Dr. Kendal Williams: Welcome everyone to the Penn Primary Care podcast. I'm your host, Dr. Kendall Williams. So we're back with another series of great episodes, and we have a wonderful schedule here for the fall. And I thought we'd start out with a big success story, one that affects us all. We now have virtually universal screening for hepatitis C.

And Hepatitis C has been a real success over the last, 10 or 20 years. So I brought on two experts to talk to us about it. Dr. Vin Lo Re is an associate professor of medicine Penn and also a professor of epidemiology and biostats. He is the co-director for the clinical core of the Penn Center for AIDS Research and does a lot of work with Hepatitis C as well. VIn thank you for coming.

Dr. Jessie Torgersen is an assistant professor of medicine at Penn. She is the clinical director for the Center for Viral Hepatitis at Penn Presbyterian Medical center.

And with Dr. Lo Re as a member of the Division of Infectious Diseases at Penn. Thanks, Jessie. So, this is a very interesting subject because we all know something about Hepatitis C, but even I have found, and I try to keep up with these things, that things have progressed so quickly in the last, 10 years or so, that it's been a little tough to keep up.

But I wanna start with the basics and just go over the virus itself, how you get it, how common it is, and so forth. And Jessie, maybe we'll start with that. How does one get Hepatitis C?

Dr. Jessie Torgersen: Yeah. A great question. So, hepatitis C is, predominantly transmitted through exposure to infected blood and into a lesser extent, to exposure to bodily secretions. The most effective way for hepatitis C to be transmitted is really through that blood exposure. And that's really where we saw a lot of the risk, drived in our, birth cohort or baby boomers, those born between 1945 and 1965 with prior exposure to blood products that may not have been screened effectively for hepatitis C. Up until about 1992 when rigorous screening was really implemented.

But this is also why we've seen hepatitis C emerges really a major concern in people who inject drugs because blood containing the virus can contaminate not only needles and syringes that are used to inject and potentially shared, but can also and contaminate materials used to repair drugs, including water filters and cookers. Additionally, hepatitis C can be transmitted via non injection drug use through again, bloody contamination of straws and pipes.

And the potential for that contamination to be virus inoculated into mucosa that

has been traumatized either through snorting or, smoking drugs. and then contributing to that acquisition. Other means, as I alluded to the, bodily secretion so we can cease transmission through sex, although it's relatively ineffective. Sexual transmission, again, and heterosexual sex and non discordant couples, is pretty rare. Somewhere between, less than 0.07 percent per year. Where we do see a bit higher risk with sexual exposure or sexual transmission is among those who have unprotected anal sex, multiple sex partners or, chem sex where there may be a disinhibition with regards to barrier protection and such.

So, that's one of the reasons why oftentimes men who have sex with men or people who engage in chem sex are recommended for more regular screening. Lastly, I think transmission can. Perinatal infection and this is becoming more and more recognized, but currently estimates suggest maybe about 6% of pregnancies with Hepatitis C will result in infection in the baby.

Dr. Kendal Williams: So the people at risk are primarily those with a history of intravenous drug use, but those other groups that you mentioned, what are some of the cohorts that we're seeing now other than the baby boomer cohort? Is there another group that's sort of at risk?

Dr. Jessie Torgersen: Yeah. I think you hit the nail on the head with people who inject drugs or, people with, substance use disorder. We're really seeing that this distribution of, people with new infections, or newly recognized infections is really at a. Bimodal distribution across the age groups. With a really impressive peak over the last 10 years in people between, 18 and 45 and really owing to the explosion of the opioid epidemic. So, our clinic population is, certainly, a representative of that. Where a half are our young people whose major risk factor is injection drug use or substance use, while the other half are, those in the birth cohort.

Dr. Vincent Lo Re: I should just add that, new hepatitis C infections in the US have nearly tripled since 2010. And as Jessie alluded to, really driven by the opioid epidemic, and particularly in persons who were, between 20 and 40 years of age, so a much younger group.

