,
but it’s it’s.

It’s the starting point for this discussion or any discussion about prevention. Which sometimes I think UM, sort of gets put into the second row here, but. As you can see in the slide here on the in the left panel is the expenditures in billions of dollars annually. As you can see in the slide here on the in the left panel is the expenditures in billions of dollars annually. As you can see in the slide here on the in the left panel is the expenditures in billions of dollars annually.
And then for the most common cancers are the most lethal cancers you can see that it’s not billions, but it’s tens of billions of dollars, and in fact the national costs of cancer were estimated to be 190 billion in 2015 and now 209 billion in 2020, an increase of 10% over that period of time. And that doesn’t really even account for the hidden costs of cancer, which is a product approximated to be 100 billion. And as I’ll show you the next slide, we’ve made a lot of advances. Certainly in the treatment of cancer. But we still have 1.5 million cancers.
and .6 million related deaths every year. And just to give you a perspective and on that as bad as COVID was and is a point 6 million deaths is almost two full. Not quite, but almost twofold more deaths than those than that caused by COVID. So, uh, what’s happened over the last 45 years? You can see that arguably, I’m here are there’s a CDC data rate per 100,000 of the population. We’ve really not made any significant headway in the incidence of cancer in males and females.
There's a sort of a peak in males in the early 90s, and that's come back down, but it's about the same level as it was in 1975 and in females it's gone up slightly. I mean partly in dude and aging population to be sure. But you know, these are not the kinds of numbers we'd like to see. Certainly we've made some advances in survival, particularly well in both sexes, maybe perhaps more in males than females, but I would say also here that even preventing cancer related death.
It’s a long life or longer life of significant morbidity and lower quality of life to live with cancer, as I know from my own family members. So the mission of the division of Cancer Prevention is as follows. Lead supports and promotes rigorous innovative research and training to reduce risk burdens. Consequences of cancer to improve the health of all people, and you’ll understand this a little better as I go through and give you a this at a glance of view of
the division of cancer prevention.

Uh, just to highlight that I almost do nothing, this everything that you're going to hear about it has to do with an amazing staff.

Uhm, shown here we have groups focused on method more methodologic approaches or exposures and we also have organ specific areas of research as well.

I will highlight some of these, but that is not to say that there I mean we could talk for hours about what everybody is doing.

Uh, I put up this translational continuum,
and again, you’ll see why here in a moment to really sort of highlight this, the stepwise development of interventions and therefore where we fit into that from basic science to translation and these are approximations. I wouldn’t say that any one of these you know nobody’s limited perception completely to this area, but I would say 90 to 95% of the work. Each of the division is sort of showing up. This in terms of the divisions and these are approximations.
00:07:54.050 --> 00:07:57.304 represented here and in over with an
NOTE Confidence: 0.928211687142857
00:07:57.304 --> 00:07:59.859 overlay of the translational continuum.
NOTE Confidence: 0.928211687142857
00:07:59.860 --> 00:08:03.330 We really focus on the.
NOTE Confidence: 0.928211687142857
00:08:03.330 --> 00:08:05.820 An innovation to prevent cancer
NOTE Confidence: 0.928211687142857
00:08:05.820 --> 00:08:07.812 and to manage symptoms.
NOTE Confidence: 0.928211687142857
00:08:07.820 --> 00:08:10.016 As I would talk about later
NOTE Confidence: 0.928211687142857
00:08:10.020 --> 00:08:11.240 and try to you know.
NOTE Confidence: 0.928211687142857
00:08:11.240 --> 00:08:13.403 So we identify and we do early
NOTE Confidence: 0.928211687142857
00:08:13.403 --> 00:08:15.444 validation work with the hopes that
NOTE Confidence: 0.928211687142857
00:08:15.444 --> 00:08:17.199 successful strategies then get more
NOTE Confidence: 0.928211687142857
00:08:17.199 --> 00:08:20.107 or less handed off to the division of
NOTE Confidence: 0.928211687142857
NOTE Confidence: 0.928211687142857
00:08:21.993 --> 00:08:25.164 So we really there really are two.
NOTE Confidence: 0.928211687142857
00:08:25.170 --> 00:08:27.310 Population science groups at the
NOTE Confidence: 0.928211687142857
00:08:27.310 --> 00:08:30.169 NCI were a little bit sort of.
NOTE Confidence: 0.928211687142857
00:08:30.170 --> 00:08:32.914 I would say the forgotten group or the
00:08:32.914 --> 00:08:35.989 I think people are generally more familiar with cancer control and population sciences because it tends to dovetail more. More easily with the Cancer Center in the those renewals, particularly related to. Uh, uh, outreach? Uh, we’re actually probably more aligned in terms of the work we do with the division of cancer treatment and diagnosis, Albert. We spend a lot more. We invest a lot more in
treatment and diagnosis.

We work closely with the division of Cancer Biology, particularly on identifying pathways for cancer or carcinogenesis that can be then translated into prevention strategies and then the intramural program with the center of Cancer Research and division of cancer epigenetics, which we're increasingly working closely with to try to get their innovations into clinical practice and into public health. So you all know this, but it's always useful to
sort of declare these things.

Cancer prevention is really, really hard.

There’s certainly an event bias or what I call an event by success is the absence of events, and therefore there are no champions. This is also referred to as the prevention paradox. Our first mission is to keep healthy people healthy. First do no harm, and I’d say this applies more to public health and even medicine, and I point out that you know when we do screening people think of
screening as a one step process,

but it’s really a two step process.

