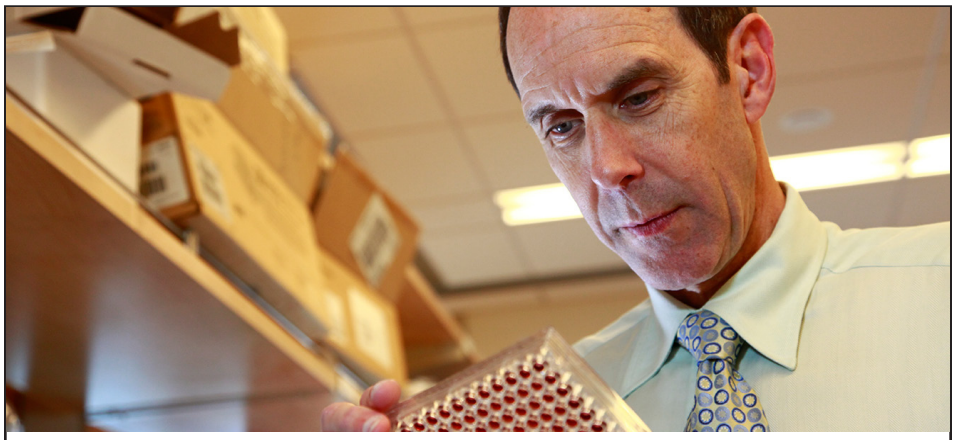
THE CANCER LETTER

May 9, 2014 • www.cancerletter.com • Vol. 40 No. 19



Oregon Center Launching $1 Billion Program To Identify Lethal Cancers Before They Kill

By Paul Goldberg

Brian Druker has some awesome jobs to fill.

As many as 30 scientists and their teams will get to focus on cancer research without having to worry about applying for grants.

"It's about bringing 20 to 30 people together, giving them sufficient funding—almost like [Howard Hughes Medical Institute] level funding," Druker said to The Cancer Letter. "If you have 20 to 30 people who are focused on science, working as a team to solve a problem, judged on progress toward the goal, as opposed to how many grants and publications do you have, we think we can make a more rapid contribution in this area.

(Continued to page 2)

CMS Advisors Express Low Confidence In Low-Dose CT Screening for Lung Cancer

By Matthew Bin Han Ong

An advisory panel for the Centers for Medicare and Medicaid Services expressed low confidence in low-dose computed tomography as a method for screening for lung cancer in the Medicare population.

Evidence is inadequate to ensure that benefits of the procedure would outweigh harms, the Medicare Evidence Development & Coverage Advisory Committee said at the hearing April 30.

(Continued to page 3)

In Brief

David Cole Named President of MUSC

DAVID COLE was named president of **The Medical University of South Carolina** and its affiliated medical centers.

Cole is an oncology surgeon and researcher at Hollings Cancer Center. He also currently serves as president of MUSC Physicians and as chairman of the Department of Surgery.

(Continued to page 17)

OHSU Knight Cancer Institute To Recruit 20-30 Researchers

(Continued from page 1)

"And, in addition, if 20 or 30 people are spending their time focused on science, that's like 40 to 60 people in a regular research environment, because they have their administrative responsibilities, their teaching responsibilities, and their grant-writing responsibilities."

The new goal is a logical continuation of Druker's work with Gleevec (imatinib), a spectacularly effective treatment for chronic myelogenous leukemia and several other cancers.

The difference, of course, is that Druker, director of the Knight Cancer Institute at Oregon Health & Science University, and a member of the small club of people whose work has revolutionalized cancer therapy, wants to move identification of cancer's lethal characteristics to an earlier stage in the disease process.

The research program Druker envisions will require $1 billion, of which $300 million is already on hand, and $200 million more will need to be raised by February 2016, which will then trigger a matching gift of $500 million from Nike co-founder Phil Knight and his wife Penny. To help raise the rest of the money, OHSU began running a series of advertisements in The Wall Street Journal and The New York Times earlier this week.

The new program doesn't yet have a formal name, but OHSU is moving forward. "Right now we are just calling it the Knight Cancer Institute, which we are," Druker said. "I don't even know what we are going to call it."

The words "lethal cancers" may figure in the name—or they may not. With the name a work in progress, the program is moving forward.

"We are going to start recruiting the leader of this program immediately," Druker said. "We are actually putting the job description together as we speak.

"The reality is we want to approach this as the most efficient way to solve the problem, if you think about how do we do better at accurately detecting breast cancer. What do we need to know about the basic biology? How do we collect information to understand the basic biology? What technologies do we need to deploy to detect the changes as cancer moves from nonlethal to lethal? It becomes as much an engineering problem as you can possibly make it.

"So we will hire the people that we need who will approach the problem and solve the problem."

OHSU's focus is what distinguishes it from other cancer centers.

"I am not saying this work isn't being done anywhere," Druker said. "I am just saying we are going to make a major push into this issue. We are the only ones investing $1 billion—that's for sure.

"If we are successful, in a decade, when people say, 'Where is the best early detection research occurring?' we want to be among the handful of institutions where the best work is being done.

"I think the important point is, we are looking at this in terms of how we solve the problem and what resources do we need to apply, what disciplines, what investigators do we need to bring together to solve the problem," Druker said.

The room for improvement in early diagnostics is vast.

"If you look back 30 years ago, when I started my training, we had chemotherapy, which nonspecifically killed cancer, didn't distinguish cancer from normal, and we had mammograms and PSA," Druker said.

"Thirty years later, we have hundreds of targeted cancer therapies—and we have mammograms and PSA. If you think about the natural evolution of where the field goes, it moves from molecularly targeted therapy for advanced cancer to molecularly targeted early detection and, ultimately, to prevention.

In part, the strategy is similar to the development of Gleevec.

"With Gleevec we said, 'Let's stop non-specifically killing cancer and understand what drives the growth,'" Druker said. "What we are saying with early detection

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

Editor & Publisher: Paul Goldberg
Associate Editor: Conor Hale
Reporter: Matthew Bin Han Ong

Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

is, let's stop detecting something like a PSA and start detecting it based on what we know about what turns it from a precancerous lesion into a lethal cancer.

"It's the same molecular approach that we took with Gleevec. What do we need to detect? How do we need to detect it, and that becomes what we translate into reality."

Knight's $500 Million Gift

Druker has been talking about this approach to diagnostics for at least a decade.

In 2008, the Knight family gave OHSU $100 million, a part of which was spent to recruit molecular geneticists.

Among those recruited were Joe Gray, Lisa Coussens, and Paul Spellman.

By last spring, Druker was plotting the next step.

In April, 2013, Druker met with Knight and presented him with a proposal to invest $1 billion, which would be built around the lead gift of $300 million to $500 million.

"He was stunned and shocked, but he didn't throw us out of the room," Druker said. "He said he was actually thinking about it."

On Sept. 20, the Knights were expected to attend an OHSU event.

A few days earlier, Knight called and said that he wanted to introduce him.

"Of course, I said, 'Yes, you can introduce me,'" Druker said. "The only people in the room who knew what he was going to say were himself and his wife—and he announced that he would give us $500 million, if it's matched with $500 million in a fundraising campaign over the next two years."

His surprise introduction was videotaped by OHSU.

OHSU has until Feb. 6, 2016, to raise these funds. If the center raises $499 million, the Knights would be relieved of their obligation (The Cancer Letter, Sept. 27, 2013).

OHSU put together an economic impact statement, and in February the state authorized $200 million in bonds to fund construction of a building. While this counts toward matching funds, the goal is now to raise $1.2 billion, which would give OHSU $1 billion to spend on research.

About a quarter of these funds will be placed into an endowment, and the rest will be expended over about a decade, Druker said.

So far, philanthropy has contributed a bit over $100 million to the effort, in addition to the state's $200 million commitment.

When Knight made his announcement, his friend Dan Weiden, founder of the advertising firm Weiden+Kennedy, was in the room. The firm, based in Portland, has donated the creative work for the national campaign OHSU has just launched.

Druker said the campaign's initial media buy would be several million dollars, with a lot on emphasis placed on social media.

"The focus of the campaign is, we've done this before," he said. "We can do it again."

CMS Advisors: Lung Screening May Do More Harm Than Good

(Continued from page 1)

Panel members gave low average confidence scores in response to two questions focusing on harms—2.22 for whether there is adequate evidence for significant benefit over harm, and 2.33 for whether harm will be minimized in the Medicare population.

"I got stuck on 'adequate', and I just didn't feel that there is really adequate evidence at this time," said MEDCAC member Jo Carol Hiatt, chair of the Inter-Regional New Technology Committee at Kaiser Permanente. "It's promising, but we certainly need more information before making a broad statement about benefit to the Medicare population."