Dr. Kendal Williams: And we'll see that cohort, continuing to progress through the stages. So, let's talk about the natural history, because it's a virus that usually doesn't produce acute symptoms, right? And most of the problems are down the line. I don't know that I've seen that much acute Hepatitis C, but both of you have, What is it like?

Dr. Vincent Lo Re: Yeah, so, It could really span the spectrum from asymptomatic, to a clinician will identify fluctuations in liver amino

transferases to, in very rare cases, acute hepatitis C, can go on to ful hepatitis. So, given the fact that, it's such a spectrum and the fact that in 55 to 86% of individuals with acute Hepatitis C, they will go on to chronic hepatitis C infection. And then that chronic hepatitis C will lead to liver inflammation, liver fibrosis, and typically about 20% of individuals in 20 years with hepatic fibrosis will go on to cirrhosis.

And then once you get cirrhosis, you're at risk for primary liver cancer, paracetic carcinoma, and end stage liver disease decompensated cirrhosis, but, 14 to 45% of individuals who are exposed to hepatitis C and get acutely infected will spontaneously clear. And so when you see these patients in clinical practice, you'll see that their hepatitis C antibody is positive, but their hepatitis C RNA is negative with no history of antiviral therapy.

Dr. Kendal Williams: And you said that that numbers about 15% will clear?

Dr. Vincent Lo Re: Yeah, I mean it's generally about 15%, about 85%. I mean, the range is anywhere from 55 to 86% will go on to chronic, and the range is around 14 to 45% for spontaneous clearance. but typically, the rough rules are 85 and 1585 will go on a chronic infection in 15 will spontaneously clear.

Dr. Kendal Williams: Yeah, you know, I remember this 15%, just even going back 15 or 20 years, when I learned about Hepatitis C, it was, 15% would clear. Now you can correct me on this fan, but 15% of those who do not clear will go on to cirrhosis. And then there was something like, 15% of those who become cirrhosis will develop hepatic cellular cancer. Maybe you can correct me on those numbers.

Dr. Vincent Lo Re: Yeah, you're close. Typically, about 20% of individuals in 20 years will develop cirrhosis and then once individuals with chronic hepatitis C have cirrhosis around two to 4% per year will develop primary, liver failure, hepatic decompensation. And that's characterized by the complications of cirrhosis, so things like ascites, spontaneous bacterial peritonitis, varial hemorrhage and hepatic encephalopathy.

Dr. Kendal Williams: And what's the time course here from say, infection to cirrhosis in those who are going to develop cirrhosis, I mean to advance cirrhosis.

Dr. Vincent Lo Re: Yeah, usually it takes about seven years to advance each stage of hepatic fibrosis. So, typically we're talking about 25 to 30 years after acute infection that a subset of individuals will go on to advance hepatic fibrosis or cirrho.Is.

Dr. Kendal Williams: Yeah, when you hear the numbers, it's surprising because of course there are a lot of people with hepatitis C, but the, prevalence in that population of cirrhosis is very high. and yet you also have this very long window in which you can intervene, which is of course why we have you on this podcast today to talk about this, Because we can intervene. right?

Dr. Vincent Lo Re: That's the beauty, because in 2014, really the advent of all oral, direct acting antiviral agents completely revolutionized how we care for chronic Hepatitis C, and it's one of the few, as you alluded to in the beginning of this podcast, amazing success stories that we can now cure with 95% plus likelihood a chronic viral infection. So to recall in my early days, treating people with 48 weeks of pegulated interferon and riboviron, and all of the attendant severe adverse effects to now in essence, an eight to 12 week duration of antiviral treatment with almost no side effects. All oral easily tolerated is really, the holy grail of a chronic hepatitis C treatment.

Dr. Kendal Williams: Yeah, it's remarkable. So I wanna spend a, fair amount of time on those treatment regiments, but I wanna go back and actually there was a few questions that people had asked me and the one to capture, and that was interestingly, some of the questions about what hepatitis can do that is sort of extra hepatic, in terms of arthritis, in terms of porphyria and some of these other things, because these things show up for folks as well?