The first step in screening is to tell healthy people there. Healthy and they don’t need to be screened again for whatever is an acceptable interval. And then among the positives we try to rule in. Who needs immediate care. But it’s also important to remember in the general population, most people at any one time will not be. Uh, you know, will not get cancer or particular cancer so 49 out of 50 women would never
NOTE Confidence: 0.986315853636364
00:10:35.519 --> 00:10:37.898 get cervical cancer if we did nothing of all.
NOTE Confidence: 0.986315853636364
00:10:37.900 --> 00:10:39.304 We didn’t screen them.
NOTE Confidence: 0.986315853636364
00:10:39.304 --> 00:10:40.708 We didn’t vaccinate them,
NOTE Confidence: 0.986315853636364
00:10:40.710 --> 00:10:41.332 etc etc.
NOTE Confidence: 0.986315853636364
00:10:41.332 --> 00:10:43.820 It’s a high bar because of the rare
NOTE Confidence: 0.986315853636364
00:10:43.897 --> 00:10:46.795 events and the relatively small benefits,
NOTE Confidence: 0.986315853636364
00:10:46.800 --> 00:10:49.085 and there’s very little tolerance
NOTE Confidence: 0.986315853636364
00:10:49.085 --> 00:10:51.570 for toxicity and and then the final
NOTE Confidence: 0.986315853636364
00:10:51.570 --> 00:10:53.436 barrier if you will, is there.
NOTE Confidence: 0.986315853636364
00:10:53.436 --> 00:10:55.254 I think there’s a perception that
NOTE Confidence: 0.986315853636364
00:10:55.254 --> 00:10:57.401 there’s no money in prevention and I
NOTE Confidence: 0.986315853636364
00:10:57.401 --> 00:10:59.619 I would challenge that only to say that.
NOTE Confidence: 0.986315853636364
00:10:59.620 --> 00:11:01.130 Nobody wants to get cancer,
NOTE Confidence: 0.986315853636364
00:11:01.130 --> 00:11:02.594 and so there’s a lot of people out
NOTE Confidence: 0.986315853636364
00:11:02.594 --> 00:11:04.017 there that don’t want to get cancer.
NOTE Confidence: 0.986315853636364
I mean, uh, you know, so that I think that there's actually, given the big denominator, there's a big opportunity for industry to get involved in and prevention. I think that what scares them off is the expense and difficulties of doing large trials to demonstrate. Efficacy and effectiveness and the very low tolerance for toxicity or adverse events. Obviously obesity is and tobacco or...
the main causes of cancer tobacco, you know, we even do some work in this area, particularly for anti nicotine approaches. Obesity I think hangs over all of us in terms of how do we tackle this problem? How do we mitigate the effects of BC? What is the causal relationship of obesity with cancer? Is it inflammation? And then a variety of other causes. Viruses are near and dear to my heart.
because of my work on human papilloma virus, which causes 5% of cancers globally, so it's. And HPV been my training ground on. I started off as a lab scientist but moved into molecular epidemiology 20 years ago and continue to learn from the study of HPV in many ways. So if we think about this causal model where we go from normal to initiate it to precursor States and invasive cancer, it really helps us sort of identify the roles of different groups. But also where we where the opportunities for intervention now precursor states, I mean those are somewhat artificial slices of the pathway,
and in case of cervical cancer that probably really aren’t distinct states, just clinical diagnosis that fall within this area somewhere between. Initiated and pre cancer. 

So what can we do right now? Obviously and I will say highlight that I recently published an OP Ed in Stat to talk about really these same strategies that are being used for COVID can be used for cancer prevention and that we really need a pandemic response for cancer prevention because of the annual burden of cancer. So avoidance is one strategy or
00:13:47.356 --> 00:13:50.090 primary prevention if you will,
NOTE Confidence: 0.987055714285714
00:13:50.090 --> 00:13:53.768 through tobacco prevention, HPV and HB.
NOTE Confidence: 0.987055714285714
00:13:53.770 --> 00:13:56.762 HPV vaccination treatment of
NOTE Confidence: 0.987055714285714
00:13:56.762 --> 00:13:59.006 H pylori potentially.
NOTE Confidence: 0.987055714285714
00:13:59.010 --> 00:14:01.590 And then sex sort of secondary
NOTE Confidence: 0.987055714285714
00:14:01.590 --> 00:14:03.310 prevention through tobacco cessation,
NOTE Confidence: 0.987055714285714
00:14:03.310 --> 00:14:05.083 screening and diagnosis.
NOTE Confidence: 0.987055714285714
00:14:05.083 --> 00:14:07.788 And those tools, avoidance vaccinations,
NOTE Confidence: 0.987055714285714
00:14:07.788 --> 00:14:08.716 bringing treatment,
NOTE Confidence: 0.987055714285714
00:14:08.716 --> 00:14:11.500 or the very things that we’re
NOTE Confidence: 0.987055714285714
00:14:11.566 --> 00:14:13.216 using now to battle COVID.
NOTE Confidence: 0.987055714285714
00:14:13.220 --> 00:14:15.698 And really we need to highlight
NOTE Confidence: 0.987055714285714
00:14:15.698 --> 00:14:18.574 those and bring them back into
NOTE Confidence: 0.987055714285714
00:14:18.574 --> 00:14:20.290 the prevention discussion.
NOTE Confidence: 0.987055714285714
00:14:20.290 --> 00:14:21.921 Uh, we’re working more and more in
NOTE Confidence: 0.987055714285714
00:14:21.921 --> 00:14:23.814 the area of interception of cancer and
we’ll talk more about this in moment, right? And this is sort of moving us towards what people refer to as precision cancer prevention, and I’ll talk about that a couple times through this and even propose a broader definition of precision cancer prevention. But obviously, tamoxifen and its derivatives for breast cancer for those who are at high risk and seats for colon cancer immune modulators. Drugs that target oncogenic drivers and
re activators of tumor suppressor genes, for example.

