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FLATIRON CEO CAROLYN STARRETT: WE'RE REIMAGINING THE INFRASTRUCTURE OF CANCER CARE, AND WE'RE GOING GLOBAL

As real-world evidence becomes ever more essential, a cancer health technology company that played a key role in modernizing 21st-century health data is capitalizing on its accomplishments in the U.S.

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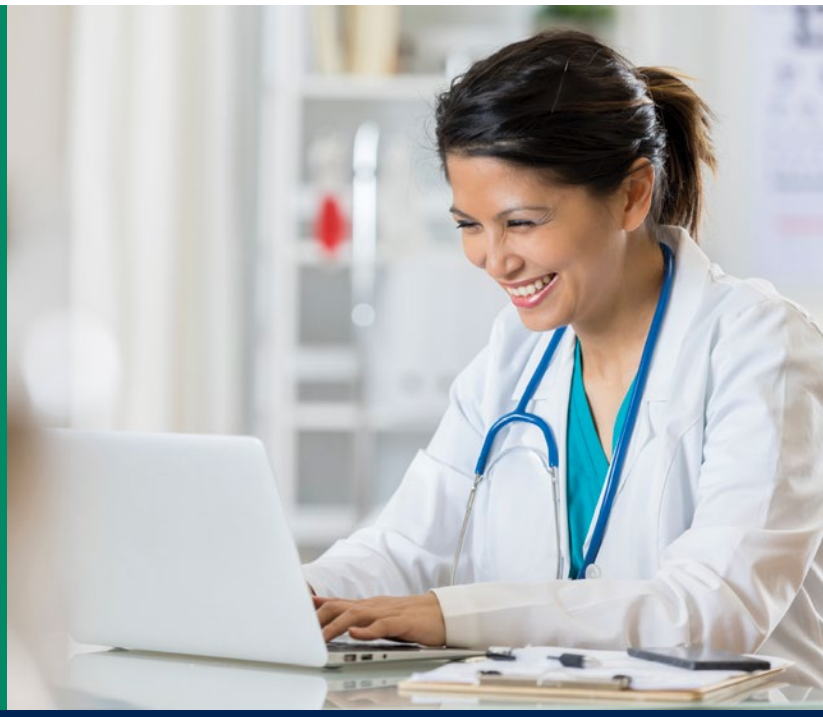

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CONVERSATION WITH THE CANCER LETTER

> To us, reimagining the infrastructure of cancer care means generating better and more actionable integrated evidence and technology to continue to reduce the time it takes to bring new therapies to market.

As real-world evidence becomes ever more essential, a cancer health technology company that played a key role in modernizing 21st-century health data is capitalizing on its accomplishments in the U.S.—and moving into international markets to meet the growing demand for actionable data.

Founded in 2012, Flatiron Health, now in its 10th year, is entering the third phase of its evolution as a pioneer of real-world data and machine learning applications in cancer informatics.

Carolyn Starrett, a long-time business operations and strategic development executive at the company, was named CEO in April 2021, after Flatiron co-founders Nat Turner and Zach Weinberg stepped down from management.

"We had our startup phase and days early on. We then had an acquisition and a period of learning what it meant to exist post-acquisition," Starrett said to *The Cancer Letter*. "Now, we're internally talking about Flatiron 3.0. And I think 3.0 is an opportunity to really think about how we further advance and realize the mission that we set out to achieve 10 years ago."

A decade ago, Flatiron was conceived when its founders went on a road trip to visit community oncology clinics and cancer centers.

In 2018, Roche acquired the company for $2.1 billion, signaling a turning point in cancer Big Data and sparking a heady race among health IT companies to expand their offerings.

The company remains autonomous as an independent affiliate of the Roche Group (*The Cancer Letter*, March 2, 2018).

Now headquartered in a swanky open-plan office building between Hudson Square and SoHo in New York City, Flatiron has subsidiaries in Japan, Germany, and the U.K., works with the top 20 pharmaceutical companies, and serves a growing portfolio of academic cancer centers and community practices.

Today, the company is composed of more than 1,000 full-time employees and 1,500 flex-time employees around the world.

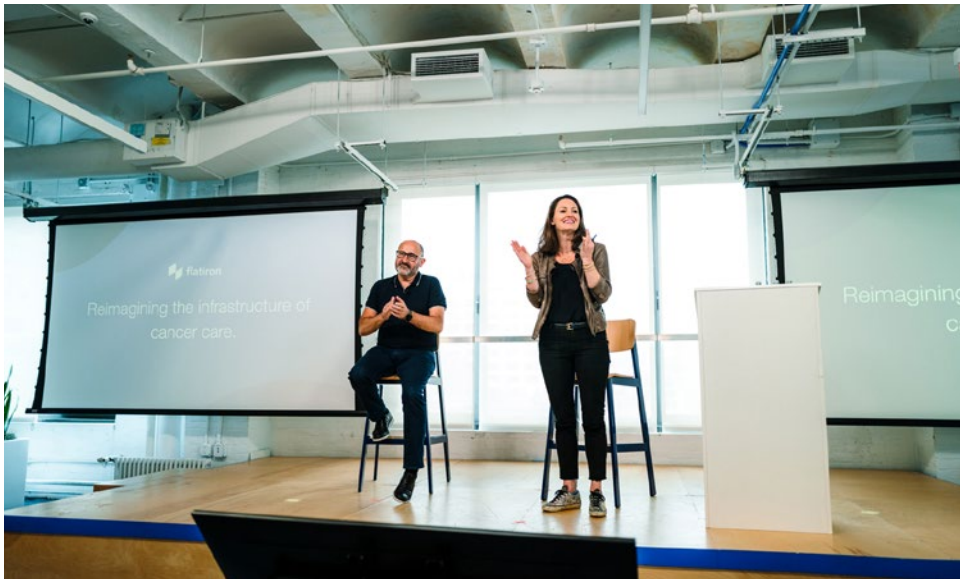
"We've learned that it's going to be important to understand not just U.S. populations, but also a broader global population," Starrett said. "We're in the process of designing custom approaches for the context that exists within each one of those markets.

"It's now been, I think, a three-year investment in understanding the legal regulatory and compliance requirements and forging our first early partnerships. We announced our first partnership in Japan last year to study patients with gastro-intestinal cancers and you can expect more coming in the U.K. and Germany."

Starrett's vision for Flatiron focuses on providing answers to the big questions in health informatics, cancer care, and research of the next decade:

- Speeding up translational science and the approval of new medicines,
- Steering the development of integrated evidence by building an ecosystem that links disparate sources of data,
- Creating access to high-quality real-world evidence across emerging markets and global populations, and
- Expose inequities in cancer care and improve outcomes for patients with cancer.

"If we look at the landscape today, there are just so many core problems that still persist," Starrett said. "It still takes over 10 years to bring new oncology treat-



Carolyn Starrett with Flatiron's chief medical officer, Javier Jimenez, presenting last month at the company's first in-person mid-year "All Hands" meeting, and celebrating Flatiron's 10-year anniversary.

ments and therapies to market. Clinical trials are expensive, inefficient, and slow. They don't really represent the patients who might ultimately receive and benefit from those medicines."

As definitions of scientific and clinical significance broaden, and as researchers and regulators move towards more holistic interpretations of health data, Flatiron is viewing real-world evidence—and its many facets—as one component in a much larger ecosystem in which previously siloed streams of information are becoming more interdependent.

"What we've learned over the last 10 years as we got started with real-world evidence is that a lot of the questions we want to answer require careful synthesis and analysis of healthcare data that comes from multiple different data streams and sources and methods," Starrett said. "And EHR data alone doesn't solve the problems that we want to tackle."

Flatiron is a founding member of the Real-World Evidence Alliance, which now includes 10 health organizations that collaborate and advocate for novel applications of real-world data.

"The goal here is to think about how to provide guidance, so that the best practices for planning and conducting and reporting on real-world evidence studies are clear to everyone involved," Starrett said. "The hope is that will then help to improve the quality and the transparency of the evidence and the acceptance of these data sources."

Flatiron and other alliance members have been working together with Friends of Cancer Research to develop real-world endpoints, with the goal of convincing FDA that these endpoints can be validated and used to inform drug approvals and regulatory decisions (*The Cancer Letter*, Sept. 25, 2020; Nov. 22, 2019).

"It's been an important area of collaboration, because the endpoints in clinical trials are operationally defined quite differently than real-world evidence endpoints," Starrett said. "They are captured in very different ways. So, the scientific bar for use of any type of data, including real-world data, is really high and needs to be reliable and relevant to the scientific question."

Flatiron's renewed commitment to health equity is led by Cleo A. Ryals, who drives the company's priorities and research strategy on disparities. Because of its ability to rapidly identify gaps in care delivery, real-world evidence is able provide timely snapshots of unmet needs in communities, at scale.

"We found out, for instance, that socioeconomic status information was not captured well in the EHR," Starrett said.

"And so, we had to take a step back and think about how do we pull the right external markers and validation with full respect to patient privacy and practice privacy, and all of the different considerations that are important to define new variables, that we can then add into our integrated evidence to really start to understand where the inequities exist."

Starrett said the company is directing its resources into generating actionable integrated evidence and technology to reduce the time it takes to bring new therapies to market.

"The real potential is still very much ahead of us," Starrett said. "We are, at Flatiron, deeply focused on reimagining the infrastructure of cancer care, so that we can come together across the ecosystem and accelerate this learning and do it more efficiently and more sustainably."

Starrett spoke with Matthew Ong, associate editor of *The Cancer Letter.*

Matthew Ong: You've been CEO of Flatiron for a year now, but you've been there since 2016, and you've watched the company evolve.

From these six years, what are your takeaways, or lessons, about Flatiron, and what do we need to know about the future of real-world data in oncology?

Carolyn Starrett: Like many at Flatiron, I have a deeply personal connection

to cancer. I found my first early-stage melanoma when I was 28, and all of my grandparents have experienced cancer.

What's been cool over the last six years is seeing how Flatiron has evolved. We've started to talk about the three chapters of the company, if you will. We had our startup phase and days early on. We then had an acquisition and a period of learning what it meant to exist post-acquisition.

Now, we're internally talking about Flatiron 3.0. And I think 3.0 is an opportunity to really think about how we further advance and realize the mission that we set out to achieve 10 years ago.

Flatiron was founded to answer a pretty simple question: Can we take the data that's generated via routine care and make it useful? How can we improve lives by learning from the experience of every person with cancer?

We've really lived that mission over the last 10 years. We were pioneers in the evolution of real-world evidence in oncology, we see patients with cancer who have new treatment alternatives and options as a result of that real-world evidence, and we're proud to have contributed to some of these meaningful advances.

Moving forward, the things that get me excited are how we take this vision even further. We cultivate a virtuous learning cycle where we can learn from real-world experience, and then embed that back into research and development and access decisions around the world, and then, importantly, back into the treatment decisions that are made at the point of care.

That, in and of itself, is really the opportunity. It's how do we truly reimagine the infrastructure of cancer care, so that we are creating a more modern and connected oncology ecosystem together with clinicians and researchers and regulators, and how do we leverage technology and AI and data that's already captured to transform and accelerate clinical trials, so that we can better understand the right treatments for very targeted patient populations.

So, that's really our goal moving forward: Closing this loop and starting to bring new options and insights back to the point of care, and continuing to partner with our biopharma customers, independent cancer centers, and academic medical centers across the ecosystem to drive systemic change.

I've seen that happen over the years; I'm looking forward to seeing more. What's your vision for Flatiron, as CEO, and what should we be paying attention to as folks in oncology?

CS: I love that you asked that. My vision as CEO is to empower teams at Flatiron to build a world where technology and science can help close the gap between care and research.

If we look at the landscape today, there are just so many core problems that still persist. It still takes over 10 years to bring new oncology treatments and therapies to market. Clinical trials are expensive, inefficient, and slow. They don't really represent the patients who might ultimately receive and benefit from those medicines.

And then, with the rise of new modalities and personalized medicine, understanding the best treatment for every patient is increasingly complex. And I don't think we've fully maximized the potential of all the new therapies and learning how to best use them.

To us, reimagining the infrastructure of cancer care means generating better and more actionable integrated evidence and technology to continue to reduce the time it takes to bring new therapies to market.

It means understanding exactly who can benefit from these therapies, and then making them available to the patients who need them around the world.

It means integrating clinical research into routine care and making it easy for every patient with cancer to participate in a clinical trial to close the gap in access and ensure that we're learning from patients who look more like the real world.

Lastly, there is an important need to use data for good—to surface and understand healthcare disparities that continue to exist in cancer and to partner with our network of cancer centers to drive towards improving the outcomes for their patients.

It's great that you mentioned integrated evidence, because the field seems to be thinking of the utility of RWE in the context of an integrated framework, and how different facets can be used to complement or complete other types of data.

What does that look like? And what does integrated evidence in this context mean for researchers, physicians, and patients?

CS: I think of integrated evidence as an emerging discipline.

And what we've learned over the last 10 years, as we got started with real-world evidence, is that a lot of the questions we want to answer require careful synthesis and analysis of healthcare data that comes from multiple different data streams and sources and methods.

And EHR data alone doesn't solve the problems that we want to tackle.

Taking the EHR data that we cultivated and linking it to claims and genomics and imaging to map in critical contextual information—e.g., mortality, socioeconomic status, smoking status. There are a lot of values that just aren't captured consistently or accurately, and you can't learn from data that isn't captured.

