

Support comes from AstraZeneca, working to change how cancer is treated with personalized medicine. Learn more at [astrazeneca-us.com](http://astrazeneca-us.com) Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. 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 is a conversation about clinical treatment pathways with Dr. Kerin Adelson. Dr. Adelson is an Associate Professor of Medical Oncology at Yale School of Medicine, and Dr. Chagpar is an Associate Professor of Surgery at Yale and the Assistant Director for Global Oncology at Yale Comprehensive Cancer Center.

Chagpar Let's talk a little bit about what exactly is a clinical treatment pathway?

Adelson A treatment pathway is a standardized way of treating patients who have similar disease presentations in a consistent way. Pathways are a narrower version of clinical guidelines, which say, "we have seen that patients have the best outcomes if you treat them in a certain way, and so a guideline would say, you should make sure to do it that way." A pathway is a little bit narrower and it becomes a way of standardizing care across a larger enterprise. While there may be 4 or 5 effective options that you could give a patient, there are reasons why you might want to prioritize one over another, and pathways do that. They are really a way of influencing how we deliver care.

Chagpar Help me to understand this a little bit better. A patient comes in with a cancer, say breast cancer, and they go to their doctor and their doctor does their history and their physical exam and finds out more about them and looks at their images and checks their pathology, how exactly does that then correlate to this what seems to be kind of cookie-cutter medicine?

Adelson There are different kinds of pathways. Pathways could just be institutional preferences where a group of doctors get together and say "we believe this is the best way to treat this disease," or pathways could actually be clinical decision support where they are embedded in the electronic health record. A physician would go through and enter a patient's stage and other factors, sometimes they can enter things about the patient's other medical problems which might influence which treatments you would give a patient, and at the end of that, the pathway will make a suggestion of the treatment that is perhaps best for that patient. And so, the doctor then can either choose to use that recommendation or not. And we always say that while we want to standardize care, if we ever hit a time where 100% of the doctors were using the pathway, we would know that we have a problem because there are always times where you need to look at other factors, other clinical scenarios, patient's personal preferences, but overall, pathways are a way of knowing how you're treating very, very different presentations across a larger organization.

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Chagpar Because it sounds to me, from an outsider perspective, that taken to an extreme, pathways can be 'bot-like' medicine. The computer is saying, well we put in all of this data and it is going to spit out what you should do, in which case why go to medical school?

Adelson That is a really great and really interesting point. I think there are different degrees of how personalized patients should want their medicine to be. So, patients want doctors to take into account their values, their preferences, their living situation, their economic situation and all of that is tremendously important, and to be honest, I do not think the criteria that go into developing today's pathways do a great job of reflecting those personal elements. At the same time, we know that there are proven treatments that are better than others and the idea of the sort of oncology chef or the doctor who says, "I am going to give you a pinch of this and a pinch of that and a little of this, and for you, it is going to be just perfect." Patients who are treated that way do not do as well, and the patients want to know that they are getting the most effective regimen possible. So, when they develop clinical pathways in oncology, especially in medical and hematologic oncology, the very drug-based specialties, there is a hierarchy they go through and that hierarchy says, okay for looking at several different treatment options, the first thing we are going to do is prioritize the most effective, and if several regimens are equally effective, then we are going to go with the one that is the least toxic, that is going to have the least number of side effects for a patient, and finally, if those things are equal too, then we will use the less expensive regimen. And in most pathways that are around today, cost only ends up figuring in 5 or 10% of the time because the efficacy and toxicity, there are substantial differences. Where I think pathways are not doing a great job addressing patient preferences is in a few realms. There can be different treatment options that require a tremendously different amount of time and effort given by a patient. So, we always say in breast cancer you have heard me talk about this before, you can give a drug called paclitaxel. You can give it once a week 12 times which is very popular and is the chosen priority in most pathways, particularly because you do not have to give a shot to boost white blood cells, that is a very expensive option, or you can give it once every 2 weeks 4 times. Well, the difference between those two to an individual patient could be a month longer out of work and an extra 8 visits to an infusion center. So, a patient really should understand what factors are going into determining what is on a pathway, and a working, very busy patient may prefer to get the less frequent treatment that would be over sooner.

