Welcome to Yale Cancer Answers with your host doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it’s a conversation about outcomes research in kidney cancer with Doctor Michaela Dinan. Michaela, maybe we can start off by you telling us a little bit more about yourself and what exactly you do. I call myself a cancer outcomes or health services researcher so people aren’t always familiar with cancer outcomes or health services research. They tend to be more familiar with basic or clinical Cancer Research. Basic Cancer Research relates to
studies done in a lab with cancer cells, either in a Petri dish or in animals where researchers can directly manipulate and study cancer cells to learn more about basic biology of cancer. And then, clinical Cancer Research refers to when advances in basic science are being translated into actual medical tests or treatments and are then tested in humans to see if they work. My focus of research health services is the part that comes after this, after a new medical treatment or diagnostic tool is found to work in clinical trials, I study how it actually gets used in the real world. You have to remember that only around 3% of patients are treated on a clinical trial. And other people who take part in clinical trials are not like the general cancer population. In order to be enrolled in a clinical trial, you have to be healthy enough to qualify for participation and every clinical trial has a set of very strict inclusion and exclusion criteria. And if you don’t meet every single one, you can’t participate as you can imagine, the vast majority of patients who receive treatment are not part of a clinical trial,
so trial participants don’t look like everyone else who gets treatment for their cancer in the real world. Many people that are not included in trials are often older adults. People who have other medical conditions or people who don’t live near an academic Medical Center or who can’t make all the extra visits that are often required, or people that don’t otherwise want to participate in trials for some reason. Health Services Research, which is what I do, looks at how cancer treatments happen quote in the real world. So for example, we get to ask questions like how is cancer treated within the entire country as opposed to just one center? Who has access to new treatments? What are the outcomes associated with these new treatments? How much does it cost to get these treatments? And are there racial or economic or other disparities in access to cancer care? Wow, I mean that sounds so relevant when you think about the subpopulation, as you say, who get treated on clinical trials.
being so small and yet the outcomes of those clinical trials are applied to the entire population, it seems to be particularly important to see what happens out there in the real world on patients who may not have looked exactly like the people who were in the trials.

Yes, that’s exactly right. And the other point about clinical trials is that they tend to be highly controlled settings, right? So patients who are participating in a clinical trial not only have gone through the litany of inclusion exclusion criteria just to be enrolled, but once they are enrolled they are very closely monitored and followed in terms of their treatment and their outcomes that someone is keeping a very watchful eye on them. This is very different from a patient in the real world who’s kind of coming into and going out of the healthcare system on a regular basis and may not be being followed as closely.