So, real-world evidence is certainly one component of the broader discipline of integrated evidence, but what we're working to do is think about how we bring together evidence from across the ecosystem to learn more quickly and efficiently whether it's captured in routine care, intentionally collected in a trial, or prospective study reported by patients.

And we're seeing a real need to start to link those disparate sources of data.

And we're seeing the FDA moving in that direction as well, with the use of real-world evidence, for instance from Flatiron, for approvals.

What would you say are some of Flatiron's biggest research and regulatory accomplishments, and how do those advancements inform Flatiron's research priorities right now?

CS: We have active partnerships underway now with the U.S. FDA, Friends of Cancer Research, the National Comprehensive Cancer Network, NICE, among many others.

And those are our research partnerships, where we pick research questions and actually explore these topics together, so that we can collectively learn from one another.

We are also a founding member of the Real-World Evidence Alliance, which now includes 10 organizations working in the real-world evidence field. And we're working to come together to champion collaboration around important novel applications, and the policies that will enable them.

It's been exciting to see the momentum in guidance from the FDA, and the same thing is now happening in Europe around HTA applications. And so, we are looking closely at those, and think we can play a meaningful role in providing guidance, because we have firsthand experience looking at these data over many years.

Some of the big wins we've seen to date include—and thank you to *The Cancer Letter* for covering many of these over the years—men with breast cancer now have an approved therapy option in Ibrance. And this is a population which was historically too small and challenging to study in a randomized clinical trial [*The Cancer Letter*, April 19, 2019].

Similarly, last year, we saw a new dosing regimen approved for patients with EGFR mutations for some cancers, which enabled patients to go in for chemotherapy once every two weeks instead of once a week, which means half as much time is spent in the infusion chair and days back in each of these patients' lives.

And maybe one last one—I was really excited to see this. We have a partnership with Foundation Medicine (FMI) where we build a clinical genomics database, and their Foundation One CDX genomic test was recently approved by the FDA as a companion diagnostic to identify patients for a couple different indications of Rozlytrek (entrectinib).

What was interesting here is, first and foremost, this is going to enable broader access to genomic testing and potentially breakthrough therapies for patients. But also as a condition of this approval, the FDA requested that FMI conduct a post-approval study powered by our joint clinical genomics database, which spans over 100,000 patients.

So, now there is a new companion diagnostic that was approved last month. And we already have the built-in data set that's going to enable FMI to address those FDA requirements via retrospective real world evidence.

That's exciting to hear. How has the Roche acquisition informed Flatiron's work and priorities, and what do Flatiron's partnerships, research collaborations, and business transactions with other pharma companies look like now, post-acquisition?

CS: We're an independent affiliate of the Roche Group and we remain a separate legal entity, and that autonomy has always underpinned our work with many life sciences companies, with cancer centers, with academic medical centers, with the regulatory groups. We continue to work independently and our priorities are informed through input from all of our customers.

We have strict firewalls in place and confidentiality obligations that ensure that we can do this work in a connected way across the ecosystem. And this is critically important for us to maintain. We work with all of the top 20 global pharmaceutical organizations that develop oncology therapeutics now. And part of what we learned from them are about the new possibilities that are emerging and the joint use cases that we think are most exciting.

What we're seeing is that demand for real-world data and real-world evidence is continuing to grow, and we're seeing across the landscape a continued increase in investment in R&D in oncology.

At the same time, the drugs themselves—and I think COVID has contributed to a lot of this—are being approved sooner with more limited data.

There's an increasing need to think about this concept, as I described, of integrated evidence to understand what happens after that first approval. If the first approval determination is made looking at results across 30 patients, that doesn't tell you how the drug is going to work when we then bring it to a much broader patient population around the world.

And so, we're seeing that our partners are excited to further explore integrated evidence approaches for post-marketing commitments and to make the case for reimbursement around the world more quickly. These market access use cases are an important area of investment.

And there's also a very broad recognition that we need to do better in terms of diversity and representativeness in research and in trials. We're working with our biopharma customers on both fronts, to both broaden and expand the solution set in how we run clinical trials, and then to think about how we build more diversity and representativeness to all of the research that we do and the decisions that are made.

Speaking of market access, I see that you're also investing in international collaborations. You were recently in Japan; you're still working with them. Why are these partnerships important?

Is market access a primary consideration? Are the collaborations mostly focused on research or are you also looking to grow your client base abroad?

CS: We've learned that it's going to be important to understand not just U.S. populations, but also a broader global population.

First, in the context of learning from real-world evidence, and, second, in the context of broadening our approaches for clinical trials around the world.

Today, we have international subsidiaries in Japan, Germany, and the U.K. And we're in the process of designing custom approaches for the context that exists within each one of those markets.

It's now been, I think, a three-year investment in understanding the legal regulatory and compliance requirements and forging our first early partnerships. We announced our first partnership in Japan last year to study patients with gastro-intestinal cancers and you can expect more coming in the U.K. and Germany.

Why is this important? There are two million people diagnosed with cancer and 750,000 of them lose their battle with cancer every year across these three countries.

So, first and foremost, in service of our mission to improve and extend lives for every person with cancer, this is an important focus area.

But then, as you said, when we talk to our biopharma clients, it's important to them to tackle the challenge of access to high-quality real-world evidence from global patient populations. We are following their lead, following their priorities. And we're seeing really, really great momentum here.

We also have a three-year partnership with NICE that started in 2020, and we were able to work together most recently to help provide input and feedback on the real-world evidence framework that they just launched.

The goal here is to think about how to provide guidance, so that the best practices for planning and conducting and reporting on real-world evidence studies are clear to everyone involved. The hope is that will then help to improve the quality and the transparency of the evidence and the acceptance of these data sources.

How far along are the real-world evidence frameworks that are being developed in other countries? Is it still primarily driven by the U.S. market and the intellectual advancements here? What is the landscape looking like elsewhere?

CS: There's a ton of activity in this space. It's been encouraging to see the momentum in the U.S. and with NICE and ISPOR in particular and across Europe, we're seeing similar activities underway. I think that the theme and trend is consistent around the world, from what I see.

We recently had the chance to participate and help shape the NICE Real-World Evidence framework earlier this year. The research coming out of our ongoing NICE Research Collaboration not only helped inform the development of this framework, but has been critical in making greater use of real-world data to resolve gaps in knowledge and driving forward access to innovations.

We hope to continue partnering with countries to advance impact and use of RWE.

How has your suite of services grown in recent years? And what should we know about Flatiron's latest work in AI and machine learning? For instance, is clinical decision support—versus resource, depending on clinical utility—a reality now for users in your ecosystem?

CS: I'll start with AI and machine learning. ML and AI have been the foundation of the way we've designed our products from the very beginning.

In the early days, we pioneered the use of machine learning technology, paired with natural language processing to

start to extract clinically relevant information from EHRs and make that more available for research.

What we started to see very quickly was that that wasn't necessarily enough to ensure that these clinical data points were captured with the level of transparency and quality that we know are necessary.

So, we built a clinically-trained abstraction workforce who look directly at the chart and make clinical determinations around, for example, line of therapy or progression of disease, actually looking at the core source data.

Now, machine learning is getting much better and much more accurate. So, we're in the process of running a lot of tests to understand what's the best technique for any given data variable, and it looks different depending on the data field that we're working on.

The right approach for line of therapy, for instance, might look different than smoking status, or extracting biomarkers or genomic information. And so, we have an opportunity to get much more customized and create the frameworks to properly evaluate and transparently communicate the quality of the data that's being produced with machine learning.

In addition to using ML for building our cohorts, I would say the other thing I'm excited about is using ML to start to tackle some of these really important needle-in-a-haystack problems that would just be impossible to manually extract from the chart at scale.

When we have a very rare patient population in question, we can use machine learning to get an early read and quickly answer a specific research question. We have also built ML models to predict patient data fields that aren't captured well in the EHR in real time at the point of care, so that those data can inform treatment decisions and get to the clinician much more quickly. These data live in the EHR, but they might be buried in a document and are liable to be missed.

What we continue to see is that the AI is really only as good as the humans who are using it and the judgment they apply. There's the art and the science and we continue to believe that it's going to be really important to blend both of those.

I'll highlight one interesting product in particular, called Flatiron Assist. It's a clinical decision support tool that works in our EHR, OncoEMR, but is also platform agnostic and integrates with Epic, and over time, other large EHRs.

It pulls all of the important information that you might use to make a clinical treatment decision and then showcases and integrates all of the guideline-concordant therapeutic options and available clinical trials to consider.

And it also highlights preferred practice protocols and regimens—and unique payer considerations—to ensure clinicians are aware of all of these options and can make the best possible treatment decisions at that critical moment.

In this very complex world, I think that's a really important starting point. How do we actually make use of all of the data that does already exist?

It also is an exciting opportunity coming back to the vision to start to close the gap between research and care. As an example, the DESTINY-4 trial that was reported out of ASCO this year, which is going to change the standard of care for women with HER2-low breast cancer.

We actually had implemented that early finding and that HER2-low status into the OncoEMR several months before that study was released.

We think we can play an important role in compressing that cycle and getting new guidelines out to clinicians as soon as they're available, and then building the right mechanisms to make use of all of the data that may exist, if not in the perfect form that we might like to see it.

Six years ago, many players in cancer informatics were, in my opinion, at the start of a race to offer clinical trial matching services. And you just mentioned that your CDS also supports that, and it's part of the suite.

How far have we come as a field in that regard, and what is Flatiron's focus now in clinical trials?

CS: Very few patients take part in clinical trials, and it's well recognized that those who do are not broadly representative.

Today, clinical trials data is collected in one stream and routine clinical data is collected in another, and they don't really talk unless humans move them back and forth. It's crazy when you actually think about how much of the clinical trials workflow still exists on paper logs on walls in the clinic.

We think there's an opportunity to use technology to tackle that challenge and integrate these two different research approaches.

You may have seen we acquired a company called Protocol First last year, which has built software that automates the direct transfer of data from EHRs into EDCs, reducing the need for human transcription. The Protocol First suite of solutions is rolled out across many academic medical institutions, and trials with sponsors, and CROs around the world.

We are excited to bring that solution, which is so deeply complimentary to the work we've already done in trials management and in the EHR embed-

ded software, together to think end-to-end, how do we map out the entire value chain of what does it take to design a trial, start a trial, find the patients, get them enrolled and make that process digital instead of deeply manual in the way that it is today.

You asked about clinical trials matching. I think many folks are indeed trying to tackle this one, and that's fantastic. We're excited to be part of the solution.

The place and the role that I think we can play most uniquely is in thinking about how do we, as I mentioned earlier, use machine learning to understand how to automate that pre-screening process, so that we can not only figure out which patients might be eligible for a trial, and do that in the background, rather than having a human manually go through all of the different inclusion and exclusion criteria.

But then, also build the workflows that put that information at the hands of clinicians at the right time when they're making a treatment decision. That's what we hear from our practices has been really challenging.

They might find a patient who might be eligible, but then, by the time the patient is seen and they think about talking to them about a clinical trial, they actually already went on standard-of-care therapy.

So, they missed that window, and didn't get to the doctor at the right time of the visit—leading to a big missed opportunity.

We integrate these pre-screening and research team decisions and alerting directly into the clinician workflow, and we think that's going to really help improve enrollment.

What about rare diseases? Is Flatiron focused on expanding not only evidence generation for rare diseases, but also to be able to say:

"Hey, we might be able to help you get data and enroll patients—either on the real-world evidence side or in combination with a prospective study or retrospective study—in order to look at potential indications for these rare diseases"?

CS: Yes. I think this is a perfect application of that integrated evidence concept we talked about, and we're starting to get smarter about determining the right approach for each particular question at hand.

With rare patient populations, it may be that a real-world evidence approach and a retrospective study makes a lot of sense, but we also need to think about that in a broader context—that's a unique decision depending on the specific question at hand.

Rare diseases are one of the important applications that we see for both retrospective real-world evidence and better clinical trials that are faster and more efficient and enroll more simply. But the trial technology we're building is actually platform agnostic.

We are in trials today, and the solutions, the technology, supports all phases of trials across all settings.

And so, the same benefit we can offer in rare patient populations we can also offer holistically in lots of different disease areas.

What about your projects with FDA? You mentioned a few things that you were working on with FDA.

Last I looked, you were also working on developing real-world endpoints in a multi-year, multi-phase collaboration with Friends of Cancer Research (*The Cancer Letter*, Sept. 25, 2020; Nov. 22, 2019). How's that going, and what does your FDA portfolio look like now?

CS: We've had a partnership in place with the FDA over the last five years, and we also have a decent amount now of direct experience engaging with regulators on behalf of sponsors, in the context of specific regulatory submissions using Flatiron real-world data.

These are important sources of learning for us, because we can then help bring guidance back to all of the other customers that we work with and better inform the way we are designing our evidence solutions.

One of the research collaboration projects we're excited about is focused on understanding similarities and differences between metastatic breast cancer patients treated in the real world and patients treated in clinical trials.

We're effectively producing trial-like populations using Flatiron real-world data to understand how replicable those results are in real-world data. And we're excited that projects like this can start to advance our shared knowledge in oncology for research and regulatory purposes, and further help to define what the right quality bar and methods are for evaluating fit for use in real-world data.

On endpoints in particular, it's been an important area of collaboration, because the endpoints in clinical trials are operationally defined quite differently than real-world evidence endpoints. They are captured in very different ways.

So, the scientific bar for use of any type of data, including real-world data, is re-

ally high and needs to be reliable and relevant to the scientific question.