So I’m going to present this chart or this picture for our three main programs here. It’s what I call our preventive agent R&D pipeline. And the thing that I want to point out is that people don’t always recognize these programs, particularly in DCP. We gave a presentation for this new program called Capital, which I'll explain in a moment to the BSA members. The NCI Board of Scientific advisors.
And one of the members didn’t even know what prevented. So let me so I’m going to drag you through this because I want to engage you in the process of developing new prevention strategies. So Cap is a new program. It’s a targeted agent identification program for preventive agents. Prevent is our preclinical development and validation program and even you know, to the extent of producing GMP grade drug for trials seek Tenet is our early stage clinical trials network and then core, which I’m sure everybody’s heard of, is our.
00:16:04.306 --> 00:16:05.192 You know,
NOTE Confidence: 0.985103935
00:16:05.192 --> 00:16:07.407 our big clinical trials network.
NOTE Confidence: 0.985103935
00:16:07.410 --> 00:16:10.106 For primarily for phase three trials like T.
NOTE Confidence: 0.985103935
00:16:10.110 --> 00:16:11.930 Mist.
NOTE Confidence: 0.985103935
00:16:11.930 --> 00:16:14.198 We had a moon shot consortium
NOTE Confidence: 0.985103935
00:16:14.198 --> 00:16:16.450 on come on novel advents.
NOTE Confidence: 0.985103935
00:16:16.450 --> 00:16:20.184 You lack net is to look at prevention of
NOTE Confidence: 0.985103935
00:16:20.184 --> 00:16:23.103 HPV related disease in HIV and people
NOTE Confidence: 0.985103935
00:16:23.103 --> 00:16:25.468 living with HIV in Latin America.
NOTE Confidence: 0.985103935
00:16:25.470 --> 00:16:28.140 We have funding opportunities for cancer
NOTE Confidence: 0.985103935
00:16:28.140 --> 00:16:30.861 prevention and control trials and a new
NOTE Confidence: 0.985103935
00:16:30.861 --> 00:16:32.905 one hitting the street on in yellow.
NOTE Confidence: 0.985103935
00:16:32.910 --> 00:16:33.483 Here,
NOTE Confidence: 0.985103935
00:16:33.483 --> 00:16:34.629 cancer trials,
NOTE Confidence: 0.985103935
00:16:34.629 --> 00:16:36.348 planning and feasibility.
NOTE Confidence: 0.985103935
00:16:36.350 --> 00:16:39.030 It’s kind of like a P20 funding opportunity.
I can’t remember what the mechanism is. But the basic idea is that these trials are very hard to do and to do denovo, and if we spent some money investing in, we would. You know, get the planning done in the and test the feasibility before they came for an R1 level funding. Precision Cancer Prevention centers is is the future. I hope it’s my dream and fantasy that it would and it would dovetail with this R&D pipeline. But basically two engaged centers to kind of create their own pipeline that would move.
Move from discovery to early translation to early human trials and. I emphasize here as shown below that although these programs sit at the NCI, they’re open for investigator initiated research to take advantage of these programs, and we encourage it. We want you to come forward with new prevention strategies, and again I want to emphasize that what DCP focuses on innovation, new strategies that we haven’t that you know are not. You know that need development and early validation. This just shows the CPCT net,
which is really this early phase clinical trials group that’s across the country. With data monitoring and uhm, uhm? A board that’s a data management and that coordinates these activities, optimizes clinical trial designs, developed surrogate and intermediate endpoint biomarkers, test novel imaging technologies, and develop further insights into the mechanisms of cancer prevention by agents. This is led by even zabbo. Here’s a couple of the approved trials that are already underway, one on NAFLD,
00:18:47.278 --> 00:18:51.574 a HPV vaccine delayed booster trial.
NOTE Confidence: 0.942205678333333
00:18:51.580 --> 00:18:54.116 Uhm and prostate uhm.
NOTE Confidence: 0.942205678333333
00:18:54.116 --> 00:18:57.286 A management trial as well.
NOTE Confidence: 0.974324832
00:19:00.080 --> 00:19:02.780 These are some of the.
NOTE Confidence: 0.974324832
00:19:02.780 --> 00:19:05.495 Protocols that are under development
NOTE Confidence: 0.974324832
00:19:05.495 --> 00:19:09.099 a wide range from breast cancer to
NOTE Confidence: 0.974324832
00:19:09.100 --> 00:19:11.245 FAPA metformin as a chemopreventive
NOTE Confidence: 0.974324832
00:19:11.245 --> 00:19:13.390 agent for lung cancer and
NOTE Confidence: 0.974324832
00:19:13.468 --> 00:19:15.438 high risk of these patients.
NOTE Confidence: 0.974324832
00:19:15.440 --> 00:19:17.200 I’m not going to read through all these.
NOTE Confidence: 0.974324832
00:19:17.200 --> 00:19:19.228 You can have these slides and
NOTE Confidence: 0.974324832
00:19:19.228 --> 00:19:21.675 kind of see the the breadth and
NOTE Confidence: 0.974324832
00:19:21.675 --> 00:19:24.230 depth of the trials at the NCI.
NOTE Confidence: 0.948990096521739
00:19:26.460 --> 00:19:29.100 We’re doing a number of studies
NOTE Confidence: 0.948990096521739
00:19:29.100 --> 00:19:31.740 on topical tamoxifen to look at
NOTE Confidence: 0.948990096521739
00:19:31.740 --> 00:19:34.140 whether we can sort of change
the benefits to harms ratio, I'll come back to that point. By delivering tamox into that issue at risk, and in this case breast cancer. Looking at some biomarkers in DCIS breast density. Measuring inter individual variation and looking at serum and tissue concentrations of the drug being delivered topically.

Are you lacnet which I mentioned before? Is our HPV prevention clinical trials network in Latin American Caribbean, and there are three consortium members working on a variety.
interventions from some vaccination

work to screening to pre cancer

therapeutics and people living with HIV.

So then that leads us into discussions of screening early detection,

Obviously, Plco is one of the major U S trials that was sponsored by the Division of Cancer Prevention and here above,

Obvious here in the yellow.

I just wanted to state that we are more and more thinking about what I call risk informed screening,

so using risk to decide who and when people need to be screened or to modify the management of the screen positives.
And it also provides a possible or potential for intervention with targeted preventive agents if we know the biology of what that risk is, then we could then combine both screening strategy with a preventive agent strategy. So this is our screening early detection R&D pipeline at the core of this is Dern, which has been just renewed and is now 20 years in the making or in its life and it continues. I will present a few slides on that, but we have some related projects around pancreas cancer, PCDC, liver cancer, TLC,
we have a liquid biopsy consortium and we have an image ingane. Biomarkers consortium T bells and new program to help us differentiate between indolent and aggressive cancer. I’m sure many of you have heard of H Tan which is the human tumor Atlas network and we built off of that a pilot study called the Pre Cancer Atlas which we’re hoping to renew in the subsequent year or so. One of the big gaps that we need to fill is a screening and early detection network. Not that Encor doesn’t do some of that, but.
We really need to engage the primary care providers to recruit average risk populations into our trials,

We're developing a new lung cancer image library for improved interpretation of those images I mentioned you last time.