And I wanted to cover that before we jump into the regimens. You both have some experience with the extra hepatic manifestations of hepatitis C. What's real in that and what's not real?

Dr. Vincent Lo Re: Jess, do you mind if I take this just because we've done a lot of research in the area. The thought Kendall is that the chronic, inflammation that is associated with hepatitis often is associated with release of cytokines and that these cytokines really have a number of untoward effects in organ systems outside the liver. And the combination of this chronic inflammation and the cytokines can induce damage in the kidneys, damage in the coronary arteries. Our group has done a lot of work actually on, you mentioned, arthritis, and we've done a lot of work on, bone disease and have demonstrated that in high resolution peripheral quantitative CT, that in essence there is endothelial thinning of cortical bone in patients with chronic hepatitis C compared to uninfected controls.

Mimicking a pattern that is seen in other chronic inflammatory disorders. So, and does appear that more hepatic inflammation may be implicated as a worsening factor associated with greater extra hepatic complications. So I think

it's this combination of chronic hepatitis, chronic inflammation and the cytokine release that's really driving a lot of these extra hepatic complications. And what we have seen in clinical practice and what we're studying right now as to sort of the biology of this, is that cure of hepatitis C does appear to ameliorate these extra hepatic complications and it leads to people having improved cognitive function, reductions in bone and joint disorders improvements of skin abnormalities. So, these are additional off shot benefits from antiviral treatment, not just directed at the liver.

Dr. Kendal Williams: I had a patient years ago, 20 years ago, I was just out of residency as one of my first patients in practice and he had hepatitis C and I don't even know if he'd gotten interferon. It was very new. And you know, he had terrible arthritis and we could never really figure out why nothing really was effective. He would go to Jamaica and just sit on the beach and spend months on end just sitting on the beach because the only thing that would make him feel good.

And now looking back, I know that, he just had all of these extra articular or extra hepatic manifestations of hepatitis C I think, and that was, really devastating for him at the time. So we talked about the natural history, developing a dys, cirrhosis and hepatocellular cancer. And then you just answered a question I had and that was whether or not these extra hepatic manifestations, the risk is reduced and we'll get to how we screen and monitor people who have been treated who still have, some residual cerotic damage.

But let's go back and just talk about the screening. It seems it's universal. I don't actually know the laws out there now in terms of, the standards are for screening for Hepatitis C, it almost see all my primary care patients. It comes up as a flag, as something to do. There may be some standards behind that. Jessie, can you speak to that?

Dr. Jessie Torgersen: Yeah. Yeah. So as you mentioned, screening is now, recommended by, both the Center for Diseases Control but also the United States Preventative Service Task Force. And in 2020, they both organizations recommended Universal one time screening for all adults US PSTF recommended up 18 to 79. And this really speaks to the need to transition away from risk based screening since we really found that about 50% of people were being missed with that risk based screening. Now, how does that translate into laws for screening? Is still a bit state specific.

Currently in the state of Pennsylvania where we practice there's a state mandate on the books from 2016 Act 87, which mandates offering of screening for Hepatitis C and linkage to care for those born in between 1945 and 65. So it

hasn't yet caught up to the current recommendations for screening all adults. State of New York. Has similar mandates, but again, varies by each state. It, is certainly since it's endorsed by the CDC and US Preventative Service Task Force. It's reimbursable as part of that care and really is as critical to identifying people before they develop those more severe end stage manifestations of hepatitis C cirrhosis and hepatocellular carcinoma.

And it's really helps to reduce stigma by just offering this test to every adult since people either may not recall risk factors or maybe reluctant to disclose those factors due to stigma. And it also takes away any clinician concern about, you know, is this person truly have hepatitis C if there's no, amino transfer free elevations, or trying to find whether or not there's an indication to screen somebody by putting out these universal recommendations. Particularly look with lft changes, we know, about a quarter of people with hepatitis C will have persistently normal immuno trans raises.

