Kendal Williams (Host): Welcome to the Penn Primary Care Podcast. I'm your host, Dr. Kendall Williams. So pancreatic cancer is a very common cancer and we all see it, frequently in primary care. it's the second leading cause of cancer death in the United States. And as we all know, it has a poor five year survival. The lowest of all the cancers. There are no current screening test validated for pancreatic cancer but we do detect lesions frequently on imaging done for other reasons, that need to be evaluated by us as primary care physicians. And oftentimes we don't know exactly what to do with. So I asked two experts in this field to help us work through this challenge.

Two of the, co-directors of the Pancreatic CYS and Multidisciplinary Program at Penn. so. Dr. Charles Volmer is the chief of GI surgery at Penn and the director of pancreatic surgery. He is the co-director with our other guest of the Pancreatic CYS Multidisciplinary Program at Penn. Dr. Volmer is an internationally recognized expert on pancreatic cancer and pancreatic surgery. He graduated from the Sydney Kimmel Medical College in Philadelphia to general surgery residency at Wash U in St. Louis and the fellowship at the university of Toronto. He came to Penn from Harvard, where he had been further trained and was on the faculty there. Chuck, thank you for coming.

Dr. Charles Vollmer: Thank you.

Kendal Williams (Host): Dr. Nuzhat Ahmad is the vice chief for the division of gastroenterology here at Penn. she is the co-director of the Penn Pancreatic CYS Program. As I noted, she did medical school in her native Pakistan at Dow Medical College, followed by residency at the university of Illinois in Chicago and a fellowship, at Penn before joining the faculty. Nuzhat is an expert in the management of pancreatic diseases and therapeutic pancreatic Obilio endoscopy. Nuzhat, thanks for coming.

Dr. Nuzhat Ahmad: Thank you.

Kendal Williams (Host): So we see these lesions a lot, those who listen to the podcast know that, I have said before that one of the most challenging things, when I went back to primary care was managing incidentalomas of various forms. but these are a little more than that. I actually wanna start with pancreatic cancer itself, the real deal and what that looks like on imaging and the various types of pancreatic cancer, maybe Nuzhat, we will start with you.

Dr. Nuzhat Ahmad: So, the most common type of pancreatic cancer is, the ductal adenocarcinomas, about, I would say 85 to 90% of cancers that are diagnosed these. And when we refer to pancreatic cancers, most people are actually referring to ductal adenocarcinomas. The rest are actually a mixture.

Predominant being adenocarcinomas associated with pancreatic cysts most notably IPMN and MCNs, which are both musinist cysts. And then you sort of have, the less common ones, Cera cyst, adenocarcinomas, pancreatic or blastomas and asiner cell cancers.

And the typical pancreatic adenocarcinoma, when you see it on imaging has an appearance that is, often unmistakable it's a solid mass, patients will present with painless jaundice, abdominal pain, weight loss. And when we look at imaging, we are able to determine with, a significant degree of confidence that the patient does have a pancreatic cancer. There are however other lesions that can mimic a. Pancreatic adenocarcinoma, but that they're much, much less common.

Kendal Williams (Host): Can you take me through, I have always thought of these as solid masses as well, but we're about to talk about a variety of cystic lesions that can potentially evolve into cancer. Can you take me through the cyst solid transition if you will?

Dr. Nuzhat Ahmad: So, I think it's prudent to lay out the landscape of pancreatic Cysts, if you will. And the reason is that I think it's important to understand the number of cysts that exist actually in the population or are the incidents of pancreatic cysts. And I think the reason why this is important is that the consequence of cyst developing into pancreatic cancer, obviously so devastating that you'll see extremely nervous patients with very, very small cysts.

So there have been a number of studies done and the, prevalence of pancreatic cysts is anywhere from 24%. Chuck, you can correct me if I'm, inaccurate, but 24% in autopsy series, imaging studies have, demonstrated incidental pancreatic cysts in up to, 14 to 16% of patients. And it's unclear if we are seeing an increased detection or increased prevalence because there is overuse of imaging or is there an aging population or is it because of something else that's happening?

We think that it's the former meaning that people are getting scanned for almost everything. I mean, you know. Patient walks with a broken toenail and gets a CT scan and there you have it. Most of these are picked up incidentally and the significance is that a small number of them, very, very small number of them will go on to develop cancer. And if you look at the incidents of pancreatic cancer in surveillance studies, these are pancreatic cysts that have been watched over years is only 0.4% per year during surveillance.

If you look at the surgical literature, the rate of malignancy pancreatic cyst that

are resected is about 15%, but we think there's significant bias there. And if you look at anyone who walks through the door with an asymptomatic incidental cyst, the risk of cancer is 0.01% for small cyst. It's a little bit higher in cyst that are greater than two centimeters. So I think it's important for primary care to understand. This context, because they are typically the ones who have the initial conversation with the patient.