We're now have on the street at Cascade, which is another consortium to look at best practices for screening women living with HIV for cervical cancer.

How best to screen them?
Last Mile is a project that I'm Co leading on getting self collection and HPV testing approved. For routine screening in the United States and so forth. Uh, we're hoping to stand up some risk informed screening for cancer trials, or what I call risk trials, and we have a large trans NCI liquid biopsy, multi cancer early detection program that I've initiated and we will be working on that, including what I hope is a large platform trial to look at some of these technologies going forward.
This just gives you a sense of end core which is involved in all of those activities that preventive agent development program as well as the screening early detection. There are over 1000 clinical sites, 46 centers and affiliates and more than 4000 investigators. This is led by Warden Mckaskle Stevenson who’s doing an incredible job of. Herding the cats if you will. Uh, I’m sure you’ve heard of a team nest, which is a randomized clinical trial to compare 2D versus 3D mammography.
I'll show you some of the not results, but there are recruitment in our recruitment struggles during COVID. We've just launched Forte, which is to look at best rap best management of. You know low, fairly low risk. Populations who have wanted two non advanced polyps. And then a management trial for pancreatic cysts. You can see here the team missed was, as was many of our activities adversely affected by the COVID pandemic, shown here highlighted down here, you can see that the enrollment almost went
to zero during the height of the pandemic.

It’s now come back and exceeded the monthly recruitment levels.

So we’re very excited about that and over time will start getting some readouts from the trial itself on.

3D versus 2D mammography.

Uhm, this just highlights the cascade, which is a global multicenter cooperative agreement.

Clinical trials network.

To optimize this cervical cancer screening and treatment cascade for women living with HIV.

Looking at all these issues in...
the care continuum care of care.

From screening uptake to management of positives,

Although this will be a will have sites in the United States,

we will also include sites in low and middle income countries.

A last mile, as I mentioned, is really going to, we hope,

we will also include sites in low and middle income countries.

A last mile, as I mentioned, is really going to, we hope,

A last mile, as I mentioned, is really going to, we hope,
this topic more than 15 years.

I know I look young, but it has been more than 15 years working on this particular one,

that the idea that we can democratize screening by bringing screening to the homes or to convenient areas for participation in screening, I think, is going to be a game changer, not just nationally but globally.

Although most countries don’t necessarily take FDA approval.

Directly in consideration,

it is a big deal to have an FDA approval for a particular intervention so.
We're very excited about this initiative, which we're hoping to launch in the next year or so. And the other thing to say about this is from the meta analysis that I've participated in and others know that women prefer this. It's kind of a no brainer and using a PCR based HPV test there’s really little or no decrement in clinical performance, so this is a big deal. If we can get it underway.

And it’s a big deal in the global battle against cervical cancer.
ERN was established in 2000, UM, to support investigator initiated research for the development and validation of biomarkers, foster interaction cooperation between academic, clinical, industrial partners or leaders. Furnish and apply standardized biomarker validation criterion quality assurance and facilitate regulatory process to bring biomarkers rapidly into clinical use. This is really our core biomarker for you know, screening for prevention and early detection, and Sudhir has done an
amazing job on this program. This just gives you a sense of the different components of this. There are four main research groups shown here. On the left there's a steering executive, committees that oversee and review the program on a regular basis. We have a consulting team and the breadth and depth, earn because of its breadth and depth, is really started to come. You know, permeate all areas related to. Early detection biomarkers related to early detection and prevention projects. Collaborations with Japan, India, France.
Uhm, we’ve gotten Co funding from a variety of organizations. As I mentioned, there are tangential collaborative groups that expand on particular areas of EDR, and many associate members, federal partners, and we engage directly with pharma biotech industry.

These are just some of the tests and I won’t go over them. Obviously the perhaps the one that you’re you know.

Hearing a lot about his cancer seek which is a multi cancer early detection.
which was supported by the DRN.

But there are many more and with this next round of renewal we’re really hoping to push more things to FDA approval and into clinical practice.

And that’s really going to be our metric going forward is how much of this gets into routine care?

Uh, I sort of alluded to this before, but the idea that we could bring these two pipelines together one is biomarker discovery, as well as and as well as bringing a preventive agent into the mix and so that you could detect and mitigate cancer risk, but.
As I will talk about later, I really want to expand what we call precision cancer prevention and I will talk about that a little bit later. We also do symptom management, which seems odd, but that’s the way it is. And actually I’m very excited about this. I think there’s tremendous opportunity to improve symptom management and supportive care. What’s really important about this to me is that the prevention and treatment of symptoms from cancer really has a profound effect on the quality of life.
Of patients, but also their ability to survive the cancer and cancer treatment if we can manage symptoms better. As you well know, many of you are oncologists. The clinical performance remains high and so patients really not only get their first line of treatment, they get their second and third line treatment and even treatments that haven't been invented today but will be tomorrow.

So we have a very broad portfolio, big and broad portfolio and in symptom management shown here.
Uh, those are the number in the upper left hand panel is the number of grants per per year.

Are we really the only group at the NCI that focuses on pain management? And much of these activities happen within our clinical trials network, now called Encor. It used to be sikap. So this is again the pipeline and I use this as a is a sort of a platform for thinking about where we want to go. We have a lot of. You know, activities in our clinical trials, but what’s really lacking is an investment in the biology and genetics.
What we'll call here is precision symptom management, or symptom science.
to do and not much.

We can’t show anything.

So the this moon shot that tolerability consortium focused on analyzing,

interpreting,

clinician and patient adverse event data to better understand Taler ability.

Doing so by creating a consortium to share analytic approaches and so let me conclude with a few slides here and then it will open up for questions.