What we've seen is that it's helpful to sit together, to look at the methods, to look at and understand the feedback, and come together transparently around the best methodology to tackle what is inherently really complex and messy data.

And we're continuing to pursue this partnership.

As you know, I recently invited Rebecca Miksad, Flatiron's senior medical director, to speak on a panel about the role of real-world evidence at the intersection of COVID and cancer—in part because I spent significant time covering that space during the pandemic, particularly as it pertains to inequities (*The Cancer Letter*, May 13, 2022).

How is Flatiron positioned to inform these conversations, not only at a local level, but also nationally? And what are some highlights that you'd want to communicate?

CS: One of the great things about real-world evidence is that it is an important mechanism to expose inequities and expose the gaps that exist.

You actually wrote a cover feature story about a hackathon we did back in 2019 that ended up on the ASCO plenary stage.

At the hackathon, we looked at the difference and disparities in time to treatment in states that had rolled out the ACA Medicaid Act. [*The Cancer Letter*, June 21, 2019]

And that's the type of investment that we've continued.

We now have a head of health equity and disparities research who drives our research strategy and cross company priorities in this respect. We've had a team most recently focused on building out the data inputs necessary to do the type of research we think is missing. And this comes back to the infrastructure of cancer care.

We found out, for instance, that socioeconomic status information was not captured well in the EHR. And so, we had to take a step back and think about how do we pull the right external markers and validation with full respect to patient privacy and practice privacy, and all of the different considerations that are important to define new variables, that we can then add into our integrated evidence to really start to understand where the inequities exist.

We also have an ongoing partnership with the American Cancer Society, where we are actually funding grants to support research in the study of quality and equity in cancer care and outcomes, called the Real-World Data Impact Awards.

It's been cool to see where those grants have gone and the research they have enabled.

To give a current example related specifically to COVID, one of our researchers wrote a paper that was presented at ASCO in June looking at the increase of telemedicine use among patients with cancer during the COVID-19 pandemic.

On the one hand, we saw a very large increase in the use of telemedicine in cancer care, which historically has been a place where that was very, very low.

On the other hand, we saw that there were pretty substantial inequities in where that telemedicine was used. And so, Black, uninsured, non-urban, lower socioeconomic status patients were less likely to be able to use telemedicine services.

We certainly don't have all of the answers, but taking a step back, I hope that we'll continue to see coverage of telemedicine services be permanent instead of tied to the emergency health declaration that came out via COVID, and continue to increase the reimbursement rates for these services from the commercial payers and the private insurers.

Thinking about everything we've talked about over the last 45 minutes, what are we looking forward to next?

CS: Thank you so much for having me, Matt. This has been a ton of fun.

Reflecting on the last 10 years of Flatiron, I'm so proud of the progress we made, the milestones we talked about, the patients who have access to new therapies as a result of all of the work that we've done across the ecosystem to understand their stories.

Looking forward, I think we're really at an inflection point, and the real potential is still very much ahead of us. We are, at Flatiron, deeply focused on reimagining the infrastructure of cancer care, so that we can come together across the ecosystem and accelerate this learning and do it more efficiently and more sustainably.

I think if we can do this, we will be on a path to accelerate the approval of new medicines, accelerate the understanding of who should receive those medicines, accelerate ensuring that they can be reimbursed around the world and then ultimately ensuring better patient outcomes for all of the people experiencing cancer today.

That is a problem and a vision that gets me really, really fired up. And I'm just really excited to be part of this journey.

Thank you for taking the time to speak with me.

CS: Thank you.

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As *U.S. News* tweaks methodology, top four cancer hospitals remain unchanged from last year

(1) MD Anderson, (2) MSK, (3) Mayo, (4) DFCI

By Jacquelyn Cobb, Matthew Bin Han Ong, and Paul Goldberg

Don't sack the director because your cancer center's score and ranking by *U.S. News & World Report* have slipped.

By the same token, don't reward the director too generously if your center has gone up a notch, or two. Or seven.

As careers of cancer center directors are made and cut short based on shifts in *U.S. News* rankings from year to year, it's easy to forget that the news organization regularly changes the methodology it employs as it assesses and ranks healthcare institutions.

Often, readers—and, by extension, folks who decide on employment contracts of center directors—are urged to refrain from comparing specific cancer centers' overall "specialty score" from year to year.

"It is a statistical truth, and we try to be transparent about how we've calculated the rankings and what our results are," Ben Harder, managing editor and chief of health analysis at *U.S. News*, said to *The Cancer Letter*. "But it's not as though a hospital falling on that score from one year to the next is actually meaningful. It can't be translated as, 'Oh, this hospital got worse year over year.'"

The *U.S. News* metrics are used exclusively by the media company, and every year, RTI International, the contractor employed by *U.S. News*, publishes a methodology report. While sometimes statisticians and directors of cancer centers gripe about the news organization's methodology, it's unclear whether any have critiqued it in a rigorous manner.

The *U.S. News* methodology is a moving target.

This year, *U.S. News* added cancer surgery for three diseases—prostate, ovarian, and uterine malignancies—to the evaluation criteria. Prior to the 2022-2023 rankings, only performance in co-

Best Hospitals 2022-23: Cancer

Rank	Hospital	U.S. News Specialty Score	30-day survival	Discharging patients to home	Patient experience	Number of patients	Nurse staffing	Intensivists	Advanced technologies	Patient services	Recognized as Nurse Magnet hospital	NCI-designated cancer center	Accredited by FACT	Expert opinion	Current AHA responder
1	University of Texas MD Anderson Cancer Center, Houston	100.0	5	5	NA	13,187	1.9	Yes	8	8	1	Yes	2	33.4	Yes
2	Memorial Sloan Kettering Cancer Center, New York	85.7	5	5	5	6,496	2.4	Yes	8	8	1	Yes	2	31.2	Yes
3	Mayo Clinic, Rochester, Minn.	79.9	5	5	5	4,527	2.9	Yes	8	8	1	Yes	2	16.1	Yes
4	Dana-Farber/Brigham and Women's Cancer Center, Boston	76.0	5	5	5	4,376	2.4	Yes	8	8	1	Yes	2	18.9	Yes
5	UCLA Medical Center, Los Angeles	73.2	5	5	5	1,942	3.2	Yes	8	8	1	Yes	2	4.5	Yes
6	Cleveland Clinic	71.9	5	5	4	3,446	2.4	Yes	8	8	1	Yes	2	6.4	Yes
7	City of Hope Comprehensive Cancer Center, Duarte, Calif.	69.9	5	5	4	3,666	2.6	Yes	8	8	1	Yes	2	5.4	Yes
8	Hospitals of the University of Pennsylvania-Penn Presbyterian, Philadelphia	69.2	5	5	4	3,589	2.5	Yes	8	8	1	Yes	2	6.8	Yes
9	Northwestern Memorial Hospital, Chicago	68.9	5	5	4	2,616	2.0	Yes	8	8	1	Yes	2	2.3	Yes
10	Siteman Cancer Center at Barnes-Jewish Hospital, Saint Louis	68.4	5	5	4	4,540	2.5	Yes	8	8	1	Yes	2	4.0	Yes
11	Cedars-Sinai Medical Center, Los Angeles	67.7	5	5	4	2,237	2.7	Yes	8	8	1	No	2	1.8	Yes
12	New York-Presbyterian Hospital-Columbia and Cornell	67.6	5	5	4	5,741	3.1	Yes	8	8	1	Yes	2	2.9	Yes
13	Johns Hopkins Hospital, Baltimore	67.4	5	5	4	2,396	2.4	Yes	8	8	1	Yes	2	11.9	Yes
14	University of Chicago Medical Center	66.4	5	5	4	2,318	2.3	Yes	8	8	1	Yes	2	3.0	Yes
15	Stanford Health Care-Stanford Hospital, Stanford, Calif.	66.2	5	5	5	2,468	2.7	Yes	8	8	1	Yes	2	4.7	Yes
15	UCSF Health-UCSF Medical Center, San Francisco, Calif.	66.2	5	5	4	2,480	2.6	Yes	8	8	1	Yes	2	5.4	Yes
16	UPMC Presbyterian Shadyside, Pittsburgh	64.3	5	5	4	4,325	2.3	Yes	8	8	1	Yes	2	3.0	Yes
18	USC Norris Cancer Hospital-Keck Medical Center of USC, Los Angeles	64.0	5	5	5	1,184	2.5	Yes	8	8	1	Yes	2	2.7	Yes
19	Perlmutter Cancer Center at NYU Langone Hospitals, New York	62.9	5	5	4	3,277	2.4	Yes	8	8	1	Yes	2	2.6	Yes
20	UC San Diego Health-Moores Cancer Center	62.8	5	5	4	1,674	2.1	Yes	8	8	1	Yes	2	2.2	Yes
21	Massachusetts General Hospital, Boston	61.0	5	5	5	3,649	2.6	Yes	8	8	1	Yes	2	7.2	Yes
22	Duke University Hospital, Durham, N.C.	60.5	5	5	4	2,898	2.1	Yes	8	8	1	Yes	2	4.9	Yes
23	Mayo Clinic-Phoenix	60.4	5	5	5	1,517	3.2	Yes	8	8	1	No	2	2.7	Yes
24	Ohio State University James Cancer Hospital, Columbus	60.3	5	5	5	4,627	2.2	Yes	8	8	1	Yes	2	5.2	Yes
25	H. Lee Moffitt Cancer Center and Research Institute, Tampa	60.2	5	5	5	2,266	1.2	Yes	8	8	1	Yes	2	6.2	Yes
25	UT Southwestern Medical Center, Dallas	60.2	5	5	5	2,014	2.2	Yes	8	8	1	Yes	2	1.3	Yes
27	Seattle Cancer Care Alliance/University of Washington Medical Center	59.7	5	5	4	2,346	2.3	Yes	8	8	1	Yes	2	7.0	Yes
28	Mount Sinai Hospital, New York	59.0	5	5	3	2,661	2.3	Yes	8	8	1	Yes	2	1.4	Yes
29	Houston Methodist Hospital	58.2	5	5	4	1,859	2.1	Yes	8	8	1	No	2	0.3	Yes
30	AdventHealth Orlando	57.9	5	5	4	4,131	1.9	Yes	8	8	0	No	2	0.2	Yes
31	Beth Israel Deaconess Medical Center, Boston	57.7	5	5	4	2,108	1.5	Yes	8	8	0	Yes	2	0.5	Yes
31	Rush University Medical Center, Chicago	57.7	5	5	4	1,645	2.1	Yes	8	8	1	No	2	0.6	Yes
33	Huntsman Cancer Institute at the University of Utah, Salt Lake City	57.4	5	5	4	1,443	2.2	Yes	8	8	0	Yes	2	1.3	Yes
33	University of Kentucky Albert B. Chandler Hospital, Lexington	57.4	5	5	3	1,452	1.8	Yes	8	8	1	Yes	2	1.0	Yes
35	Dan L Duncan Comprehensive Cancer Ctr. at Baylor St. Luke's Med. Ctr., Houston	57.3	5	5	3	866	2.0	Yes	7	8	1	Yes	0	0.5	Yes
35	Montefiore Medical Center, Bronx, N.Y.	57.3	5	5	2	2,716	2.5	Yes	8	8	0	Yes	2	0.6	Yes
37	OHSU Hospital-Knight Cancer Institute, Portland, Ore.	57.2	5	5	4	1,780	2.2	Yes	8	8	1	Yes	2	0.9	Yes
38	Vanderbilt University Medical Center, Nashville, Tenn.	57.0	5	5	4	2,379	2.3	Yes	8	8	1	Yes	2	3.0	Yes
39	UC Davis Medical Center, Sacramento, Calif.	56.8	5	5	4	1,621	2.7	Yes	8	8	1	Yes	2	0.9	Yes
40	University of Michigan Health Rogel Cancer Center, Ann Arbor	56.5	5	5	4	2,865	2.7	Yes	8	8	1	Yes	2	3.6	Yes
41	North Shore University Hospital at Northwell Health, Manhasset, N.Y.	55.5	5	5	4	2,043	2.4	Yes	8	8	1	No	2	0.5	Yes
41	Thomas Jefferson University Hospitals-Sidney Kimmel Cancer Center, Philadelphia	55.5	5	5	4	1,933	2.1	Yes	8	8	1	Yes	2	1.0	Yes
43	Emory University Hospital, Atlanta	55.3	5	5	4	2,376	2.2	Yes	8	8	1	Yes	2	1.5	Yes
44	MedStar Georgetown University Hospital, Washington, D.C.	55.1	5	5	3	934	1.7	Yes	8	8	1	Yes	2	0.9	Yes
45	M Health Fairview University of Minnesota Medical Center, Minneapolis	54.7	5	5	4	1,615	2.0	Yes	8	8	0	Yes	2	0.6	Yes
46	UCI Medical Center, Orange, Calif.	54.5	5	5	4	1,055	2.0	Yes	8	8	1	Yes	2	1.3	Yes
46	University of Kansas Hospital, Kansas City	54.5	5	5	5	2,283	2.1	Yes	8	8	1	Yes	2	0.5	Yes
48	Queen's Medical Center, Honolulu	54.4	5	5	4	1,750	1.5	Yes	6	8	1	Yes	0	0.0	Yes
48	Sylvester Comprehensive Cancer Center-Univ. of Miami Hosp. and Clinics, Miami	54.4	5	5	3	1,633	1.3	Yes	8	8	0	Yes	2	1.8	Yes
50	Lenox Hill Hospital at Northwell Health, New York	54.1	5	5	4	848	2.9	Yes	8	8	1	No	0	0.6	Yes

Rankings are based on all of the above measures.

lon cancer and lung cancer surgery was being measured.