So tell us a little bit more about your more recent research and what your more recent research and what
you’ve been doing in this realm. Sure, right now I currently have a study funded by the National Cancer Institute to look at oral Anti cancer agent utilization in patients with kidney cancer. So kidney cancer, like most cancers, can either be early stage or more advanced stage. Stage refers to how far a cancer has spread throughout a person’s body. So for kidney cancer, early stage disease is confined to the kidney. Whereas for advanced or metastatic disease, the disease has learned to travel through the bloodstream and has spread to other parts of the body, such as the lungs, bones or brain. So early stage disease is typically treated with a surgery or if it’s small enough, in an elderly or unhealthy person, it is sometimes just observed. Advanced kidney cancer for most patients is not curable. However, the treatments for advanced kidney cancer have improved dramatically in recent years. One of the biggest changes has been the development of these oral cancer treatments or pills that target kidney cancer to help shrink
These oral cancer treatments have been allowing people to live years longer, even for people who have what traditionally would have been considered incurable kidney cancer. However, these oral treatments are relatively new to kidney cancer. The first oral agents for kidney cancer became available or were approved by the FDA in 2005 and 2006, but with many similar treatments having been discovered since then. In fact now the 10 first new drugs approved for kidney cancer in recent years, 7 out of 10 were oral agents. The interesting thing about oral anti-cancer agents is that they represent a shift from how cancer treatment used to be delivered. So as most folks know, cancer treatment used to be almost always intravenous or given by injection at the hospital. So you know it required patients to come to a cancer hospital or clinic in order to receive treatment. However, oral agents are picked up by the patient from the pharmacy and taken home.
and unlike intravenous treatments, these oral agents are not taken in front of a medical staff. Instead, they are taken at home by the patients when patients come to a cancer clinic and receive an intravenous chemotherapy, obviously, the doctors know that they’re getting the treatment there. The same is not necessarily true for oral agents, however. Patients can forget to take their medications. They can forget or delay refilling their prescriptions. They may not follow the instructions as to when and how to take their medications exactly, or they may choose to stop taking their medication altogether, particularly if they are concerned that they might be having side effects from it, or if the cost of filling the prescription is too high. So my current research has been looking at the use of these oral anti-cancer agents and kidney cancer. I’m looking at things like who are receiving them.
disparities in access to these drugs? Are patients doing as well as they did in clinical trials when taking these drugs? Because like we were just talking about, when a patient when these drugs were being first studied in a clinical trial, they were being studied in a highly controlled setting, whereas now in the real world, patients are on their own, taking them at home, and then finally, I'm interested in questions like can patients afford to continue taking these drugs based on the cost? Those all sound like really interesting questions. What have you found? What’s interesting is that we have found that by 2015 a little over 1/3 of patients with kidney cancer with renal cell carcinoma specifically, which is a subset of kidney cancer, were receiving an oral anti cancer agent for their advanced kidney cancer. We know that previous studies have shown that black patients have had about a 10% worse mortality associated with kidney cancer, and we know that this
difference is not improved with
the introduction of these
oral anti cancer agents.
We wanted to see if access to these drugs
was a potential driver of these disparities.
Surprisingly, when we looked we didn’t see any difference
in access to these drugs by race, ethnicity or any other indicators
of socioeconomic status.
However, we did see decreased use in these
oral agents in patients who were
unmarried, patients who were living
in the South, and patients who
were in older age groups and in
this specific patient population
that means patients who
were in the age group 80 plus.
We were surprised to see that
access to these drugs was not
different by race or ethnicity,
so we next wanted to see if something
else could be driving disparities in
kidney cancer outcomes that we know exist.
So we looked at adherence to these
medications and what we observed
was that about half of the patients
studied were adhering to the
medication during the first
three months of their treatment.
So we were interested in the patients who live in areas with high levels of poverty were much less likely to take their medication almost half as likely as those who did not live in high poverty neighborhoods. Also, we found that patients that had to pay more than $200 a month for their medications they were about 30% less likely to be adherent as compared to patients paying less than $200 a month for their medication. So when we take a step back from all this, what we think we’re seeing is that although poor patients are able to start these drugs because we’re not seeing any difference in their initiation, they may not be able to continue to take them or to continue to take them as often as they are prescribed, because we’re seeing decreases in the adherence to these drugs and that could be affecting the differential outcomes that we know exist in patients with kidney cancer. So when you control for socioeconomic status and you look at the impact on race did you find that that was a
driver that mediated the relationship between race and outcomes? I think that is a good interpretation of what we’re seeing, right? So I think what you’re asking is, when you look at everything in the same model, we’re seeing that yes, poverty is driving this measure of adherence, but we’re not seeing an association with race, but I think what you’re getting at, which is correct, is that the kind of interaction between race and poverty, those are two very closely related.