And they can provide some degree of reassurance with these numbers. Now, having said that the risk of cancer, even though small is real. And the problem is that we don't know exactly who will go on to develop cancer and who won't as a result, we've end up watching the whole cohort. I must say that, our understanding and Chuck feel free to chime in on this. Our understanding of pancreatic cysts has evolved greatly over the last 10 years. And even in our multidisciplinary group, we've seen pretty much everything.

But even to this day, we are still surprised by this very unexpected cancer in a pancreatic cyst. So the risk is there. It's very small, given the overall, general population, but it is real. So the dilemma always is how do we recognize the cysts that are at a higher risk of developing into cancer? And yes, they do follow an orderly progression, especially the type that are called IPMN they follow an orderly progression from mucinous to an adenocarcinoma. But we don't know whether the driver for IPM turning into ano carcinoma is the same driver. That is for a pancreatic adenocarcinoma, the more conventional pancreatic adenocarcinoma.

Dr. Charles Vollmer: So if I could chime in on that, it came up while she was speaking. I wanted to make a point. This concept of the cyst based cancer is newish in our lifetime basically, about 1982 is when the first reports really came around, of this IPMN condition. And it really didn't hit its adolescence or such till the 2000s. I still think we're sort of in the adolescents of the disease. We really haven't gotten to a state of really understanding it. But, when I was training back in the nineties and such, it was always taught to us that cysts of the pancreas were, pseudo cysts by default.

Like 90% plus were going to be benign, pseudo cysts, largely from pancreatitis. It was only in and around 2000, or so that we started to get relevant enough surgical series of upwards to a hundred cases at one institution or two or three of them that we started to understand pathologies from these resections. Because these patients were actually presenting with symptomatic problems. a lot of the time pancreatitis in fact, and that's when we started to understand that the cyst process was associated with cancer.

It's funny, because I've asked my peers or actually my forefathers in the surgical

community, the generation before me about this, were you ever doing operations for this stuff? And when you were doing your pancreas cancer operations, you know, were they cystic in nature in the likes and they all kind of shrug their shoulders and said not really, they don't remember it that way at all. So is this a disease phenomena that's come up in the last 50 years a new, probably not. It's hard to believe that that's the case, but it certainly has been, a new finding for us in our field.

And I would tell you that now this becomes the third pillar of our practices, both for Nuzhat and I, whereas previously we would've said we take care of cancer and pancreatitis. Now an equal dominant pillar of our, clinical practices is cyst processes. I make one other quick point about what she said earlier. Two other things to follow up. First of all, the prevalence is somewhere on that 15 to 20% range, based, mostly on series where people were having imaging of the abdomen for something, and they were found to have ay in the pancreas on that imaging.

So it could be more than that in the general population. And, the second thing is that you, are more likely to have assist the older than you are. That number goes up closer to 40% perhaps in, age 70 and above. And the older you are, the larger, your cysts will be. So it's sort of an acquired thing over life and it is natural for these things to grow bigger. And then the third thing I'd make to, clean up the first question is, we didn't drop in that term neuroendocrine tumor as a pancreatic cancer.

Nuzhat and I would not really think of that in the same, setting as pancreatic adenocarcinoma, but, many of the patients and other doctors, will call neuroendocrine tumors, pancreatic cancer. So it's really a totally different ball of wax. And the neuroendocrine tumor would be maybe about 10%, the, all the tumors that we would encounter of the pancreas. And it's actually the most common thing found on screening for high risk patients for pancreatic adenocarcinoma.

And you can actually think of neuroendocrine as sort of, straddling both of these concepts, the cyst concept and the pancreatic adenocarcinoma. It behaves a little bit like, both. it's like the cysts in that it is a pre-malignant condition, with a true propensity to become a pancreatic cancer, but at a low rate and the biology of it is very, finicky and unpredictable.

Dr. Kendal Williams: So just to summarize the normal progression of pancreatic adenocarcinoma is not to go through a cystic phase. And as Chuck, as you had said, cyst that were felt to be benign or even pseudocysts early in your training. but now we're getting these cysts back on imaging and it's been

now recognized that some of them do progress to malignancy. Nuzhat, am I thinking about this correctly?

Dr. Nuzhat Ahmad: Yes you are. We don't know if the conventional pancreatic adenocarcinoma, as we understand it. And the cancer that develops in pancreatic CTS have the same drivers. We do know that up to, I would say 3% is about two to 3% of patients who have pancreatic cysts, a specific type of pancrea Cy, called IPMN, which will come to later, have concurrent pancreatic ductal adenocarcinoma, and it's still clear, there has been some work done on this to try and identify if they're related or not. And I think it's been 50/50 so far, whether the pancreatic cyst cancer and the pancreatic cancer have similar drivers or not. But I think this is important to recognize that up to 3% of patients who have the IPM and kind of cyst can have a concurrent pancreatic adenocarcinoma.

