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TRANSCRIPT - GR 03 18 22 “Colorectal cancer screening: When there is a fork in the road, take it!” *Mary Pachapin, MD, from the NYU Grossman School of Medicine*

UVA IMR Chiefs

00:24:13 To introduce Dr Marc Shaiman from the New York University so we're delighted to welcome to the UVA and American College of Gastroenterology visiting scholar and equity diversity.

- 00:24:24 Taken obtained his medical degree from Cornell and residents gave you are hearing hospital.
- 00:24:30 That came in followed his residency training with fellowship training and Jasper Generality at Montefiore Medical Center and Albert Einstein College of Medicine.
- 00:24:37 Before returning to New York Presbyterian for chief resident here, Dr Potato and Jordan faculty at Cornell and 1994 before transitioning to NYU where he now holds a plethora of leadership.
- 00:24:48 Positions, including the Shoals Leads Professor of Gastroenterology Director of the Division of Guests Raj Gastroenterology Hepatology and Vice, Chair of Clinical Affairs for the Department of Medicine.
- 00:24:59 Doctor Potato and it's a devoted clinic clinician educator, as noted from his conference teaching awards, including the Steam Master Clinician Award by NYU School of Medicine.
- 00:25:08 Beyond this, he sits as the immediate president of the ACG as well as a co-director of the Physicians Leadership Scholars Program.
- 00:25:15 He's committed significant research and leadership time to the study of colorectal cancer detection and prevention.
- 00:25:20 With numerous publications in the American Journal of Gastroenterology and Clinical Gastroenterology Hepatology to name a few.
- 00:25:27 Today, we look forward to taking advantage of Dr Evans expertise and learning more about advances in the world of color for cancer screening, please join me in welcoming Dr Jason to the virtual screen.

Mark Pochapin

00:25:45 Thank you.

- 00:25:47 First of all, it's so nice to see all of you I'm very disappointed because I've never been to UVA and I hear it's one of the most beautiful campuses in the country.
- 00:25:55 So I'm hoping that this will be a potential rain check to come back and meet all of you in person that's what we've missed most with this pandemic.

- 00:26:03 But on the other hand, I think this is an ability for us to all communicate to learn from each other and still awake for us to continue on, so let me share my screen.
- 00:26:19 Okay, you should all be seeing my screen now I'm talking about forks in the road.
- 00:26:24 that's a quote from Yogi Berra a famous Yankee and philosopher and we'll see where we are at a fork in road and colorectal cancer screening and according to yogi we should take it.
- 00:26:36 So I am now broadcasting right from the city that's actually the view, not from my window, but on the river, it really is beautiful on the east river and not quite uva type beauty, but.
- 00:26:49 has its own unique city duty and itself, so what I want to do is go through a timeline.
- 00:26:55 just very briefly because the story of colorectal cancer prevention is actually quite a remarkable one and one that's really unique.
- 00:27:02 To our country and to a lot of investigators in different institutions and it doesn't go back that far i'm starting in 1973 when the concept that Paul a peck to me actually using a snare to remove a polyp.
- 00:27:16 During colonoscopy was first developed by to New York surgeons actually in 1973 RON Reagan was diagnosed in 1985.
- 00:27:27 And also that same year we identified the biology for focusing through the vocal gram or the different genetic mutations which will discuss.
- 00:27:36 In 88 we showed that checking microscopic blood installed using why I actually prevents colon cancer in 93 the national pulp study showed that colonoscopy and removing polyps.
- 00:27:48 actually prevents cancer and 97 there now new guidelines that use colonoscopy as a primary screening modality prior to that it was old diagnostic.
- 00:27:57 In 2000 public education became key when Katie Kirk went on the air we'll talk more about that and literally the public ran to get screening colonoscopy after that 2006 we started focusing on quality and in 2014.
- 00:28:12 Going forward we've now had these national campaigns to increase the screen right.
- 00:28:18 So I want to start with the case of a 52-year-old male who has a history, who has a family history of colon cancer.
- 00:28:24 His mother had colon cancer at age 58 she was genetically tested and did not show any high risk mutations there's no other family history, he had his first colonoscopy at age 40 which was normal.
- 00:28:36 The patient has had regular bowel habits and physical exam is completely normal.
- 00:28:41 Now, like so many after he goes through that bow prep once he doesn't want to take the bow prep again.
- 00:28:47 he's do for his follow up screening evaluation and he says, I don't want to go through a colonoscopy can I do a color guard or blood tests and so, how do you respond a fine we'll order color guard because it's over 90% sensitive.
- 00:29:01 Let me introduce you to my dog who could sniff out colon cancer we'll talk about that this will not work because colonoscopy is the only appropriate test for someone who's at high risk with a family history like yours.
- 00:29:12 Or, this will work, because your mother was genetically tested and she didn't have any mutation so we don't have to worry about you.

- 00:29:18 Or we could just skip the colonoscopy all together and do a blood test so we're going to talk about all of these things.
- 00:29:24 first thing I want everybody to recognize is that colon cancer for each gender represents the number three cause of cancer related death so for men it's prostate long and.
- 00:29:34 Excuse me it's long prostate and colon for women it's long breast and colon for men and women it's actually number two.
- 00:29:41 it's long colon and then either breasts or prostate bottom line is it's still a pretty significant killer as cancers go and it's something that we need to do better with.
- 00:29:51 So I want to start off by just reviewing some of the genetics, I know we have a crowd of people who are going to be.
- 00:29:58 either going into internal medicine or practicing and so much now comes down to precision medicine and understanding the genetics.
- 00:30:05 So this was the vocal gram or what Burt Vogelstein first described in 1988 which shows how normal tissue can turn into an adenoma to an advanced adenoma to cancer.
- 00:30:17 So here's normal tissue going to advance that a normal to cancer and this process takes about 10¹⁵ years to occur.
- 00:30:26 Usually the mutations or stop codons and we have both oncogene to tumor suppressor genes the oncogene is I like to think of as the gas pedal I love cars as you'll see in this talk.
- 00:30:37 And if you think about an oncogene going awry it's like getting the gas pedal stuck to the ground we can't take your foot off the gas so K Ras would be a good example of an oncogene.
- 00:30:47 Where the other mutations describe mostly tumor suppressor gene, this would be like the brake not working so either your gas is stuck or your brakes not working, but the process of going.
- 00:30:57 To more disk plastic tissue through the set mutations ultimately leads to cancer and you probably recognize some of these like p.
- 00:31:05 The APC gene or 18 Q, these are tumor suppressor genes that in the set sequence or P 53 is late in the sequence and K Ras is earlier.
- 00:31:16 But there's this other component this EPI genetic component, where you can hyper methylation and change the function of the genes, so this is known as.
- 00:31:25 hyper methylation activation known as CpG so about half of all the protein gene promoters actually are cytosine guanine and I have down here CpG promoter.
- 00:31:38 And these are called CpG islands, and if they are turned off by hyper methylation they This is called a CpG island method later of.
- 00:31:48 phenotype which I have here, so what can happen is, if we take our CpG promoter tumor suppressor gene and we hyper methylation it.
- 00:31:56 We could actually inactivated we inactivated tumor suppressor gene it's almost as if we inherited and inactivation of a tumor suppressor gene or that sequence of genetic mutations can further move along towards a mutation that can lead to cancer.
- 00:32:12 So this works in the setting of mismatch repair proteins, that we can inherit a genetic mutation that affects our ability to make the mismatch repair complex that's called lynch syndrome or HNPCC as we used to call it.