The panel votes in a manner that differs from the FDA Oncologic Drugs Advisory Committee, which usually votes up-or-down on the approval questions. In contrast, MEDCAC members are asked to rate the benefit-harm ratio on a five-point scale, after which the committee members' scores are averaged.

In the case of CT screening, the two most important scores fell into the low confidence range.

It is unclear how CMS will interpret MEDCAC's recommendation, but insiders say it's plausible that low-dose CT screening for lung cancer could be denied coverage.

Committee members largely based their votes on results from the NCI-funded National Lung Screening Trial, a $256 million randomized trial that accrued over 53,000 participants.

The trial documented a 20 percent decrease in lung cancer specific mortality (95% CI, 6.8 to 26.7; p=0.004) for patients between the ages of 55 and 75.

The U.S. Preventive Services Task Force gave a B rating to the procedure last fall, recommending screening for people between the ages of 55 and 80 who have a 30-pack-year history of smoking (The Cancer Letter, March 21).

The upcoming decision will ultimately determine how a positive trial and a positive USPSTF recommendation translate into a coverage policy. CMS expects to release a decision memo in November, with a final coverage determination by February 2015.

Many of the principal advocates of screening, including those who once slammed the NLST and tried to derail it, showed up at the MEDCAC hearing to argue for broad coverage. These advocates and care providers sought full coverage within the risk group described by the USPSTF as well as limited coverage with evidence development for lower-risk groups.

One advocacy organization, the Lung Cancer Alliance, had launched a program to certify "centers of excellence" for providing screening. The reliability of that certification came under fire from skeptics at the hearing (See story on p. 8)

Reacting to the negative recommendation from MEDCAC, Laurie Fenton-Ambrose, president and CEO of the alliance, said panel members had failed to grasp the data on lung cancer screening.

"This is a nonbinding poll by a group of committee members outside of lung cancer screening on their understanding of the level of existing evidence and data existing," she said to a reporter.

Fenton-Ambrose had previously called the NLST a "failed" and "outdated" trial (The Cancer Letter, April 18).

The American College of Radiology called the MEDCAC vote a "failure" that may "place many seniors at risk."

"The ACR is deeply disappointed at the failure of the MEDCAC to vote in support of national Medicare coverage of LDCT screening for patients at high risk for lung cancer," the statement reads.

"Without national Medicare coverage for CT lung cancer screening, seniors face a two-tier coverage system in which those with private insurance will be covered for these exams and many of their lives saved, while Medicare beneficiaries are left with lesser access to these exams and placed at increased risk of dying from lung cancer," said Ella Kazerooni, chair of the ACR Lung Cancer Screening Committee. "CMS needs to move for full national coverage as the USPSTF recommendations would indicate."

Members of the advisory committee said they were not convinced that the NLST results would be generalizable to the Medicare population, largely because that population is highly heterogeneous, and because there are no mandatory screening criteria in community practice for the procedure.

"I'm essentially concerned about generalizability and implementation," said Michael Gould, a senior research scientist and director for Health Services Research and Implementation Science in the Department of Research and Evaluation at Kaiser Permanente. "I think this is an opportunity, and should our coverage decision be made to cover with evidence, really, the only possible way we are going to learn about harms in usual clinical practice is to make that kind of decision, and have that kind of policy."

Several panel members said there was no way to predict whether medical practitioners would limit availability of the procedure to the cohorts that match the NLST population or meet the USPSTF criteria.

"We had a lot of discussion about how we will implement a policy of ensuring that all radiographic facilities that are doing low-dose CT screening would adhere to the criteria of the NLST," said Steven Woolf, director of the Center on Society and Health, and professor in the Department of Family Medicine and Population Health at the Virginia Commonwealth University. "There are wonderful efforts we've heard about today from the professional societies trying to make that happen.

"Most sound like they are going to be voluntary, and I agree with my colleagues that the only way to actually set limits on a runaway problem like we've had with other forms of cancer screening is to tie reimbursement to that, so that coverage would not be possible unless there was documentation that those criteria are being met."

It's almost impossible to extrapolate the NLST results to the Medicare population, said Curtis Mock, a senior medical director at UnitedHealthcare Medicare & Retirement.

"I feel it's our obligation to first, do no harm," Mock said. "I didn't find it, I thought I would today, and I didn't hear that the evidence is there to support benefit beyond harm."

Loose screening criteria could harm patients, said Harry Burke, associate professor of biomedical

informatics and medicine at the University of the Health Sciences, and a clinician at the Walter Reed National Military Medical Center.

"I think the low positive predictive value drives harm—whether you can balance that harm with benefit is a very difficult business," he said. "But the low predictive value is a major problem for me."

Jeffrey Rich, a cardiothoracic surgeon at Mid-Atlantic Cardiothoracic Surgeons Ltd., warned that serious implementation problems would arise if the committee recommends coverage.

"I'm worried that when you take away the benefit part of it, and are left with just the harm part, I want to be certain that we implement this thing right," Rich said. "I think there's potential harm in poor implementation."

Panel: Is It Really Up to LCA to Certify Centers?

Moments before the hearing was closed to public comments, guest committee member Michael Gould asked Fenton-Ambrose to describe LCA's certification program for screening centers:

Gould: My question for Ms. Ambrose—first of all, thank you for your presentation, and thank you for the work that your organization is doing. I think we need to have a frank discussion about generalizability, and to me, there's a very clear tension here.

On the one hand, we want to make sure that the technology is available to as many people as possible who can benefit from that. On the other hand, we want to make sure that it's done safely, and I think your organization recognizes that.

And, given what we know about the highly variable quality of health care in diverse settings throughout the United States, would it not be reasonable, and would your organization support a coverage determination that says, 'We need to make sure this is done right, and these are the following conditions that we would attach to make sure that screening is done safely in the right patients who have the right information, can make an informed decision, who get followed-up appropriately and are not exposed to unnecessary harm from a false positive?'

Fenton-Ambrose: Thank you so much for that question, because clearly, it is a goal that every one of us here shares, and asks, 'How do we take a proven benefit and make sure that it is deployed safely and responsibly?'

What we were hearing from our patients and consumers is, 'Am I at risk? Should I be screened? Where do I go?' And that's what we attempt to address immediately. The key is whether or not we need to make screening contingent on the collection of more evidence for the USPSTF population.

And I believe that we can uniformly say here, with some exceptions, that we can move this forward, and that we do have structured reporting systems, we have protocols, we have technological capacities, and we have the desire by health care teams to do this. And the key is saying, 'Here are the requirements to do this well and right, are the principles, and allow these community centers within the context of those principles to then deploy it based on what their community's needs are…

Rita Redberg [MEDCAC chair, professor of medicine in the Division of Cardiology at the University of California, San Francisco Medical Center]: Thank you. Thank you.

LFA: So yes, that's what the guiding principles are saying and we're seeing pushed out across the country. But I don't think we have to make screening this population contingent on the collection of more evidence.

MG: Well, how can we be sure that those principles are going to be followed? And, with no disrespect intended, is it really up to the Lung Cancer Alliance to determine who is a center of excellence?

And would you support CMS having some criteria for who becomes a center of excellence?

LFA: I think we could probably all gather and figure that out, as ACR, Society of Thoracic Surgeons, our organization, among others, has done, and that would be a wonderful opportunity to really go through this in far more detail than, perhaps, time allows here, to again reinforce what is in place, what is being observed, and how we can work together collectively to embed it properly in public health infrastructure.

But I would like to say, please have confidence in the professional societies, whose direct responsibility is to set up these screening criteria and protocols to know they're doing it well and right, right now.

Kazerooni [professor and director of the Division of Cardiothoracic Radiology and vice-chair of the Department of Radiology at the University of Michigan]: I just want to reinforce the point that was said earlier. The ACR accredits the majority of outpatient CT scanners in the U.S. Those criteria are part of that, and CMS recognizes that already today.

RR: OK, you did make that point. Thank you.

Practices Could Bill Without ACR Accreditation

If CMS provides national coverage without stringent reporting requirements, community radiologists could bill Medicare for low-dose CT, regardless of whether the practices are accredited by ACR or whether the patients meet the NLST criteria.

It's important for practices to adhere to the dose levels in the NLST and perform low-dose CT only on patients in the right age groups, said committee member Gerald White, a medical physicist at Penrose Cancer Center at the St. Mary Corwin Regional Medical Center:

White: I had a question for Dr. Kazerooni, and Dr. [Michael] McNitt-Gray. We've established the existence of standards. I want to ask the ACR accreditation process for low-dose CT screening.