These are certain my informal, UM, unofficial priorities,

really understanding biologic risk and using that to guide what we do for patients,
but also population risk to
NOTE Confidence: 0.96990851
00:32:56.190 -- 00:32:58.550 decide who gets screened and how.
NOTE Confidence: 0.96990851
00:32:58.550 -- 00:32:59.798 How to screen,
NOTE Confidence: 0.96990851
00:32:59.798 -- 00:33:01.890 how to screen positives are
NOTE Confidence: 0.96990851
00:33:01.890 -- 00:33:04.410 managed and how to harmonize care.
NOTE Confidence: 0.96990851
00:33:04.410 -- 00:33:06.336 What I call equal risk equal
NOTE Confidence: 0.96990851
00:33:06.336 -- 00:33:07.620 care for equal risk,
NOTE Confidence: 0.96990851
00:33:07.620 -- 00:33:10.148 which is an idea that we had promulgated
NOTE Confidence: 0.96990851
00:33:10.148 -- 00:33:12.429 over 15 years ago in the cervix.
NOTE Confidence: 0.96990851
00:33:12.430 -- 00:33:12.679 World,
NOTE Confidence: 0.96990851
00:33:12.679 -- 00:33:14.671 as we saw that there were the all
NOTE Confidence: 0.96990851
00:33:14.671 -- 00:33:16.168 these new tools coming and there
NOTE Confidence: 0.96990851
00:33:16.168 -- 00:33:18.485 was going to be a great deal of
NOTE Confidence: 0.96990851
00:33:18.485 -- 00:33:19.909 heterogeneity in the population.
NOTE Confidence: 0.96990851
00:33:19.910 -- 00:33:21.918 Risk to their vaccination.
NOTE Confidence: 0.96990851
00:33:21.918 -- 00:33:25.390 We really needed a organizing principle here.
Obesity, as I mentioned before, causes so much of the burden of cancer and we really don’t understand it. If we did, we could mitigate its effects. Obviously, changing lifestyle behavior would be ideal, but I think it’s a real challenge to get people to change their lifestyle behavior over a course of decades. And so I’m not saying that we shouldn’t invest in that, but I’m saying complementary to that. We really should understand the pathways and how obesity contributes.
to carcinogenesis so that we can.

Combine that with changes in lifestyle and behavior.

I think I’ve said enough about precision, symptom, prevention, and management, but I you know, just to emphasize that I, I think we need to move away from the trial and error that often occurs in clinical management. That’s not a criticism of the clinicians at all, it’s just that we haven’t. We haven’t really taken this as seriously as we should in terms of bringing the same kind of focus on precision medicine.
to this area as we have in other areas.

Health disparities I think there's a lot of opportunity for innovation.

I mentioned self-collection developing points of care testing like for HCV. You know, bringing the tests to the people, or bringing the intervention of the people rather than just relying on them to come to the clinic.

I know that persistent reality is a major risk factor for cancer, and then we're being bombarded with new technologies, AI multi-cancer, early detection, synthetic biomarkers, etc.

We really the NCI plays a pivotal role in sort of getting out in front and figuring out what’s good and what’s not without bias without. And gender and I think we need to do that more and more as these new technologies rollout faster and faster. Uhm, I wanna pose something that might be a little bit controversial, which is a broader definition of precision cancer prevention. To achieve equitable care for all. And the core principles here are the benefits to harms ratio and understanding. All causes of differences, not just biological,
which informs how we can be more precise.

So what we've typically figured is the what, which is based on an understanding of carcinogenic processes.

Target early changes via screening or interception, but I want to add The Who into this, which isn't always integrated into this, which is who's at risk and how much risk. And that really tells us, not just.

What age but what kind of screen? To use or what kind of intervention to use and what's the follow-up care? Where a?
Alternative delivery strategies, like I mentioned home based sample collection of testing, app based interventions and so forth and then how benefits and harms can be manipulated by alternative routes of administration like topical tamoxifen, maintaining effective doses more consistently through sustained release to reduce toxicity and perhaps even increase improve the benefits. The cancer prevention, benefits and even strategies. For immunization and we we often focus on active immunization, but sometimes you can’t develop a good
response or a sufficient response. So maybe we have to make antibodies like anti nicotine antibiotics which we are supporting right now to give people the immune spot immune response that they need. I think this is my final slide, which is just a call out for our cancer prevention fellowship program, from which I spawned. So how bad can it be? This is a multidisciplinary, diverse, and highly competitive postdoctoral training program that provides flexibility.
for fellows to generate and pursue original scientific ideas and structure, to develop competencies, support their future as leaders in the field. But I’m very proud of is we’ve got now cancer prevention fellows from Costa Rica and we are working towards the idea of having an ongoing international training component to this cancer prevention fellowship. And then the Cancer Prevention Fellowship program has alumni across all across the country in the world. You know it’s been around for 35 years now and fellows are at major cancer centers and leadership positions.
Government agencies, research firms, foundations, and policy organizations, and the website for the Cancer Prevention Fellowship program. Shown there at the bottom. So with that, I'll say thank you and I'll take any questions. From the audience and thanks again for the invitation to Yale Cancer Center. Thank you very much. Doctor Castle and Great talking, kind of a whirlwind overview. What’s been going on with exciting preview of next steps? So I’ll ask people to send questions.
via the chat button while we’re waiting

for some other questions that they

had one just to get the ball rolling.

So. In your position,

the decisions need to be made

with regarding prioritization of

large scale efforts forward in

overarching strategies at the center.

Beneath that there are four

tactical decisions which.

Which plans to find out which teams he

grants or program projects so for WhatsApp.