So helpful to have this universal guideline. Beyond the universal one time screening. There's certainly people who should have ongoing, assessments for Hepatitis C exposure. This is often people with those risk factors we discussed previously. So those who inject drugs or men who have sex with men, people on hemodialysis. And additionally, the American College of Obstetrics and Gynecology also recommends Hepatitis C screening with every pregnancy. So you'll likely see obstetrician screening their patients more frequently too. And so that's really, I think where the screening is coming into play to try and become a more regular assay in routine healthcare.

Dr. Kendal Williams: And so there's two tests, right? So the first is an antibody screen followed by an RNA PCR, is it an automatic reflex now?

Dr. Jessie Torgersen: Yeah, that's preferred. And, as you can imagine it, you know, the reflex is needed to confirm if somebody has current infection that is with detectable Viremia or past slash spontaneously cleared infection with no detectable viremia. So most laboratory assays, most commercial laboratory assays will have an option for a hepatitis C antibody IgG or total with an automatic reflex to a PCR assay. And this is often quantitative, so you get a, viral load amount with that assay.

And what's important to know is that, depending on where the potential exposure may have occurred it's important to understand the potential window period for those antibodies as well. We know that antibodies can take maybe about two or three months to really develop following exposure. And so this would be a standard screening test to complete an antibody with reflex to viral load if that antibody's reactive. However, If somebody had an exposure within

that window period, then potentially going straight to a viral load would be helpful since breia can be detected much sooner, about a week or two after that exposure.

Dr. Kendal Williams: So this is where you guys are gonna help us peak behind the veil because in primary care we'll do a screen we'll get a positive test. An antibody test, a reflex PCR is positive. Patient has active, albeit maybe indolent hepatitis C and needs to be seen. So, Jessie, let's say we send this patient to you. What do you do? What happens then? This is peeking behind the veil a little.

Dr. Jessie Torgersen: Yeah. My first visit is often, the pre-treatment evaluation. And this is really to take an opportunity to talk to the patient about hepatitis C transmission, Hepatitis C, natural history and talk about these amazing curative therapies that we have. Particularly talking about the anticipated treatment duration. The optimal, treatment outcomes with strict adherence. And also to set the stage for the challenges that may lie ahead, particularly with prior authorization of medications. Part of that pretreatment evaluation, a critical part I think, is to really assess the degree of hepatic fibrosis.

And fortunately, we don't require liver biopsies these days. So since we have a number of noninvasive modalities to assess liver fibro, and what we do here at our clinic is to assess liver fibrosis with transient lastography. And that gives us a nice point of care test with a quantitative number that correlates to the metavir stages of fibrosis with F4 being cirrhosis, F0 being essentially normal liver. So that's generally the first part of that at the, at the pretreatment evaluation. I also make sure that people have been screened for other bloodborne pathogens, specifically HIV and hepatitis B because of those. common routes of transmission.

Additionally we've had a hepatitis A outbreak in Philadelphia for the last couple years with transmission noted to be via percutaneous routes too. So viremic people are transmitting, often through injection drug use. So we'll also assess for hepatitis A as both Hep A and Hep B serologies can inform, our vaccination needs. And lastly if we do see people co-infected with hepatitis B, specifically those with detectable surface antigen that, may impact, how we treat them because, they're somewhat antagonist, if you will, hepatitis B and hepatitis C infection. And so once we treat hepatitis C, there's the potential for a hepatitis B flare in that setting. So some patients weren't initiation of hepatitis B therapy in that setting prior to Hep C treatment.

Dr. Vincent Lo Re: I think one of the things that you're getting a sense of Kendall from Jessie's response is we do a fair amount of education at the initial

visit because most of the patients that we see, they don't know anything about Hepatitis C. They don't have, they generally don't have any symptoms. They're not really clear totally why they're presenting to us. So really spending the time, as Jesse had said, to really go over what is hepatitis C? How might you have acquired it? What is it doing to your liver and to organs outside of your liver?