Two questions: One, are the standards for the accreditation process on both the clinical and the physics side comparable to what was done in the NLST? Are they higher or lower or different in some way?

Kazerooni: I'm happy to report that Dr. McNitt-Gray, the physicist on the CT accreditation program that helps us develop the ACR lung cancer screening CT scanner and technical parameters. So we can both speak to that question.

The ACR is one of three designated organizations under MIPPA [Medicare Improvements for Patients and Providers Act] to accredit ambulatory care facilities for purposes of Medicare coverage and reimbursement. So currently, the ACR accredits the majority of outpatient CT scanners in the United States.

Under the CT accreditation program, we have developed a specific center of excellence or programs designated lung cancer screening programs, which have lower radiation exposure CT scans, which meet, if not exceed—in the lower direction—the lower limits of radiation exposure that was set by NLST.

So we expect, through our accreditation program, that radiation exposures will be lower than what was in NLST.

GW: So my question was not just about the radiation exposures, but about things like criteria for entry into the screening program, things like that.

EK: Yes. As well, we have standards about the physicians and who interprets lung cancer screening CTs. We have standards about entry criteria into eligibility for lung cancer screening. We also mandate smoking cessation as part of lung cancer screening programs.

GW: And the second part of my question is: If a facility wishes to be ACR-accredited for CT and they do low-dose CT lung screening, do you require that they have your credential in low-dose CT screening in order to be accredited by the ACR, or can they be accredited by the ACR for CT, do the low-dose screening, but not meet your low-dose standards?

EK: So, in order to get designation of being a lung cancer screening designated center, they have to meet our criteria.

These are subject both to attestation as well as to practice audit. They cannot receive the designation from the ACR unless they're part of the ACR CT accreditation program.

GW: So my question is not about the designation; it's a MIPPA-related question.

If someone wishes to use the ACR accreditation to qualify for MIPPA payment from CMS, and they wish to do low-dose CT screening, do they need to meet your low-dose requirements, or do you pull the accreditation entirely if they don't meet the low-dose requirements and claim to do low-dose CT?

EK: The CT accreditation program is broad one. It does not just lung cancer screening CT; it covers neuro CT, musculoskeletal CT, cardiac CT. So the global designation for CT accreditation depends on the type of exam that you perform at your center.

Sites can specify the types of exams they perform—for example, some sites don't perform pediatric CT, and they would not submit that for accreditation. So if they want to pursue lung cancer screening CT designation, they have to submit and conform to the requirements of lung cancer screening designation.

GW: I hate to belabor this, because this is an important point. Under your program, if someone wishes to do, say, neuro CT, they can't just say, we're going to skip the neuro part, but we're going to get accredited for abdomen, and then continue to do neuro, you don't allow them to do that? Do you allow them to do the low-dose CT screening if they're otherwise accredited, but don't meet your low-dose requirements?

EK: I think we're kind of saying the same thing, but just using different language. If you want to have designation for accreditation from the ACR's lung cancer screening program as a designated center for lung cancer screening, you'd be required to follow the requirements for low-dose CT, smoking cessation, and the appropriate population being screened. If you did not meet those requirements, you could not have ACR designation as a center for lung cancer screening.

GW: But you could still bill CMS for the low-dose procedures? I'm trying to…

EK: As a global question under MIPPA, that's probably already existed. We're trying to improve that by having a specific lung cancer screening designation.

RR: My question, from the patient point of view—it's not clear if a patient knows they going to an accredited place or not, and then, beyond that, as I read from the public comments and published literature, even if you have a low-dose protocol, doesn't mean what a patient gets is actually a low-dose CT.

We know, for example, Rebecca Smith-Bindman published a study in the Archives of Internal Medicine in 2009 showing, even at the same institution, there was 30, 40, 50-fold variability in the amount of radiation.

I know there were hearings held after that study was published, and there was talk of changing this. Have there been any changes since then that have minimized that variability?

EK: Part of practice audit under the ACR CT accreditation program is radiation exposure as a quality parameter. So that is an important quality component of the accreditation program.

RR: And do patients know how much radiation they're getting from a CT screening?

EK: The amounts of radiation exposure and how it's implemented varies wildly across U.S. in terms of how information is communicated to patients. As you're probably aware, in some states like California, there are requirements for documentation in the radiology report.

What information that is and whether it's the right or the best way to communicate radiation exposure and risk, I don't think people yet understand the answer to that question.

Radiation risk is a relative one, and to simply report a number without risk assessment of what that means, whether it's a two year old, 15 year old, or 65 year old, is very important. To just simply convey a number to a patient without explanation, I think, would be inappropriate.

ACR's Lung-RADS is Now Open to Public

The ACR's Lung Imaging Reporting and Data System was made available to the public the day after the hearing.

Curtis Mock: Dr. Redberg, there still seems to be some confusion, I wonder if we could clarify before we move on. Even though there is an interest to move forward to identify those that are screened, there still is some misunderstanding about whether the follow-up radiation exposure is the same as that of the low-dose or whether it's higher.

And not being certain about how many scans the patient gets in follow-up before they drop back into the screening. I'm getting two different answers and I want to clarify that.

RR: Well, I think, certainly, when you read NLST, there was no protocol and they were all over the place, and a lot of the follow-ups were full chest CTs that were reported at much higher doses—eight millisieverts—and I am certain that in actual practice, it would be even more variable and at higher doses because…

EK: I'd like to address your question directly. Because of the reduction of false positives with Lung-RADS, fewer people require interim CTs. For the people who do require a downstream diagnostic test…

RR: Dr. Kazerooni, you haven't actually shown us any data from Lung-RADS, so that's why I'd prefer to keep discussing the evidence. We look forward to seeing data from Lung-RADS, but right now we haven't.

EK: Lung-RADS uses the evidence that is already available in the ELCAP and NLST databases.

RR: Can you give us those references?

EK: I think you have much of that in USPSTF references already from which we've extrapolated the data and developed Lung-RADS…

RR: I haven't seen it.

EK: It means that the follow-up CTs will all be low-dose CTs, except for the 2 percent that are at the very highest risk for cancer who may undergo more aggressive diagnostic pathways. So that is a very important point. Most people with a positive CT who need a follow-up test, will get a low-dose CT.

RR: So my understanding is you'll get the same CT that you got that showed the nodule in the first place, but you will just wait over time. And while you are waiting over time, of course, it's unclear whether or not you have cancer or not, you are waiting over time to find out, and there's a lot of uncertainty and anxiety associated with that.

Claudia Henschke [professor of radiology at the Icahn School of Medicine at Mount Sinai and principal investigator of I-ELCAP]: Well, I'd just want to say that our protocol is always, specifically ask for a low-dose follow-up CT, one. If there's no growth, then you go to the next annual screening, and that has not created a lot of anxiety in all the patients that we've done. You have to talk to the patients; you have to talk to the participants.

RR: I would love to see the quality of life data from the NLST.

Bach: LCA Center Certification Untrustworthy; CISNET Models Don't Match

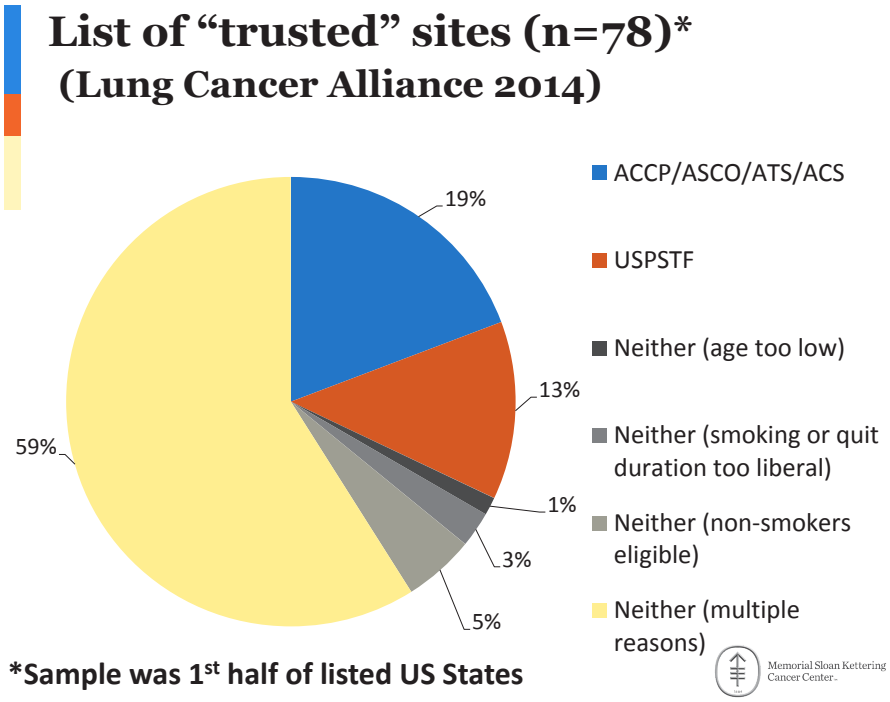
By Matthew Bin Han Ong

When it appeared that CT screening for lung cancer was a shoo-in for Medicare coverage, the Lung Cancer Alliance, an advocacy group, started to certify "screening centers of excellence."