All five cancer surgery ratings are now factored into the Honor Roll, which is the overall non-specialty *U.S. News* ranking of best hospitals.

Adding these procedures "expands what we offer to patients and the data they can use to make data-informed decisions about where to get care," Harder said. "What each of the new ratings does is zoom in on a particular population of cancer patients and provide them with a rating of hospitals on the basis of their performance in surgically treating those specific types of cancer."

The cancer surgery ratings, however, do not directly factor in the specialty Best Hospitals for Cancer ranking. Patients with diverse cancer diagnoses, including prostate and gynecological cancers, are already included in the oncology-specific ranking design.

"I think our expansion of those ratings to cover prostate cancer, uterine cancer, and ovarian cancer is the most notable change that we made to the methodology this year," Harder said. "We've made a number of other methodology changes that are maybe more under the hood, but they are important nevertheless. Among those is this was the first year that we had data from the pandemic period that was included in the analysis."

Among cancer hospitals, MD Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, Mayo Clinic, and Dana-Farber Cancer Institute retained the top four spots in the 2022-2023 ranking.

There was minor reshuffling among the top 20 in this year's ranking, but one in particular stood out—Johns Hopkins Hospital and City of Hope Comprehensive Cancer Center traded spots. Hopkins moved from No. 6 to No. 13, and City of Hope moved from No. 13 to No. 7.

Harder said changes in outcome data—specifically, survival and discharge to home—tend to be a primary factor in year-to-year fluctuations in hospitals' rankings.

"Both hospitals scored in the same scoring tier, which ranges from one to five, for both those outcome measures," Harder said. "What you are noting is that this is an exception to an overall pattern of quite a bit of stability in the rankings from last year to this year."

In the ranking methodology, patient survival is measured for 30 days after being admitted, relative to other hospitals treating similarly complex conditions. Discharge to home is assessed according to how often patients go directly home from a hospital, rather than being discharged to another facility.

Other movements from 2021 to 2022 include:

- UCLA Medical Center ascended to No. 5 from No. 8,
- Hospitals of the University of Pennsylvania-Penn Presbyterian moved up two spots from No. 10 to No. 8,
- Cleveland Clinic moved from No. 5 to No. 6,
- Northwestern Memorial Hospital dropped from No. 6 to No. 9, and
- Cedars-Sinai dropped from the No. 9 spot to the No. 11 spot, leaving the Siteman Cancer Center at Barnes-Jewish Hospital to close out the top ten.

"As our methodology report describes in detail, the value that gets factored into our rankings calculation isn't the one-to-five tier, but rather the underlying, continuous performance measure, which is what's known as a 'random effect,' or RE," Harder said.

U.S. News doesn't publish RE values because they are "too arcane for most members of the public to find useful," Harder said. In the case of Hopkins v. City of Hope, the higher-ranking hospital earned better REs this year, even though both hospitals had REs that were good enough to put them in the same scoring tier.

The *U.S. News* metrics show comparable performance between Johns Hopkins and City of Hope. An exception is that Johns Hopkins ranked higher than City of Hope on expert opinion scoring (11.9% vs 5.4%). Additionally, City of Hope is reported as scoring "Average" for uterine cancer surgery, while Johns Hopkins is rated "High Performing" for all cancer surgery procedures.

"We did not make any major methodology changes in terms of excluding or including a new swath of patients, or changing how we do risk adjustment," Harder said. "So, I wouldn't attribute it to methodology changes."

The gap in overall score that separated the nearly perpetual No. 1 (MD Anderson) from No. 2 (MSK), has sometimes been as small as 0.1%. This year, this gap has widened to 14.3%—without affecting rankings (*The Cancer Letter*, July 24, 2015).

For what it's worth, MD Anderson scored "High Performing" on all cancer surgery measures, while MSK scored "Average" on uterine cancer surgery, which was being rated for the first time this year.

COVID adjustments; health equity metrics

To control for COVID-related oscillations in patient volume and outcome, *U.S. News* excluded visits in which a patient had a COVID-19 diagnosis.

Pre-COVID patient volumes, circa 2017-2019, were used as benchmarks.

"We feel pretty comfortable that we've removed that effect," Harder said. "We removed some cases that arguably didn't need to be removed from our analysis—I guess the cancer surgery metaphor would be to cut a wide margin around the problem."

These measures would ensure that the rankings are relevant to patients this year.

> We want to make sure that we have a relatively comprehensive, if not 100% holistic, view of what hospitals are doing around health equity before we start integrating that into the ranking methodology.
>
> – *Ben Harder*

"We're using data from a prior time period, but our goal is to help patients make a decision in the here and now," Harder said. "For that reason, any historical perturbations that are not germane to how those hospitals are providing care today is sort of beside the point—it's a distraction."

The rankings methodology does not include a suite of health equity measures developed in 2021, which found that the vast majority of hospitals in the United States—up to 80%—treat patient populations that are disproportionately white. These measures largely relied on inpatient Medicare data from 2015 through 2019 to evaluate more than 1,900 hospitals, primarily by comparing the racial demographics of patients to community benchmarks (*The Cancer Letter*, July 30, 2021).

These measures were expanded in the 2022-23 rankings. Starting July 26, hospital profiles on the *U.S. News* website will feature metrics on racial disparities in unplanned readmission, which aim to measure how much "charity care" each hospital provides, and how well low-income patients are represented among the patients each hospital serves.

"What we don't yet know is to what extent is racial disparity the fault of the hospital, something that the hospital is failing to do for its Black patients that it's doing toward its white patients, versus to what extent is this a reflection of the systemic racism that exists in the community surrounding that hospital," Harder said.

Research has demonstrated that targeted efforts to reduce disparities can be effective, but the boundary between a hospital's capabilities vs. systemic hurdles can be blurry. For instance, existing financial and logistical barriers in access to care in underserved communities play a critical role in determining care delivery and health outcomes, Harder said.

"You can imagine if Hospital A is flinging its doors open wide to patients of lower socioeconomic status, but as a result some of those patients aren't able to see their primary care doctor after their surgery, they don't have the money to afford medications, they have trouble getting transportation to follow up care, they end up getting readmitted at a higher rate," Harder said. "That hospital may appear to have a larger racial disparity than one that treats all the white patients at its doorstep, and well-to-do, well-insured African American patients.

"We want to make sure that we have a relatively comprehensive, if not 100% holistic, view of what hospitals are doing around health equity before we start integrating that into the ranking methodology." Harder said. "If you're only measuring one aspect of something, then that can have, again, unintended consequences in terms of what institutions focus on and where they may let their guard down."

Bigger gaps in overall score

The latest rankings for cancer hospitals appear to show a growing gap in the *U.S. News* overall "specialty score" between MD Anderson and MSK.

The overall specialty score is determined based on the statistical distribution of all variables between all of the ranked hospitals. While the overall score is not necessarily meaningful for individual patients looking for specific clinical information, does this gap actually suggest a larger difference in overall quality between MD Anderson and MSK than in previous years?

"All the scores are relative to each other. So, one hospital could get better, and the other one could stay the same—and the gap between them expands," Harder said. "And then the other thing is that we're looking at different data each year. And so those measures are calculated on the basis of the data from that year across all hospitals."

Changes in the ranking methodology or in the underlying data can affect a hospital's score—leading to an expanded gap between, say, MD Anderson and MSK—but it doesn't necessarily mean that the quality of care has wors-

ened at the hospital in the lower-ranking position.

"You could say that the gap between those two hospitals has widened. If that is meaningful for patients or not, I think that might be a little bit too much of a stretch," Harder said. "But from a statistical standpoint, in terms of what we measure, yes, it does reflect a widening gap."

Marketing claims notwithstanding, *U.S. News* ranks centers for one reason only: to help patients make informed decisions.

"Each patient is different, has different clinical needs, has a different diagnosis," Harder said. "We need to treat each patient according to what their needs and medical conditions are."

The Cancer Letter's previous coverage of the *U.S. News* best cancer hospital rankings follows:

- **2021:** Racial minority patients underrepresented in 80% of hospitals, *U.S. News* "equity measures" find
- **2019:** MD Anderson retains top spot on *U.S. News* rankings; Johns Hopkins moves up to No. 4
- **2016:** MD Anderson (Again) On Top of *U.S. News* and World Report Ranking
- **2015:** MD Anderson No. 1 (Again) in Rankings by *U.S. News*
- **2014:** Memorial Sloan Kettering Seizes Top Cancer Hospital Prize from MD Anderson in *U.S. News* & World Report Ranking
- **2013:** A "Screw-Up" Worked in MD Anderson's Favor In Seven-Year Stint as *U.S. News* & World Report Top-Ranked Cancer Center

> "We're using data from a prior time period, but our goal is to help patients make a decision in the here and now."
>
> *– Ben Harder*

City of Hope opens ambulatory cancer center in Irvine as part of $1B expansion

By Paul Goldberg

In the latest phase of its plan to invest over $1 billion in Orange County, City of Hope has opened a multi-specialty outpatient cancer center in the county and hired 29 physicians to practice there.

City of Hope Orange County Lennar Foundation Cancer Center is financed in part with a $50 million gift from Lennar Foundation, the charitable arm of Lennar Corp, a Miami-based publicly traded home building company.

"In 2018, we committed $1 billion to develop and support [the Orange County Campus], as part of changing the way cancer care is delivered across the country," Robert Stone, president, CEO, and Helen and Morgan Chu Chief Executive Officer Distinguished Chair of City of Hope, said to *The Cancer Letter.*

The opening of the outpatient center and the groundbreaking for the planned hospital that is slated to be completed in three years occurred on July 27. Facilities are located on an 11-acre campus at the Orange County FivePoint Gateway in Irvine.

In addition to campuses in Duarte and Orange County, City of Hope is building a national cancer research and cancer care system that includes: a network of clinical care locations across Southern California, the newly acquired Cancer Treatment Centers of America, Translational Genomics Research Institute and AccessHope, a company that partners with employers to provide their employees with cancer information and clinical decision support (*The Cancer Letter,* Feb. 4, 2022; Jan. 21, 2022; Dec. 10, 2021; April 2, 2021; Jan. 29, 2021; Oct. 9, 2020; June 28, 2019).

In the next phase of the Orange County project, City of Hope plans to build a 70-plus bed cancer hospital that would be contiguous to the just-opened ambulatory cancer center. That project is expected to be completed in 2025, City of Hope officials said.

By way of comparison, the hospital on the Duarte campus of the NCI-designated Comprehensive Cancer Center has about 200 beds. City of Hope's basic science facilities will remain on the Duarte campus.

When the expansion is completed, City of Hope will operate two cancer campuses in its four-county primary service area. The other academic cancer center in Orange County, the Chao Family Comprehensive Cancer Center, is a part of UC Irvine.

Academic cancer centers in greater Los Angeles area include UCLA Jonsson Comprehensive Cancer Center, USC Norris Comprehensive Cancer Center, and Cedars-Sinai Samuel Oschin Cancer Center.

City of Hope's new ambulatory center will offer specialized cancer care, phase I through phase III clinical trials, precision medicine, and early detection and prevention programs. City of Hope has recruited a team of physicians with expertise in lung, breast, gastrointestinal, gynecological, genitourinary, blood, and other cancers. These physicians will practice exclusively in Orange County.

"You observe many places talk about hiring a new single person. But it's rare to see an entire comprehensive team hired," Edward S. Kim, physician-in-chief at City of Hope Orange County and vice physician-in-chief at City of Hope National Medical Center, said to *The Cancer Letter.*

The newly hired faculty members will be working exclusively on the Orange County campus, Kim said.

"We have a singular faculty model, in that all of these folks will work together, because the best way to magnify our expertise is to put more people's brains together," Kim said. "And so, it synergistically adds to the already existing exceptional faculty at City of Hope."

A list of the 25 faculty members newly recruited from other institutions and four who are transfering to Orange County from other City of Hope locations appears here.

According to City of Hope's numbers, today nearly 20% of residents with cancer leave Orange County for advanced care. Those who get care at the City of Hope main campus drive for up to two hours each way to get there.

Orange County has 3.2 million residents, which makes it the sixth largest county in the U.S. Since the county has a higher-than-U.S.-average percentage of seniors, cancer incidence there is expected to rise by 18% over the next decade, City of Hope officials estimate.

"We had hoped that we would be able to recruit the type of talent that Ed has now been able to recruit, but you don't really know until you go out to do it," Stone said. "And we have gotten an overwhelming message from the oncology community that this is a model that people wanted to participate in."

> "We have a singular faculty model, in that all of these folks will work together, because the best way to magnify our expertise is to put more people's brains together."
>
> *– Edward S. Kim*

A portion of the Lennar's $50 million gift to City of Hope will support collaborative translational research between City of Hope and the Sylvester Comprehensive Cancer Center of the University of Miami. Both City of Hope and Sylvester serve diverse populations, and both have received investments from Lennar in the past.

