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HIV LUNCH AND LEARN SERIES: HIV UPDATES FROM CROI 2024

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[video transcript]

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great. Well, thank you, and it's a pleasure to be here. I definitely need to shorten that bio in the future, but I have had the privilege of working at Johns Hopkins for more than 25 years, and have been a part of the effort to improve outcomes in people with hepatitis C. And it really all starts with hepatitis C screening and pre treatment evaluation. So I want to really get into that over the next 45 minutes or so, and hopefully leave some time for discussion. These are my financial disclosures. These are the learning objectives for today. We're going to talk about how to identify people for whom screening is indicated. The punchline, there is screenings indicated for everyone in the United States. We'll talk about the testing algorithms, and we'll list the components of the pre treatment evaluation of people with hepatitis C. So let me start by getting into the rationale for screening recommendations and Hep C and how that ties into Hep C elimination, I think, as many of you know, in 2016 the who made it, what I think was a very bold proposition, they challenged countries and society to eliminate hepatitis C as a public health threat envisioned in a world where hepatitis C viral, where viral transmission was halted and everyone had access to safe, affordable, effective care. So specifically for hepatitis C, what they wanted to do was see a 90% reduction in chronic hep C infections treatment of 80% or more of eligible persons, and if that were to be achieved, that would lead to a 65% reduction in mortality. We'll talk a bit about this, but you can see the issue if we look over in the bottom of this PowerPoint figure in 2015 they estimated there were 170 5 million new cases, and the 90% reduction would come down to 175 and the number of deaths would come down from nearly 400,000 so a lot of work to be done, and there has been some progress made in a number of countries already meeting these metrics, including countries like Iceland and Egypt. In the

United States, we've gotten off to a little bit slower start, but we have, as Francis Collins put it, in this Jama viewpoint and historic opportunity to eliminate hepatitis C's of public health throughout the United States. And this is literally in front of the United States Congress for funding, but it really starts with the identification of people who are infected. That is screening. Before we even think about things like Linkage to Care, we've got to get people diagnosed, and we'll talk a bit more about that. So just as a quick level setting on hepatitis C this is primarily a blood borne pathogen. I'll talk a little bit more about that. After someone becomes infected with the hepatitis C virus, the virus enters the liver cells, begins to replicate. So what you can see in the panel to your left is that within a couple weeks after exposure, you start to see the viral load, or hep, C, RNA, go up. Alt levels also climb, typically after the virus level, and then in some people, they will clear the path of. Okay, they'll no longer have chronic active hepatitis C infection. So the RNA is negative, but you'll note that the antibody test listed here as anti HCV remain goes up and remains positive in the people for whom they don't clear, and that clearance occurs in about 25% as high as 40% of people, but for people for whom they don't clear, figure in the right they RNA becomes positive and remains positive beyond six months, and remains positive really indefinitely, until that person is successfully treated. But you'll notice in both cases, the anti HCV test is positive. So acute clearance positive antibody, acute onto chronic positive antibody, with the difference being in the RNA. You'll also notice in the kind of jagged line towards the bottom that the alt can pop into the normal range with chronic infection. So Alt can't be used for chronicity. To test chronicity, it has to be RNA. We'll come back to that point. So the CDC data was updated in 2021 for the United States, and these are risk factors that were identified in people with acute hepatitis C infection, and I mentioned earlier that it's a blood borne pathogen. You'll note along the top of this figure that injection drug use that ranks as the most commonly identified risk factor. A number of people had missing data, of course. So what this means is that when we talk about the opiate epidemic, when we talk about the opiate mortalities and fentanyl mortalities, we need to remember that needles used for injection drugs can transmit hepatitis C quite readily, more transmissible by blood than HIV. So other factors on here, you'll see sexual risk factors also occurring. Hepatitis C is expected to transmit pathogen, particularly among men who have sex with men, less efficiently transmitted in other settings, needle stick exposures, some exposures through transfusion, but fortunately, the blood supply has been screened since 1992 if we look at the issue of acute hepatitis C, I mentioned that the goal was to reduce the number of new infections by 90% the who wants to see this number going down? Francis Collins in the US national plan, I want to see this number coming down, but indeed, that's not been the case. What we have seen dating back to around 2010 has been a steady, persistent increase in the number of new hepatitis C infections. So reported to the CDC in 2021 was 5000 new infections. They do some modeling to assess, well, okay, what is the real number? And that's around 70,000 there was just a paper published that indicated 84,000 people were treated in the most recent year that they were able to get data from the CDC. So think about it, if we're treating 84 and we have 70,000 new infections, we're really not making progress towards elimination because we're failing on