- 00:32:26hereditary non-Paul posters colon cancer, but it's really referred to, mainly now is lynch.
- 00:32:31So if we have, for example, an MMR H1 or an MSA that interfered with genetically we're not going to have the complex that's going to run up and down the DNA, be able to exercise abnormal DNA and repair.
- 00:32:45But the same can happen if we hyper methylation we can inactivated as an EPI genetic phenomenon not something inherited but something that's in quiet acquired.
- 00:32:56Now, when we think of the pathways to cancer, we think that all cancers, by and large, come from polyps not that.
- 00:33:04All polyps turn cancers, but all cancers and average risk patients do come from polyps.
- 00:33:09So how can that happen well one is I just mentioned to you this concept of chromosome on stability, the set genetic sequences that go awry.
- 00:33:18which can take 10 to 15 years usually working through an advanced at an omen.
- 00:33:22assess ulcerated Paul is a type of polyp as well, a little different from adenoma that's much flatter a little different and histology but it can lead to cancer Those are the two pre cancers are potentially precancerous polyps at an ominous POPs says all sorted polyps.
- 00:33:40Now I mentioned lynch syndrome that's a loss of the mismatch repair protein due to a genetic abnormality inherited.
- 00:33:48And that can lead to microsatellite instability, which is an accumulation of these defects within the DNA.
- 00:33:55And within a year, it could very rapidly move through polyp and into cancer so where chromosomal instability can be 10 to 15 years.
- 00:34:03lynch syndrome, we actually screen every year because the polyp the cancer sequences accelerated since we don't have the normal mechanisms in place.
- 00:34:12To try and prevent the abnormalities in DNA and the DNA abnormalities accumulate lead the polyps lead to cancer.
- 00:34:18That works through a K Ras pathway, but it doesn't have these hyper methylation sense, because this is something inherited, however.
- 00:34:27If we hyper methylation we have the CpG islands or the CpIs that's really more of a CpG ref pathway that can lead to the same microsatellite instability and accelerated pathway to cancer.
- 00:34:39Or can lead to adenomas polyps going through a standard pathway, but not through the chromosomal instability, but through a hyper methylation.
- 00:34:47And we see this as people get older where there's more hyper methylation so the three pathways of chromosomal instability genetic or as a.
- 00:34:56construct adenoma or hyper methylation ultimately can lead through the polyp to cancer.
- 00:35:02But most cancers are actually average risk 75% are the 25% are primarily group and family histories, where the real genetic miss.
- 00:35:12The genetic inherited type of colon cancer, we see in familial I didn't know but as Paula posts or lynch is the minority.

- 00:35:20 5% lynch 1% SAP and inflammatory bowel disease, a whole different pathway going through an inflammatory pathway that although may go through dysplasia may not necessarily go through Adenoma.
- 00:35:33 that's the only pathway that doesn't really go through the polyp because it's inflammatory based all the others are polypoid some because of inherited genetic mutation.
- 00:35:42 Others acquired, but even with a family history there's a higher risk, even if we don't know what that genetic pathway is yet, as you know, we're fighting all these mutations out in real time and we keep finding more and more genetic mutations that lead to colorectal cancer.
- 00:35:58 This is what an adenoma known as Paul looks like on a colonoscopy when it's larger like this it's quite obvious, you could see it is protruding from the background wall and the way we remove this as we put a loop of wire around called a snare and we're able to cut this off.
- 00:36:15 These are also polyps these are called adenomas adenomatous polyps you're probably looking at them and saying, where are the polyps so let me show you.
- 00:36:23 In a here I'm outlining the polyp now, and you can see, this little bit of yellow mucus sometimes the only way you get a clue to these polyps.
- 00:36:32 That they produce more mucin and that mucin gets thing with bottle here I call this the egg drop soup sign because it looks a little bit like egg drop soup again the museum picking up some of the background material but here's the polyp here and then see here's the polyp.
- 00:36:49 So these polyps are difficult to see, but they can be 20 to 35%.
- 00:36:55 Of the polyps that lead to cancers, so we have to be able to detect these polyps as well, very easy to see the large polyp I showed you previously, but these flat adenomas are more difficult.
- 00:37:06 This is the enemy, this is what cancer looks like it's ugly you could see it bleeds it's friable and it's beginning to dip down you see that central component.
- 00:37:16 Where it actually looks like it is being pulled into the tissue is how the cancer grows into the wall into the lymph nodes and ultimately to the liver and the rest of the body that's what we want to avoid at all costs.
- 00:37:29 So how do we prevent colon cancer well there's a real paradox, I told you that colon cancers and number three cause of cancer related death.
- 00:37:37 But the other thing, because we can find the pre-cancerous growth, the polyp we could prevent colon cancer colon cancer is one of the most preventable and even when picked up early one of the most curable cancers, we have.
- 00:37:49 So the number three cause of cancer related death yet one of the most preventable and curable of all cancers that paradox is really frustrating when you're in this field and the question is, what can we do about it.
- 00:38:01 Well, let me show you a little video of what a polyp looks like and how we remove it, because I know not all of your gastroenterologist watching today.
- 00:38:09 So we're looking at the colon you'll see little purple rubber fingers it's a little tough I use on the scope.
- 00:38:16 And you'll see a polyp now appearing at the six o'clock position, not a large polyp, this is about probably about six millimeters or so the snare wire is pushed out.