Dr. Charles Vollmer: I tend to say that it's sort of like the IPMN or the cyst is like the smoke signal for the cancer. In other words, it travels with it. You could biologically talk in the same way that you would about LCIS with breast cancer, something to that effect. There's also a little bit of controversy while we're on this line of thought about whether one of these cancers through cyst pathway is actually less aggressive then a sporadic pancreatic cancer. There's a lot of data that would suggest that they behave a little bit better and your survival could be better if you have a cancer and assist, but it's clouded by the fact that there's probably stage migration.

And that these things are found much earlier. in the process. and they're so infrequent, we haven't had yet the volume to do the proper head-to-head analyses of that. so we really don't know there's a lot of animal, lab work going on and developing models that are exclusive for cysts, versus, sporadic tumors. So that's the next wave is sort of understanding those kind of insights.

Dr. Nuzhat Ahmad: Yeah. And just to build on that it's again, this is why they're so fascinating is that even within one subtype of cyst, there can be different histological, subtypes, and they will go on to develop different kinds of adenocarcinoma like coloid versus tubular. And the prognosis is different depending on what kind of a cancer develops and what we don't know. Why do certain morphological subtypes pretend such a poor prognosis. and I think this is why it's so fascinating that they don't have the same biological behavior.

And very interestingly, Chuck and I were discussing this, whether all these cysts in a patient have the same biological behavior, are they all identical or are they gonna behave differently? We don't know this, but I mean, this is what makes pancrea exist. So fascinating.

Dr. Kendal Williams: So for us as primary care physicians, let's let me set a scenario here. It's a very common scenario. We do a CAT scan. the abdomen for some reason, and it scans through the pancreas and there's a cyst revealed. This is apparently very common up to 20%. I think one of you had said earlier, I read two to 19% of the general population may have these cysts and they may give us something more specific about it. And then, we're basically asked to follow up on it. And for a lot of us, we're really not sure what to do.

So let's just go over the types of cysts that may come off a radiographic read. and then maybe you can help us work through what to do with them. So, you've mentioned IPMN so introducal popular mucinous neoplasms. Let's just start with that, which I understand to be the most common cystic pancreatic legion.

Dr. Nuzhat Ahmad: Correct. So, there's several ways to slice and dice this. First of all, I think from the primary care perspective, what you can provide to the patient initially is reassurance and the reason why I say that is sometimes patients come to us completely freaked out thinking that they have a cancer. So you can, reassure them that most patients will go the rest of their lives without developing any problems from the cyst. But I think you do need some expertise to figure out what kind of assist it is and whether it needs to be surveyed or acted upon.

Like I said, there's several ways you can slice and dice Cysts, but the major way would be to divide cysts into the type that have malignant potential. And those that don't, I think that's perhaps the simplest way when you're managing cysts. The ones that don't have a malignant potential are typically cysts that you're born with, retention cysts or cysts associated with pancreatitis. In these cases, history will be there. And of course, sometimes you see cyst in patients with, polycystic kidney disease.

These patients, will have typically not always, they will have a history that will guide you towards what these could be. The other group, which is the one that has a malignant potential is a much larger group. We call them pancreatic cystic neoplasms. And in that bucket, you have several types. The three main types that are pertinent to this conversation are, IPMNs, which are basically seen in males and females equally. And there are different subtypes of that. And we can talk about that if you would like, and then we have new synergistic neoplasms.

Which are almost exclusively seen in middle-aged females. And then we have a third type which is in this bucket, but does not have malignant potential for all intents and purposes. These are the serious cyst adenomas. Most typically they have a characteristic appearance on imaging. And when you see that, you can

make a diagnosis with a great degree of confidence that this is what it. There are very, very few cases reported in the literature of progression of these kind of cysts to cancer. And for all intents and purposes, we don't follow them.

Now again, the caveat is some of them, I would say about one third of them will have a different appearance. Will have an appearance, which will be most consistent with the mucinous cystic neoplasm or with an IPMN. And then we have to, try and define that. But I think this definition is important because you're going to decide whether the patient is going to undergo surveillance, are we going to biopsy the cyst or are we just gonna ignore it? These are our options, right? They ignore the cyst, you survey the cyst or you resect the cyst. So which pathway is the patient going to go down depends on factors, such as the appearance of the cyst and what we think the cyst is.

Dr. Kendal Williams: So I'm gonna ask a basic question that was asked of me. So you get the cat scan and they recommend MRI imaging often. What type of MRI imaging should we get? You know, one of the primary providers I spoke with about this podcast said, should I be doing an MRI with contrast to the abdomen? Should I be doing an MRCP? What are the difference between those tests? And he said, sometimes I order one, and then I'm told to order the other one and the insurance company won't let me order the other one. So maybe you could educate us on that, just in terms of sorting through which kind of cyst it is, we gotta have to get good imaging.