that goal of new infections. I also want to point out that there's been an increase among black, non Hispanic Americans really, in the last couple of years, rising relatively dramatically. And in fact, you'll see that we expect that number to continue to increase, because it's the sharpest line we're seeing here among different racial and ethnic groups. So we really do need to identify people with active hepatitis C, because that is how Hepatitis C is transmitted. This shows the data in a bit of different way, men and women. And I want to make two points in this slide. One is that you're seeing in the two kind of peaks. This is the baby boomer generation in the now listed as 60 to 70 years old men predominant in both settings. But you'll note that the number of women in the 20 to 40 year age group is substantially higher, and now the peak of chronic hep C is actually greatest in 20 to 40 as baby boomers get treated and have other cause of mortality. Now, one of the consequences of women of childbearing age acquiring Hepatitis C is that there is a substantial. Initial increase in mother to child transmission and Perinatal hepatitis C, which is increased 21%

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so looking at a bit of a different way that the prevalence hepatitis C among women and people who are pregnant is continuing to increase that's shown here in the figure to the right, and the heat map of the US kind of shows you where maternal hepatitis C infection is being identified, and it tracks very well with where we're seeing acute hepatitis C cases. So this has really been something that has come to the fore of many clinicians that we need to pay attention to people who are pregnant and move towards testing. We'll talk a bit more about that. Now, of course, what we worry about with Hepatitis C is the potential progression of liver disease from fibrosis to cirrhosis, and once cirrhosis develops, we can see things like decompensated disease, ascites, varices and liver cancer. So the goal is to diagnose people early when they're at this end of the spectrum, the early fibrosis, and prevent the progression to cirrhosis over time. So certainly that's one of the reasons we want to diagnose people as soon as we can, because they age with this pathogen, they could have more disease. Now, one of the problems, and these are data from the MFWR in 2000 when they looked in the NHANES survey, where they people enrolled in this national survey gay blood they were identified to have hepatitis C, they estimate that about 40% were unaware of their hepatitis C infection. Now other estimates suggest these numbers are increasing, but because chronic Hepatitis C is largely asymptomatic, people are unaware that they are infected, that many people don't know they have the infection until they are tested. So people don't walk into a healthcare setting and say, I would like to be tested because I feel X, Y or Z. In fact, it's quite the opposite. Many people assume that because they don't feel sick and because no one's mentioned it to them that they must be okay, and it really does require a proactive testing approach. Now, before the updated guidelines for screening was done, the there was a systematic review and a look at the evidence of what could happen if we screened more people. So this was an analysis that was done before the recommendation for all adults in the United States to be screened. And what the researchers showed published in 2020 was that sustained virologic response or cure was associated with a decrease in all cause mortality, a