- 00:38:27 And then you could see a little cup of normal tissue under the Paul is being removed a small amount to heat is being produced and that lupa wire, known as the snare literally cuts through the polyp.
- 00:38:37 And now we're going to advance the Kaleidoscope where there's a little channel where that Cathy just came out.
- 00:38:43 suction the tissue and that tissue is going to be sent the pathology and that little divot that you see there is going to heal and if you go back.
- 00:38:51 and say six or eight weeks, you wouldn't even know that something was removed that heals completely as if nothing was ever there.
- 00:38:58 So that's why we want to find the polyps and remove them because not only are they easy to identify but they're easy to remove and obviously prevented from ever having the chance of turning cancerous.
- 00:39:09 Now let's imagine for a minute that we now turn the clock 10 years to the future, or maybe eight years, so the future and what we're going to see here.
- 00:39:21 So now we're moving that clock forward imagine that we didn't remove the polyp.
- 00:39:26 And now again coming back on a colonoscopy, this is another patient.
- 00:39:30 But this is no longer polyp, this is a cancer it's a regular it's bleeding the tissues tribal.
- 00:39:37 And you can imagine if you turn the clock back, it would have looked like the polyp I just showed you in the previous video this one, you cannot remove because it's already growing into the wall.
- 00:39:46 We do have some techniques now where we could remove full thickness cancers if they don't seem to have invaded using endoscopic ultrasound and imaging.
- 00:39:55 But most of the time, this needs to be removed surgically now again if it's early this could be curable but we don't want to wait till someone develops a cancer.
- 00:40:04 The US preventive services Task Force involves three GI societies together come together with recommendations, the last group of recommendations was in 2017.
- 00:40:15 had three tiers tier one being colonoscopy every 10 years and annual fecal them, you know chemical test that's looking for microscopic blood i'll go into a little bit more detail on these tests.
- 00:40:27 tier two is using virtual colonoscopy known as CT colonography every five years or using sequel mino chemical test the fit but adding DNA to it that's known as color guard.
- 00:40:38 or flexing every five or 10 years and tier three is a capsule study which honestly is not us, because it requires quite a rigorous prep and what we don't recommend is the current blood tests, known as set the nine.
- 00:40:51 Something that I think is very important and that we've put a lot of attention to is the disparities we've seen in colorectal cancer incidence and mortality and what we see.
- 00:41:01 Is for both incidents on the left and green and mortality on the right and green, we see a higher incidence and mortality rate.
- 00:41:10 For black Americans, and this is something we've known for a while, but we've been focusing on it to figure out what causes it I could tell you that the focus in the past.
- 00:41:20 has been to look for genetic determinants, what are the genetic but now we're looking at not only genetic and epigenetic but also social determinants and how they may play a role.

- 00:41:31 And it's important for people and families, like the Davis Atkins family because Len adkins here on the Left was diagnosed at age 48 and died six months later, for colorectal cancer.
- 00:41:42 This is a time where screening started at age 50 and the young man in the picture actually has become a big advocate now 10 years later, and was very helpful getting the age move to age 45.
- 00:41:54 Also, we know that there's been a lot of high profile people like black panther star Chadwick Bozeman.
- 00:42:01 Who was 43 so even at age 45 screening Chadwick Bozeman would not have been picked up in screening.
- 00:42:07 But Lynn Atkins might have so we have to figure out what's going on and why are we seeing younger adults and particularly black Americans affected more from this disease.
- 00:42:18 Well, this concept of black Americans having an increased incidence and mortality started with the recommendations 2017 stating let's start screening black Americans at age 45 but moving forward now the current guidelines are that all Americans start at age 45.
- 00:42:38 When we look at the disparities, one of the things that we've recognized, not just in colorectal cancer pretty much in everything in medicine is that coven really unmasked these disparities.
- 00:42:49 And it certainly did so with colorectal cancer screening and what I liked about this article by Sophie bells or and colleagues, is that they not only.
- 00:42:58 listed the impacted areas, but also the potential solutions and Sophie is actually interviewed about this there's a little.
- 00:43:07 code here that I would suggest, if you have an interest in this area to listen to Sophie talk about this topic because.
- 00:43:14 it's really something that we haven't put enough attention into recently, and one that is critically important if we're going to be able to equitably screen and prevent colorectal cancer.
- 00:43:24 So what we have here is trying to come up with solutions that will allow us moving forward to have the ability to screen and prevent cancer in a way that's.
- 00:43:36 Has equity and equality, so that we don't see the disparities using multiple modalities, not everybody can get to a colonoscopy so maybe fit or color guard might be an option.
- 00:43:50 making sure that the test is positive, like a fecal amino chemical pesticide positive it gets followed up, unfortunately, there are a lot of people who get tested but don't get the appropriate follow up for positive non-colonoscopy based test.
- 00:44:02 making sure that we have Community partners a lot of research has been done, looking at.
- 00:44:07 How Community partners can increase screening rates in place that we might not recognize where people get together like barbershops, for example, Joe ravenel here at nyu is published some really interesting data.
- 00:44:17 That getting information at barbershops may actually disseminate it better than just giving it out in other locations.
- 00:44:25 Houses of worship or another place but getting partners to get the information out, making sure that we fund the appropriate screening and not just screening but also things like transportation and education.