Assessing about alcohol use and how this critically important co-factor can further damage the liver and really doing a good medication reconciliation to, to look for what possible medications might interfere in the form of drug interactions with the antivirals really critical in addition to all the laboratory studies that she mentioned.

Dr. Kendal Williams: And you mentioned lastography, and this is a new thing, right? So many of us weren't exposed to this in residency. Can you go over what this is?

Dr. Jessie Torgersen: Yeah, it's, a point of care test. It's, been available since around 2013 in the United States. And more and more, liver clinics viral hepatitis clinics are starting to try and access them because of the availability of a relatively reliable point of care, fibrosis assessment. So this is patients need to be fasting for at least three hours. If they're not, that any food can actually increase the blood flow to the liver and falsely elevate the fibrosis readings from that transient lastography. But basically it sends sound waves through a pulsitile probe to get a measure of how elastic or how stiff that liver is. And using a proprietary calculation can, measure that, sound wave flow, to, come up with a quantitative value of that fibrosis.

And so that's incredibly helpful. A rapid test. Noninvasive, it's, unfortunately not currently approved for women who are pregnant, or people with pacemaker or defibrillator. But otherwise quite reliable, taking about five, 10 minutes max to complete. It again gives us a, point of care printout right away, and it gives us a measurement that's essentially calculated over a mean of 10 individual measurements. So quite reliable to get a sense of not only how much fibrosis is there, but that stage as well.

Dr. Vincent Lo Re: I, would just add that, you know, because we're talking about, determining liver fibrosis, it's actually an incredibly important part of chronic Hepatitis C evaluation because you really wanna identify individuals with advanced hepatic fibrosis and cirrhosis. Because those are the individuals that you really are ultimately you really wanna make sure that they're gonna get antiviral therapy, but these are the individuals that, as primary care clinicians, you wanna make sure that they are gonna be monitored on an every six month basis for primary liver cancer, hepatistatic carcinoma. These are the individuals

that you're really gonna wanna refer for upper endoscopy, to monitor for Varicies.

And these are the people that you really wanna make sure that you are evaluating for decompensated liver disease. And there is what's called a child turcot pew score, that's based on the presence of encephalopathy societies. Biliruben, the albumine cutoff, INR cutoff that you really want to make sure, because if these individuals are manifesting laboratory findings or signs of decompensated liver disease, then hepatology referral is really crucial in these individuals.

Dr. Kendal Williams: So let's talk about treatment, and I wanna come back to this afterwards, sort of the post-treatment management, because then we're gonna have to, you know, this whole question of how much damage is there to begin with and who needs to follow them after the treatment and so forth. But let's talk about the treatment regimens. You know, those of us who followed this from afar a little bit. went through the interferon. Petulated interferon phase and then various regimens that were genotype specific. But now it seems that the most effective regimens, it doesn't seem to matter which genotype you have. Is that right?

Dr. Jessie Torgersen: Yeah, there's fourth, first line, direct acting antiviral regimens, that are available. And two of those are pan genotypic. They cover all genotypes from one to six. And what's nice is that, most insurers have at least one of those pan genotypic regimens on their formulary. So, it's easily accessible and pick that, regimen for our initial treatment. I think what's important when thinking about treatment too is, thinking about, who should get treated, which is really just about everybody. And really the only people who should not be treated are those with a life expectancy less than one year, from non-liver related disease processes.

I like to highlight this because there's still providers that think there needs to be a period of abstinence among people who with substance use disorder or people with ongoing alcohol use disorder. And we really know that people with substance use disorder can certainly achieve cure rates as high as those without, so really not a reason to withhold treatment in that setting.

Dr. Kendal Williams: And this is one of the reasons I wanted to have you on because this has progressed so much. A lot of us have these sort of. Ideas in our head from previous sort of intermediate stages, if you will, of the treatment paradigm where you had to be selective. And of course, there was a toxicity associated with each of the regimens and so forth. So now knowing that you know that pretty much universally effective and universally tolerated, it changes

the whole dynamic.