So yes, seeing an association in one might be attenuating the association in the other. Did you look at that? The reason I ask is because we’ve seen a similar thing across a number of disease sites. I did a study just recently looking at breast cancer survivors and their use of endocrine therapy, which is also an oral agent that women take for at least five years.
and very similar to your findings, did not find that there was necessarily a difference by race, which we had thought might have been a factor when looking at whether people took these medications, but we were looking at the question of did you not take this medication as prescribed due to cost and we thought there may be a racial disparity in terms of that. But when we looked at it, we didn't find a racial disparity but really found a difference very much as you say in terms of poverty and in terms of whether or not people had insurance. I'm wondering if you controlled for poverty and whether we still see a difference in outcomes between black and Caucasian patients. So in our city we did not see a difference by race, but we did see a difference by poverty. So by both indicators of poverty and race were in the model and the association by race, as you said, for your city was not significant where it was for the indicators of poverty level. Does that make sense?
So even though they were both in the model race, we did not find an association with race, but we did with poverty, and I guess the point that I was trying to make earlier is that we know you that unfortunately, in this country, poverty differentially impacts folks by race and ethnicity. This is such an interesting conversation, but we need to take a short break for a medical minute. Please stay tuned to learn more about colorectal cancer. When detected early, colorectal cancer is easily treated on highly curable and as a result it’s recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer.
cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents, resulting in more patient specific treatments. More information is available at yalecancercenter.org. You’re listening to Connecticut Public Radio. Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest Doctor Michaela Dinan and we’re talking about cancer prevention and more, specifically, right before the break Michaela you were telling us about your research looking at disparities that we see in outcomes between African American patients and Caucasian patients with regards to kidney cancer and renal cell cancer. In particular, you were looking specifically at oral agents and found that really poverty was, so a couple of questions. Has anybody gone back and looked at the correlation between race and outcomes? Has anybody gone back and looked at the correlation between race and outcomes?
begin with and took a step back and said uncoupling that from poverty is it really poverty that is the driver of those outcomes, or is it really race and the poverty by association with nonadherence is a separate issue? Yeah, so the overall question of why is there differential outcomes for patients of black race with kidney cancer? That’s a bigger question and the studies that have looked at that question have still found a significant association between race and outcomes as well. You’re right and our study was specifically a subset of that question. Because we were specifically interested in how are oral anti cancer agents either contributing or not contributing to this kind of pre observed disparity that we’ve seen in kidney cancer patients? So because oral anti cancer agents were a relatively knew technology in the kidney cancer space, we wanted to see whether or not they were contributing to an attenuation of
this disparity in outcomes, or whether it was contributing to a potential widening of these disparities in outcomes. Because previous research of both mine and other folks looking at the emergence of medical technologies and cancers has shown that sometimes it can go either way. It can either help mitigate disparities or sometimes it can help widen disparities if there's an additional element of decreased access for certain populations. The other question that I had was when we were talking earlier before the break about the whole concept of health services research, one of the really important points you made is that health services research really looks at real world outcomes as opposed to trials. And clinical trials sadly do not necessarily include the population at large, and so when we think about clinical trials, particularly with oral agents for kidney cancer, did those include African American patients, and were the outcomes in those African American patients equivalent
0:19:01.299 –> 0:19:03.69 to Caucasian patients?
0:19:03.69 –> 0:19:06.678 I mean, could that partly explain
0:19:06.678 –> 0:19:08.93 some of these disparities as well?
0:19:08.93 –> 0:19:11.78 That’s a great question,
0:19:11.78 –> 0:19:14.594 and again, it points to a broader
0:19:14.594 –> 0:19:17.983 issue where clinical trials in
0:19:17.983 –> 0:19:20.608 general struggle to be representative
0:19:20.608 –> 0:19:23.678 of the general population,
0:19:23.68 –> 0:19:25.83 and there are certainly efforts
0:19:25.83 –> 0:19:28.595 to make those clinical trials more
0:19:28.595 –> 0:19:31.3 representative of the general population.
0:19:31.3 –> 0:19:34.975 But that’s something that continues to be
0:19:38.074 –> 0:19:40.576 addressed and certainly race is 1
0:19:40.576 –> 0:19:42.76 area where there have been efforts
0:19:42.76 –> 0:19:45.539 to make them more representative.
0:19:45.54 –> 0:19:48.38 I think 1 area where trials continue to
0:19:48.38 –> 0:19:50.299 struggle with their representativeness
0:19:50.299 –> 0:19:52.575 is with older populations,
0:19:52.58 –> 0:19:55.442 and I think that’s something that’s
0:19:55.442 –> 0:19:57.35 particularly relevant to cancer
0:19:57.429 –> 0:20:00.208 patients because a lot of cancers tend
0:20:00.21 –> 0:20:02.664 to have median age of diagnosis
0:20:02.664 –> 0:20:06.05 for the 65 plus patient population,
0:20:06.05 –> 0:20:10.082 and yet those people tend to be very
0:20:10.082 –> 0:20:12.868 under represented in trials.
0:20:12.87 –> 0:20:13.844 For instance,
0:20:13.844 –> 0:20:17.74 I think one great example of this is
0:20:18.69 –> 0:20:21.065 with an you emerging medical
0:20:21.065 –> 0:20:23.558 technology which is relevant to
0:20:23.558 –> 0:20:26.504 kidney cancer but also other
0:20:26.51 –> 0:20:29.125 cancers are immunotherapies
0:20:29.125 –> 0:20:31.217 or immune checkpoint inhibitors.
0:20:31.22 –> 0:20:32.152 And again,
0:20:32.152 –> 0:20:34.482 older folks in those clinical
0:20:34.482 –> 0:20:37.199 trials are under represented and
0:20:37.2 –> 0:20:40.182 yet there’s this kind of assumption
0:20:40.182 –> 0:20:42.646 that these immune checkpoint inhibitors
0:20:42.646 –> 0:20:45.418 are going to be less toxic than
0:20:45.418 –> 0:20:48.773 the standard or previously
0:20:48.773 –> 0:20:50.636 used cytotoxic chemotherapies.
0:20:50.64 –> 0:20:52.212 And so you know,
0:20:52.212 –> 0:20:55.229 a lot of physicians have been operating
0:20:55.229 –> 0:20:58.619 under the assumption that the toxicity
0:20:58.619 –> 0:21:01.77 profiles of these immune oncology
0:21:01.77 –> 0:21:04.212 agents is less than traditional
0:21:04.212 –> 0:21:06.778 therapies and so have been more
0:21:06.778 –> 0:21:08.923 willing to give these therapies
0:21:08.923 –> 0:21:11.467 to older patients and yet it’s
0:21:11.467 –> 0:21:13.825 not really based on clinical trial
0:21:13.825 –> 0:21:15.88 data because that clinical trial
0:21:15.88 –> 0:21:17.54 data doesn’t readily exist,
0:21:17.54 –> 0:21:20.34 and so one of the things I’m interested
0:21:20.34 –> 0:21:23.529 in potentially looking at in the
0:21:23.529 –> 0:21:26.418 future is real world utilization of
0:21:26.418 –> 0:21:29.19 these drugs in patients who were again
0:21:29.19 –> 0:21:32.105 not going to be represented and in
0:21:32.105 –> 0:21:34.22 standard trials and whose outcomes,
0:21:34.22 –> 0:21:36.728 whose toxicity profiles may look very
0:21:36.728 –> 0:21:38.838 different than what is typically
0:21:38.838 –> 0:21:40.286 seen in a trial.
0:21:40.71 –> 0:21:43.242 I think that
0:21:43.242 –> 0:21:44.93 it’s so important,
especially when we think about the fact that these drugs may affect different people differently, right? I mean, I think we’ve seen this even in the cardiology world back in the day when only men were included in some of the heart attack trials and we realized that women’s heart attacks present differently than men’s heart attacks and drugs may affect different genders differently, and similarly we may find that there are differences based on race and other things, trying to tease out what really is at the root of these disparities, it really does require some as you call it real world kind of investigation. Yes, and this is all so relevant right now in the times of COVID-19 where we have this very big need to get vaccines approved and treatments approved as quickly as possible. But again, we already know that COVID-19 is affecting minority racial and ethnic patients differently than it is white patients. We know that there’s differential outcomes.
Covid is affecting minority patients much more severely than it is Caucasian patients. What I think is really important, thinking about COVID-19 is that you know the clinical trials that were done really did have a reasonably robust representation of minority patients and so it’s led us to believe that the vaccines should work equally efficaciously for minority patients. For African American patients, as it should for Caucasian patients. But bringing it back to kind of health services research and real world science is this vaccine hesitancy and the fact that we’re seeing, at least by anecdote, that there may be more reluctance to really embrace the vaccine amongst African Americans, who sadly are the most affected and who probably could use the vaccine the most. So how do you address that in terms of trying to understand data from clinical trials are applied in the real world?
Yeah, it’s an interesting conundrum. I think that in terms of people’s willingness to take a vaccine, their willingness to kind of accept data from clinical trials as relevant to them I think that largely depends on the messaging and inconsistent messaging. I think that part of the problem is that some of these issues are incredibly entrenched and systemic issues that are longstanding for some of these populations, right? And so they’re not specific to necessarily one vaccine or one trial, but generations of a health care system that hasn’t necessarily always acted in their best interest, right? So I think just going forward a consistent message of representation for everyone concerned for everyone, I think is going to be really important and I think that that’s true of Covid, I think that’s true of cancer, because one of the issues that we’re talking about today is cancer prevention and some of the most important factors for cancer prevention are things that have been long known as perhaps
one area where there’s not been a ton of really large steps and advances, but things like not smoking things like maintaining a healthy weight, eating a healthy diet these are kind of the standards of cancer prevention across the board, and again, it’s certain messaging to different populations to make sure that they are receiving the message. Make sure that they understand how important it is. It is something that needs to be considered.