Dr. Nuzhat Ahmad: So we tend to like MRIs better, just because of the MRCP, so it's really like a 3d reconstruction of the ducts. And what they can define is they can define a couple of things for us. One is in the case of IPMN the cyst actually communicates with the pancreatic duct, which may or may not be obvious on C scan imaging. So MRI helps us with that. And the second thing is that it helps us by looking at the internal architecture of the cyst to define whether there is any high risk features within the cyst, like a solid component.

And then the other reason why sometimes, radiologists will recommend an MRI is if the CT scan is not done in a pancreatic protocol, they may actually really not get that great imaging of the pancreas. So they're not able to pick up more subtle lesions. That's typically the reason you don't need, Contrast MRI, you can actually do it without contrast. In fact, when we survey people with pancreatic C radiology, even if we order it with contrast, they will convert it to an MRI without contrast.

Dr. Kendal Williams: And so is there a distinction between an MRI of the abdomen and an MRCP in the performance of the test, or is it just having to do with how they reconstruct the images in terms of trying to, I see Chuck shaking

his head? No?

Dr. Charles Vollmer: Not really, essentially you should think about the MRI as the best test to look at the plumbing and, the MRCP element. I've not found that, it adds like you have to order it specifically. when I look at the test, I'm just scouring the way the duct looks, throughout the gland. I don't need the 3d reconstructions. They actually tend to be pretty pictures for us, but when you're a practitioner in the field, you're looking at that pancreas in a different way than that. So, I don't find that, that particular moniker, provides added value or specificity or anything like that.

So, the other thing to think here is that CAT scan is a better test to look at the Parinkama. And so if you're really looking for cancer, or mass lesions or those kind of things, the CT scan is the imaging you want primarily if you don't get it first. And then the MRI is the plumbing system. Often actually the thing that drives this first and foremost is ultrasound. It's the ultrasound that's done for, kidney lesions or kidney disease or gynecologic purposes or right upper quadrant gallbladder looks. That, the technician strays and wants to see what they can delineate about the pancreas.

Now, the pancreas pretty hard to deal with, with ultrasound because of bowel gas in the way. So, in very thin people, you can achieve it, but most of the time, you can't really look at that, full gland that way, but they get a peak there and they can get the pancreatic head and just see enough to see there's something abnormal. Then it goes to the next axial imaging. We would say that the primary thing that we would use is the MRI. And in fact, I make it a policy that I get a baseline MRI regardless of what's happened because we're gonna govern everything off of that in the future. The other thing to remember is that MRI does not give you radiation.

So when you get to see us, then we're gonna be talking by and large about surveillance for almost everyone. So we're talking about repetitive scanning, maybe for 40 or 50 years, in some cases, etcetera. So CT scans are not, ideal for us. The issue with MRI that comes up a lot is, pacemaker and contraindications. And then a lot of it is patient driven anxiety, those kind of issues. But we're getting around that all the time. There are protocols and I wouldn't put this in your lap as a primary care doctor. I think this is, for us in our office to guide the process to get these things done.

But there are, protocols now for pacemaker and metallic objects, and there are open air MRIs and they're sitting upright MRIs at this point for people. So almost all the time we can get that done through that process.

Dr. Kendal Williams: So you had mentioned on the MRI, you're trying to look at the plumbing and just to go back to, IPMNs. My understanding is it depends on where this thing is in relationship to the main pancreatic duct, that kind of determines how risky it is as a lesion that may progress to malignancy. Is that correct?

Dr. Charles Vollmer: So if I could take that, at the outset here, the way I talk to the patients is, we show them a picture of the pancreas and it's a depiction that we have in the office, and it's basically got a long tube going through it. And that is the main duct and it goes from left to right. And it's about a two to three millimeter macroscopic tube in real life. And then the rest of it is tributaries forcing into that, that are going to be purely microscopic. You can only see them basically by, transaction of the pancreas by the pathologist. And at the end of, this system, the periphery are the cul-de-sac of the asinine all around it.

So, I talked them in those terms, like the cul-de-sac of your community, each house is a cell that's making pancreatic juice into the sac. So, the Genesis of this problem is the cells that are lining the tube. and when they go dysplastic, they will turn into mucinous based cells that are creating mucus. And that's the definition of, IPMN for the most part. I make some analogies that, if you wanna put it in your mind's eye, it's like, a cherry hanging off of vine. The vine is the main duct. The side branch is. the tributary or is the stem of the cherry. And then the cherry itself is the cyst.

and how do those cyst, those, what we call side branch cyst happen? It's some sort of obstructive process in that flow of that river. at the very simplistic thought process, you can think of it like a babbling brook in the woods. It's kind of babbling along there. And then the beaver comes along and he throws the sticks, in there and it backs it up and you get a pond behind it. and whatever that obstruction is, whether it's from the heaping of the cells, in an abnormal disease process. Or it's the mucus plugging that goes on. That's how these little blebs, so to speak of cystic cavity are conceived. so that's just like a primer on the topography of this.