Dr. Vincent Lo Re: These direct acting antivirals have heralded in for the first time, the opportunity that, potentially Hepatitis C could be eliminated as a public health problem.

Dr. Kendal Williams: I was reading a little bit about the Egyptian experience as I was preparing for this, and apparently it was 20% of the Egyptian population had Hepatitis C and, they, have made great strides towards eliminating it in the population.

Dr. Vincent Lo Re: Yeah, as has the country actually, of Georgia, has done, and also just really focused the attention on the public health infrastructure given the high prevalence in that country as well.

Dr. Kendal Williams: So, just digging down into the regimens and talking about them again, we don't have to go through the specific regimens. It's probably not important that all of us know these, but just to know that it's a 12 week regimen relative, it's all PO, it's all nontoxic. What else should we know, Jessie, about this?

Dr. Jessie Torgersen: Of the four regimens, they're all, combinations of at least two drugs. And these are just for reference purposes, NS3/4A protease inhibitors or NS 5B preliminary inhibitors, NS5A directed inhibitors, and these combined are anywhere between eight weeks to 12 weeks for a treatment duration. With that duration, dependent upon which regimen is, selected largely, they are incredibly well tolerated with the most common side effects that I quote to my patients are things like, Headache, GI upset and fatigue. With really fatigue, I think being the most common at around, anywhere between the 15 to 30%, depending on the regimen.

Headache I think is probably one of the lesser side effects that are, in that common realm anywhere between five and 10%. So I find that the fatigue is something most of my patients notice, but with that advanced counseling, advanced warning they notice it and say, Oh, that didn't bother me. And I've had nobody who's discontinued their direct acting antiviral regimen because of these side effects. So, again, incredibly safe, incredibly well tolerated, and fortunately, incredibly effective.

Dr. Kendal Williams: And then if you have somebody come back, they've completed their eight to 12 weeks, what's your next step? What do you do then?

Dr. Vincent Lo Re: I think Kendall really depends on whether or not they're,

cerotic. If an individual is not erotic and achieves cure there's really no follow up recommended for non-erotic patients. You just wanna make sure you're advising them against, excess alcohol use and particularly if they're at risk for Hepatitis C reinfection, which can occur just because you have hepatitis C antibody, it's not protective against reinfection. We spend a fair amount of time counseling on risk reduction, and for those at risk, we're typically testing for hepatitis C RNA annually, or at any point if they come in with elevated liver immuno transferases.

However, if the, if an individual is after treatment, cerotic and achieves cure even in that individual, we're continuing to perform liver ultrasounds every six months for a hepatacilic carcinoma. Surveillance we're referring them for upper endoscopy to evaluate for varisies. We're doing the same kind of risk, counseling on risk reduction and really making, sure in that subgroup, those patients with cirrhosis, that we're advising abstinence from alcohol.

Dr. Kendal Williams: And you know, we all know that within the cerotic group there's people with early cirrhosis that just may, even if we're doing an ultrasound, we'll see early cirrhosis even without any other manifestations. But those people need to be followed too, even if their INR'S normal, their albumin's normal, they don't have any varisies and so forth?

Dr. Vincent Lo Re: That's absolutely correct.

Dr. Kendal Williams: And you know that from Elastography, right? So a certain level of fibrosis tells you that a patient is cerotic even if they don't have any other manifestations, right?

Dr. Vincent Lo Re: That's exactly right. It certainly, technically cirrhosis is a pathological diagnosis. Obviously, as Jessie mentioned, we're not doing liver biopsy, so we're looking either with elastography or in some instances, it will be identified on abdominal imaging where either an ultrasound or a CT or MRI may note cerotic changes in the liver.

Dr. Kendal Williams: So some of these you're gonna send back to us and say all good. Nothing to do, just watch the Tylenol all dosing, watch the alcohol, watch any risk factors for being reinfected. What percentage would you say are in that stage that they leave and they're done and there's nothing else to do? I don't know if there's data on this. This might be just an estimate off the top of your head.