I think your point about systemic racism and the absolutely important tragedies that have happened in the US health care system over centuries really, that has propagated the lack of trust for minority populations is going to be a hard mountain to climb, but I think it is so important, particularly when we think about not only therapeutics but as you say, about prevention.

Whether we’re talking about Covid or whether we’re talking about cancer and so really thinking about all of the ways that we can prevent cancer,
February being Cancer Prevention Month, have we seen any impact in terms of really driving forward some of those behaviors? Some of those primary prevention techniques that all of us know about in terms of cancer prevention. Are we making a dent? I think so. There’s a long way to go and I think there’s a lot more to be done in those primary areas that you mentioned. But for a lot of cancers we do see that the incidence of cancer is going down, not for all of them, but for sure we’re seeing some improvements there. One of the easiest things to do for younger boys and girls is to make sure that they received their HPV vaccinations in the terms of cancer prevention, and certainly since the HPV vaccination has come on the scene, we’ve certainly seen decreases in HPV related cancers associated with utilization of that vaccine.
And then the other area is that we're seeing this kind of increase in the number of cancer survivors, so even folks who are unfortunate to receive a diagnosis, cancer survival for many cancers is going up as well, and I think some of that you know a lot of that, is attributable to these advances in diagnostic or treatment technologies.

But to some extent as well people trying to reduce or quit smoking, eat healthier diets, maintaining a healthy body weight. All of these things are only going to help.

Doctor Michaela Dinan is an associate professor of chronic disease Epidemiology at the Yale School of Public Health. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org. We hope you'll join us next week to learn more about the fight against cancer here on Connecticut Public Radio.