And I kind of say, this is like the Nile or the Mississippi running through the pancreas that way. The main element, the main river is gonna be what we call main duct disease. And it indeed is the more, charged up or virulent type. And it'll Harbor about a 50, maybe 75% chance of developing a cancer within it, if it can be localized to that. The side branches are more like 5% or less. Chance of developing. So there's a different biology that goes on in that real estate, so to speak. And now we have a third category that is a mixture of the two it's called mixed variant. And that's when you see dilation the main duct with one of these

blebs, so to speak and that, by and large, behaves like the main duct. So any dilation, the main duct puts you in a bad place for this.

Dr. Kendal Williams: That's very helpful. Let's talk about EUS and Nuzhat I know this is sort of your area. when do you go and do an ultrasound and EUS on one of these lesions?

Dr. Nuzhat Ahmad: So let's say you get a CAT scan on somebody for Hemoteri or something else, and you see a 1.5 centimeter cyst in the head of the pancreas. The patient is like a 66-year-old male. You send them to me. So I'm gonna assume that the cyst is musinous. So the question then is, do we have to prove that the CST is musinous or. And the EUS basically helps us define two things. Whether the cyst is musinous or not. And second does it have any high risk features or high risk cells? Is the cytology abnormal or not? So, it's a safe test.

It's well tolerated, but it does require anesthesia and it is invasive. So we are judicious about it, meaning that we don't order it for everyone. And there's a lot of debate about this in the pancreas world as to who should get an EUS. And if you go to 10 different academic institutions, you'll get 10 different answers. Some people will do an EUS FNA on everyone who has assist grader than a centimeter. Others won't touch anyone unless the cyst is greater than three centimeters. I think we are somewhere in between.

I look at a cyst and if it has no high risk features and it's about, let's say 1.5 centimeters, I'm gonna assume that this is a side branch IPMN just based on the numbers and I'm going to say, look, we are just gonna enter you in a surveillance protocol and we'll do an MRI every year. And if the CS starts to change and character our size, then I'll go ahead and do an EUS with an aspiration. And at that point, I'm assuming that the cyst is musinous. Frankly, speaking to define whether the is musinous or not is really an old conversation from 10 years ago. I think currently the conversation should be, how can we predict which cysts are gonna be the bad actors and we don't have that answer yet.

Dr. Charles Vollmer: the listeners of the podcast will absolutely remember back to medical school the courses you had on diagnostic testing and, everything you do has the chance of a false, positive and false negative. And a good test, if my recollection was is that you're getting good accuracy with two to 4% chances of each of those categories. That kind of makes a good test. So absolutely we have issues mostly with the cytology element, where you can have false positives and we really don't know false negatives, per se as, easily, but definitely false positives.

So, it's kind of my conception and I don't know if I'm right about this and Nuzhat could tell me what she thinks. I think the smaller the sys there is the more likely you're gonna have more variance on that call. the larger, probably it's gonna be more authentic for what you're gathering from it. in the past Well, we have to say that this improved greatly the cytopathologist skillset and their nomenclature and how they report things to us is totally different than 20 years ago. Now they have a lot more specificity in terms of the degree of dysplasia that they're able to talk about.

And for us, if we hear high grade dysplasia or adenocarcinoma, you can pretty much take it to the bank that that's correct. Pretty much, but anything short of that is not as dependable. And it used to be that the wording was atypical cells and 20 years ago that was code speak for it's probably cancer. It could be cancer. And we've sort of grown out of that, and you have to get back to the idea that atypical is exactly what it is at face value it's cells that don't look right for that area of the body, okay. But it does not necessarily mean cancer.

So it can be, dysplastic cells as this disease process is, but it doesn't mean that they're certainly aggressive or that kind of thing. In other cases, you can just have stranger calls of the cells that are there that may take you to alternative diagnoses than IPMN, but the word Atypia drove for many years, us crazy as surgeons, because we were basically handcuffed when we saw that because, and there was a lot of ignorance at that point in time. So we operated aggressively based on that. And I can tell you now, I'm very skeptical when that's the read.

And I'm not going to the operating room, but there was a whole fervor our whole field on this has gone from aggression to holding back and conservative approaches on this. So, we would be doing one centimeter cysts back then that we knew the numbers, the odds would say it was 1% chance of having a cancer in those cysts. Even back then, that was the thing, but a one centimeter cyst with an atypical finding. And then you throw in quite often the family history of pancreatic cancer, maybe like one person in the family and that sort of cluster was like red alert, red alert. We've gotta go take these things out.

And lo and behold, what we find through that most of the time we were taking out dysplasia, premalignancy. Largely at low levels. And we don't know the biological progression processes that way. And you also have to understand that, pancreas surgeries, not kids play. so to do that and suffer consequences, both in the short term and long term, was, pretty, impressive on patients. So we have definitely grown in our careers. We have grown with the times and adapted to the quality of inputs that we're getting to help make these decisions.