Centers all over the country received this designation from LCA and were listed on the group's website.

However, as he prepared for a recent Medicare advisory committee meeting, Peter Bach, a pulmonologist and health systems researcher at the Memorial Sloan-Kettering Cancer Center, checked the list of LCA-certified centers.

He found that the vast majority of the centers did not meet either the multi-society or the criteria recommended by the U.S. Preventive Services Task Force for lung cancer screening eligibility.



About 68 percent of 78 LCA-certified screening sites that Bach examined did not meet the criteria, Bach said at the April 30 Medicare Evidence Development & Coverage Advisory Committee hearing.

Though a MEDCAC member himself, Bach testified independently. He was also a requestor for the National Coverage Determination.

"Here's a pie chart we generated in my office—we just took the list of 'trusted' sites from the Lung Cancer Alliance," said Bach, an attending physician and director of the Center for Health Policy and Outcomes at MSKCC. "We stopped when we got halfway into the alphabet.

"These sites publish their screening eligibility criteria," he said. "The small blue slice of 19 percent meets the multi-society guidelines for eligibility. The orange meets USPSTF. Every other site listed enrolls people who don't meet those criteria."

Bach's presentation is available on The Cancer Letter website.

The LCA's list is important because it is one of the concerns regarding implementation of measures aimed at minimizing harms to the Medicare population, should the Centers for Medicare and Medicaid provide coverage for low-dose CT screening for lung cancer.

"There are good things happening in harm minimization," Bach said. "The American College of Radiology's efforts, the BI-RADS effort is one thing that is going on, but there are serious concerns, in my mind, that coverage from Medicare will lead to an explosion of inappropriate activities driven by probably a mix of both good intentions and entrepreneurialism.

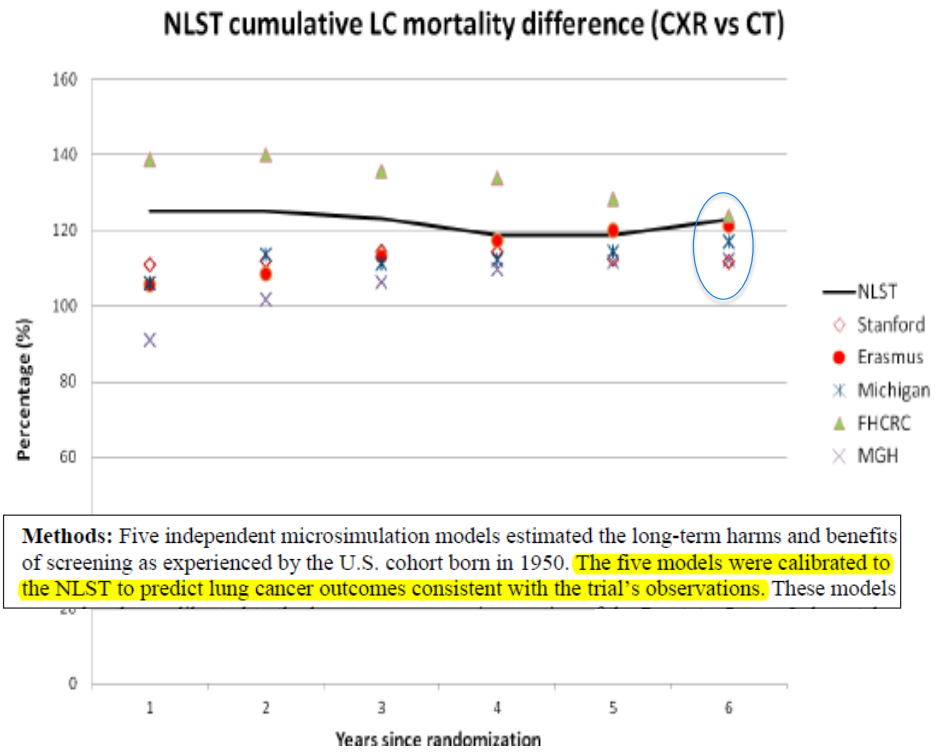
"And remember that the coding and capturing of smoking history as an eligibility criteria is something we have no experience with, doesn't fall under the meaningful use criteria, and we have a long history of behavior by doctors coding things like minimal bowel symptoms to do colonoscopy screening as our backdrop for this."

Existing studies that claim CT screening's false-positive rate can be reduced are plagued with problems, Bach said.

"There's a recent study from ELCAP where they talk about changing the threshold," he said. The data coming from that, which extrapolate to the number of cancers found in things like that, has little relevance to the question at hand."

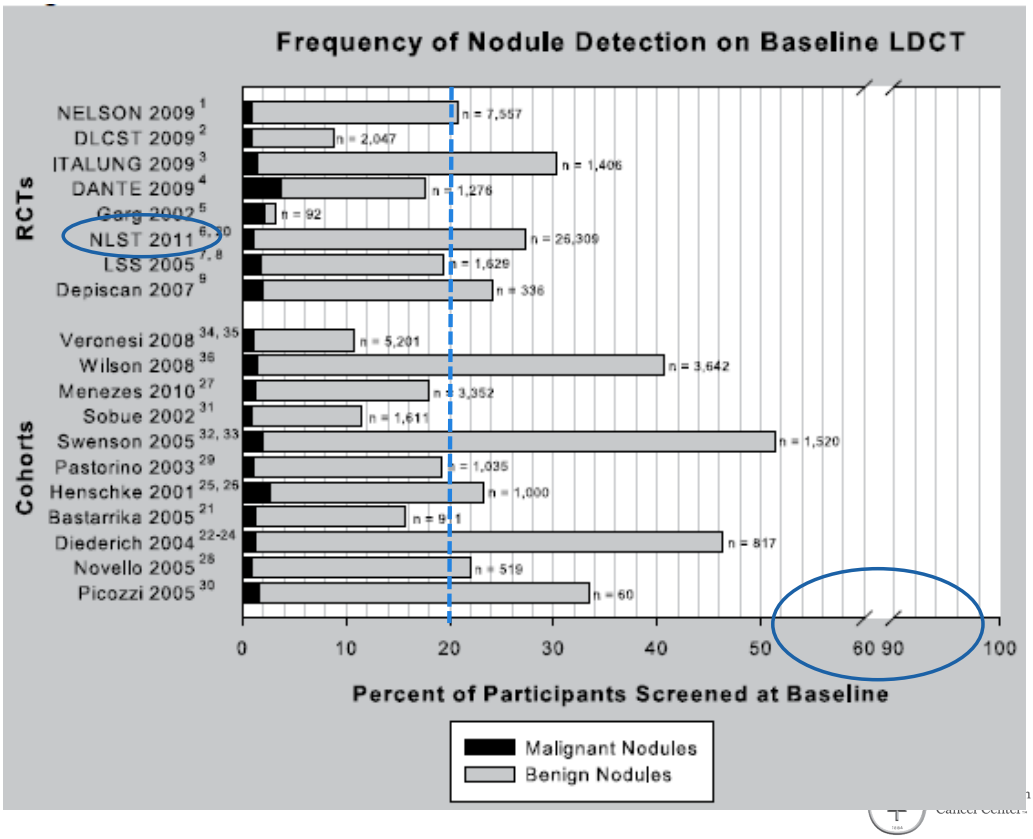
Bach said that at least two decades of research on screening in academic centers—such as the ones used in the National Lung Screening Trial—demonstrate that care in those centers is less harmful and more

CISNET models don't predict shape of NLST benefit



Methods: Five independent microsimulation models estimated the long-term harms and benefits of screening as experienced by the U.S. cohort born in 1950. The five models were calibrated to the NLST to predict lung cancer outcomes consistent with the trial's observations. These models

False positive rates: not consistent



efficacious, leading to questions about extrapolation to community practice settings.