- 00:44:36The education is critically important and cannot be done just by healthcare practitioners those partners that I talked about are also people could make sure that people are getting screened for colorectal cancer.
- 00:44:47And finally advocacy and this is going to our Congressional leaders, the people who are going to represent us to make sure that screening is not only available but cover.
- 00:44:57And I will tell you that Virginia played a major role in making sure that colonoscopy was covered and I'll get to that shortly, but Virginia plays.
- 00:45:04A big role in paving the way, but we have to do better, we need coverage for everybody, with all different types of socio economic status and different types of backgrounds and locations.
- 00:45:16So this is those disparities that I mentioned to you, looking at the incidence and mortality of black Americans versus nonblack Americans, the good news here is that we are doing better.
- 00:45:27And what I want to show you is that the slope here is beginning to narrow.
- 00:45:32And when we look at the ratio between black and white mortality.
- 00:45:37We could see that it's beginning to level off and actually it's beginning to come down, meaning that black American mortality rate is actually coming down in comparison to white American mortality rate.
- 00:45:47This is huge, it means that we can make a difference.
- 00:45:50We focus on this, and this that is really just over the past five years and we're focusing on it more we're going to be able to make differences I'm really hopeful.
- 00:45:59That we can show that in colorectal cancer, we can really eradicate some of these disparities, we see, because we know how to prevent it.
- 00:46:08As I mentioned, the American cancer society came out with their recommendations in 2018 that all Americans to start screening at age 45 mainly because we're seeing younger people get colorectal cancer.
- 00:46:21And the American cancer society used modeling data which showed in the blue bars, starting at age 45 and in the Gray bars age 50 and on the y axis the life here is gained, so this is colonoscopy CT colonography flexible sigmoidoscopy.
- 00:46:40we're seeing that for each type of modality life years gain improve when you start at age 45 and one of the things that is really important.
- 00:46:50Is that when we do life years gain starting at age 45 the colonoscopy we get the greatest number of life years gains we get 429 and that's really the modality that we've been putting forward is starting at age 45 and if possible with colonoscopy.
- 00:47:05and actually the US preventive services Task Force came around recently and they now recommend for H 50 to 75 great day.
- 00:47:13And age 45 to 49 great because the data isn't quite as good for age 45 to 49 but great a n grade be both must be covered by Medicare, meaning that.
- 00:47:25It doesn't matter that it's a be compared to an A A and B will be covered, this is a game changer now because all commercial insurance.
- 00:47:32will follow suit of Medicare and the US preventive services task force so basically now everybody by and large, should be covered, who has insurance or has Medicare age 45 and above.

- 00:47:46 And by the way for older adults, although I'm not going to get into this much but for older adults it's really about a discussion and life expectancy and again this is for average risk with an older adult.
- 00:47:58 Has a family history, they themselves have had cancer polyps that surveillance not screening, we talked about screening we're talking about people are average risk or not high risk.
- 00:48:09 So what about school based test, this is something we've known about since the early 90s, as I showed you in that timeline and it turns out, it works so even a very simple test which isn't the best test.
- 00:48:20 Has a 30 some percent reduction in mortality, this was shown in a Minnesota colon cancer control 30 year follow up study they look 30 years later, people who had fecal cold blood testing that's using old school Wyatt testing.
- 00:48:34 which a number of us used to use for colorectal cancer now fecal immuno chemical test is really the main thing not quiet base but quiet place showed a 32% reduction.
- 00:48:46 In colorectal cancer mortality, that is quite good for a test that's really not that good so there's no excuse for people to get no testing, in other words there's no excuse for people to at least at a minimum get a fecal called blood tests using fit testing.
- 00:49:04 And it doesn't work in the office, so we can't just check the patients in the hospital or check them in the office by digital rectal exam smear.
- 00:49:14 The the sample and see if there's any microscopic blood this study showed that at home, a six sample test of the old school Guayaquil at about a 24% pickup advanced neo pleasure.
- 00:49:27 But in the hospital or in the office only about a 5% meaning doesn't mean you shouldn't do rectal exam.
- 00:49:33 You can do a rectal exam to check a prostate if you think there might be a lesion there or, if you think someone might be actually GI bleeding.
- 00:49:40 If someone has melanin what i'm talking about is doing a rectal exam and checking the school for microscopic occult blood as a screening colon cancer screening modality it doesn't work with just a single digital rectal exam, it has to be an at home test.
- 00:49:56 Well, we were talking about fit this is a fecal amino chemical test that detects the globe and loyalty of hemoglobin.
- 00:50:03 It doesn't require dietary modification, it has to be done every year, and it also can be quantified and this is actually quite a good test.
- 00:50:10 It has a food sensitivity in this Meta analysis of 70% and a specificity and 94% for test that's really inexpensive it's about \$20 that's really easy to do.
- 00:50:22 is actually fairly good 70% is not bad and a specificity and 94 is actually pretty good as well, so again no excuse.
- 00:50:31 That we're not doing some form of testing and a fit test is perfectly adequate as an alternative to colonoscopy And what about the DNA, so this is a.
- 00:50:41 Little video that was created, years ago, almost 20 years ago and the initial DNA testing looked at 21 point mutations in the mutations we talked about when I started this presentation that occur when a polyp is turning cancer and K Ras and ABC and.

- 00:50:58 It looks at microsatellite instability that accumulation of those genetic mutations we talked about and DNA integrity, but the concept being as a polyp grows in this video it's going to shed cells and those cells might be able to be picked up in the stool as it moves forward.
- 00:51:16 So when the first data came out, we were really excited to see, not surprisingly it's a very specific tests, because you're picking up DNA.
- 00:51:25 But unfortunately as a screening tests and have very poor sensitivity, only about 50% it was an expensive tests as expensive as calling us be was not covered by.
- 00:51:35 Insurance it really looked like this test was dead in the water, but they did something really smart what they did is they took the DNA and they added the fit.
- 00:51:45 So now you have what we call a multi targeted tests which took that same DNA type testing and added the communal chemical testing to it.
- 00:51:53 One that I just showed you had a pretty high sensitivity to begin with, and a row, and even a higher specificity and combine them, this is the color guard test is the test, you see advertised on TV.
- 00:52:04 Where you're looking for fit and DNA it uses to gene methylation markers seven K Ras mutation markers and fit and it actually has a much better sensitivity for cancer sensitivity that 20% higher but note.
- 00:52:18 Is that the fit is actually doing the heavy lifting here that still is about 74% effective similar to the data I just showed you on fit.
- 00:52:26 polyps it's doing better picking up polyps not great.
- 00:52:30 42% that's Okay, but this is not a polyp detection test, this is a cancer detection test, we have to recognize the difference we're calling asked me is really a polyp.
- 00:52:40 removal and a cancer detection this really isn't looking for polyps.
- 00:52:45 The other problem is that the specificity is lower, because we've actually ratcheted up the sensitivity and this is important because the incidence of colon cancer for any screen individually is relatively low.
- 00:52:56 So we actually see a lot of false positives and, of course, causes panic, not only for the patient.
- 00:53:01 But for the doctor when they do the colonoscopy and they don't find anything on the colonoscopy very often will go back to make sure we didn't miss something.
- 00:53:09 So there is a lot to understand, about the color guard test it's a good cancer detection test and it's only mediocre for finding POPs should not be used for patients, finding POPs Oregon for anybody at high risk.
- 00:53:22 CT colonography is really a cool name, when you say virtual colonoscopy but it requires the same prep a small tube is putting the rectum and the colon is inflated an air is used as a contract a contrast and then CT scan is done, the three dimensional configuration has made.
- 00:53:45 The 3D reconfiguration makes these beautiful images.
- 00:53:50 And it actually isn't bad for polyps it picks up polyps over six or seven millimeters over 85% of the time that's not bad.
- 00:53:59 So this will not only pick up cancer, but also larger polyps, the problem is, all the other stuff cat scans pick up, and we know this to be true just in our own scans of our own patients.