PHYSICIANS PRACTICING AT CITY OF HOPE ORANGE COUNTY LENNAR FOUNDATION CANCER CENTER

Name of Physician	Academic Rank Appointment Title	Admin Title	Previous Institution
Edward S. Kim, M.D., M.B.A.	Professor, Department of Medical Oncology & Therapeutics Research	Physician-in-Chief, City of Hope Orange County Vice Physician-inChief, City of Hope National Medical Center	
Richard Lee, M.D.	Clinical Professor, Department of Supportive & Integrative Care	Medical Director, Supportive Care & Integrative Medicine, City of Hope Orange County Medical Director, Integrative Medicine, City of Hope National Medical Center	University Hospitals Seidman Cancer Center
Jyoti Malhotra, M.D., M.P.H.	Associate Professor, Department of Medical Oncology & Therapeutics Research	Director of Thoracic Medical Oncology, City of Hope Orange County	Rutgers Cancer Institute of New Jersey
Jennifer Tseng, M.D., F.A.C.S.	Associate Clinical Professor, Division of Breast Surgery, Department of Surgery	Director of Breast Surgery, City of Hope Orange County	The University of Chicago Medicine
Sandy Liu, M.D.	Assistant Clinical Professor, Department of Medical Oncology and Therapeutics Research	Medical Director of Genitourinary Medical Oncology, City of Hope Orange County	UCLA David Geffen School of Medicine

Jason Salsamendi, M.D.	Clinical Professor, Division of Interventional Radiology, Department of Diagnostic Radiology	Lead Interventional Radiologist, City of Hope Orange County	Kaiser Riverside Medical Center
Dina Ragheb, M.D.	Associate Clinical Professor, Department of Diagnostic Radiology	Medical Director of Diagnostic Imaging, City of Hope Orange County	Riverside Medical Clinic
Amanda Schwer, M.D.	Assistant Clinical Professor, Department of Radiation Oncology	N/A	Newport Beach Radiosugery Center (Hoag Memorial Hospital Presbyterian)
Jennifer S. Woo, M.D.	Assistant Clinical Professor, Department of Pathology	N/A	University of California, Irvine, Department of Pathology
Percy Lee, M.D.	Professor, Department of Radiation Oncology	Medical Director of Orange County & Coastal Region Radiation Oncology; Vice-Chair of Clinical Research in the Department of Radiation Oncology	University of Texas MD Anderson Cancer Center
Priscilla Grace Harrell, M.D., M.P.H.	Associate Clinical Professor, Department of Anesthesiology	Medical Director of Anesthesia, City of Hope Orange County	Tufts Medical Center
Jeffrey S. Yoshida, M.D.	Clinical Professor, Division of Urologic Oncology, Department of Surgery	Medical Director of Urologic Surgery, City of Hope Orange County	Hoag Family Cancer Institute/Hoag Memorial Hospital Presbyterian
Joshua G. Cohen, M.D, F.A.C.O.G, F.A.C.S	Associate Clinical Professor, Division of Gynecologic Oncology, Department of Surgery	Medical Director, Gynecologic Cancer Program, City of Hope Orange County	UCLA David Geffen School of Medicine
Irene Morae Kang, M.D.	Assistant Professor, Department of Medical Oncology & Therapeutics Research	Medical Director, Women's Health Medical Oncology, City of Hope Orange County	USC - Norris Cancer Hospital
Samar Singh, M.D.	Associate Clinical Professor, Department of Diabetes, Endocrinology and Metabolism	N/A	University of California, Irvine, Department of Endocrinology
Nairi Berner, M.D.	Associate Clinical Professor, Department of Diabetes, Endocrinology and Metabolism	N/A	University of California, Irvine, Department of Endocrinology
Azra Borogovac, M.D., M.S.	Assistant Clinical Professor, Department of Hematology & HTC	N/A	University of Oklahoma Health Stephenson Cancer Center - Transplant & Cellular Therapy Clinic

Lance Uradomo, M.D., M.P.H.	Associate Clinical Professor, Division of Gastroenterology, Department of Medicine	N/A	University of Maryland School of Medicine
Cory M. Hugen, M.D.	Associate Clinical Professor, Division of Urologic Oncology, Department of Surgery	N/A	University of California, Irvine, Department of Urology
Jessica Cheng, M.D.	Assistant Clinical Professor, Department of Supportive Care Medicine	N/A	University of Texas MD Anderson Cancer Center
Misagh Karimi, M.D.	Assistant Clinical Professor, Department of Medical Oncology& Therapeutics Research	Director of Clinical Operations, City of Hope Newport Beach Fashion Island	City of Hope
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Photos courtesy of the Boyle family

OBITUARY

Peter Boyle, one of the great epidemiologists of our time, dies at 71

By Otis W. Brawley, MD

Peter Boyle, FRSE, FFPH, FRCPS(Glas), FRCP(Edin), FMedSci, died after a long illness on July 23 at his home in Lyon, France. He was 71.

He is known for his work in tobacco control, bringing orthodoxy and truth to interpretation of scientific data, his forecast of a cancer epidemic in the developing world, his advocacy of cancer prevention and his mentorship of young scientists.

Boyle is among the great epidemiologists of our time, such as Sir Austin Bradford Hill, Sir Richard Doll, Sir Richard Peto, Julian Peto, Abraham Lilienfeld, Peter Greenwald, Fred Li, Joe Fraumeni, and Brian MacMahon. Indeed, most were friends, colleagues, and collaborators.

Boyle was born and raised in Glasglow. He obtained a doctorate in statistics from the University of Glasgow and initially worked for the West of Scotland Cancer Surveillance Unit. In 1984, he joined the faculty of the Harvard School of Public Health in the Departments of Biostatistics and Epidemiology, and became a member of Dana-Farber Cancer Institute.

In 1986, he left Harvard for the International Agency for Research on Cancer (IARC), the United Nations cancer agency. There, he ran the Surveillance of Environmental Factors Related to Cancer in Humans (SEARCH) Program—launching a trailblazing series of international case- control studies assessing the causal factors of a number of cancers.

In 1991, the famous cancer surgeon, Umberto Veronesi, invited Boyle to head the Department of Epidemiology and Biostatistics at the newly formed European Institute of Oncology in Milan. There, Boyle built a high-functioning research unit that not only did research, but made sure that research findings impacted policy.

It was from The European Institute of Oncology that Boyle rose to international prominence with work that included reassessments of the European Code Against Cancer and developing a cancer atlas for the European Union. He served as a member of the European Cancer Advisory Board and worked as scientific advisor to the European Commission on the European Tobacco Contents Directive. Boyle's work in the 1990s with the European Parliament to pass groundbreaking tobacco control regulation is lowering European tobacco consumption even today.

In 2004, Boyle was named director general of IARC. From there, he designed and gathered support for the first randomized prospective study to show that cervical cancer screening saves lives.

The study showed that very low-tech visual inspection of the cervix and immediate treatment of abnormalities prevented deaths. "See and Treat" is now commonly used in resource-poor regions of India, Africa, South America and even on the southern border of the United States.

In 2009, Boyle left IARC to found the International Prevention Research Institute in Milan, a private agency that would do epidemiology research to influence policy.

Over his career, Boyle was a both a critic and a supporter of modern medicine and science. In the mid 1980s he wrote a scathing criticism of a then widely ac-

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In 2017, Boyle was presented the Royal Medal of the Royal Society of Edinburgh by Queen Elizabeth II.

claimed study with exaggerated claims of the success of chemotherapy.

The paper, in the journal *Science*, said chemotherapy was preventing 150,000 cancer deaths a year in the U.S. Boyle pointed out that the data was not analyzed appropriately. He reanalyzed it and showed that the paper's authors were off by an order of magnitude. Boyle then noted there are 10,000 medical oncologists in the US preventing 15,000 deaths per year. "That is 1.5 lives saved per year per oncologist."

When it was announced that a paper would be presented in the plenary session of the American Society for Clinical Oncology (ASCO) annual conference, claiming that prostate specific antigen testing reduced prostate cancer mortality—it got huge publicity even before presentation. ASCO asked Boyle to be the discussant of the paper.

He noted that the study did not use the required "intent to treat" analysis, and when analyzed appropriately the data showed there was absolutely no evidence of a protective effect and there was possibly even evidence that PSA screening was net harmful. Boyle proclaimed, "This publicity machine is wrong and a disservice to the cancer community."

Perhaps the contribution Boyle was most proud of was his gathering of health experts and mentoring of young scientists. From the mid 1990s onward, his annual National Cancer Institute Directors (NCID) Meeting was a coveted invitation.

He always made sure that a large number of young scientists were invited to "hang out" with the movers and shakers in the cancer public health community. He always found sponsorship for those from developing nations who could not afford to pay their way. He had the ability to bring the best out in people from diverse backgrounds.

The annual group picture would have such unusual things as the director of the National Cancer Institute of Korea standing next to a medical oncology trainee from Tanzania. Through this meeting, he fostered the creation of many unusual friendships and valuable collaborations.

It was at the NCID meeting that he began a series of projects to bring attention to the growth of the cancer problem in Africa. Boyle was very concerned about the fact that cancer mortality was beginning to rise in developing countries just as it was starting to decline in developed countries.

He was among the first to point out the evolution of the cancer epidemic and point out that this demanded greater implementation of prevention and risk reduction. He was also concerned about the difficulty in getting adequate pain treatment into Africa.

In 2017, Boyle was presented the Royal Medal of the Royal Society of Edinburgh by Her Majesty, Queen Elizabeth II. Other honors, including the Knight's Cross of Order of Merit of the Republic of Poland and honorary doctorates from the Universities of Aberdeen and Dundee and a professorship at the University of Strathclyde.

He is a member of the National Academy of Science of Hungary, a fellow of the Royal College of Physicians and Surgeons of Glasgow, a fellow of the Royal College of Physicians of Edinburgh, and an honorary fellow of the Royal College of Physicians of Ireland.

Boyle was known for being intense and orthodox in his work, but he was also fun to be around. He was passionate about football (soccer to Americans). His favorite club was the Celtics. He would often explain to Americans "The Celtics I follow are a soccer team based in Glasgow, not a basketball team in Boston."

A constant traveler, he was known to have a favorite Chinese restaurant in every city he visited. If he was in Bogota, Mumbai, Krakow, or Quebec City, he knew what the best Chinese restaurant was. His obsession with Chinese restaurants was so serious that one of his friends suggested that *The Cancer Letter* publish a list of Boyle's favorite Chinese restaurants as a tribute to him.

Here it is:

- Restaurant La Chine, Lyon
- Mr Mann, Glasgow
- KuKu Taiwanese Food, Krakow
- House of Foong Lin, Bethesda
- Din Tai Fung, a chain of restaurants originally from Taipei

For Indian food, there was always Gaylord Fine Indian Cuisine in London and San Francisco (Boyle believed the London restaurant to be slightly better).

Boyle is survived by his wife, a brother, three daughters, two sons-in-law and three grandchildren. He was very proud of his three daughters. Each daughter has distinguished herself in medicine. Boyle often joked that the stream of strange foreign medical people arriving for dinner over the years was a clear risk factor in their career choices.

> "Boyle built a high-functioning research unit that not only did research, but made sure that research findings impacted policy."

In true Boyle family fashion, the night before his funeral, his wife Helena said to some of those whose careers he helped, that we best pay tribute to Peter by supporting his passion and continuing his work.

Boyle with wife Helena and their three daughters as he received an honorary doctorate from the University of Aberdeen.

Otis W. Brawley, MD, is the Bloomberg Distinguished Professor of Oncology and Epidemiology at Johns Hopkins University.

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GUEST EDITORIAL

Climate change and cancer

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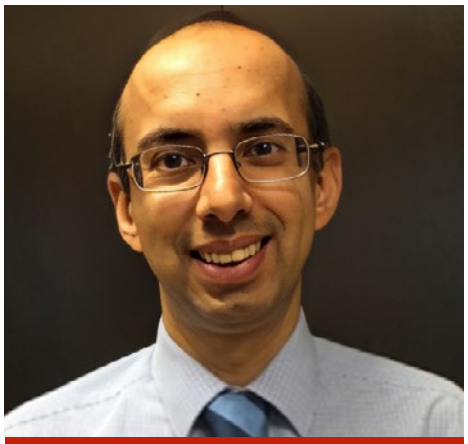

Sharan Majumdar, PhD
Professor, Department of Atmospheric Sciences; University of Miami Rosenstiel School of Marine and Atmospheric Science

A growing body of evidence is pointing to the obvious ways in which climate change impacts the environment. But those of us who study the impact of climate change on health have noted that the long-term shifts in temperatures and weather patterns also have not-so-obvious, downstream health implications, specifically for cancer.

Here in South Florida, we are at ground zero of the global climate change issue. Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine is in an area that provides a unique opportunity to study and understand how changes occurring in the natural environment influence disease risk and outcomes for all people.

This includes people in the Miami-Dade County catchment area who may experience compounded effects, because they are already medically underserved and underrepresented.

A problem of global proportions

The fallout from climate change is happening worldwide.

Just think: The third consecutive dry season across the Horn of Africa has resulted in the worst climate-induced emergency in four decades, leading to malnutrition and soaring disease risk. In September 2021, 17 COVID-19 patients

died when severe flooding inundated a hospital in the central Mexican state of Hidalgo.

And the wildfires that predictably and more frequently rage across the Western United States each year are fueling dangerous levels of pollutants, potentially increasing risks that include heart and lung disease.

Extremes of climate change

In the past two years, the U.S. has had a record number of severe weather events, from wildfires and ice storms to hurricanes, that each resulted in $1 billion or more in damages.

According to Gallup findings released in 2022, there were at least 20 such incidents in 2020 and 2021, versus nine or more events totaling $1 billion or more in damages each year since 2011.

One in three U.S. adults report they have been personally affected by an extreme weather event in the past two years, according to Gallup.

Studies suggest with very high confidence that climate change is leading to increased temperatures, and hence increased heat stress. Jane Gilbert, Miami-Dade County's Chief Heat Officer, was the keynote speaker at the inaugural University of Miami Climate Resilience Academy Symposium in April 2022.