"The NLST also had an overeducated population relative to the tobacco-using population as a whole," Bach said. "Both of those things, I would speculate, would tend to make CT screening look more efficacious and less harmful than if it would if the right population had been representative.

"Paul Pinsky [acting chief of the Early Detection Research Group in the Division of Cancer Prevention at NCI] showed a nice slide at the radiologist level from the NLST," Bach said. "This is a slide looking at the false positive rates of all the published studies from our recent JAMA article. In the top are the RCTs, in the bottom are the observational arms. False positive rates vary as do the lung cancer detection rate shown in the dark part of each of these bars.

"A pooled average of these represents about 20 percent of false-positive rate—that's just one number that really does depend on care setting.

"This is the clinical problem: 19 CTs of 20 have a false positive," Bach said. "One has lung cancer—everyone else is potentially harmed."

Also, the rates of follow-up procedures and invasive procedures for lung cancer are inconsistent across four other studies, Bach said.

"These trials have weaknesses; they're all in the evidence review," he said. "They had smaller sample sizes and inconsistent follow-up, there's actually some data ascertainment problems as well. But nevertheless, the NLST result has not be reproduced in three other randomized trials in terms of lung cancer mortality reduction.

"That is not the case in terms of the effective cause of death on other causes than lung cancer. Paul [Pinsky] correctly reported that the NLST reduced overall cause of death, but that was purely for mediation reduction death from lung cancer.

"If you look at their rate of death from causes other than lung cancer in the NLST and these other four studies, there is no evidence that CT screening reduces the rate of death from anything like cardiac disease or any other cause."

Adherence to Criteria and Models are Inconsistent

Adherence to lung cancer screening eligibility criteria was inconsistent, but achieved a high of 95 percent in the NLST's CT screening arm, Bach said.

"We have some important questions," he said. "Is this group's study generalizable? Are the findings in terms of mortality false positives and adherence generalizable? Were the settings generalizable? What to do when we don't have data? What about unstudied groups? What about unstudied durations?

"We don't have data for screening over 74, and in fact, the NLST is underpowered in the over-65 group. We don't have data for longer duration; we don't have data for real world settings. What can we infer, and can we trust our models?

"The risk of lung cancer rises with advancing age—shown here in two prototypical patients—somebody who is 80 with a 50-pack-year smoking history has about a 6- to about 11-time greater risk of death from lung cancer than somebody who would barely be eligible through NLST entry criteria—a 55 year-old with 30-pack-years.

"But there are bad things that happen, too, with advancing age in terms of net benefit tradeoff: rising risks of false positives, life expectancy reductions, and risk of surgical death. All three of those things are shown empirically on this slide.

"These are the three bad trends, if you will, as you go into advanced age in terms of net benefit tradeoff. The point is obvious. The harms that are related to false positives will rise with advancing age.

"As people age, unfortunately, the risk from surgery rise, and even mortality at 30 days rises."

Questions about the long-term benefits of low-dose CT lung cancer screening are dependent on models, Bach said.

"From the CISNET group, I've taken the view—and I wrote one of the two editorials that went with the CISNET paper and the task force—that the CISNET models probably are not adequate to determine what will happen over a long period of time of screening," Bach said. "It's not out of disrespect, it's just an empiric observation.

"The basic argument is, there were five separate modeling groups. Those groups each produce estimates, and they match so poorly to one another, that I think we're left wondering, 'Are any of these right? But for sure four out of the five have to be wrong because there is no overlap.'

"And the variation in what these models produce was extremely wide. One model, for example, per

100,000 people, estimated 22,000 life-years gained in the population, another five axed that.

One model on overdiagnosis estimated that about 72 people would be overdiagnosed, another estimated five or six times that number.

"The models, I believe, are not reliable, and they're fundamentally not in agreement—no meaningful outcome data and reasons for concerns about selecting setting," Bach said. "The first test of a model is, 'Does it mimic what we can actually observe in real nature?' and they don't.

"It's clear in the technical report that these models were all post-hoc, recalibrated to match at six years. This is not a critique of the methods, please don't misunderstand me—I'm unable to find to what extent these things had to be recalibrated. But if you don't hit the target, that means you can't trust the data going forward."

Steven Woolf: Why CMS Should Not Cover LDCT

National coverage for low-dose computed tomography may result in more harm than benefit to the Medicare population at this time, said Steven Woolf, a member of the Medicare Evidence Development & Coverage Advisory Committee.

Speaking at the April 30 MEDCAC hearing, Woolf said coverage would run into many implementation challenges and adherence problems—it would be unlikely that all practices would observe the strict criteria set by the U.S. Preventive Services Task Force and the National Lung Screening Trial, he said.

Woolf is director of the Center on Society and Health, and professor in the Department of Family Medicine and Population Health at the Virginia Commonwealth University.

Following is Woolf's response to the panel's first voting question: "How confident are you that there is adequate evidence to determine if the benefits outweigh the harms of lung cancer screening with LDCT in the Medicare population?"

I voted 'one' [on a five-point scale]. My reasons are similar to my colleagues in comments I made earlier about questions about whether the magnitude of benefit observed in the NLST is generalizable to the other populations, and concerns about whether the harms could potentially offset some of those benefits, especially if screening extends beyond the narrow risk group that the recommendation applies to.

The point I want to reinforce that my colleagues made is that it's not realistic to expect lots of NLSTs to get conducted. We're probably not going to get a better randomized trial than the one we have, but the solution to that is modeling. But those of you who have studied modeling understand that, when you see one model, you've seen one model.

This CISNET model is very interesting, very sophisticated, very informative, but we can cite many examples of other cancer screening tests where modeling studies, over the years, have reached different conclusions based on different assumptions that go into the model, different kinds of models—simulation models and so forth—and I think, in the literature, the more that modeling is done on this type of screening, we'll continue to see a more diverse set of outcomes and results than what we've seen now.

I have a series of concerns about challenges that we might face if CMS were to cover this in trying to replicate the conditions and the recommendations.

The recommendations from the [U.S. Preventive Services] Task Force that are the basis for this [National Coverage Determination] specify that screening be offered within certain parameters, and if we look closely at those parameters, I see implementation challenges in keeping to that risk group, both in terms of the feasibility that practices will face, and actually following through on this.

We have plenty of experience in health care to know that these challenges are real, and the tendency is for those criteria to slip, and that means the lower risk group will end up getting screened and the risk benefit relationships that we are basing this recommendation on will no longer apply.

First of all, the age is supposed to be age 55 to 80, but we already know from discussions today that there is a sentiment to move that to an earlier age group to start screening earlier.

Also, we've heard comments made about the inappropriateness of cutting off screening at the proposed stopping age. So it is quite likely that it would not be limited to that age group.

The 30-pack-year and the 15-year quit rule, operationally, pragmatically, the implementation of that will be challenging because of difficulties with screening and intake.

We have heard testimony from centers of excellence that have developed systems for doing this, and I applaud them for it. But the feasibility of expecting that to be done nationwide with implementation of this coverage policy are quite challenging.

Plus, there is a strong sentiment from many of the

organizations that testified today and others to loosen those criteria and accept a 20-pack-year history and so forth. Dr. [Peter] Bach [attending physician and director of the Center for Health Policy and Outcomes at Memorial Sloan-Kettering Cancer Center] had noted that, when you do that, the number needed to screen now shoots up to 3,000, and the whole risk-benefit ratio potentially starts changing.

A detail, a nuance in the task force recommendation that no one has discussed today is the provision that this only be done for people who are able and willing to have curative surgery.

Those are two different things, but we haven't discussed either of them. How will we define who is able to have curative surgery?

We've had some surgeons indicate today that there's hardly any patient who would not be eligible for curative surgery. And even those who are considered clinically appropriate for this surgery—willingness to have surgery—once informed of the potential consequences, how would that actually be implemented?

Challenges to image interpretation—I won't belabor that, because we had a lot of discussion about how we will implement a policy of ensuring that all radiographic facilities that are doing low-dose CT screening would adhere to the criteria of the NLST. And there are wonderful efforts we've heard about today from the professional societies trying to make that happen.

Most sound like they are going to be voluntary, and I agree with my colleagues that the only way to actually set limits on a runaway problem like we've had with other forms of cancer screening is to tie reimbursement to that so that coverage would not be possible, unless there was documentation that those criteria are being met.

The concern has been raised that if we limit screening only to facilities that are state-of-the-art, such as those at academic centers or even community-based facilities that are state-of-the-art, we are contributing to health inequalities because so much of the population—especially geographic areas at high risk of lung cancer—don't have access to those facilities.