- 00:54:09 If we were to refer every patient who had a polyp over five millimeters then almost 20% after the CT colonography are going to need to take another prep and they're going to have to have a colonoscopy to find and remove the polyp.
- 00:54:21 If we look for every color every extra colonic finding over half a page.
- 00:54:41 issues are going to have a lot of other stuff and we're exposing patients to very small mouth radiation.
- 00:54:46 And many patients are still going to call and ask me so, this has not really picked up the way.
- 00:54:50 It was hope when it was first developed but it's still there is a tool and, by the way, it's an excellent tool for patients who have an incomplete colonoscopy for one reason or another.
- 00:54:58 Either have a very torturous colon adhesions from prior scarring or maybe there's actually an obstruction from a tumor this can be used at the day of a colonoscopy to look at the part of the colon that wasn't visualized on colonoscopy.
- 00:55:14 So how do we know colonoscopy is effective.
- 00:55:17 Well, this was the national polyp study that was done in 1993 they looked at about 1500 patients and they said, what are the expected numbers based on things like our sphere database, the Mayo clinic data St marks that on the right.
- 00:55:30 You could see that the expected number of cancers were much higher than the actual observed cancers, which is the solid bold line on the bottom.
- 00:55:38 By 76 to 90% so by doing a colonoscopy and removing polyps there's a 76 to 90% reduction in colon cancer that's pretty significant.
- 00:55:50 And what's great for anybody who's involved in outcomes research it's really important to follow your database because.
- 00:55:56 It becomes even more powerful as time goes on, and 20 years later, the same group said when we're an answer and colleagues.
- 00:56:04 took that data and they looked at the number of that somewhere they expected to see 25 deaths, they saw 12 deaths, so the good news is it's a 53% reduction.
- 00:56:13 The bad news is it's only a 53% reduction if we're thinking that all cancers come from polyps and removing the polyps why isn't it 100%.
- 00:56:23 Well, there are a number of reasons that have been proposed one, this is a high risk cohort from beginning, because these patients already were known to have polyps.
- 00:56:31 too is that technique is improved greatly finding these flat tops that we talked about and three is that we can't find every polyp and we have to do better.
- 00:56:40 So I think if we were to repeat a study like this now, the rate would be significantly more reduced, but not yet zero and that's why we do have to do better.
- 00:56:51 Well, we have tried to follow the route of other successful screening modalities mammography and pap smear which is on the top the very top line is pap smears the.
- 00:57:02 middle line is mammography these are in the 70 to 90% screening rate and the bottom line is colon cancer screening, which since the year 2000 has been dramatically increasing.
- 00:57:13 And while that's been happening, this has been a real public health success story we've seen a decrease in incidents and mortality and colorectal cancer, something we should

all feel very proud of that we're able to really impact this disease by decreasing incidents and mortality.

- 00:57:30and public health is comes in interesting ways and unfortunately Jay Monahan.
- 00:57:35Who was diagnosed in 1997 from colon cancer passed away just nine months later, from this disease and his wife Katie Kirk who was cohost of the today show, at the time.
- 00:57:47decided she had to do something about this, and she went on the air and had our own on air colonoscopy.
- 00:57:53which was quite dramatic at the time, because and morning TV you're not talking about colonoscopy and stool and bow preps.
- 00:58:02But Katie and the producers actually Jeff zucker was the producer at the time, and he actually a survivor of colon cancer and that that is public knowledge.
- 00:58:11There was a lot of interest to try and do something about it and boy did they do something.
- 00:58:16it's as if people went and ran and got their colonoscopy in the year 2000 when she had a colonoscopy you almost never see this type of break here just a break in the curve.
- 00:58:27Where Katie had her on air colonoscopy and 20% more people ran out and got their colonoscopy and it was sustained.
- 00:58:34So when you get someone who is a trusted source of information, and they have such a loss and they go through this themselves.
- 00:58:42as a role model, it becomes a real asset to medical people like all of us trying to get the word to our patients as an example, they can show that they can do it if it can happen to them, and they can get a colonoscopy any of us can as well.
- 00:58:57Well, brings us to Virginia and the Kirk sister Senator Kirk was a State senator for Virginia.
- 00:59:04In 2000 and she decided that she wanted to put legislation and to make sure it actually mandated colorectal cancer screening and have not been done before.
- 00:59:14And Senator Kirk work with one of your own faculty David Johnson has been a role model and mentor for me.
- 00:59:21he's on your faculty he is a past President the acg he's a real icon in this field and It just shows the power of the two of them getting together and they wrote this legislation.
- 00:59:31That health care services shall provide coverage for colorectal cancer screening under any such policy contract or plan delivered this was a game changer and I have to thank.
- 00:59:41Senator Kirk unfortunately has passed away for pancreatic cancer and Dave Johnson, and all of you who may have been involved in putting forward this legislation that changed for the country.
- 00:59:52And in fact this is the photo of Governor Jim Gilmore at the time, signing the legislation with Emily Kurt to his left and Dave Johnson to the right a real team effort.
- 01:00:03And unfortunately, you could see how thin Emily Kirk is in this photo she was diagnosed just two weeks later with pancreatic cancer and I know you have a name.
- 01:00:17Center for in her name and also a lecture series for the acg and the Kirk sisters have really changed the face of colorectal cancer by screening and public advocacy.
- 01:00:30Now, what about the increase in young patients, so I mentioned that screening, he was dropped page 45 here's the reason why.