Among other points, she emphasized that hundreds of thousands of workers in South Florida are exposed to extreme heat while working outdoors. Vulnerable populations, such as manual or unskilled laborers, are disproportionately affected by extreme heat.

We also can say with high confidence that climate change is resulting in rising sea levels. A third major and well-recognized consequence of climate change is increased rainfall, which increases concerns about flooding and standing water, heightening the risk of vector-borne diseases.

We witnessed this with Tropical Storm Alex at the beginning of the 2022 hurricane season here in South Florida.

While people in many areas of the U.S. are worried about potential flooding, others are concerned about droughts, another well-recognized consequence of climate change.

Climate change might lead to more frequent extreme weather events. Take tropical storms and hurricanes, for example. Their average forward-motion speed may be slower in a warming world.

The consequences of slower-moving tropical cyclones include longer durations of wind damage and intense rainfall, leading to increased infrastructure damage and flooding. For urgent issues such as maintaining or evacuating hospitals, the duration of the storm's impact is critically important.

As an extreme example, Hurricane Harvey sat over Houston for five straight days in 2017. The downstream effects of Harvey were flooded chemical plants, oil refineries, and Superfund sites, causing industrial pollution. Even hospital generators were flooded post-Harvey.

There are studies that have looked specifically at patients, including how these weather events create downstream effects such as reduced access to health care. For example, longer-lasting and potentially more devastating tropical storms and hurricanes can negatively impact care access and overall survival for lung cancer patients, researchers reported in *JAMA* in 2019.

Given the rising sea levels, coastal inundation from tropical cyclones may become worse in future years. Climate change may be increasing the proportion of major hurricanes (Category 3 and above), bringing more wind damage to residences, hospitals, and overall, although this data is based on one recent study and more research is needed.

Direct and not-so-direct impacts on cancer

An additional 250,000 people worldwide are expected to die annually between 2030 and 2050 because of climate change from malnutrition, malaria, diarrhea, and heat stress, according to the World Health Organization.

Climate change affects the social and environmental determinants of health—everything from clean air and safe drinking water to adequate food supply. It also affects such things as access to care, including cancer screenings.

For cancer risk specifically, it is safe to say that climate change can increase cancer risk through a variety of mechanisms, including increased UV exposure, risk of exposure to toxic chemicals, heat, reduced access to cancer screening and care, and more.

In the commentary "Climate Change and Cancer," published in *CA: A Cancer Journal for Physicians*, authors write that climate change increases exposure to known carcinogens.

For example, wildfires release pollutants, such as particulate matter. We have found that heat and pollutant exposure from wildfires affect our first responders. Moreover, the foam they use to put out fires is a known carcinogen and may contaminate the groundwater.

It's likely that the most impactful cancer challenge facing the world from climate change will be disruption to systems of cancer care, including diagnosis, treat-

ment, and management, according to a review in *The Lancet Oncology*.

Examples include not only severe weather conditions that restrict access to care, but also damage to cancer centers, hospitals, laboratories, and other facilities that provide needed oncology services.

> An additional 250,000 people worldwide are expected to die annually between 2030 and 2050 because of climate change from malnutrition, malaria, diarrhea, and heat stress, according to the World Health Organization.

A not-so-obvious impact of climate change on health is climate gentrification, in which residents of places that are elevation secure (meaning they are at higher elevations where the risk of flooding is lower) are displaced from those areas.

That can diminish their ability to access health care including cancer preventive services and social support, which we know attenuates cancer risk and improves survivorship for people navigating a diagnosis.

In an example of gentrification, Little Haiti is one of the most elevation secure areas in all of Miami-Dade County. As a result, there is significant development occurring within the boundaries of this neighborhood that has traditionally been the largest enclave of Haitian settlement in the U.S.

That development is causing the outmigration of Haitian families who have lived in this community for decades. Consequently, they are being dislocated from health-promoting resources that are important for prevention and earlier detection of cancer.

There are additional consequences facing more vulnerable populations. For minorities, there are the compounding issues of increased risk, for a variety of other reasons that are broadly influenced by social determinants of health, and gentrification.

Add to all this what happens when we experience extreme weather and the issues are further compounded, with minorities at even greater risk.

We also know that minorities may be less likely to live in areas with abundant green space. Without natural tree cover, there is increased UV exposure. Increased UV exposure drives the risk of melanoma.

Melanoma in racial/ethnic minorities tends to be diagnosed at later stages, when treatment efficacy is lower. Part of that is because of a lack of awareness, both within communities and among physicians, about how melanoma may present in people with darker skin.

The Washington Post summed it up when it reported last year: "Racial minorities in the United States will bear a disproportionate burden of the negative health and environmental impacts from a warming planet, the Environmental Protection Agency said Thursday, including more deaths from extreme heat and property loss from flooding in the wake of sea-level rise."

The time to act is now

This is a health crisis, and the time to act is now.

The National Cancer Institute (NCI) is taking great interest in the topic of climate change and cancer, and NCI-designated cancer centers around the nation, including Sylvester, are taking action.

"The NCI is interested in supporting research relevant to advancing the understanding of the effects of climate change on cancer risks, control, and survivorship, and ways to prevent or mitigate negative health effects," according to the Notice of Special Interest: Climate Change and Health.

Hopefully, it's not too little, too late. Addressing and limiting the impact of climate change on health will require great minds, lots of quality research, and collaboration.

In 2022, the University of Miami hosted a daylong Climate and Health Symposium, during which researchers, clinicians, and policymakers gathered to examine how climate change and extreme weather pose a threat to public health across the globe.

Participants addressed the obvious and not-so-obvious effects of climate change on health. For example, using Florida data, one researcher presented a link between exposure to heat waves and premature births. Another investigator presented evidence about climate and COVID-19 incidence.

We are hosting other university-wide symposiums to bring faculty together, including those who do not regularly interact. For example, our Syl-

vester cancer faculty, clinicians, and researchers are collaborating with faculty from outside the cancer center and the medical school to identify problems and devise solutions.

Sylvester researchers are giving talks, including National Cancer Institute Dissemination and Implementation fireside chats on the topics of climate change, cancer, and health. We spoke at The American Society for Preventive Oncology 2022 annual meeting on such subjects as how climate change alters the behavior of extreme weather events and the resulting impact on cancer rates and outcomes.

Health systems, including cancer centers, should find ways to promote collaboration and action. We have been supporting a mechanism called U-LINK, an intermural funding opportunity to catalyze interdisciplinary collaboration around social issues like climate change.

This year's focus was on resilience, and we funded three projects that were health specific, two of which had direct implications for cancer.

And of course, we have ongoing research programs looking at the impact of climate change on cancer and health.

Creating better access to health care by increasing the number of mobile medical units in vulnerable communities, building greener and more sustainable structures, and disseminating information on heat wave warnings in real time are just some of the strategies that can serve as a prescription to cure the climate crisis.

Cancer centers can start looking within their own walls to protect people and communities from the health impacts of climate change.

"Cancer care—including chemotherapy, immunotherapy, and surgery anesthetics; imaging devices; and radiation therapy equipment—contributes to greenhouse gas emissions and climate change," according to *The ASCO Post*. "Studies have shown that the biggest contributors to the carbon footprint in the U.S. health care system are the hospital and pharmaceutical industry sectors, so optimizing operating room ventilation based on occupancy and demand and using more energy-efficient computed tomography and magnetic resonance imaging machines can help to reduce greenhouse gas emissions."

"Although some may view these issues as beyond the scope of responsibility of the nation's cancer treatment facilities, one need look no further than their mission statements, all of which speak to eradicating cancer," according to "Climate change and cancer," referenced above.

"Climate change and continued reliance on fossil fuels push that noble goal further from reach. However, if all those whose life work is to care for those with cancer made clear to the communities they serve that actions to combat climate change and lessen our use of fossil fuels could prevent cancers and improve cancer outcomes, we might see actions that address climate change flourish and the attainment of our mission to reduce suffering from cancer grow nearer," the authors wrote.

IN THE ARCHIVES

CANCER HISTORY PROJECT

Jerry Yates on building a cancer center in a rural environment—Vermont

By Alexandria Carolan

As Jerome Yates reflects on starting up the University of Vermont Cancer Center in the early 1970s, he quotes Joe Simone: "When you've seen one cancer center, you've seen one cancer center."

"That's basically true, because it's heavily dependent on what the existing expertise is and what the population is like, what the geography is like," Yates, 85, a retired oncologist who has practiced and administered research at Roswell Park Comprehensive Cancer Center, the University of Vermont, NCI, and the American Cancer Society, said to *The Cancer Letter*. "It's a combination of the environment, the expertise that's available, and the opportunities. And you never know when some of the opportunities are going to occur."

Yates started at the University of Vermont in 1974 with the goal of building a cancer center. At the time, he was the only medical oncologist in the state.

In 1976, Yates and UVM basic scientist Richard Albertini convinced Irwin Krakoff to move to Vermont from Memorial Sloan Kettering and become cancer center director.

An announcement of Krakoff's move from MSK appears in *The Cancer Letter*'s archives:

> IRWIN KRAKOFF, who heads the Div. of Chemotherapy Research at Memorial Sloan Kettering, will become director of the Univ. of Vermont Cancer Center. That center is being developed as a prototype cancer center in a rural setting; university officials were delighted to land someone with Krakoff's prestige to run it.

"We really had an extremely strong program in the late '70s. And in fact, it was probably as strong as some of the programs that were in the major cancer centers, fortuitously, because the science was there, and the opportunity to develop a training program in medical oncology and to expand the medical oncology expertise, locally, was really rich at that time," Yates said.

How do you develop a cancer center?

"It was really the three of us working together that put this together," Yates said.

"We had strong basic science and drug development—brought [Krakoff's] expertise to Vermont. He was able to get a contract for studying phase I, phase II drugs. I maintained the affiliation with the Cancer and Acute Leukemia Group B," he said. "There were people doing basic cancer research. Dick Albertini was an MD, PhD who was looking at carcinogenesis and testing to determine what chemicals or exposures might be carcinogenic."

Yates and Albertini received a planning grant in 1974 to develop a cancer center in Vermont at a time when funds were flowing from NCI.

"The ability to get a planning grant to develop the cancer center was also critical to stimulate the pursuit of R01s and build programs," he said. "It was an opportune time. And you look at the way it is now where they're funding 10 to 15% of the approved grants, it's not so good. It's a lot tougher for the young people today."

"The planning grant on the research side allowed the development of cancer research programs that were really the forerunners of the core grant that we got three years later," Yates said.

Yates also received a rehabilitation grant from NCI for patients with advanced cancer—which helped develop a clinical infrastructure for the future cancer center.

"I wrote a grant to look at the rehabilitation of cancer patients with advanced cancer, because I felt that the rural environment deprived them of a lot of opportunities that one could find in a cancer center like Roswell Park," he said. "We essentially laid out a comparison between counties, in which we did this in an intensive way with periodic home visits, versus counties where the patients received customary care being followed only in the clinic."

The rehabilitation grant allowed Yates to spend a lot of time getting to know the rural populations of Vermont.

He would give talks at social centers for people all around the Green Mountains—churches, and grange halls that organized activities for farmers, a part of Americana.

"That was the social access to lay communities," he said. "And so, oftentimes, there'd be family practitioners who would be the point people to introduce you to the leaders in these areas, in the small communities."

In getting to know the communities, Yates learned that the wives of farmers kept impeccable records, which allowed his team to determine what carcinogens

may or may not have been present in these rural environments.

"There were lots of anecdotal reports of acute leukemia occurring in populations, and primarily childhood populations, where the residents were close to high tension wires," he said. "One of the doctors thought we ought to take a look, because the other concern was—were there more miscarriages among the women who were pregnant in these areas?"

These records tracked the health of dairy cows, including any bovine miscarriages.

"Because of the kinds of records they kept, we were able to speculate that the high tension wires were not important in terms of malformations that occurred in the dairy cows," he said. "And probably, to some extent, that the threat of the electromagnetic fields from high tension wires was not as important as some people had thought."

There were other theories too. Were fiddlehead ferns, eaten by Vermonters in the springtime, causing bladder cancer? Were microwaves to blame for other cancers?

"We looked at the association of bladder cancer and eating fiddlehead ferns. It turned out not to be real," he said. "There were studies then that subsequently were done in radar men on ships, where they got exposed to massive doses of microwaves. And they didn't find that there was an increased incidence of cancer."

"These are niches that provide unique opportunities to look at exposures and what the relationship between exposures are and cancers."

Lung cancer was the most prevalent cancer in these populations, and Yates estimated that the smoking rates among farmers hovered somewhere around 70%—a proportion that is significantly lower today.

Yates, through the cancer prevention program he developed at UVM, decided to focus on smoking cessation programs.

"They were beneficial, but they were also difficult at the time," he said. "Smoking was widespread, and, needless to say, in restaurants and actually even in schools, there were areas where people could smoke."

The breakdown of labor—men had driver's licenses and handled farm equipment, while women balanced checkbooks and kept records—proved to cause difficulties when a member of the family became sick.

"When the women would get breast cancer, there were difficulties with the male counterparts handling the financial side of the operation," Yates said. "When the males got their lung cancer, and had to get treated either with radiation or chemotherapy or surgery, many of the wives couldn't drive a car."

Yates hoped to acquire state funding to set up a rehabilitation program for the spouses of patients: the men would learn to manage checkbooks, and the women would take driving lessons.