That argument only holds if one accepts the premise that screening results in more benefit than harm. Screening done poorly—if one is open to the premise of screening done poorly—results in more harm than good, then one is actually committing an ethical error by exposing disadvantaged populations or people who are disadvantaged geographically to a form of imaging or follow-up work ups that are actually going to cause more deaths or cause more adverse outcomes than benefit. And that is equally troubling, ethically, as barriers to access.

Another concern is whether clinicians will actually wait for the annual interval.

We have, time and time again, with other forms of cancer screening, PAP smears, and many others we can mention, where recommended intervals for screening have had a slippery slope, and there's been a creep in the interval of frequency of screening that I think will be hard to adhere to.

Another topic we haven't discussed today is the 95 percent adherence rate in the NLST.

Our ability to ensure that the millions of Americans who would be offered this form of screening will achieve 95 percent adherence—a rate that I have not seen achieved for other forms of cancer screening—is very doubtful, especially when one considers that 95 percent was achieved in a population that higher socioeconomic status, higher educational attainment, and a younger age, than the population that would actually be receiving this screening.

There's reason to believe that lower SES patients and older patients might face more barriers in actually following through on the recommended protocol.

Will treatment in the community follow the same protocol? We've seen evidence presented of wide variation, even within the NLST centers—the centers of excellence.

It's only reasonable to assume that there would continue to be variation in widespread population use, and even worse, potentially.

And the point made about the surgical complication rate, the very good results that were observed in the NLST—and, if I understood correctly, from the NLST paper and Dr. Bach's testimony, and so forth—the complication rate was one quarter of what's typically reported.

So, again, when we are talking about a tenuous risk-benefit ratio, these substantial differences and outcomes could tip the scales in the wrong direction.

Cancer Treatment

Growth of the Cost of Drugs Slows to 5.4 Percent per Year; 21 Therapies Launched in 2 Years

The growth of global spending on oncology medicines has slowed over the past five years, according to a report by the IMS Institute for Healthcare Informatics.

Spending on cancer drugs, including those used for supportive care, increased at a compound annual growth rate of 5.4 percent during the past five years, reaching $91 billion in 2013, compared with 14.2 percent from 2003 to 2008.

The slowed growth rate reflects fewer breakthrough therapies for very large patient populations, as well as patent expirations, reductions in the use of supportive care medicines, and stronger management on the part of payers, the report states.

Targeted therapies have dramatically increased their share of global oncology sales, from 11 percent a decade ago to 46 percent last year. Payers have intensified their scrutiny of the value of these medicines relative to their incremental benefits over existing treatments.

At the same time, the average cost per month for a branded oncology drug in the U.S. is now approximately $10,000, up from an average of $5,000 a decade ago. Concentrated or single-payer health systems, and those utilizing health technology assessments to evaluate the value of treatments, tend to pay less than U.S. prices for medicines. The pricing discount mechanisms used in major European markets typically drive net prices down by approximately 20-40 percent in comparison.

"As the cancer patient population mix shifts from mature and developed markets to low- and middle-income countries, oncology is bringing higher levels of uncertainty to health systems across the globe--both in terms of the nature and rate of innovative treatments, and levels of reimbursement for patient care," said Murray Aitken, executive director of the IMS institute.

"While an estimated 30 percent of cancers are preventable and early diagnosis and treatment can reduce or delay mortality significantly, the reality is that countries struggle to bring together the right combination of preventive measures and clinical interventions including vaccines, diagnostics and therapeutics."

The full version of the report, including a detailed description of the methodology, is available at www.theimsinstitute.org.

The report's key findings are:

Global market growth for oncology spending has moderated. The global market for oncology drugs, including those used in supportive care, reached $91 billion in 2013 as measured at ex-manufacturer prices and not reflecting off-invoice discounts and rebates. This compares with $71 billion in 2008 and $37 billion a decade ago.

Global growth has been less than 10 percent each year since 2008, and the U.S. market for oncology drugs has grown at a rate of 3.5 percent over the past five years, reaching $37 billion last year. Biologic products now represent less than half of the oncology market, a slight decline over the past 10 years as new drug launches have been concentrated in small molecules, including kinase inhibitors.

Innovation in cancer therapies is becoming more targeted. New drug development has yielded significant innovation across cancer types and therapeutic approaches, including preventive vaccines. Pharmaceutical company investments remain high and cancer therapies account for more than 30 percent of all preclinical and phase I clinical development products, with 21 new molecular entities being launched and reaching patients in the past two years alone.

These new medicines have increased the complexity of treating cancer, leading to more combination therapies and additional lines of therapy. Clusters of innovation based on similar underlying science and multiple development pathways have transformed patient care in areas such as advanced melanoma, as well as sub-populations of cancers with higher prevalence.

Although sales for certain recently launched oncology drugs have rivaled those of earlier blockbusters, many new drugs are targeted to small patient populations and face strong competition, resulting in comparatively modest sales levels.

Pricing and the value of treatments face more payer scrutiny. The high number of new targeted therapies launched and available for cancer patients has also escalated payer scrutiny of their value relative to incremental benefits over existing treatments. Judging the additional value of these treatments for individual patients is fraught with challenges due to the high level of variability in patient response, the frequent changes in protocol, and underlying issues of equity and patient care.

Newly launched treatments typically bring

between two and six months of incremental overall survival, although this can vary by patient. The American Society of Clinical Oncology recently issued recommended targets for meaningful clinical trial outcomes, a useful step to guide those investing in innovation as well as those paying for patient care. In the E.U., there is a trend toward lower list prices at the time of launch compared to U.S. list pricing, and European markets have other discount mechanisms, which may be employed across national, regional and local levels.

Impact of biosimilars and non-original biologics is growing. The introduction of regulatory pathways for biosimilars and increased production capacity around the world are driving a new competitive dynamic in the $40+ billion biologics portion of the oncology market. However, the potential role of biosimilars in developed countries will be limited by the expected flow of patent-protected innovative products that will displace older, off-patent products subject to biosimilar competition.

These agents already play a role in the supportive care segment of the oncology market in Europe, and are expected to do the same in the U.S. in the near term. In low- and middle-income countries, non-original biologics—those based on an original molecule not introduced by its manufacturer in a particular market—are expected to play a significant role in oncology and already capture 60 percent or more of certain recombinant and synthesized biologics.

On a global basis, biosimilars are expected to generate $6-12 billion in oncology sales by 2020, increasing the level of competition but accounting for less than 5 percent of the total biologics market at that time.

Unique dynamics in U.S. contribute to changes in oncology care. In the U.S. market, which contributes 41 percent of total oncology drug sales, changes in the structure of healthcare delivery are impacting cancer treatment site of care, reimbursement and patient out-of-pocket costs.

Physician practices are becoming larger, and healthcare organizations that care for underserved populations and are covered by the 340B Drug Discount Program have expanded their oncology presence, as have accountable care organizations.

This is resulting in a shift in patient care from physician offices to hospital outpatient facilities. Since hospitals incur higher costs and overhead for the delivery of care, their reimbursement levels for the administration of drugs are higher than those for physician offices. For typical targeted therapies that are infused or injected by an oncologist, reimbursed costs for hospitals are at least double those for physician offices and have brought sharply higher costs to payers over the past two years.

These higher costs are also associated with higher patient out-of-pocket costs depending on insurance plans and benefit designs, and can trigger reduced levels of therapeutic persistence by patients and higher overall cost of care.

Women's Health Initiative Trial Produced $37.1 Bil in Returns

The overall economic return from the Women's Health Initiative estrogen plus progestin trial indicates that the changes in practice it produced provided a net economic return of $37.1 billion over 10 years.

The paper, a collaboration between WHI investigators and faculty at the Hutchinson Institute for Cancer Outcomes Research, states that during the 10-year period since the main study findings were published, the changes in practice returned approximately $140 for every dollar invested in the trial. The paper was published in the Annals of Internal Medicine.

The WHI is one of the largest NIH-funded studies ever conducted on women. Housed at the Fred Hutchinson Cancer Research Center in Seattle, it is a 15-year, multimillion-dollar study established in 1991, involving more than 160,000 women throughout the U.S.

Researchers created a disease simulation model to evaluate clinical and economic outcomes for combined hormone therapy eligible women since the initial publication of the E+P trial results in 2003.

The study first estimated clinical outcomes for women taking cHT following the study versus a counterfactual scenario where the E+P trial was not conducted and cHT use persisted at historical (pre-2003) trends. Based on the projected clinical outcomes, the study then calculated the net economic return of the trial, minus the trial cost of about $260 million.