substantial decrease in liver cancer, by 70% reduction. And so if we screened all persons, either identified 256 additional people infected have cured 80,000 additional cures and 4400 fewer cases of liver cancer. And in this modeling, identification can be very cost effective. So these are the recommendations that currently exist in the HCV guidelines, and I'll talk a bit more about the CDC recommendations one time opt out Hep C testing for all individuals 18 years or older. And then testing should be performed in people younger than 18 if they have behaviors, exposures or other circumstances that put them at risk. So examples of that might be a baby born to a mother who is Hepatitis C positive, a person with recent or any injection drug use in the past, or a number of other factors that might lead to infections, such as men who have sex with men, particularly those who are HIV infected. So the one time testing applies to people without ongoing potential risk for infection, but annual testing is recommended for all persons who are actively injecting drugs and all people with HIV infection, particularly men who have unprotected sex with men, all pregnant women should be tested. That's also been updated in the US guidelines, although, as you'll see along the bottom, the US premise services task force recommended screening from 18 to 79 they put an upper age limit on that and the CDC when they. Recommended screening pregnant people with each pregnancy, they talked about regions with low prevalence of type C, but I think there's a growing consensus that we should be testing all pregnant people, because it's very difficult to apply prevalence data the way it's suggested in this particular slide. So this was the publication April 2020, where the recommendation was for essentially testing all adults, 18 to 79 including pregnant persons, independent of any signs or symptoms of HCV infection, independent of any identified risk factors. Routine testing, this was given a Grade B recommendation, ensuring that payers would cover this. They do recommend regular testing in people with ongoing risk factors, and the evolution is shown along the bottom of the slide with this arrow, we've gone from blood and organ donors to risk based testing the Baby Boomers to now all adults. This is the consensus recommendations for testing during Age pregnancy. And I think this is something that really is an important step if we're going to control and understand how to prevent mother to child transmission, because if we stop and think about the CDC data that I shared earlier, we're at a time where we're actually seeing More newborns and young children under the age of five with hepatitis C than really any time in the last 20 years. That number is going up when indeed we want to eliminate hepatitis C, particularly among newborns and children. So let's talk about approaches to screening. The screening test really have been fairly consistent over time. There is an antibody test, and as I tell patients, this is your immune memory of the infection. And we anticipate that most people once infected, whether they undergo a spontaneous elimination of the virus that is spontaneous clearance or treatment induced cure, they will remain antibody positive. In fact, I was in clinic yesterday, and one of my consults was the woman who had been cured more than 10 years ago, who was very concerned that she had recurrent hepatitis C because her antibody test was positive, that was a very quick, easy

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situation to rectify by checking HDR name, but it is the first line screening test. Now there are rapid tests that could be done at point of care with results that come back in roughly 20 minutes, and a reactive test indicates current or resolved infection and is the primary screening. But there is really a much greater emphasis on testing all positive antibodies for a RNA. Now, the patient I described did not have a reflex RNA testing on her antibody. So she came to me with a lab report that said anti HCB reactive. It did not have reflex RNA testing, so we had to send her back for another blood draw. It is important that HCV RNA testing is done when the antibody test is positive. Now, there are some circumstances where you may want to screen with RNA if you have someone with recent infection. If we go back to that figure, I showed RNA positive around two weeks, antibody positive as early as two or three weeks, but sometimes as late as four to six to eight weeks, depending on the circumstances, maybe slower and people say, for example, with HIV. So if you're concerned about acute hepatitis C and the anti HCV is negative, you would want to test with RNA as a screening modality. That would be a good example of where you'd use HRNA first. Now this is what I alluded to. The CDC recently updated their kind of advice, if you will. They said that all samples collected should have HCV RNA testing performed automatically when the antibody is reactive. Automatic testing happens in the laboratory on the same tube of blood that was sent to them. This allows for a single visit to conduct both test parts of the screening sequence. So that that patient, I'll go back to the patient I saw yesterday. So. If we had had a automatic reflex testing, then the information that that patient got in the MyChart app would have said, antibody reactive RNA not detected. That would have been reassuring to her and reduced the period of concern. So this is the CDC has supported this and is working with laboratories across the United States to implement this. And many of the large commercial laboratories are already doing that. What they want to do is they want to eliminate the ability to order the test that is anti HCV independent of the reflex testing. So in the future, you would not have the option to order just the antihcp antibody. And the idea here is we want to link people. We want to get people diagnosed so we can link them to care and receive curative therapy. So this is the algorithm, if the test is non reactive. Already talked about a couple areas where you might use RNA for when you with acute Hep C, where you think that might be important, but if the test is reactive, RNA testing is done. If it's not detected, there's no current infection. And in general, you can tell that person that they had hepatitis C in the past and had cleared initially enough we're seeing at our community based screening events where we do point of care testing. More people that have been treated coming back and getting tested for antibodies. They want to be screened again. And I would strongly discourage that. I tell people who have been successfully treated, please don't get an antibody test if your healthcare provider recommends it, tell them that you don't need to be screened for hepatitis C and that this is not a way to confirm that you're still cured, if you will. If the RNA is positive, of course, that means a current infection. It doesn't distinguish acute versus chronic, and we'll come back to that point in a minute, but it does mean that the virus is actively replicating in the liver, and that person needs medical care for hepatitis C. And this is just a lot of what I've talked about in terms of interpreting the results, and I think that, in general, we've covered most of this,