Dr. Nuzhat Ahmad: I just wanted to say that just going back to, what I was saying earlier about EUSs. If you have a patient who's younger, like if somebody's older with a pancreatic CYT, then I'm going to not automatically go to an EUS FNA, because I'm gonna assume this is a musin cyst, but if it's somebody younger, let's say 40 years old. Then I'm going to do an EUS FNA, because I want to define what kind of a cyst it is before we commit them down to 40 years of surveillance. And the two things like Chuck said, we look for are psychology, which basically tells us whether there's malignancy or not.

And like Chuck said, it's not overall accuracy, it is only about 50% and we do miss cancers. And the other test we have is a CEA level, which is also, not the best test, but it tells us that the cyst is musinous or not. And, in previous years, a very high CEA level was taken as an indication of malignancy and that's absolutely inaccurate. The only thing it tells us is that the cyst is mucinous. There are some caveats here as well, because we can see some inflammatory cysts that can have very high CEA levels. And sometimes we can have CEA levels, which are almost at the cutoff.

Like, what does that mean? if this was two points more, would it be mucinous versus not? So both the tests that we have are not perfect, so we need something else. And that's where, you know, DNA analysis comes in.

Dr. Charles Vollmer: Similarly CA 19-9 tumor marker. which is, what we have for pancreatic, biliary cancers, can be tested in that fluid and it gets really confusing then. Right. We also contest it in the blood and often there are a lot of people who do that as a baseline to see if there's a cancer then and there, when the diagnosis is made. So we always have to distinguish, is it from the blood or is it from the, fluid first of all, and what's the relevance? So CA 19-9 within the cyst fluid is meaningless. And we, probably, I don't know, Nuzhat if you even send it Out?

Dr. Nuzhat Ahmad: We don't, I've never done it.

Dr. Charles Vollmer: Whereas a CA 19-9 in the blood in that kind of patient would put your antenna up. Well, maybe we are sitting on a cancer here.

Dr. Nuzhat Ahmad: But I don't recommend it. I don't recommend obtaining even a blood CA- 19-9 because they can sometimes be elevated falsely and then, you know, you're gonna be chasing your tails. So I recommend against that.

Dr. Charles Vollmer: Personally I am sitting on five patients right now with that scenario of a CA 19-9 in the serum that's high. and they may have cyst, or

we have not been able to identify a lesion in the pancreas that corresponds with it. So the more you do here, the more you chase, the more vexing it becomes.

Dr. Kendal Williams: Chuck, I'm getting an appreciation for your job because. This is not an easy decision. And as you noted, pancreatic surgery is a big deal. And I, still remember it was a veteran, actually a patient I met at the VA who had had a Whipple. And I said, why did you have a Whipple? And of course he had, at that time, turned out to be a benign lesion. I was shocked that somebody would undergo a Whipple for a benign lesion, but obviously this is what you're dealing with every day is trying to figure out who's gonna undergo an eight hour operation with considerable morbidity?

Dr. Charles Vollmer: Yeah. So, things have changed a lot. The operation is now about five and a half, six hours. If we're talking a Whipple, distal pancreatectomy is an hour and a half to three hours, depending on complexity. But those were both double those when I started my career and we've come a long, long way. My era now, I'm like generation 2.5 or three in terms of pancreatic surgeon lineage and mine was really the first era to incorporate fellowship training. And then the group after us now is all exclusively that.

So the training and education process made things better and, anesthesia has made things a lot better in terms of the, conduct of the operations. And finally radiology has improved for us because, the roadmaps to the operations are there for us ahead of time, but more than anything else, the, decision making on what the type of lesion is and its relationships to things in the Abdomen is, defined, whereas in the old days it was explore and let your hands do the talking, right? So we put all those together. And, in terms of this decision making, you gotta go onto the gastroenterologist, contribution too.

So having the EUS and then finally putting this all together in a multidisciplinary group, makes the decision making a lot more, codified and relevant. I'm gonna tell you that in general, our field is regressing pulling away from the aggression of doing these operations. When I started, half pancreatic cyst must be pretty malignant, gonna get an operation, knee jerk response. It was the heyday. The heyday of our, field was 2000 or so, or, volume is huge on this stuff. And now everything is getting more tempered about what we do with this.

And we're learning, more and more about different, degrees of aggression. That also comes with despite the fact that the operation is, more swift safe and everything, the complication profile, the mortality aspects, all that kind of stuff, they're all the same still. I would warn one thing, there's a lot of nihilism in the field of medicine about the Whipple operation. there's a lot of people in the

audience here, who's gonna span 30 year olds to 75 year olds practicing in this.

But generations passed, this was just felt to be brutal because people went into those operations then they were scarred by being there as a medical student. They remember the patient's recovery on the floor and they know people who survive for long periods of time. There's just sort of bad mojo, bad vibes about that out there. And I have to tell you that it's a lot different than it was back in the time. So the ability for people to sustain these operations and do well after it is much, much better now.