The WHI clinical trial was funded by the National Heart, Lung, and Blood Institute. Assuming that 75 percent of the change in cHT prescribing can be directly attributed to the WHI, and subtracting the cost of the study itself, the net economic return of WHI E+P trial was $37.1 billion.

During the 10 years following publication of WHI E+P findings, the investigators estimated that 4.3 million fewer women used cHT. As a result there

were 126,000 fewer breast cancer cases, 76,000 fewer cardiovascular events, 263,000 more osteoporotic fractures, and 15,000 more colorectal cancer cases compared to the no trial scenario.

"It is important to consider the potential value of studies when making decisions about how to invest limited public research dollars," said Scott Ramsey, director of the Hutchinson institute.

"Many stakeholders have talked about the high cost of the WHI estrogen plus progestin trial, but few have considered the potential value of the trial. These findings show that the trial was a high-value use of public funds with a substantial return on investment."

The observed reduction in cHT prescribing saved $49.5 billion in direct medical care costs. In addition, the net health yield for women in the U.S. was approximately 145,000 more quality-adjusted life years than would have occurred in absence of the trial.

"The WHI trial is often discussed as having a major impact on post-menopausal combined hormone therapy use, but I'm not aware of any other studies that have projected how many fewer women used combined hormone therapy as a result of the trial," said the study's lead author, Joshua Roth, of the Hutchinson institute.

"It really brings the point home when you crunch the numbers, to see that millions of U.S. women likely stopped or never used combined hormone therapy based on the trial's findings, and that the change in use resulted in important reductions in disease incidence and associated medical spending."

Of the $37.1 billion credited to the WHI trial, $26.4 billion was attributable to medical expenditure savings. These savings were driven by 25 million fewer person-years of cHT use, as well as cost savings from avoided diseases. The remaining $10.7 billion represents the value of additional quality-adjusted life expectancy resulting from lower incidence of breast cancer, cardiovascular disease, and venous thromboembolism.

"The motivation for the first WHI trial was to see if we could prevent heart disease, the number one killer of women; that's why we did it—the economics never occurred to me," said Garnet Anderson, lead Women's Health Initiative investigator and director of Fred Hutchinson Cancer Research Center's Public Health Sciences Division.

"What these findings underscore is the significant role clinical trials play in science and the importance of continuing to find ways to strategically invest public research funds to maximize value to society."

FDA News

Cancer Unit Fastest in Approval Despite Having Highest Workload

By Paul Goldberg

A study by a conservative think tank found large differences in performance of the FDA divisions, with oncology demonstrating the agency's fastest time from application submission to approval.

Paradoxically, the Manhattan Institute found that the oncology division's staff members had the agency's highest workload—measured in INDs per staff member at the division.

In the study, the median time for approval at the slowest division is three times as long as the approval time at the fastest. The agency's two fastest units, oncology and anti-viral, took under 200 days to make a decision on a drug. The neurology division took nearly 600 days to approve a drug.

Researchers gathered data measuring output and workload from the review divisions of the Center for Drug Evaluation and Research from 2004 to 2012. The divisions accounted for 184 new drugs or biologics and 80 percent of all new CDER-approved drugs over the period.

"We agree that there are differences in the average time it takes to approve drugs across CDER's different review divisions," said Stephanie Yao, an FDA press officer. "However, we believe that these differences are not an indicator of inconsistencies in efficiency but are rather a reflection of the different types of drugs and disease conditions we review, which also vary considerably across CDERs numerous review divisions.

"For example, some review divisions, such as oncology and anti-viral drugs, receive a high proportion of drugs designated for 'priority review,' which provides for a shorter regulatory review clock for drugs that represent significant improvements over existing therapies," Yao said.

"In many instances, these same priority-reviewed cancer and anti-viral drugs treat serious conditions and address unmet medical needs, where it may be easier to clearly establish that the benefits of the drug outweighs the risks," Yao said.

"On the other hand, other FDA review divisions, because of their area of medical specialty, may receive relatively few priority review drugs by comparison, and may also have a higher proportion of drugs that demonstrate modest efficacy in conditions for which there are many similarly-effective treatment options, which may present a less clear benefit-risk balance."

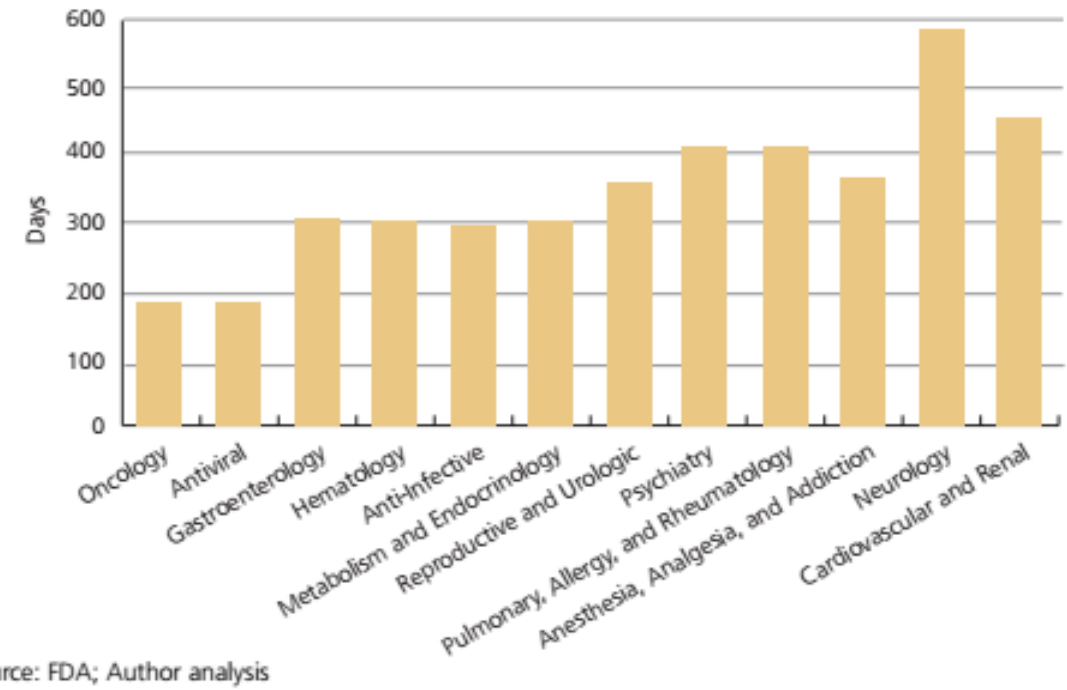
Table 1. Workload Factors by FDA Reviewing Division[1]

Division	INDs/yr/staffer[2]	NDAs/yr/staffer[3]	Priority Rating	Special Program[4]
Anesthesia, Analgesia, and Addiction	0.965	0.167	42.9%	0.0%
Anti-infective	0.782	0.181	40.0%	10.0%
Antiviral	0.725	0.250	72.7%	45.5%
Cardiovascular and Renal	0.634	0.165	40.0%	6.7%
Gastroenterology	0.812	0.196	38.5%	23.1%
Hematology	0.835	0.121	41.7%	50.0%
Metabolism and Endocrinology	1.037	0.182	15.8%	0.0%
Neurology	0.742	0.137	33.3%	6.7%
Oncology	1.622	0.161	86.4%	51.1%
Psychiatry	0.651	0.071	0.0%	0.0%
Pulmonary, Allergy, and Rheumatology	0.700	0.138	41.7%	25.0%
Reproductive and Urologic	0.630	0.181	0.0%	0.0%
Average (12 divisions)	0.845	0.162	46.4%	15.2%

[1] New drug and biologic approvals, 2004–12. Green cells indicate above-average workloads; red cells indicate below-average workloads
[2] Average annual number of INDs received divided by division staff level
[3] Average annual number of NDAs submitted divided by division staff level
[4] Drug was designated for accelerated approval or fast-track status

Source: FDA; Author analysis

Figure 5: Median Time to Approval by FDA Division



Source: FDA; Author analysis

In Brief

David Cole Named President Of Medical University of S.C.

(Continued from page 1)

Former President **Raymond Greenberg** stepped down in August 2013 to become executive vice chancellor for health affairs of the University of Texas Health System.

In 1994, Cole became an assistant professor in the MUSC College of Medicine and since then he has served in a variety of faculty and leadership positions at MUSC, earning tenure in 2001.

Cole earned his medical degree from Cornell University Medical College in Maryland and completed his residency training in general surgery at Emory University. He then completed a surgical oncology fellowship at NIH and NCI's Surgery Branch.