- 01:00:37 If we look at the statistics, we could see that for younger patients eight zero to 49 years old, we see an increased incidence and mortality in both.
- 01:00:47 colorectal cancer and rectal cancer for age 50 to 64 we are seeing a nice decline and then a little bit of a leveling off, it is still declining, but not to the same rate.
- 01:00:59 And then for older adults, aged 65 and over we're really winning the war and colorectal cancer these graphs continued decrease but something's happened, where we actually see a increase risk.
- 01:01:12 of incidents and mortality for younger patients.
- 01:01:17 And we don't see that in older patients and truthfully we don't know why now I don't want to cause too much alarm whenever you look at graphs like this it's very important to look at the y axis we look at the 65 and up.
- 01:01:28 We see rates per hundred thousand 100 200 300 if we look in the middle, we see 25 50 75 and on the top with the youngest it's two four.
- 01:01:41 And six OK, so the numbers are not the same, the graphs are positioned Similarly, but the numbers are still much, much higher for those 65 and over, but the trends are going up for younger patients.
- 01:01:53 When we put it on the graph like this, we could see by birth cohort now our younger adults are way low in the incidents, but the graphs are going up.
- 01:02:03 Whereas our older adults are much higher incidence and numbers, but the graphs are coming down.
- 01:02:08 And the question is one of these going to overlap when are we actually going to see younger people starting to have higher rates overall numbers of colon cancer as we started eradicating more of the older individuals with colorectal cancer, for both the colon and the rectum.
- 01:02:23 So why is it increasing and younger adults, well, we don't really know can be a change in the microbiome and overuse of antibiotics.
- 01:02:30 All the diet that we eat that has processed meats and sugar carbohydrates fat obesity decrease physical exercise, the truth is we really don't know.
- 01:02:40 What we do know is that young colorectal cancer presents for the rectal bleeding.
- 01:02:44 And also distilled disease, so we cannot attribute in younger adults in their 20s and 30s.
- 01:02:50 Any rectal bleeding just to hemorrhoids really have to make sure that they get appropriately evaluated and, if necessary, a colonoscopy.
- 01:02:57 there's data to suggest that young adults get diagnosed three to six months later, because people attribute rectal bleeding to other causes and don't consider colorectal cancer.
- 01:03:07 And it's not all because of genetics, we talked about genetics at the beginning of this talk, but only 20% of these young folks actually are associated with the germline mutation.
- 01:03:17 And those that did have the mutation about half didn't even have a tip of family him family history.
- 01:03:23 And one in four had not even first degree relative to have colorectal cancer, so we need to really expand our genetic criteria, I think all patients who are young.
- 01:03:33 In the 30s and 40s who get colorectal cancer should be genetically tested and, by the way, notice, we have lynch syndrome and a PC.

- 01:03:41me why ah, but also brought up may have an increased risk and in one study broccoli showed a relative risk of anywhere between 1.2 to 1.4 so family history is really important, I think we need a much lower threshold of genetic testing.
- 01:03:55So we're doing a great job I've shown you the curves are improving, how can we do better.
- 01:04:00Well colon asked be finds polyps as shown here, but what happens if the polyp is hitting hidden behind the phone.
- 01:04:07colonoscopy also Mrs polyps and we find that it's very operator dependent in this study dating back to 97.
- 01:04:14Doug REX looked at different operators and found the penny on who's doing the procedure depends on how many polyps or miss, meaning that there's technique.
- 01:04:22and skill involved not just the procedure itself and for polyps greater than one person, one centimeter which are significant POPs he found 6%.
- 01:04:31Miss rate at that point, but an overall miss rate of about 25% that's a lot of POPs we're not finding and that's why as societies we've been really focused on quality.
- 01:04:40You have to start with what we're doing and doing the best way now what I'm showing you I love cars, I mentioned that before, this is a 1968 chevelle malibu convertible has a 327.
- 01:04:51Small block engine with four barrel carburetor and a dual exhaust, this is what quality was represented automotive industry in the 60s it's just it exudes it loses quality.
- 01:05:06We could do the same doesn't have to be a car, we could do the same and, obviously, our ability to care for patients, much more important than any car, no matter how beautiful, it might be.
- 01:05:16We want to look at how many adenomas we pick up per patient that's called an anomaly detection rate.
- 01:05:21how long it takes to withdraw the scope, so we don't withdraw too quickly the technique use, making sure people know what they're at an omen detection rates are.
- 01:05:29So they can do better, or there can be intervention to make sure that they get up to the standard that others have and making sure that the prep is really high quality and split between evening and morning.
- 01:05:42So this is a picture I can see by show hands there, how many people see a picture, but I can tell you it's a picture of a cow.
- 01:05:50What is interesting about this picture is that when I was moving out of my home, I had not seen this picture for about 30 years.
- 01:05:57And I had my son with man, I say Oh, this is that fun picture of a cow, he says, I don't see a cow.
- 01:06:02And 30 years later I haven't seen this picture I still saw the cow, meaning that we have to know what we're looking for here's the head here's the body.
- 01:06:11Now, hopefully, you all see the picture of the cow that's just the way the brain works, we need to be trained what to look for.
- 01:06:17So, once you see the cow, we can start recognizing that through these flat lesions that we need to see when we do colonoscopy.