Dr. Kendal Williams: That's great. I'm in that generation that remember them as being the big deal. Let me try to kind of figure out who among the patients that we get reads back on. Are we gonna send to you, because clearly it's probably not appropriate for us to have you see everybody. Right? So how are we gonna screen who we send to you? How do you want us to do that?

Dr. Nuzhat Ahmad: First of all, you're right. We can see everyone. I don't think we need to see the cysts that are five millimeter, six millimeters, seven millimeters, like the sub centimeter cysts, unless there's something else in the pancreas. There's actually some conversation whether these should just be ignored. We do have several guidelines, none of which are perfect by the way, from different societies. And some of them say that if the syst is sub centimeters, you can just go ahead and do an MRI every two to three years. I don't wanna speak for Chuck, but I'm happy to curbside.

Like if somebody sends me an epic message on a patient, I can quickly review the MRI and give you an opinion. And I do that quite routinely with some of the physicians. If a cyst is greater than 1 centimeter. I think they should come in to see us, just to have a conversation about the risk. Number two, there are some other things, the pancreatic duct, if there is dilation of the pancreatic duct, then you know, we are talking about most likely a mixed type IBMN. And those are the patients I think who should see us.

Obviously, if there's something else in the pancreas, if they're symptomatic in any ways, if they've had acute recurrent pancreatitis, they should see us. Family history of pancreatic cancer, I think it's reasonable to see us just because we can have a more detailed conversation about their risk. And I personally think to be honest, if a primary care physician is uncomfortable about having a conversation with the patient about any aspect of this, they're welcome to send the patient to us and we'll have that conversation.

Dr. Charles Vollmer: I'm happy to see anyone. I'll even take it down to the sub centimeter thing. So for a lot of reasons, first of all, this is what we do. We're

happy to take the burden off of you. Whether it's out of ignorance about the disease process or the lack of ability to counsel, people on this discreetly. Anyone who comes to me actually gets at least a half hour long conversation about this and what the disease process is and it's an educational process for the patient. And I actually think that it's a controversy about the sub centimeter things because we could be drowning in them, but you also can't blow them off.

And, it's gonna be, hard for busy primary care doctors to remember this and keep up with the schedule on this and, we're happy to do it. The second thing is, we've developed a multidisciplinary team that basically mimics a tumor board process for any other thing that you have in the healthcare system, breast cancer, lung cancer, the likes. Okay. So, it's for purpose is to have all these experts in this field, laying eyes on the situation. I will, admit this is a growth industry for us and I guess we'll take care of that problem.

And we are basically in how. deal with this because once these are identified, it really becomes part of a, person's regular healthcare maintenance process. there's some medical legal aspects to this that's not really brought up and haven't been problematic, but you can understand that if a person never finds out about it or it gets dropped and it's not surveilled when it should be or they don't get counseling on something like that, someone's gonna be on the hook when the badness happens down the line.

So, I would just say that in general, in my practice, I have three pillars to the practice cancer. pancreatitis and cyst is the new player in this era now. And they are all probably equal and there's a Venn diagram of how they all overlap each other. But in my pancreatic surgical practice, as a super expert in this is all I do, I'm absolutely willing to take on that third pillar of the cyst disease. And even if it's not surgical in nature, so we're happy for the Penn community here, we're very happy to take this on.

The last thing that helps us here is it builds up our knowledge base and our research capabilities that, pretty much everyone that comes to us, we acquire, a story on and it helps us understand things. And, not only do it ourselves, but to collaborate with other, groups around the country in trying to figure this out, many of the things we're gonna need to figure out are gonna be about large population, data. That's gonna help us understand how to surveil people properly cost benefit analyses and these kind of things.

Dr. Nuzhat Ahmad: One thing Kendall, I think where primary physicians can really help us is when we consider stopping surveillance. So this is a blind spot in this entire world of pancreatic cysts. When do we stop surveillance? I mean, I definitely, and I'm sure Chuck you, so do you, we have patients in the eighties,

late eighties with pancreatic cysts. We know they're gonna grow the big cyst for small cyst at one point. So we know that they're gonna grow. and the second thing is the likelihood of cancer also increases with age.

So when do we stop surveillance? But this is when I think primary care also comes in. We have guidelines we should stop, screening for patients for colon cancer after the age of 75. And a Hemi colectomy is much simpler surgery than a Whipple, but yet we are continuing to follow these cysts. There's no answer to this. This really is a blind spot in this conversation, but if a patient walks in and I know I eyeball them and I know regardless of what we find, they're not going to be resectable.

Because of the [inaudible] conditions. That's I think when we need the help to have a conversation with primary care, just because they know the patient best. This is not a one and done. It's typically a process that goes on over a few meetings about, okay. You know, maybe it's time to stop surveying this.