PETER BACH's account of his wife's death from breast cancer—**"The Day I Started Lying to Ruth"**—was published in New York Magazine May 6.

Bach is a pulmonologist and director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center.

MD ANDERSON CANCER CENTER honored 16 junior faculty members with the first **R. Lee Clark Fellow awards**. The award was established to recognize outstanding work by junior faculty members.

The program is named in honor of MD Anderson's first full-time director and president, who served from 1946 to 1978. The awards are being given to three groups of MD Anderson faculty members: those with a clinical focus, those with a clinical and research focus, and those with a scientific focus. Each recipient receives $100,000 to fund their research over the next one to two years.

The following are the 2014 R. Lee Clark Fellows:

Clinical Innovators

• Courtney DiNardo, assistant professor, Leukemia

• Steven Lin, assistant professor, Radiation Oncology

• Simrit Parmar, assistant professor, Stem Cell Transplant and Cellular Therapy

• Kathleen Schmeler, associate professor, Gynecologic Oncology and Reproductive Medicine

• Jason Westin, assistant professor, Lymphoma and Myeloma

Physician Scientists

• Lauren Byers, assistant professor, Thoracic/Head and Neck Medical Oncology

• Don Gibbons, assistant professor, Thoracic/Head and Neck Medical Oncology

• Elizabeth Mittendorf, associate professor, Surgical Oncology

• Samuel Shelburne, associate professor, Infectious Diseases

Scientists

• Jichao Chen, assistant professor, Pulmonary Medicine

• Francesca Cole, assistant professor, Molecular Carcinogenesis

• Michael Galko, associate professor, Biochemistry and Molecular Biology

• Han Liang, assistant professor, Bioinformatics and Computational Biology

• Hui-Kuan Lin, associate professor, Molecular and Cellular Oncology

• Li Ma, assistant professor, Experimental Radiation Oncology

• Xiaobing Shi, assistant professor, Biochemistry and Molecular Biology

THE US ONCOLOGY NETWORK and the **Community Oncology Alliance** sponsored a "Virtual Hill Day" to persuade members of Congress to stop the Centers for Medicare and Medicaid Services from applying the sequester cut to Medicare payments for cancer care drugs.

The event, which took place May 7, was intended to boost support for the **Cancer Patient Protection Act** (H.R. 1416), which instructs CMS to stop applying the 2 percent sequester cut to payments for Medicare Part B drugs, including cancer drugs and therapies. The bill, introduced by Rep. Renee Ellmers (R-N.C.), has 110 co-sponsors.

"Cancer patients and their care teams are witnessing the direct impact of the sequester on the delivery of community cancer care and it is time that lawmakers hear this directly from their constituents—and take action," said Barry Brooks, chairman of the Pharmacy & Therapeutics Committee for The US Oncology Network.

Follow us on Twitter: @TheCancerLetter

THE ATHENA BREAST HEALTH NETWORK adopted the **Health Level Seven International-approved guide** for sharing electronic data for breast cancer treatment. The guide was developed by the American Society for Clinical Oncology and approved through HL7 to become a national data standard.

In adopting this guide, Athena can now use a standardized format to transmit data across the systems supporting its projects, and plans to begin transmission of patient data starting this summer.

ASCO hosted a Data Interoperability Standards Summit in February 2013 to encourage collaboration in developing standards that will overcome the barriers facing electronic health records. The society selected adjuvant treatment for breast cancer as the focus for the first oncology standard.

Athena's network participated in the larger Interoperability to Support Practice Improvement project, which is sponsored by the University of California Davis Institute for Population Health Improvement and the California Office of Health Information Integrity. INSPIRE will produce breast cancer treatment plans and summaries for the Health Information Home, a patient-centered repository supporting care coordination.

ASCO is now expanding the guide for electronic data sharing with data relevant to the treatment of colon cancer and plans to submit to HL7 in the summer of this year.

ELI LILLY & COMPANY signed an agreement with **Prasco Laboratories** to market the authorized generic version of Evista (raloxifene hydrochloride tablets), in 60 mg strength in the U.S. Prasco will begin shipping the product immediately. The financial terms of the agreement were not disclosed.

Evista is an estrogen agonist/antagonist indicated for: treatment and prevention of osteoporosis in postmenopausal women; reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis; reduction in risk of invasive breast cancer in postmenopausal women at high risk for invasive breast cancer.

THE JOHNS HOPKINS Kimmel Cancer Center received $10 million from **Under Armour** to help build a breast health center. The gift comes from the company's Power in Pink Campaign, and the facility will be named the Under Armour LiveWell Center.

The money will be used to construct and outfit a center dedicated to breast health-related programs in the Kimmel Cancer Center's newest facility, the Skip Viragh Outpatient Cancer Building.

Slated to open in 2017, the Skip Viragh Building will serve as the primary entry point for cancer care at Johns Hopkins, with the breast health center located on the top floor.

THE MELANOMA RESEARCH ALLIANCE and **L'Oreal Paris** launched It's THAT Worth It, a campaign to support melanoma research.

As part of a three-year partnership, L'Oreal is donating $750,000 to the alliance for the L'Oreal Paris-MRA Team Science Award, led by researcher Meenhard Herlyn, director of The Wistar Institute Melanoma Research Center, the Caspar Wistar Professor in Melanoma Research, and a professor in the Molecular and Cellular Oncogenesis Program. The donation will fund research exploring the role of 16 variant genes as co-drivers in melanoma susceptibility, development and progression.

Celebrity broadcast and print public service announcements are the first in a series of initiatives to urge women of all skin tones to use sunscreen, and commit to supporting melanoma research. L'Oreal will donate $1 to MRA for each supporter who signs up through the campaign's website, and $1 for each L'Oreal suncare product sold in the U.S., up to $250,000 in 2014.

KRISTIN DARBY was named chief information officer of **Cancer Treatment Centers of America**. She will be the principal architect of the organization's Information Services function, including all clinical and non-clinical hardware and software applications, data infrastructure, warehousing and security, informatics, and system-wide technology support services.

Darby most recently served as CIO of the Northeast Region for Tenet Healthcare, overseeing the IT and informatics functions at nine acute care hospitals as well as nearly 100 ancillary locations. Prior to that, she was the CIO, VP of information solutions for Risk Management Foundation of the Harvard Medical Institutions.

Drug Approvals

Accelerated Approval Granted To Zykadia in ALK+ NSCLC

FDA granted accelerated approval to Zykadia (ceritinib) for patients with a certain type of metastatic non-small cell lung cancer.

Zykadia is the fourth drug with breakthrough therapy designation to receive FDA approval. It is being approved four months ahead of the product's goal date of Aug. 24. The FDA had also granted Zykadia priority review and orphan product designations.

Zykadia is an anaplastic lymphoma kinase tyrosine kinase inhibitor that blocks proteins that promote the development of cancerous cells. It is intended for patients with metastatic ALK-positive NSCLC who were previously treated with crizotinib, the only other approved ALK tyrosine kinase inhibitor. Only 2 to 7 percent of patients with NSCLC are ALK-positive.

Zykadia's safety and effectiveness were established in a clinical trial of 163 participants with metastatic ALK-positive NSCLC. All participants were treated with Zykadia. Results showed that about half of the participants had their tumors shrink, and this effect lasted an average of about seven months.

Common side effects of Zykadia include gastrointestinal symptoms such as diarrhea, nausea, vomiting and abdominal pain. Laboratory abnormalities such as increased liver enzymes, pancreatic enzymes and increased glucose levels were also observed.

Zykadia is marketed by Novartis. The FDA's accelerated approval program allows approval of a drug to treat a serious disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising drugs while the company conducts confirmatory clinical trials.

FDA granted orphan drug designation to ADXS-HPV for the treatment of stage II-IV invasive cervical cancer.

ADXS-HPV is an immunotherapy drug candidate, developed by Advaxis Inc., which is designed to target cells expressing the HPV gene E7. Expression of the E7 gene from high-risk HPV variants is responsible for the transformation of infected cells into dysplastic and malignant tissues.

ADXS-HPV is designed to infect antigen-presenting cells and direct them to generate a powerful, cellular immune response to HPV E7. The resulting cytotoxic T cells infiltrate and attack the tumors while specifically inhibiting tumor Tregs and MDSCs in the tumors that are protecting it, according to the drug's sponsor.

Orphan drug designation is granted to drug therapies intended to treat diseases or conditions that affect fewer than 200,000 people in the U.S. The designation entitles the sponsor to clinical protocol assistance with the FDA, as well as annual grant funding, tax credits, waiver of PDUFA filing fees, and potentially a seven-year market exclusivity period.