So my question to you is how do

you track success that how do you?

you made the right decisions or that?
Like if you imagine an alternate universe where you could have been focused, knowing the center could have been focusing on completely different things are completely different strategies. They can have different outcomes, so I don’t. I’m just curious how you think about how you know how to evaluate the progress of the centers making it both. So what’s the time horizon is one of the metrics for evaluating success. Boy you’ve touched it. I mean you went right to the heart of it, right? Not just from a programmatic standpoint.
but from a prevention standpoint, because it often takes more than five years to show any of this stuff works, and I think. That is sort of one of the major barriers for researchers getting into the prevention field because. It's just hard, you know, even you know and and the more successful you are like for screening, even harder it is to do a prevention trial, right? 'cause then you start extending screening intervals to the point you can't even study it within an hour one. So I mean some of these things.
You know, that’s why we have to do things more, sort of directed by the NCI as a clinical trial, rather than just relying on our one. I know everybody wants to put all the money into the R1, but my calling is to come up with the best prevention strategies and sometimes it just doesn’t fit. And as you pointed out, I have to make guess I have to make informed.
I hope. Informed guesses. About where we should put our energies. I think what I've been trying to impress upon my staff and through my staff to the extramural investigators we want to ground this in the best science possible, knowing that even that may not be good enough and one of the challenges and we were. We rely particularly for preventive agents on mouse models. But there's a lot of issues. You know? How well does it recapitulate human biology?
How much can we rely on that?

Because what happens, of course,
is then we go to, you know,
human trials based on those results.

Even the phase one phase two trials are expensive.

They take a long time and and
don’t have an efficacy readout.

So let’s say the toxicity is OK.

Then you go into a five or seven or ten year trial.

And only at the end there do you figure out,
Oh my God, this doesn’t work.

We’ve just spent $100 million for something
that’s not going to help anybody.

So it really is a challenge and I don’t have a good answer.

I would say that one of the Ways forward is we really have to think hard about. Surrogate endpoints for cancer risk or cancer mortality.

So screening trials are particularly challenging because right now the only thing that we, I think everybody can completely agree upon is if it reduces cancer mortality. It works, but stage shift doesn’t necessarily translate,
at least right now into benefit, and you can see the UK ovarian cancer screening trial is an example of that. Although I believe. Eventually stage shift should translate into mortality benefit, but until we’ve shown you, Sarah did endpoint, it doesn’t. It’s hard to then recommend something for general use, so are you know one of our challenges, whether it’s and I’ve been challenging the nutritional science.
group within our that we can’t
go into this black box of like.
Eat this we you know we can get people
to do this and then we’re going to go into a clinical trial to show you know,
reduction of cancer incidence,
which will take years and years to do.
We need intermediate endpoints that we can rely on that at least.
Push us in the right direction,
right?
The screen out the you know some of the things that aren’t going to work.
I do think that we have because of the
time and the expense we’re going to
have to be more specific than sensitive.

We can’t chase after everything, so we have to place a sort of higher bar in this development process and recognizing that we’re going to miss some opportunities. But the opportunity costs of chasing after our tail are really significant and problematic. So there is no good solution. If you have one, please tell me because. You know, we talk about this all the time. It’s just hard. It’s hard to do prevention and yet everybody knows I mean.
Even the most oncologists would tell you no.

Prevention is our first line of defense, and if you know and I always say this to my audiences, they walk down the street after Kovid and if it’s safe and ask the first hundred people you walk into and say, would you like your cancer prevented or treated? I’ll take that bet with odds that every one of them is going to say. Of course, I want my cancer prevented so. We all know it’s important we...
all want it to go forward, but there are some real challenges to it and you know, as I mentioned before, the other challenge, of course, is very low tolerance for toxicity if you’re primarily dealing with average risk. People who are on that day, most of them healthy. You can’t. You know, you just can’t do bad things to them, understandably so you know the cervix world is sort of the outlier. In a way, it’s it was the low hanging fruit you have. You know you have relatively
easily accessible tissue.

You have a single causal agent.

And it takes 20 to 25 years on average to cancer.

I mean that you know, if we if I want to be honest about them, that one was supposed to be successful and the other ones are much harder.

So.

Thank you, no, I don’t have a clear answer.

That’s why I asked, you know, I believe me.

If I had an answer I would share it with you, but I I don’t.

We struggle with this. I think the best thing we can do is brown.
Listen better science, right?

Understanding the molecular mean

people wanted the magic bullet, right?

If you eat this.

This is going to work and I'm

not saying that that won't work,

but let's look at nutrition for a

second here and I apologize to any

nutritional epidemiologists or scientists.

But the challenges of going

from eating something into a

clinical trial or profound right?

So likely it's going to

be a low penetrance thing.

Even if you can measure it and the
the ability to show it both at the lab level and if you go through the hill criteria and say we’ve got to get to a certain number of those before, we’re going to go into a clinical trial. 
And then in most cases, you’re really talking about a low penetrance or weak penetrance of or weak effect, right? You know, you’re really rolling the dice on, 50 to $100 million trial to get the kinds of endpoints. And that’s and we failed. We’ve had a number of failures and you know,
the other one that people have been chasing after his metformin and were or.

And that’s really turning out to not be relevant in the prevention space, or it’s such a weak effect that we can’t measure it, right? So that’s the other problem. It might have a modifying effect, but we can’t.