Chagpar I think that doctors in general know the clinical trial data that is coming out, they all go to these big meetings and are very much on top of the data. And therefore, you would think that they, in their armamentarium of studies, that they carry around in their brain, can prioritize those studies and figure out, well I know that this regimen is equally effective to that regimen, but this one I can give you in a shorter period of time and so on and so forth, and we are already having those conversations, and doing that calculus almost organically in their head, why do we need pathways?



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Adelson I would argue I do not actually think we are doing that great a job. I think doctors develop comfort levels with regimens that they have used, that they believe are the most effective and sometimes will put on blinders to other options. If you think about the benefit for an individual patient, that is really dependent on what that patient's risk is to begin with. So, we always say, okay well this regimen is going to give you a 50% reduction in the rate of developing metastatic disease and this other regimen it may give you a 45% reduction in the risk of developing metastatic disease. So, there are a lot of doctors out there who will say well, of course we are going to give the one that gives it 50% reduction, it is 5% better. But if a patient's risk is only 5% to begin with, that difference between those two regimens is almost negligible for an individual patient and the time and effort and real burden of treatment and potentially long-term toxicity could be quite dramatically different between the two regimens, and so pathways can help to enforce us sometimes moving beyond our true beliefs in looking at more objective data. The other scenario that I think is critically important is that we are at a time in oncology where new drugs are being approved at lightning speed, and there are general oncologists out there who practice hematology and oncology, who see everything from iron-deficiency anemia to extremely rare sarcomas, and the burden on those doctors to keep up with every latest study is tremendously intense. I cannot tell how blown away and impressed I am at some of our more general oncologists and how deep their knowledge is about so many diseases, but this helps give some basis to know that the way they are practicing is current.

Chagpar Who develops these pathways? How do they come into being?

Adelson That's a great question. There are all sorts of pathways out there. There are pathways that are put out by insurance companies, that generally take some of the same factors into account, but the insurance companies are probably coming at it from a 'whatever we can do to reduce cost, we will,' perspective. In this sort of payer-driver pathway that I have seen, they tend to prioritize the most effective, least toxic regimen the exact same way, and then there are individual institutional pathways where a bunch of doctors who work together come together and say, this is how we are going to practice, these are priorities. The issue with those is that the information technology maintenance is tremendously hard, and to keep the pathways updated and current is a huge, huge institutional commitment. And then, there are one or two companies that are based on physician consensus panels, so groups or committees that come together with doctor's represented from academic centers and community practices across the country where they vote on what items should be on the pathway and that is actually the one that we have gone with at Smilow, and it is a software that is integrated into our electronic health record, but maintained by a larger company who keeps the pathways current and does a lot of that work for us.



Chagpar One would think that one of the motivations to go towards pathway-based care is really to have a standardization across providers so that you do not see lung cancer doctor A at Smilow given X

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regimen, but then your friend who has the exact same disease at the exact same stage goes and sees lung cancer doctor B and gets regimen Y. But you said it is up to the doctor to either accept or reject the pathway? How does that help in standardization if you could just simply ignore what the pathway says?

Adelson At this point what we have seen a few months into our pathway experience, is that our doctors are selecting pathway options 75-80% of the time. And good pathways, sometimes allow for individual patient scenarios and the company that we went with, which is called Via Oncology, does have really good pathway scenarios that take into account different types of patient comorbidities. For example, if you are treating lung cancer and a patient has a history of neuropathy, it is not going to recommend the drug that is going to cause the most neuropathy. So, there can be some flexibility within pathways to account for different patient presentations and to still be on pathway, but we have said to our doctors, we would like to see you use these pathways whenever they are appropriate, but if your clinical judgment tells you that something else is better for this patient, then by all means choose something off the pathway, but now we have data and we can report and we can see whether there are certain people who are always off pathway or whether or not there are certain people frankly who were always on pathway, that could be equally concerning.

Chagpar We are going to take a short break for a medical minute and then come back and learn a lot more about clinical pathways for cancer with my guest, Dr. Kerin Adelson.