- 01:06:24 This was a real pivotal study in 2008 that looked at flat lesions and said they're up to almost 10% of a population in a va population that they did spray die to find them, they did a double prep and they train their.
- 01:06:40 Their endoscopy this how to find these and so flat lesions I showed you before can be very difficult to find and can represent 20 to 35% of cancers.
- 01:06:50 may be harder to see may not believe so, they might be not be picked up by fecal mito chemical testing.
- 01:06:56 They may be more difficult to remove and there's data that almost 30% of some of some of these larger polyps.
- 01:07:02 Almost 30% of them have some residual tissue and that's why we're trying to train or in darkness, to make sure they go back six months later, after a large part that's removed and pieces, to make sure it's fully eradicated.
- 01:07:14 And like I showed you the hyper methylation may actually accelerate the process, so we have to make sure we follow our proper intervals for these lesions.
- 01:07:23 So where are the flying cars what's the technology I showed you that beautiful chevelle but where are the flying chanel's now.
- 01:07:30 So can technology bail us out well we're making all these design changes on our scopes we're putting cuffs.
- 01:07:36 In that video you saw those little purple fingers that was on this device that I was using here called an endo cuff, we have balloons on scope to try and straighten the folds and we're using Ai.
- 01:07:47 And the colon is actually a pretty long and windy type of structure which has some blind spots, so we really could use some technology to help us, starting with a good quality exam.
- 01:07:59 And when we look at mechanical versus optical can we put more lenses versus something like the cuff, the pullback the fall, the data suggests in this Meta evaluate a Meta analysis actually mechanical enhancement works, a little better.
- 01:08:13 This is a video of using that endo cuff and there's going to be a tiny little polyp that you're going to see come into play on the right I'm.
- 01:08:23 I will let you know when it when it pops up you're going to see it on the right there I don't know if you could see my arrow.
- 01:08:30 But I'm circling it here, and it could only be seen because we're able to remove these little faults I'm not sure you can see it yet.
- 01:08:38 And I'm going to move the video and show you that we have a snare out now and that lupa wires coming out and you'll see the polyp that its surrounding this pop is about four millimeters or so.
- 01:08:49 And we push the snare out down and then we're able to grab normal tissue This is called a cold snack session excision no heat is needed when it's so small, and it looks like a Friday I call this the Friday technique.
- 01:09:03 Meta analysis looking at Ai shows a 44% relative increase that anomaly detection and a 70% relative increase that until.
- 01:09:11 At noma per colonoscopy as in this diagram on the right, what Ai does is it actually will highlight the polyp and say look over here it's like someone tapping you on the shoulder and say look over here.

- 01:09:26 Well, what about other things that have been developed well we've used robots and this flexible robot that you see on the right.
- 01:09:33 is like flying the space shuttle which might allow us to bring a robotic scope and do not only better diagnostic but even better therapeutic even potentially remove surgical.
- 01:09:43 specimens like a colon cancer, and if you recognize the robot on the right that's the robot from the original lost in space TV series, and you haven't had a colonoscopy and you recognize that robot you need to get a colonoscopy.
- 01:09:56 Anyway, the title of the talk when there's a fork in the road take it.
- 01:10:00 we've talked about both invasive and non invasive testing the best test those the one that gets done, and now I want to end the last few minutes just telling you about some of the really cool things that's been worked on in non invasive testing.
- 01:10:13 So we have molecular markers DNA RNA the microbiome and breath testing for volatile organic compounds all being looked at.
- 01:10:24 molecular markers would be picking one pencil out of a series of others which what's different about this marker and although it may not be.
- 01:10:33 Great for screening, it may be helpful for staging response to treatment assessing metastatic disease.
- 01:10:40 And these markers may be growth factors and angiogenic genes factors gene expression methylation markers as we mentioned.
- 01:10:47 microbiome microsatellite instability and others so we're always looking for markers that can point us to a tumor but also using precision medicine, say, how can we best treat it.
- 01:10:58 selfie DNA is really exciting and it's, not just for colon cancer is for breast and kidney and lymphoma and head and neck.
- 01:11:06 And in colon cancer in this diagram here, you can see that, although the numbers look pretty good in the 75% range for Stage two, three and above.
- 01:11:15 Stage one is what we want to find and that was only in about the 20 to 30% range just looking at self for DNA but we've come a long way if we had machine learning.
- 01:11:25 or potentially proteomics we can get to 85% sensitivity using machine learning and Ai emerged study they got up to 94% early stage sensitivity in this pulmonary study.
- 01:11:37 We are now working collaboratively with many centers and we should have actually completion of a very large study looking at blood testing for colon cancer using DNA machine learning protein biomarkers at the genetic phenomenon.
- 01:11:51 And that should be completed, hopefully, within the next month, so i'm really looking forward to seeing that data.
- 01:11:56 RNA has a lot of different aspects that are being looked at, although it's not quite as far along as the circulating DNA.
- 01:12:03 And the microbiome is interesting because the microbiome changes from just the polyp.
- 01:12:09 To an advanced at a moment to cancer is there a way for us to check a micro biotic fingerprint or signature and that way may actually be through snippet.
- 01:12:19 now turns out that dogs can detect colon cancer and this study is one that we quote a lot.
- 01:12:25 was done in Japan, where they trained it dog to sniff colon cancer, and if you put five samples of stool in front of a dog and one of them had colon cancer, the dog can pick up.

- 01:12:36 On in this tool sensitive in 97% colon cancer, it would sit it's trying to sit in front of the sample so if a dog sits in front of somebody at an airport either they're carrying something or they may have colon cancer.
- 01:12:48 they're both bad, so I think that this is telling us something and, if anything, is going to save humanity it's going to be a dog I'm a big dog lover.
- 01:12:58 It doesn't look like this, but I found this picture on the Internet, I had to use it as an electronic knows if I was to.
- 01:13:04 If I was to make an electronic knows it would look like this picture on the left, but actually there isn't electronic knows that people are.
- 01:13:10 Working with which has a sensitivity in the 70 to 80% range and a specificity in the 67% range.
- 01:13:18 getting closer and closer to some of the early Guayaquil data that we had so I'm actually excited we may be able to do a breath test, for example, not a fecal test and see whether or not we can detect adenomas in cancer.
- 01:13:32 So back to that case this 52 year old had a colonoscopy at age who had a negative colonized page 40 with a family family history, what do we do.
- 01:13:41 Well, for those of you who love my cousin vinny I love this this movie it's a trick question.
- 01:13:47 Because this patient has a family history, a significant family history, and although genetically his mother was never found to have something.
- 01:13:55 He is at high risk and he needs to undergo colonoscopy every five years that's the recommendation so actually this is someone who needs, not a test for like a fit or color guard but someone who's at higher risk and need to colonoscopy so I show you this.
- 01:14:17 picture, again, I hope you actually see the head and the body of the cow, but this cow also can say sometimes if you really look at these images they start talking to you, and this kind of saying something very, very important.
- 01:14:32 Go hoos.
- 01:14:34 So, in summary colon cancer screening is preventable fit and calling us be a really tier one quality colonoscopy is.
- 01:14:42 Most important, that we have a lot of technology in the hopper that we're looking for the best test is the one that gets done take the fork in the road but make sure that when we do it, we do it right, with the best possible.
- 01:14:55 Quality and again the best test that gets done so with that I will end, and just say it takes a team to eradicate colon cancer, this is my team here at nyu and for those of you who ever watch looney tunes a colon looks very awfully like what they use.