Dr. Vincent Lo Re: I would say that for probably the majority of the people that we see who do not have advanced hepatic fibrosis, cirrhosis, they're done.

And we in essence, discharge them from our practice. It's just the individuals who really we continue to follow who. unable to achieve cure, in which case we go to an alternative regimen or those individuals have advanced fibrosis cirrhosis, in which case, we continue to see them even after they achieve cure for all this kind of monitoring.

Dr. Kendal Williams: Jessie, anything to add there?

Dr. Jessie Torgersen: Yeah, I think, about 20% of our patients coming into the clinic for hepatitis C treatment are cerotic. And, certainly I think that number has held as natural history, discussion mentioned. And so really that's really the patient population that we'll continue to follow to ensure that HCC screening is completed every six months. And while I also counsel my patients that. Nice with Hepatitis C. Cure is that progression of fibrosis from Hepatitis C is arrested, once that cure has achieved. And in about maybe 40, 45% of people can actually see some improvement in that degree of fibrosis. Yet even if on Elastography following Cure they're no longer erotic they still warrant those ongoing hcc screening ultrasounds until we have more data to suggest otherwise.

Dr. Kendal Williams: Yeah, I'm glad you brought that up, that was a question of, what do you do with the patients that improve over time and so forth. so that's very helpful.

Dr. Vincent Lo Re: Unfortunately, at this point there's no hard and fast rules as to when to stop this surveillance. Basically we have to count the pre hepatitis C treatment, liver fibrosis staging. And we're still, as Jessie mentioned, trying to figure out what are the parameters, the findings that may herald when we should stop surveillance for complications of cirrhosis and, hepatic fibrosis assessed, and unfortunately we're not there yet.

Dr. Kendal Williams: I think it's a key point for primary care physicians that if somebody comes into our practice, they've been treated and maybe we have a CT image that shows that they're cerotic, that these folks if they need to be monitored every six months for hepatic cellular cancer. Because that's, a trigger, that we need to follow those people.

Dr. Vincent Lo Re: Indeed.

Dr. Kendal Williams: So it strikes me, with the tolerability of these regimens and sort of the ease of this approach. We could potentially take some business away from the two of you. That some of this may migrate into primary care over time. There may be some models of that already that I'm not aware of,

have been discussion of Hep C treatment within primary care?

Dr. Jessie Torgersen: Yeah, I think that's a wonderful idea.

Dr. Vincent Lo Re: Yeah, I mean there has been, I mean, I sat on the National Academies of Science, Engineering medicines Hepatitis, B and C elimination committee, and we acknowledged very, very early on in 2017 that if we're gonna have any hope to eliminate Hepatitis C, we simply don't have the capacity. If you're just gonna rely on either hepatologists or infectious disease practitioners. And I think we're already beginning to see even at Penn, in some practices where primary care clinicians are taking up the mantle to treat hepatitis C. And we're all for that. And I think unfortunately plenty of patients with Hepatitis C that are still around, and as I mentioned with the increase in incidents of acute hepatitis C and the opioid epidemic, we need all the help we can get.

I think the other thing to know is that we're always certainly available to provide advice to clinicians just in terms of questions or things that might come up to, to help them get through. I think the only challenge with implementing Hepatitis C care in the primary care setting is the prior authorization requests that the insurers are asking to be completed, to demonstrate medical need. They can be fairly time consuming to get around. But if you have the infrastructure and the staff to assist, it could help you get over the goal line.

Dr. Jessie Torgersen: Yeah, I have to agree. I think treating hepatitis C within primary care really decreases those barriers that may be insurmountable for patients to access that care if they had to go to another provider or location. So it's a welcomed introduction and base for, to have primary care here. And, with tools like the HCV guidelines, on the org website, it really is quite easy to select a hepatitis C regimen particularly for those treatment naive patients without cirrhosis or chronic Hepatitis B. And there's very, easy streamlined strategies, to really minimize any monitoring that's needed, short of cure, to be assessed, three months or 12 weeks, specifically after completion of treatment.