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Chagpar This is Dr. Anees Chagpar and I am joined today by my guest, Dr. Kerin Adelson. We were talking about clinical pathways for cancer treatment decisions, and right before the break, we were talking about the fact that these clinical treatment pathways are really kind of decision support that is built into the electronic medical record and takes information about the patient's stage,



their comorbidities and uses that along with information that has been gathered from clinical trials and experts to come up with what we think is the best option for patients. Kerin, you

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mentioned that the three kind of tiers that are looked at in terms of these pathways, at least the ones that are being used here and one would assume it is similar for other pathways as well, are really the efficacy or effectiveness, how well the treatment regimen works for a given population, then the toxicity, how many side effects and what are the complications and third, cost, because let us face it, cost is becoming more and more of a driver of healthcare these days. But the one piece that is really missing is where is the patient in all of this, I mean the physician has a relationship with the patient, knows what their family situation is like, how far away they live, whether their working conditions are such that they are going to be able to do this regimen or not, and that is really missing from what some could perceive pathways to be in terms of cookie-cutter medicine. So, where are we going in terms of building in patient-centered care because we talk about patient-centered care but then we talk about pathways?

Adelson That is a great question and it is actually something that as I started to work on clinical pathways and thinking about implementing them, it struck me that the patient's voice was entirely missing and I think that pathways could actually be used as a tool to help patients really understand all of their different treatment options, and so we have funding now to actually look at factors that influence patient decision making and also factors that lead to decision regret or what do patients wish they had known beforehand, before they chose a specific treatment, and so the idea is that we are actually going to build a clinical pathway for different choices in early stage breast cancer as a pilot because ultimately we would love to see this roll out to every different cancer type and the doctor would use it the same way they use our current clinical pathways where they enter stage and other patient factors and are given several evidence-based options, but then the patient would access the same portal but this time patient facing and would be able to look at very specific and meaningful information. If they take one regimen over another, how much does that actually influence their individual chance at survival, what is the rate of neuropathy for the violinist, so when we talk about toxicity with pathways, we say, well if toxicity is equal, how do you compare grade 3 neuropathy or numbness and tingling to grade 3 fatigue? The violinist may feel very differently about neuropathy than the marathon runner would feel about fatigue, and so we will be able to show patients in visual representations, not just numbers that they can understand where they can see the number of people out of 100 who would experience each different toxicity with different regimens or different treatment choices and then ultimately make a decision that is in line with their preferences, and we are really talking about this as a treatment pathway to



follow a patient throughout their entire cancer journey and really give them the roadmap to have more control in the decisions they make.

Chagpar It certainly sounds exciting not having the bot, as I called it earlier, make the decision about treatment but really have it spit out, using artificial intelligence and with the capacity of IT these days, these are the potential regimens, this is the survival difference, these are toxicities and allow it to be a platform for physician and patients to communicate and think about the regimen that is best for an individual patient.

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Adelson Exactly. With this project, which we are calling My Pathway, we are trying to turn a clinical pathway into a shared decision-making tool.

Chagpar That sounds quite awesome. Are there currently any guidelines out there in terms of what should go into a pathway, how a pathway should be developed, is this part of that or is this going to now change the paradigm on how we think about clinical pathways?

Adelson In 2016, because there was a proliferation of different pathway products on the market, ASCO, the American Society of Clinical Oncology, came up with 15 criteria that would define high-quality pathways, and in those criteria are things like, is it evidence based, is it transparent, is it consensus built, and one of the factors is, is it patient-centered and does it take into account patient preferences, and I think that highlights the importance and the need for what we are developing here at Yale.

Chagpar Now, the one thing that we have not really talked about, when we think about pathways as you have defined them, it really is built on evidence that is already out there, right? They are evidence based, so these are regimens that are tried and tested and proven true in clinical trials, which begs the question of well, how do you get onto a clinical trial, and often on this show, we have talked about clinical trials and their importance and how patients who participate in clinical trials in general tend to do better than patients who are not, so where do clinical trials fit into a pathway?

Adelson Clinical trial enrollment was a very high priority in our decision to do this huge clinical pathway implementation. As you know, we have doctors practicing all over the state of Connecticut, some of them are taking care of multiple diseases and it is very hard to keep track of what trials are open for what disease and which eligibility criteria, and so what we have done is we have taken the same logic that maps a patient to a specific regimen based on their disease criteria to actually map directly to the clinical trial for that disease state, and so on the clinical pathways that we have and that we are using here at Yale, the #1 choice is always a clinical trial if it is available, and so after the doctor navigates through the pathway and sees that this patient may be eligible for a trial and they select that, a message goes to the coordinator to come and



evaluate the patient and screen them for the study. And so, even in the first month or two that we had pathways, we had 60 referrals for clinical trials.