Measure it and therefore we can’t recommend it. And more importantly EU S Preventive Services Task Force can’t recommend it. So and you know that. So I mean part of it is we want...
something that’s so cheap that you can get it off the shelf or. Or you can go to the grocery store and eat it. That has not panned out and and and And it doesn’t mean that it doesn’t work, but it’s hard to show it, and it’s hard to invest that money in showing it. So follow up question thinking about the challenge of small effect sizes. Or it could be a large sample size of getting needed and create expense. Just thinking about the experience during COVID, but the UK. Some kind of ran circles around
00:47:45.588 --> 00:47:48.406 us as a nation with regard to the
00:47:48.406 --> 00:47:50.381 facility with conducting these large
00:47:50.381 --> 00:47:52.846 trials so that they have the recovery
00:47:52.846 --> 00:47:54.774 trial which actually enrolled 10%
00:47:54.774 --> 00:47:57.282 of all patients across the country
00:47:57.282 --> 00:48:00.031 who are hospitalized in the UK were
00:48:00.031 --> 00:48:01.960 involved in this large sent.
00:48:01.960 --> 00:48:03.680 You know, it’s large,
00:48:03.680 --> 00:48:05.400 centrally coordinated trial randomization.
00:48:05.400 --> 00:48:08.574 It is generated a great deal of prompt.
00:48:08.574 --> 00:48:11.436 Really informative information is kind of.
00:48:11.440 --> 00:48:12.420 People have subsequently been
00:48:12.420 --> 00:48:13.890 saying or what can we learn?
00:48:13.890 --> 00:48:16.008 Post code it’s not covered child.
00:48:16.010 --> 00:48:17.314 The more centralized approach,
so you know building and and you 
NOTE Confidence: 0.980951666470588
00:48:19.674 --> 00:48:21.762 mentioned is that the screening and 
NOTE Confidence: 0.980951666470588
00:48:21.762 --> 00:48:23.504 early detection network and what 
NOTE Confidence: 0.980951666470588
00:48:23.504 --> 00:48:25.104 are the strategies for creating 
NOTE Confidence: 0.980951666470588
00:48:25.104 --> 00:48:26.638 this large amount of people. 
NOTE Confidence: 0.980951666470588
00:48:26.638 --> 00:48:28.342 That and other things out there 
NOTE Confidence: 0.980951666470588
00:48:28.342 --> 00:48:30.197 for large systems where we could 
NOTE Confidence: 0.980951666470588
00:48:30.197 --> 00:48:32.033 be running multiple trials at the 
NOTE Confidence: 0.980951666470588
00:48:32.094 --> 00:48:34.467 same time and have like a single 
NOTE Confidence: 0.980951666470588
00:48:34.467 --> 00:48:36.098 infrastructure that’s really, really big. 
NOTE Confidence: 0.980951666470588
00:48:36.098 --> 00:48:36.706 Well we’ve, 
NOTE Confidence: 0.980951666470588
00:48:36.706 --> 00:48:39.222 I mean to some extent we’ve done that 
NOTE Confidence: 0.980951666470588
00:48:39.222 --> 00:48:41.170 with enkor, but that tends to be, 
NOTE Confidence: 0.980951666470588
00:48:41.170 --> 00:48:41.794 you know, 
NOTE Confidence: 0.980951666470588
00:48:41.794 --> 00:48:43.666 a cancer centers and you know 
NOTE Confidence: 0.980951666470588
00:48:43.666 --> 00:48:44.290 oncology services.
I mean, so some of the things that we’re doing like Team Nest where you have to have radiology anyway, that kind of works in that network, but. We have other networks that are in place that could be leveraged. It’s a matter of coordinating them and being willing now. Some people would say Kaiser, though my experience and I’ve worked with Kaiser Permanente Northern California for 15 plus years. They’re not really set up to do clinical trials,
but one could imagine some combination of FQHC’s and other providers, but starting to link them now.

Between you and me, and I’ll deny this if if anybody quotes me.

If you start doing that, you start building a public health infrastructure which I think COVID revealed we didn’t have in the United States so.

It is easier to do some of the stuff in Europe because they have organized programs they have organized health care.

They have organized screening.

We do not.

But I think we can start pushing
along those ways and it would be hope. My hope you know, probably long after I’m gone, but that by doing these kinds of activities where he showed networks can work together that you start to build the an informal organized screening really makes a difference in terms of the effectiveness of the program, and I’ve had the privilege and just reviewing another paper from them of working with Norway.
for the last eight or nine years.

And that’s been a real pleasure to like what they can do to you know,

and how they can make switches,

how they can really get high coverage

and identify people for whom

the system is not working right.

And and come up with alternative strategies.

So we know that screening like even

for cervix we know that 2010 to 20%

of people don’t get their routine

screening or don’t get screened at all.

And that’s where half of the cervical cancers occur.

So if we can bridge that gap,

then we’re making progress.
So I mean, that’s not the typical innovation that the division is focused on the past, but I’m a population scientist who’s worked on some of this stuff, so that’s why. I’ve sort of been thinking about my own definition of precision cancer prevention and trying to expand that to say it isn’t just what we do like targeting carcinogenic pathways. It’s also how we do it and where we do it, for whom do we do it?

That’s great baby. Let me pause, I do. I don’t wanna turn this into a fireside chat would be nice.
wanna try I like fireside chats.

I'm happy to happen even separately.

I can come back. Come.

Well, I had one other question.

No other questions from the groups.

One other quick question is on.

Mr. President.

What are you thoughts about some form

of a whole of government approach

intersectoral approach were talking about?

You know things like you know.

Is it critical?

So I wanted to find out which Ave,

but you know we subsidized corn.