But the state only agreed to help patients—not their spouses—so these efforts never came to fruition.

"We thought that with a relatively simple program, if it was available, would make a big difference because one of the problems that occurs in rural populations, is transportation," he said.

Instead, Yates's team sent nurses, social workers, and physical therapists on house calls.

"There was some continuity of care, and we actually made it a little easier in terms of dealing with the problems that occurred because the nurses would see the patients in the home," he said. "Similarly, the social workers were making periodic visits in the same homes, and they could help them with other logistical problems that were really social problems at the time."

The rural environment of Vermont was different than in larger metropolitan areas, where Yates started out.

"There was an inverse relationship between how far away they were from either Hanover or from Burlington, where there were radiotherapy facilities," he said. "The people that lived long distances away were less likely to get what was then state-of-the-art therapy, because of the transportation problems. And those kinds of problems continue to exist today."

His 7 a.m. meetings with groups of 20 to 25 people to discuss patient care also wouldn't have happened in a larger cancer center.

"Some ideas work in the rural areas that don't work in the cities," Yates said. "If you ask people in Buffalo to meet once a week, at 7 in the morning, with all of the disciplines, they'd look at you and say, 'Well, why is that necessary? That seems like a crazy idea.'"

Meetings included social workers and members of the clergy—"and they would develop expertise in areas that you might consider kind of different."

Vermont Cancer Center received its core grant in 1978. It retained an NCI-designation for three decades, until 2008, when it became the first Comprehensive Cancer Center not to seek renewal of the NCI designation (*The Cancer Letter*, Nov. 14, 2008).

VCC's new director, Randall Holcombe, intends to lead VCC to NCI designation again (*The Cancer Letter*, Oct. 1, 2021).

"What he's doing is trying to put together programs that will be competitive in terms of a core grant. And that's not easy," Yates said. "We did it way back when, because there were pharmaceutical chemists existing in the chemistry department in the university."

"And so, one's got to look at the expertise that's available there, and try to put it together into programs that will have sufficient R01 or program project, or SPORE support—there are no SPOREs in Vermont—so that they will be competitive in terms of a core grant," he said.

The 1970s was a good time to start a cancer center in Vermont—"because of the resources and the environment and the support we got from the university.

"And we're trying to help him put that back together again in Vermont," Yates said. "And I'm confident Randy knows how to do it. He did it in Hawaii. And I think with the right kind of support, he can do it in Vermont."

Yates's advice for cancer centers seeking NCI designation in 2022:

"The approach, I think, is the same, no matter where you are, You have to look at your environment. You have to look at the personnel that are available. You have to look at where the opportunities are, particularly now with the funding structure, because you could be tilting at windmills if there's not external funding available to do this.

"Now, because some of those funding sources have dried up for a variety of reasons, it's a little tougher, but the approach is still the same. You've got to have a strategic plan for how you're going to do it. And that's what we did with the people that were available and the opportunities.

"And that's what Randy is trying to do now in Vermont."

Yates spoke with Alexandria Carolan, a reporter with *The Cancer Letter* and associate editor of the Cancer History Project. The full transcript and podcast are available here.

This column features the latest posts to the Cancer History Project by our growing list of contributors.

The Cancer History Project is a free, web-based, collaborative resource intended to mark the 50th anniversary of the National Cancer Act and designed to continue in perpetuity. The objective is to assemble a robust collection of historical documents and make them freely available.

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IN BRIEF

The Parker Institute awards nearly $4.5M to nine early-career researchers

The Parker Institute for Cancer Immunotherapy has awarded nearly $4.5 million to its Early Career Researcher class of nine graduate and postdoctoral researchers.

This year, PICI partnered with the V Foundation for Cancer Research to fund four of the nine class of 2022 awardees. Known as Parker Bridge Fellows, the four recipients are senior postdoctoral investigators transitioning into faculty positions.

The 2022 Parker Bridge Fellows are:

- Katie Campbell, University of California, Los Angeles
- Kenneth Hu, University of California, San Francisco
- Derek Oldridge, University of Pennsylvania
- Bingfei Yu, Stanford Medicine

PICI's Representation In SciencE Scholar (RISE) program awards a Black, Indigenous or person of color graduate or rising postdoctoral student who has an outstanding scientific background and conducts research at a PICI Network institution.

This year, an anonymous donor committed funding to create the Parker RISE Scholar award. The inaugural RISE Scholar is Gabriel Abril Rodriguez, a postdoctoral researcher at UCLA, who plans to develop new tools to study T-cell biology.

The other award categories are:

- Parker Senior Fellow: A senior researcher who recently has earned an MD or PhD degree and is ready to establish a laboratory or independent program in cancer immunotherapy. The 2022 Parker Senior Fellow is Ya-Ting (Emma) Wang, PhD, of Memorial Sloan Kettering Cancer Center.
- Parker Scholars: graduate students and researchers focused on high-impact projects who are entering their first postdoctoral appointments. The 2022 Parker Scholars are Inaki Etxeberria, PhD, of MSK, Louai Labanieh, PhD, of Stanford, and Darwin Ye, a doctoral candidate at Penn.

PICI has recognized 37 early career researchers since 2016, awarding over $19 million in total funding.

Awardees pursue research through support from PICI's world-class network of immunotherapy experts and research institutions, as well as individual mentorship by PICI members and researchers from affiliated institutions. They also are given access to leading-edge technology, informatics and clinical data.

Cathy Eng named director for strategic relations at VICC

Cathy Eng was named director for strategic relations for the Vanderbilt-Ingram Cancer Center.

Eng is also David H. Johnson Chair in surgical and medical oncology, co-leader of the Gastrointestinal Cancer Research Program, director of VICC Young Adult Cancers Program, and professor of medicine. Eng specializes in anorectal cancer.

Eng's research focuses on phase I-III clinical trial development using novel therapeutics and approaches for biomarker discovery and enhanced drug utilization.

In this new role, Eng will oversee efforts to expand cancer center communications within VICC and across Vanderbilt University Medical Center, as well as those external to the institution.

Gulley named VP of SITC; Luke, Bruno, Warren named at-large directors

James L. Gulley was elected vice president of The Society for Immunotherapy of Cancer. Gulley is co-director of the Center for Immuno-Oncology, the director of the Medical Oncology Service, and deputy director of the Center for Cancer Research at NCI.

Gulley will begin his two-year term as SITC vice president beginning in January 2023, before becoming SITC president in January 2025.

Jason J. Luke, Tullia C. Bruno, and Sarah Warren were elected SITC at-large directors.

Bruno is an assistant professor in the Department of Immunology at the University of Pittsburgh and a faculty member in the Tumor Microenvironment Center and the Cancer Immunology and Immunotherapy Program at the UPMC Hillman Cancer Center.

Luke specializes in early-phase drug development as well as cutaneous oncology (melanoma) at UPMC Hillman Cancer Center.

Warren will soon be joining Kite Pharma as the senior director of research technology and business development planning.

Bruno, Luke and Warren will commence their three-year terms beginning in January 2023.

Nina Burbure named assistant professor at Fox Chase

Nina Burbure was named assistant professor in the Department of Radiation Oncology at Fox Chase Center.

Before being hired as assistant professor, she completed her radiation oncology residency at Fox Chase Cancer Center.

Burbure's research interests include treatment selection in hypopharynx cancer, patient-reported quality of life after prostate cancer therapy, and management of treatment delays in lung cancer.

Burbure has held teaching positions at St. Joseph's College and the New York City College of Technology.

Burbure will begin her role on Aug. 1.

Vanessa B. Wookey named assistant professor at Fox Chase

Vanessa B. Wookey was named assistant professor in the Gastrointestinal Cancer Program at Fox Chase Cancer Center.

Before coming to Fox Chase, Wookey completed an advanced gastrointestinal oncology fellowship at the Mayo Clinic in Rochester, MN.

Wookey has held teaching and leadership positions at South Dakota State University and the University of Tennessee Health Science Center.

Wookey will begin the role Aug. 1.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

ASCO, ACCC publish resources for improving diversity in clinical trials

The American Society of Clinical Oncology and the Association of Community Cancer Centers have jointly released two resources to help research sites increase racial and ethnic equity, diversity, and inclusion in cancer clinical trials.

The Just ASK Increasing Diversity in Cancer Clinical Research: An ACCC-ASCO Training Program, and the ASCO-ACCC Equity, Diversity, and Inclusion Research Site Self-Assessment are available online for free.

This release follows a pilot project with 75 research sites across the United States, which assessed the feasibility and utility of the resources.

The availability of the Just ASK Training Program and Site Self-Assessment follows the publication of the ASCO-ACCC research statement "Increasing Racial and Ethnic Diversity in Cancer Clinical Trials," which outlines actions for individual stakeholders in the cancer clinical trial ecosystem to increase diversity in research participation. The new resources directly address some of the recommendations in the research statement.

Studies have found that implicit bias reduces the likelihood of clinicians offering clinical trials to racially and ethnically marginalized patients compared to patients who are White. However, when trial participation is offered, more than half (55%) of patients agreed to enroll regardless of race and ethnicity.

The Just ASK Training Program, adapted from a course developed at Duke University, is an online implicit bias training program intended for all members of the research team. It consists of five interactive modules—which can be completed independently in about in 60-90 minutes—that present the broader context of structural and systemic racism, the role of implicit bias in clinical trial selection, vignettes with real-world examples of implicit bias, and guidance for mitigating disparities in cancer research settings.

A companion Facilitation Guide is available here.

The Site Self-Assessment helps clinical trial sites and research teams identify opportunities to improve EDI in clinical trials while doing an internal review of existing policies, programs, and procedures that offer evidence-based strategies to improve the diversity of trial participants.

The Site Self-Assessment is a quality improvement tool framed around the clinical trial enrollment continuum, and includes domains related to patient access to the site, screening patients for clinical trials, offering patients clinical trials, and participation and retention in trials. Completion of the Site Self-Assessment enables sites to identify opportunities for improvement.

The ASCO-ACCC Strategies and Resources List for EDI in Clinical Trials also provides suggestions for evidence-based strategies to address these opportunities and references to the literature. Potential strategies include diversifying the workforce, developing sustainable community partnerships, implicit bias training, and routinely collecting screening and enrollment data to assess and address disparities.

The Training Program and Site Self-Assessment resources were revised based on site feedback during the pilot testing period. The findings from the pilot study have been submitted for publication.

JNCCN paper: Chemo drugs from "rogue" online pharmacies could endanger leukemia patients

Patients seeking to purchase chemotherapy drugs online face a confusing array of websites, over half of which potentially operate unsafely or illegally, finds a new study in the July 2022 issue of *JNCCN—Journal of the National Comprehensive Cancer Network.*

A survey of online pharmacies claiming to sell the oral chemotherapy drug imatinib found that only three of the 44 identified English language sites that shipped within the United States were certified through the LegitScript online pharmacy monitoring service.

A full 52% were classified as "rogue" pharmacies that might operate without a license, sell counterfeit or expired products, steal users' payment information, or reject important safety precautions like requiring a prescription for potentially hazardous medications.

Tyrosine kinase inhibitors like imatinib have made chronic myeloid leukemia a manageable condition rather than a fatal one. Yet to work optimally, the drug must be taken for the rest of a patient's life and with high compliance.

While a generic version of imatinib became available in 2016, high prices (averaging more than $700/month at brick-and-mortar pharmacies) have remained a barrier for many patients, who then may turn to online pharmacies in the hope of finding discounts. The authors recommend physicians be aware of the marketplace to which their patients may turn, and advise patients to use LegitScript, www.legitscript.com, to check URLs and identify certified online pharmacies.

"We were struck by just how easy it is to buy an oral chemotherapy medication online, as imatinib is not a benign drug," co-author Sachiko Ozawa, associate professor, University of North Carolina Eshelman School of Pharmacy, said in a statement. "By simply searching Google, Bing, Yahoo, and DuckDuckGo, we found 44 websites that sold and shipped imatinib in the U.S.; 13 of these websites sold imatinib without a prescription, and more than three quarters did not offer a way for patients to speak with a pharmacist. This is a significant concern for patient safety."

Taking imatinib requires monitoring and frequent dosage adjustments. Even if an online pharmacy provides the medication as ordered, "patients bypassing provider interactions are likely to face much greater risks of nonadherence, discontinuation, treatment failures, and adverse events," Ozawa said.

In addition, rogue or unclassified pharmacies may not be providing patients with the real medication at all, and could even be stealing patients' medical or payment information. These sites are difficult to regulate, as they often originate abroad.

The authors said the online marketplace for drugs like imatinib is likely larger than represented in the study, as they only analyzed the first 10 pages of search engine results.

"We also found it deceiving how well some illegitimate websites mimic legitimate sites," Ozawa said. But how to address the reason patients would be using these under-regulated online pharmacies in the first place?

Patients should be encouraged to speak with their pharmacist, financial counselor, or other members of their healthcare team if they can't afford their medications, said Benyam Muluneh, PharmD, BCOP, CPP, Assistant Professor, University of North Carolina Eshelman School of Pharmacy, who was also a study co-author.

"Cancer drugs are very expensive; however, there are some resources such as third party foundation grants that may be able to help. If a medication is not affordable through regular channels, patients could also discuss alternative medication options with their providers rather than look for discounts online."

"The exorbitant price of oncology drugs is a major barrier to optimal therapy of many malignancies, including CML," Bernard Marini, clinical pharmacist specialist at Michigan Medicine, who treats patients with leukemias and other hematologic malignancies, said in a statement. Marini was not involved in the research. "As this eye-opening study found, the problem has become so bad that there is a major illegitimate online marketplace for generic oral oncology drugs.