Chagpar Are these specific clinical trials then built into the pathway?

Adelson They are. That is the customization element that we are doing at Yale, yes.

Chagpar Because you had mentioned that these pathways are from a commercial vendor, so how would the commercial vendor know what clinical trials are available?

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Adelson This was not an easy IT build. We basically had to integrate our clinical trial software with the clinical pathway software and as the clinical trials are updated and maintained in different cohorts open or closed, that information is transmitted into the clinical pathway software to keep it updated.

Chagpar It sounds like this is all moving very much ahead in terms of drug-based therapy in cancer patients, but what about when we think about best practices and evidence-based care? That really is something that we think about in the continuum from prevention, what are the best modes of prevention, all the way to survivorship, what should we be doing in the survivorship period across many modalities, not just medical oncology, but radiation oncology, surgery and so on, what role do pathways have in all of those other areas?

Adelson I think we are still in the infancy of pathways. And if you think about what the future should look like, we should have robust multi-disciplinary pathways that take into account what type of surgery a patient is having and if it is a certain type of surgery, there may or may not be radiation indicated and then which type of radiation you give, do you give a shorter course or a longer course, all of that could eventually be built into a united disease state pathway. Currently, the pathway programs that are diving into realms of radiation or surgery, even survivorship are doing it sort of within that individual discipline and I think that there will be a lot of exciting work to come.

Chagpar When we think about pathways and as you described it kind of being consensus driven, evidence based, really helping clinicians to understand what would be the best thing for their patient, especially now building in the patient perspective, do you see this as overturning or supplanting what has traditionally been the way that physicians' kind of get that information, which has been through our tumor boards right? Physicians sit down in a group every week and they talk about their patients and everybody has different ideas and talk about, well what do you think about this, and there was this recent trial and they are having this kind of surgery and maybe that influences the kind of radiation and so on and so forth. In pathways, because you now have all of this stored in IT, do you think that might take over the role of a tumor board?



Adelson I do not think so. If you think about the cases that are generally presented and bring up intense discussion at a tumor board, they are the tougher cases, the grayer cases, the harder cases and those are also most likely the ones where the doctor may go off pathway, and there is always going to be a need to share cases with your colleagues to get input from people in different disciplines and to bring that into certain cases, but there are a lot of cases that are very standard and never even really hit our tumor boards, and I think it is important to standardized care among those.

Chagpar The other question of course is, as you think about cost and you mentioned that insurance companies are also building in these pathways into their regimens, how is that going to affect

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the patients, are patients going to have their regimen covered if it is only based on the insurance company's pathways, how are insurance companies incentivizing doctors or are they incentivizing doctors based on pathways?

Adelson Anthem has a pathway program, which I have to be honest overlaps probably 85 or 90% in terms of preferred regimens with the non-payer-generated pathway program that we have gone with at Yale. And what Anthem does is, they say if you treat a patient on a pathway, which could be a very expensive brand-name pathway, if efficacy and toxicity take priority, which they always do, they are going to pay an extra fee for every month to improve care coordination, and partly what they are trying to do through that is to shift some of the dependency that cancer providers have on marking up the cost of the drug and saying we are going to pay for better care coordination and other services if you participate in these pathways which might ultimately lower the cost of drug. I think we had a very strong feeling at Smilow and at Yale that we did not want to find ourselves in a position in 5 years where every different payer was going to come to us and say you have to treat this patient that way because that is on our pathway and the other payer might say, no treat the same patient differently because that is on our pathway, and so we felt that by going with pathways that were generated by expert physicians and consensus panels, we would be able to say no we already have our own pathways and this is how we do it, and ultimately exert more control.

Dr. Kerin Adelson is an Associate Professor of Medical Oncology at Yale School of Medicine. If you have questions, the address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and past editions of the program are available in audio and written form at [YaleCancerCenter.org](http://YaleCancerCenter.org). I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.