So we our government on the one hand,

is doing things that actually
increasing the obesity our country. So just thinking are there avenues towards UM? Collaborating across sectors within the government, to, you know, think about changes at the policy level to come. I’m gonna change the diet or you know, kind of incorporate. So we to evidence based policy change under some kind of demonstration. Part projects that could relate to things, which is the change in diet? You know population efforts to
00:52:31.155 --> 00:52:33.374 to address obesity or in see how
NOTE Confidence: 0.970965175
00:52:33.374 --> 00:52:35.206 that might affect cancer, right?
NOTE Confidence: 0.970965175
00:52:35.206 --> 00:52:35.802 Well,
NOTE Confidence: 0.970965175
00:52:35.802 --> 00:52:39.378 that’s an interesting question of course.
NOTE Confidence: 0.970965175
00:52:39.380 --> 00:52:40.717 You know one of the things that
NOTE Confidence: 0.970965175
00:52:40.717 --> 00:52:42.080 I think about is, you know,
NOTE Confidence: 0.970965175
00:52:42.080 --> 00:52:43.910 this crossover of obesity and smoking.
NOTE Confidence: 0.970965175
00:52:43.910 --> 00:52:44.702 I mean,
NOTE Confidence: 0.970965175
00:52:44.702 --> 00:52:45.890 smoking suppresses diet,
NOTE Confidence: 0.970965175
00:52:45.890 --> 00:52:48.202 so is there going to be a point
NOTE Confidence: 0.970965175
00:52:48.202 --> 00:52:50.228 of crossover where where obesity
NOTE Confidence: 0.970965175
00:52:50.228 --> 00:52:52.528 becomes more important than smoking?
NOTE Confidence: 0.970965175
00:52:52.530 --> 00:52:54.780 But I’m not suggesting that anybody
NOTE Confidence: 0.970965175
00:52:54.780 --> 00:52:57.430 should start smoking to prevent recently,
NOTE Confidence: 0.970965175
00:52:57.430 --> 00:52:58.060 by the way.
NOTE Confidence: 0.922078117857143
00:53:00.150 --> 00:53:03.086 If you think about the successes of public
health successes in the United States, they've really come. They've been driven. Sort of from the ground up, right? So if you look at smoking? You know it was lawsuits and you know, demands from the public to say this is this is, you know, we have to do something. Uh, even the you know one of the most successful public health campaigns has been HIV, right and? And and that’s because. People demanded they got up on their soapbox and they said,
00:53:35.880 --> 00:53:37.080 you have to do something.
NOTE Confidence: 0.922078117857143
00:53:37.080 --> 00:53:40.200 And so I think you know one of my jobs.
NOTE Confidence: 0.922078117857143
00:53:40.200 --> 00:53:43.154 Although you know I’m not a implementation
NOTE Confidence: 0.922078117857143
00:53:43.154 --> 00:53:45.498 and dissemination person that’s in DCCPS,
NOTE Confidence: 0.922078117857143
00:53:45.500 --> 00:53:49.127 but I’ve done that work for my entire career.
NOTE Confidence: 0.922078117857143
00:53:49.130 --> 00:53:50.992 And we can speak about the audit
NOTE Confidence: 0.922078117857143
00:53:50.992 --> 00:53:52.461 evening leading the division of
NOTE Confidence: 0.922078117857143
00:53:52.461 --> 00:53:53.999 cancer prevention if you want.
NOTE Confidence: 0.922078117857143
00:53:54.000 --> 00:53:54.615 But the I.
NOTE Confidence: 0.922078117857143
00:53:54.615 --> 00:53:56.833 I do think that we have to educate the
NOTE Confidence: 0.922078117857143
00:53:56.833 --> 00:53:58.999 public on the possibility of prevention,
NOTE Confidence: 0.922078117857143
00:53:59.000 --> 00:54:00.863 which is why I wrote that OP Ed to
NOTE Confidence: 0.922078117857143
00:54:00.863 --> 00:54:02.656 say if we can do this for COVID,
NOTE Confidence: 0.922078117857143
00:54:02.660 --> 00:54:05.348 we should be doing it for cancer prevention.
NOTE Confidence: 0.922078117857143
00:54:05.350 --> 00:54:07.107 That it’s our first line of defense.
NOTE Confidence: 0.922078117857143
00:54:07.110 --> 00:54:08.790 Not that we’re going to prevent all cancer.
You know.

I have no illusions of that, but I think there’s a lot more and you have to make the investment. We invest three times just in the government.

We invest three times more into treatment than we do. Prevention, let alone pharma. It’s got to be 20 to one or more, so I think it’s it’s getting.

We need to understand obesity.

Getting voices to say.

You know we need to make these investments in prevention. We need to understand obesity.
We need to also have policies about what we make available for foods and tax. One of the most effective strategies is taxation. Ten years ago I was sitting at the UN meeting on global warming CDs and there's a lot of talk about the policy and taxation, making sugary foods less available, right? This is my opinion and I don’t mean to be offensive in any way.
It is primal and I don’t think we evolved to have unlimited access to food. But we do now. And so I know I have like no resistance and the fact that I’m sitting in home and I’m, you know, literally 20 feet away from my refrigerator is trouble. Like if I’m not around it, I’m much better off. When I was at Einstein, I wouldn’t take anything to work because I knew that, you know it just. If it’s not there, I don’t eat it.
but if it’s there, I will eat it. I have like no resistance and I don’t think I’m unusual that way. I think I’m fairly represented despite my knowledge base, so I think you know. Our challenge is understanding fundamentally what we’re hardwired to do. I mean, smoking is a little different because it’s not a survival thing, but once you’re addicted, you’re addicted, right? Your wiring, you know, you’ve you’ve done. You know, it’s haywire.
You know you’ve messed with your, you know with the program. But food is fundamental. We eat to survive so. We evolved that capacity over, you know, millennia. To you know, and when we evolved it, we evolved it when we had to go out and hunt and gather, right? So there was a lot of exercise and the marginal difference between our caloric expenditure and our intake kept things in the right place. But now I can go down to the store and get you know,
or to a restaurant and get 1000
thousand calorie lunch easily.
When we're not even supposed to exceed 2000,
right? So one meal and I,
It's all haywire,
It think it really for the obesity thing.
I mean, I do think that the NCIS responsibility
do research to understand and come
to do research to mitigate it,
recognizing that there are we may
not get these other problems solved,
but I think this is going to be a
policy ultimately just like smoking.
00:57:16.450 --> 00:57:19.090 Thank you up and down.

00:57:19.090 --> 00:57:20.938 Actually, yeah, now I feel guilty about.

00:57:20.940 --> 00:57:22.452 I’m about to walk out and buy

00:57:22.452 --> 00:57:23.590 1000 calories lunch right now.

00:57:23.590 --> 00:57:26.420 Thank you, but no thank you for so much for

00:57:26.493 --> 00:57:29.206 joining us and for your thoughts, were I.

00:57:29.206 --> 00:57:30.546 I hope it was provocative.

00:57:30.550 --> 00:57:33.320 I hope people got out a lot of it wasn’t

00:57:33.397 --> 00:57:34.836 your typical scientific presentation,

00:57:34.836 --> 00:57:37.260 but I really wanted to get out and

00:57:37.319 --> 00:57:39.153 sort of encourage people to come to

00:57:39.153 --> 00:57:40.730 the division of cancer prevention

00:57:40.730 --> 00:57:42.565 with their new prevention ideas.

00:57:42.570 --> 00:57:46.242 We really need everybody in the boat.

00:57:46.242 --> 00:57:48.670 You know, coming up with new

NOTE Confidence: 0.967927462
strategies to prevent cancer.

I think the public deserves it.

Absolutely well.

Thank you so much all right.

Good luck everyone.