Dr. Charles Vollmer: The age problem here is really, it's a frontier for us to figure out here, because it's really about the cost of the system. And when they come to my office, it's about, I'm gonna have to figure out, could I pull off this operation on you at any given age and or physiologic strength regardless of the age? Okay. So, that's there and I kind of tell these people, look as long as I can, size you up to say that you could potentially get that procedure. I'll be willing to keep an eye on you, and go with it.

But certainly if you're too decrepit to come to the doctor's at that point it's folly, to continue that kind of stuff. By and large, most of the elderly people want to keep looking at it. They want it, they want the knowledge many of them actually like going to doctors and going to those appointments and they keep it up with it. Anecdotally, I'll tell you that, I have a very vivid memory of a case that, an 89-year-old lady, came to us here at Penn, with a cystic Legion. That was, when we got to it, it was metastatic and it was cancer and it was too far gone.

She had received an opinion up at a hospital in Boston when she was age 80 about this. And they said, this is not gonna happen to you. You're gonna die before this will catch up to you, stop watching it. And they did. And there she was she died of pancreatic cancer that they're on. So you just don't know. one of the things I say in the office to people about this is like the biological process going towards cancer, it's an accumulation of multiple defects.

It's not a singular switch that goes on and off that we know of we feel it's a multi, gene based, process. But that is probably a biological process geared

towards, activation at age 130, 140 or something like that. And you're just not gonna get there. you're actually playing out the clock on life before. This disease process. I make the analogies very similar to prostate cancer for men that a lot of people will go to the grave with the cysts, but not because of them.

So this upper end is something like we will figure this out ultimately, but there's hard decisions to be made there because the patients, a lot of the patients want the continued interaction with doctors over this, and they want the knowledge base of knowing what's going on.

Dr. Kendal Williams: So that's something we can jump in with and help work patients through. So let's just, close this up. I just wanna make sure everybody knows how to get in touch with you. I didn't have any trouble. I Googled the Pancreatic Cyst Multidisciplinary Program at Penn and your center came up and a contact number. That's what I'd suggest everybody else does. And news. Audit's very kind of you to say that we could send you a note if, we're in the pen system.

I did find that when I did refer a patient down, that you guys do review, the scans before accepting them into the practice, which is fine because, you might be able to get back to us and say, listen, you don't really need to send this patient down to us. I don't know if that's common practice, but that was one experience I had.

Dr. Nuzhat Ahmad: Yeah, I do actually look at imaging beforehand. And I live in Epic constantly, as do most of us. so it's the best way to reach me for clinical stuff.

Dr. Charles Vollmer: We would always tell people if you're gonna come see us, you have to have imaging in hand. Now we're talking mostly to our Penn community here. So, stuff's gonna be there. And we are perfectly fine with this being acquired at any of the facilities. I am very keen to convenience for the patients. and It's more about the surveillance than the initial situation, by the way. What's it gonna mean to do this regularly for these people?

And I'm always filtering them back to the closest institution, Yardley, Chester, Valley Forge, Radner, whatever it's gonna be, Princeton in some cases, for their convenience purposes. And then what we've, become very flexible about how we see the patients ultimately in the follow, up. And telehealth is really good for this because there's not a lot to do other than I saw the scan. I wanna tell you about it. And then a quick question or two about how you're feeling and if you're having any problems.

But, why do they need to take these big trips down to see us for multiple hours and parking fees and all that kind stuff when it's basically a surveillance process check in. So, we've become very adaptable to that. The problem we have particularly New Jersey and Dell, like if it's out of state we can't do the telehealth now. But in state, we can do those things for the surveillance, processes. so, my clinic offers a lot of flexibility of how we can interface with patients.

Dr. Kendal Williams: you both have been so, generous with your time to go through this with us, explaining some of what's known and really helping us understand what's unknown, and how we might be able to work through this together as a healthcare community. So I really appreciate having you on, I'd like to have you back to talk specifically about pancreatic cancer down the line, maybe with an oncologist. Because I think that's it's obviously increasing as an issue for us, it's risen, I think to the second or third, most common cause of mortality. And so we'd like to have you back, to talk about that both of you Chuck and Nuzhat and we'll bring an oncologist next time.

Dr. Charles Vollmer: That's more complex than ever.

Dr. Nuzhat Ahmad: Well, thank you, Kendall.

Dr. Charles Vollmer: If I could sum up, I just say to the audience here, we're here for you. and, I didn't get to say this earlier when you kicked it off today, but those magic words on these MRIs are, the clinical correlation, suggested. And that just pose it in your lap. And I can understand you're probably sitting there scratching your head. Well, who does this? And how serious is this and all that kinda stuff. we both take great pride in being that resource, for you, and for the patients as well.

Dr. Kendal Williams: Well, that's terrific and it's a great burden off our shoulders. So with that, let's end the Penn Primary Care Podcast. Please join us again next time.