And as been mentioned, I think from a logistics standpoint, that prior authorization challenges is really the time consuming aspect of delivering Hepatitis C care in the clinic. And so if there's somebody that can address prior auth needs, some of the unique asks from each insurer with regards to that pretreatment evaluation. To have that medication approved can help patients navigate the potential need to use a mail, order specialty pharmacy and stay on top of those refills.

That's really, I think the legwork that's needed. It's really not selecting which

regimen, you know, if you're able to do that, med evaluation to evaluate for drug drug interactions, counsel the patient, really that, subsequent step with approval that becomes burdensome.

Dr. Vincent Lo Re: Yeah, and I mean the HCVguidelines.org, the way we have created it where, a practitioner could determine is the patient treatment naive or treatment experienced? What is their genotype? Do they have cirrhosis or not? It's very menu driven to facilitate implementation of Hepatitis C care in practice. And sort of new this year, we've introduced simplified approaches for those with and without compensated cirrhosis to further enable clinicians to be able to incorporate hepatitis C care in their practice.

Dr. Kendal Williams: It would seem that it ensures best interest to make it easily accessible. One of the challenges with insurance is that people don't have the same insurance for that long. And because they switch around, the insurer who pays for the Hepatitis C treatment is not necessarily the one that's gonna benefit from it in the reductions long term. But as we can get everybody on the same page about this, it would make sense to make it as easy as possible for everybody to be treated.

Dr. Vincent Lo Re: Yeah, I mean, if you think about the price and cost of complications of cirrhosis and advanced liver disease and hospitalizations and transplants, and to be able to prevent that with an eight to 12 week course of therapy. that has, over 95% chance cure, I think is fairly amazing and it's multiple studies now have come out showing the cost effectiveness of these regimen.

Dr. Kendal Williams: Well, one other question before we close, and that is, what if somebody does fail? You'd mentioned 95%, so there's a small percentage of people who do fail a regimen. Do you try then another regimen?

Dr. Jessie Torgersen: Yeah, so there is actually salvage regiment out there and the one that we often reach for is a combination of three of those medications, Vosevi being the brand name having the NS 5A direct inhibitors the NS 5B carnase polymerase inhibitors in, one of the protease inhibitors. And that's generally a one pill once a day for 12 weeks for treatment for people who have failed. One of these earlier DAA regimen. There are other agents out there to either use an extended duration of some of the other agents and for those who fail beyond that, some very limited data driven recommendations to use a number of combinations with or without riboviron as well. So still options out there to treat treatment failures after those initial treatment regimens.

Dr. Kendal Williams: I would imagine that it's virtually a hundred percent in

eventually finding, a regimen that will cure.

Dr. Jessie Torgersen: I think so. Vin has certainly had more experience than I have so far. Vin is at a fair assessment?

Dr. Vincent Lo Re: Yeah, I was gonna say just on the guidelines, we discussed some of the more challenging cases. And the number of multiple failures is exceedingly low because so many people are ultimately curing with the first round, first regimens and as Jess mentioned, the Vocevi, VosaSphere of Voxel Avir is so highly potent, and successful that it's really rare that with any of the first, and the second line agents that we can't cure anyone.

Dr. Kendal Williams: Well this has been a terrific discussion. I really appreciate both of you. coming on. It's actually, been an education for many of us. I don't think we realized how, much progress has been made. I certainly didn't. So before we leave, is there anything that you wanna say to the Penn Primary Care community?

Dr. Jessie Torgersen: I would say please use us as resources as you, look to take on hepatitis C treatment. We are always available to help provide insight in how to make that a successful endeavor in your practice.

Dr. Vincent Lo Re: I think you said it all, Jessie.

Dr. Kendal Williams: Well, thank you, Ben. Thank you, Jessie. and thanks to the audience out there for listening to another Penn Primary Care podcast. Please join us again next time.