UVA IMR Chiefs

01:15:27 ever seen me a colon like that, before.

Mark Pochapin

01:15:30 yeah you never see it again.

UVA IMR Chiefs

01:15:35 Yes, please darker questions in the chat and then or ask them you didn't get your question directly.

- 01:15:41 I'll just get it started, though I you know I wasn't aware that the sensitivity for the fit test for you know facade polyps was so low, but really the sensitivity was just there for colorectal cancer screening.
- 01:15:55 Do you feel like most providers kind of appropriately understand that difference and how it differs from a colonoscopy for screening diagnostic purposes.

Mark Pochapin

01:16:05 It's a great question, I think the answer is no, unfortunately, which is why we all need to really understand.

- 01:16:11 and actually the old guidelines he says split the test into those that prevent cancer versus those that the tech cancer truthfully I like that better because colonoscopy is a cancer prevention and fit and every other test color guard.
- 01:16:26 Are and CT colonography are really cancer detection test so unless we can find the polyp to the same level, we can find it on colonoscopy.
- 01:16:37 It's really a cancer detection so different countries have different strategies, I didn't have time to go through the data, but if you look at data from Europe.
- 01:16:46 Their mortality from colon cancer is dropping like ours, but they're incidence is going up or incidents is going down because, by and large we're using a colonoscopy prevention modality.
- 01:16:56 Their instance going up because they're using a fit cancer detection so though they're finding cancer early and preventing death from it.
- 01:17:03 Who wants to have cancer, you know you'd like to prevent it, so there is a very important difference also some people look at fit testing.
- 01:17:11 And calabar as a two stage test if it's positive, it must have a colonoscopy thinking that philosophy actually is, this is the ultimate test that everybody gets but some I get there in two stages and some I get there, and once.

UVA IMR Chiefs

01:17:26 Dr Shaw says, I find one of the biggest hurdles to convince people to get screening screen is the prep is this your experience.

Mark Pochapin

01:17:32 Yes, 100%.

- 01:17:35 And that's why I use it even in that example the patient that's a real pitch application did not want to get another call and asked, because he hated the press.
- 01:17:42 The good news is we are working on a prep we're working on a food prep and we're trying to make it so it's more palatable, but it is the biggest hurdle, on the other hand.
- 01:17:52 People recognize the benefit and how common colon cancer is and how we could prevent it usually people are willing to take the prep once every 10 years, but it is and honestly.
- 01:18:04 When people do it it's not that bad it's not painful it's just annoying and you know, hopefully, will come up with a better mechanism for prep.

UVA IMR Chiefs

01:18:14 Excellent um so Questions for Dr your sheet is excellent talk is always mark, can you speak to call it, our two, which is now in trials which may have higher specificity.

Mark Pochapin

01:18:23 yeah so calabar two is kind of in that same camp of what I was showing you with some of the blood tests and actually the people exact scientists are science are working also looking at blood testing they're trying to expand and looking into different cancers as well.

- 01:18:40 That is preliminary you'll probably have a higher sensitivity, the issue in my mind is specificity, is that we're getting a lot of false positives and causing a lot of panic so.
- 01:18:51 If the specificity could elevate as well that's going to be really important we're going to have to look at that data and also.
- 01:18:58 A lot of different companies are looking at blood testing, I honestly believe this fork in the road that I'm talking about blood testing is going to be a reality in next year or two and whether it's going to be the folks that make cola guard or other companies but it's out there.

UVA IMR Chiefs

01:19:14 And she had another question, can you also speak to the new update that colonoscopy will now be covered in insurance patients after a positive still based test, when will this start and will this include Medicare Medicaid beneficiaries.

Mark Pochapin

01:19:26 yeah So these are great questions you know I mentioned advocacy and how that can lead to disparities, this was a huge problem because previously someone had a colonoscopy they found the polyp.

- 01:19:37 And then, it was filled as a therapeutic intervention not diagnostic also now they got a copay when they were initially been screen.

- 01:19:44 We were able to act actually with all of your help in the medical community and honestly it's taken us over 10 years we fix that what I call glitch.
- 01:19:53 So now, if you have a polyp that can still be covered as a screen, but this is the next glitch so now someone gets a fit.
- 01:19:59 Now they say oh it's a positive fit it's now a diagnostic test turn therapeutic because we got to look at why they're bleeding why they're having a cold bleeding.
- 01:20:08 So there's a new update that fix that I don't know when that's going through I'm very excited again public advocacy is so.
- 01:20:14 Important I, as I said, you all know that, because your public advocate Emily Kirk put coverage on the map, so this is just an extension of what we saw with polyps and now looking at fit positivity as a diagnostic positive test, not a therapeutic intervention.

UVA IMR Chiefs

01:20:34 And then one more question since it's one but can you speak a little more to your approach to the young patient with rectal bleeding who gets a colonoscopy especially bouncing because the cost conscious care and maybe issues with insurance coverage for the younger patients.

Mark Pochapin

01:20:49 Right so there's bleeding and there's bleeding any patient who has rectal bleeding should be evaluated.

- 01:20:56 In the office with a rectal exam and it just doesn't have to be done by a gastroenterologist looking for a source do they have a hemorrhoid do they have a Fisher if I see something bleeding.
- 01:21:06 it's done in other words, I see a hemorrhoid I see a Fisher but if I don't see a source of bleeding.
- 01:21:12 And it's real bleeding they move their bowels they're seeing staining of the toilet water it's either around the stool or MIT in the stool, even if I do a black exam that's negative if they're telling me they see bleeding.
- 01:21:23 I think they should be referred for a colonoscopy I just think the risk is too high.
- 01:21:27 And the procedure typically in a young person is so well tolerated that it's not worth the risk and truthfully.
- 01:21:33 We don't see that much rectal bleeding and younger adults and young adults don't have that much hemorrhoids well let's younger women have had multiple pregnancies or people.
- 01:21:42 have other GI issues, so I think it needs to be evaluated, but without finding a source Actually, I have a very low threshold of course I'm biased, but I have a low threshold for colonoscopy.

UVA IMR Chiefs

01:21:53 Right and so much towards one on three appreciate your time and answering the questions that fantastic presentation.

Mark Pochapin

01:21:59 It seen everybody hope to meet you all in person someday soon.