"Healthcare providers need to be aware that many of these rogue and unapproved pharmacies do not even require a prescription or have access to pharmacist consultations, putting patients at high risk for adverse drug events.

"While patient-directed NCCN Guidelines for CML can be a great tool for reinforcing patient education, this study reminds us of the need to fully recognize the dangers of illegitimate online pharmacies and ensure our patients have appropriate financial support when prescribing high cost medications."

To read the entire study, visit JNCCN.org. Complimentary access to "Online Pharmacy Accessibility of Imatinib, An Oral Chemotherapy Medication" is available until Oct. 10, 2022.

Study: Adults with limited English proficiency have worse access to health care and cancer prevention services

Researchers at the American Cancer Society have found that after the implementation of the Affordable Care Act, adults in the United States with Limited English Proficiency had consistently worse access to medical care, including cancer prevention services, than adults without LEP.

The study was published in the *Journal of General Internal Medicine*.

"These findings are disappointing as there are more than 25 million individuals with LEP living in the U.S., and this number is increasing," Leticia Nogueira, senior principal scientist, health services research at the American Cancer Society and senior author of the study, said in a statement. "System-level interventions are critical, such as expanding access to health insurance coverage, providing language services, improving provider training in cultural competence, and increasing diversity in the medical workforce to help minimize barriers and be able to improve equity in access to care for this vulnerable population."

Under federal law and the civil rights provision of the, healthcare providers receiving federal funds are required to provide equal access to care for individuals with LEP. Additionally, improving access to healthcare for adults with LEP is a public health priority included in the Healthy People 2030 developing goals.

For the study, researchers identified close to 19 thousand adults with LEP, and more than 98 thousand adults without LEP in the U.S., aged 18 years or older from the 2014–2018 national Medical Expenditure Panel Survey. Associations between LEP and access to healthcare and preventive services were evaluated with multivariable logistic regression models, stratified by age groups 18–64 years old and 65 years old and older to account for Medicare age-eligibility threshold.

The study used the official government definition of LEP, which includes adults who answer, "not at all/not well/well" to the question, "How well do you speak English?" Access to care included having a usual source of care (and if so, distance from the usual source of care, difficulty contacting the usual source of care, and provision of extended hours), visiting a medical provider in the past 12 months, having to forego or delay care, and having trouble paying for medical bills. Preventive services included blood pressure and cholesterol check, flu vaccination, and cancer screening.

The study results showed adults aged 18–64 years with LEP were significantly more likely to lack a usual source of care, not have visited a medical provider, and be overdue for receipt of preventive services, including blood pressure checks, cholesterol checks, and colorectal cancer screening than adults without LEP. Results were similar among adults 65 years old and older.

"It is unacceptable that adults with LEP are less likely to have health insurance coverage, have a usual source of care, or receive preventive services compared to English proficient adults," William Dahut, chief scientific officer at the American Cancer Society, said in a statement. "Efforts to reduce barriers to care, disproportionately experienced by adults with LEP, are crucial for addressing this disparity."

"When it comes to cancer, barriers to accessing health care can become a matter of life or death," Lisa Lacasse, president of the American Cancer Society Cancer Action Network, said in a statement. "ACS CAN urges the Biden Administration to put forth regulations that provide greater patient protections under the Affordable Care Act, including strengthening and improving current provisions requiring individuals with LEP be notified of their rights and the availability of language assistance."

"We're calling on Congress to address affordability issues by closing the Medicaid coverage gap, making increased subsidies for Marketplace plans permanent, and capping Medicare Part D drug costs in their reconciliation budget deal," she said.

Other ACS authors on the study include: Robin Yabroff, Kewei Shi, and Xuesong Han.

AVIL gene responsible for glioblastoma also causes rhabdomyosarcoma, UVA researchers find

A gene that UVA Health researchers discovered is responsible for the deadliest type of brain tumor is also responsible for two forms of childhood cancer, the scientists have found.

The study was published in *PNAS*.

The discovery may open the door to the first targeted treatments for two types of rhabdomyosarcoma, a cancer of the soft tissue that primarily strikes young children.

The gene may also play an important role in other cancers that form in muscle, fat, nerves and other connective tissues in both children and adults, the research suggests.

"We accumulated multiple lines of evidence supporting [the gene] AVIL is powerful driver for both major types of rhabdomyosarcoma," researcher Hui Li, of the University of Virginia School of Medicine's Department of Pathology and UVA Cancer Center, said in a statement. "The tumors are oncogene addicted to AVIL, which supports the rationale to design therapeutic interventions to target AVIL in this childhood cancer."

Li and his team discovered in 2020 that the gene AVIL is the oncogene (cancer-causing gene) responsible for glioblastoma, the most lethal form of brain cancer. Less than 7% of patients with glioblastoma survive five years after diagnosis.

Li's 2020 discovery was named one of the year's biggest biomedical discoveries by the editors of *STAT*. Li's latest work builds on that research and suggests that AVIL is even more important than previously realized.

Malfunctions in AVIL, Li and his team found, play an essential role in the development of the two main subtypes of rhabdomyosarcoma. In a scientific paper outlining the findings, he and his colleagues describe rhabdomyosarcoma as "addicted" to the gene's excess activity. They label AVIL a "bona fide oncogene" for rhabdomyosarcoma.

AVIL may be the convergence point for two different cellular processes that cause soft-tissue cells to become cancerous, the researchers note. Blocking the activity of AVIL, they found, prevented the formation of rhabdomyosarcoma in both cell samples in lab dishes and in mouse models of the disease.

That's a promising sign for the discovery's potential to lead to a new, targeted treatment for rhabdomyosarcoma. Even with multi-modal therapeutic interventions, the survival rate for high-risk children is less than 20%.

The new research also reveals that AVIL is excessively active in other cancers of the soft tissue, known as sarcomas. The scientists found that the degree of excess activity correlates with patient outcomes, suggesting that AVIL may be a vulnerability for those cancers as well.

"These findings plus our previous work in brain tumor suggest that AVIL is an oncogene that, when over-activated, may trigger the development of multiple cancer types," Li said.

The team consisted of Zhongqiu Xie, Pawel L. Janczyk, Xinrui Shi, Qiong Wang, Sandeep Singh, Robert Cornelison, Jingjing Xu, James W. Mandell, Frederic G. Barr and Li.

Study demonstrates gender disparity in speakers at board review lectures

A study published in *Blood Advances* found that women make up 37.7% of all speakers at hematology and medical oncology board review lectures.

Its findings call attention to the many barriers people underrepresented in medicine face in obtaining educational opportunities that can be vital to career advancement and job security in academia.

Each year, students, trainees, and practicing physicians attend a collection of lectures given by leading practitioners in their selected medical specialty, in preparation to sit for their boards. Speakers are selected based on their experience in medicine, interest in education, and professional accomplishments. Through their lectures, they inform their audience on what the board exam will look like, how to tackle varying question styles, review exam content, and offer test-taking strategies.

"Hundreds of people attend these lectures and speaking at them brings faculty tremendous visibility in their field," study author Samer A. Al'Hadidi, a hematology and oncology physician at the Winthrop P. Rockefeller Cancer Institute, said in a statement. "Being selected as a speaker at these lectures is a prestigious opportunity that enhances professional development and advancement."

Al'Hadidi and colleagues collected speaker data for all board review lecture series conducted annually or biannually between 2017 through 2021. They analyzed lecture titles, speakers' names, gender, and institutional affiliation, lecture series location, and whether it was related to board certification in hematology, oncology, or both.

Their results showed that women make up roughly 37.7% of all speakers at hematology and medical oncology board review lectures. Notably, researchers found that these gender disparities only became more pronounced when sorted by subject area, with women representing 24.8% of speakers presenting on malignant hematology, 38.9% of those presenting on solid tumors, and 44.1% of speakers lecturing on classical (benign) hematology.

Investigators did observe an overall increase in female speakers over the years throughout the study period, suggesting that the field is becoming increasingly diverse. Women constituted over 50% of speakers at ASH's courses in 2020 and 2021.

In recent years, several institutions and medical societies have aimed to address this disparity by implementing working groups to promote the contributions of underrepresented minorities in hematology and oncology.

Al'Hadidi and colleagues also found that most speakers had more than 15 years of field experience since their initial certification. Choosing older and more experienced speakers over junior faculty not only keeps young professionals from engaging in educational opportunities but also poses a disadvantage for lecture attendees.

Al'Hadidi said physicians who took their boards more recently are more likely to remember the broad scope of content the exam encompasses. They will also be more familiar with the format of the test and be more likely to anticipate questions or content topics that could appear on the exam.

Limitations of the study include that authors were unable to weigh the perceived prestige of certain conferences over others, and how this may affect the value of lecture opportunities. They also did not factor in the varying levels of institutional support speakers may have been given to leave work and give the lectures, which may also have been a barrier to entry for those invited who could not take leave.

Al'Hadidi said one way to improve speaker representation is to work with academic institutions to get more women and junior faculty on lecture organizing and planning committees.

DRUGS & TARGETS

FDA accepts ImmunityBio's BLA for bladder cancer therapy N-803

FDA accepted for review a Biologics License Application from ImmunityBio, Inc. for its antibody cytokine fusion protein as a treatment for patients with BCG-unresponsive non-muscle-invasive bladder cancer carcinoma in situ with or without Ta or T1 disease.

ImmunityBio filed the BLA based on positive results from a series of studies of the investigational treatment, including the ongoing QUILT 3.032 trial. The Prescription Drug User Fee Act target action date is May 23, 2023.

If approved, N-803 plus BCG would be the first immunotherapy combination for this indication in 23 years that can be delivered directly to the bladder (intravesically) to induce natural killer cells and T cells.

N-803 has a mechanism of action that leads to the proliferation of NK and T cells. Through this action, N-803 provides a secondary boost to the immunological response generated by BCG for bladder cancer, or by a checkpoint inhibitor for other indications. In the QUILT 3.032 study, 71% of patients who had failed on previous therapies showed an over 50% increase in both response and median duration compared to the FDA-approved alternatives valrubicin and pembrolizumab, a systemic checkpoint inhibitor therapy for this indication.

The BLA submission is supported by the results from ImmunityBio's bladder cancer trials including QUILT 3.032, an open-label, three cohort, multicenter phase II/III study of intravesical BCG plus N-803 in patients with BCG-unresponsive high-grade NMIBC (NCT03022825) that was opened in 2017. The primary endpoint for Cohort A of this phase II/III study is incidence of complete response of CIS at any time.

Merck pays $35M to Kelun-Biotech for rights to investigational antibody drug conjugate

Merck has paid $35 million Kelun-Biotech to Merck for the exclusive rights to develop, manufacture and commercialize an investigational antibody drug conjugate for treatment of solid tumors.

Kelun-Biotech and Merck will also collaborate on the early clinical development of the investigational ADC.

Kelun-Biotech is eligible to receive future development, approval and commercial milestone payments totaling up to $901mm, plus tiered royalties on net sales.

The collaboration and exclusive license agreement follows Merck's decision earlier this year to exercise an option for worldwide rights, except for the Greater China region (including Mainland China, Hong Kong, Macau, and Taiwan), to SKB-264, an investigational TROP2 targeting ADC. SKB-264 is being evaluated in a phase III clinical trial for the treatment of metastatic triple-negative breast cancer and in phase II trials for non-small cell lung cancer and advanced solid tumors.

Kelun-Biotech and Merck will collaborate on certain early clinical development plans, including evaluating the potential of SKB-264 as a monotherapy and in combination with Keytruda (pembrolizumab) for advanced solid tumors.

Mission Bio establishes early access program for single-cell measurable residual disease detection in blood cancers

Mission Bio Inc. has created the first assay capable of determining measurable residual disease in cancer down to the level of individual cells.

The Single-cell Multi-omics MRD (scMRD) assay for acute myeloid leukemia improves sensitivity and specificity of commercial MRD tests used in research, and to predict cancer recurrence in patients. The assay uses the Tapestri Platform's ability to measure DNA and surface protein expression (or immunophenotype) data from the same cells.

Through Mission Bio's Early Access Program, pharma and academic partners can perform proof-of-principle studies that broaden understanding of the residual cancer cells that escape treatment for AML, by spotlighting the ones that other tests miss.

MRD is measured by physicians to help guide future therapy decisions and, potentially, prevent relapse in patients with AML and other cancers. However, these assays are limited to one type of measurement at a time, like flow cytometry for immunophenotyping or bulk sequencing for mutation detection.

Both have their limitations—certain cancer cells alter their immunophenotype in response to therapy, potentially giving a false MRD-negative result, while some rare but aggressive leukemia cells may acquire additional mutations that go undetected by bulk sequencing.

Recent research also suggests that combining both methods to measure immunophenotype and genotype information for the detection of residual disease added significant prognostic value over one method alone.

The assay yields single-cell multi-omic insights into disease evolution, therapy resistance, and transplant chimerism.

Through the Early Access Program, using fresh or cryopreserved bone marrow aspirate, academic researchers can conduct proof-of-concept studies in their labs using the Tapestri Platform, while biopharma customers can useMission Bio's Pharma Assay Development Services for initial pilot studies.

Collaborators from Memorial Sloan Kettering Cancer Center plan to present early data at the Tapestri Single-cell Multi-omics MRD for AML Summit in New York on Aug. 16, 2022. The company plans its full commercial launch for single-cell measurable residual disease detection for AML in early 2023.