so it won't be labor, but it's just nice way to summarize it. But I also do want to emphasize what the CDC says to do with current ATV infection. That's the third line down on this table, is provide the person with appropriate counseling. We'll talk about that and link the person to care and treatment. Anyone with an active HCV infection should go down that pathway of receiving appropriate counseling and appropriate care. Now, people who have cleared the infection the top row in this table, I'm sorry, the bottom row in this table, they are at risk for reinfection. So it's also important to tell people that the positive or reactive antibody does not protect them from future infection. So a great opportunity to discuss harm reduction, and a great opportunity to talk about how Hepatitis C is transmitted, what they can do to protect themselves from recurrent infection. Now, certainly, I do just want to emphasize, if someone does have recurrent infection, we can treat them again. That's not the issue. But the issue is the antibody is not protective. And along the top row, the point I want to make here is there is no vaccine for hepatitis C. There's an effort to study this, and there's been some press lately related to this, but there's no vaccine. Of course, people know there's a hep a vaccine, Hep B vaccine, but I always want to emphasize that there's no vaccine. So the negative antibody tests and the positive antibody tests, but no RNA are potentially at risk. So let's shift to talk about the pretreatment education evaluation. I talked about counseling. I think it's really important with every person newly diagnosed to educate patients about transmission, there is typically a lot of concern about people around them, family members, sexual partners. The CDC has somewhat ambivalent advice about barrier methods and that they say that because sexual transmission can be relatively low that barrier methods for monogamous heterosexual partners is not necessary. I do recommend testing of the individual's partner. That's consistent with the recommendation of testing for all people, 18 to 79 but I think it's also very important, particularly among. Men are sex with men, that we understand that this is a sexually transmitted pathogen, particularly when HIV is present. So a good example of this is people who may be entering a prep program where they're thinking about taking medication to prevent the acquisition of HIV. We want to make sure that we're thinking about hep B and C at that time, both screening and for hep B screening and vaccination, Mother Child transmission. This is something that is we need to be talking to people who have had children, women about their children. Have they been tested? And talking about this issue. And sometimes it's a challenge issue to discuss, but they should be tested, and certainly talking about and linking people to resources in the community, resources for treatment of opiate use disorder, resources for the acquisition of clean needles, equipment and works, and then screening for HIV, testing for immunity, for hepatitis A and B, and facts a if they're not immune. So spending some time to think about transmission and harm reduction, I also talk about alcohol. We're increasingly recognizing the harms of alcohol, and I think it's worth

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assessing alcohol use in everyone with hepatitis C. I tell people with hepatitis C that they the safest advice I can give them is not to drink alcohol. And I do spend some time talking about

what constitute a standard drink shown over here. And although the US Dietary Guidelines are listed and talk about moderation, there's been a big push, if you will, or recognition that the safest pathway a person can take with liver disease, whether it be metabolic associated, steatotic liver disease, hepatitis C, hepatitis B, whatever the liver disease is, the best advice we can provide is to avoid alcohol as a liver toxin. We also talk about nutrition. I talked a lot about this with patients. They ask, What should I eat? And many times the answer is, less we have certainly seen an overlay of what is now known as metabolic associated stenotic liver disease, previously known as NAFLD D or not, called fatty liver disease, and we can see this after hepatitis C cure. In fact, one of the patients I saw yesterday gained 70 pounds in the past five years. He was cured five years ago, and this is a major issue that we're talking about and dealing with. So talking about a healthy diet, in general, a Mediterranean diet is recommended as a the best approach. And then many people ask about supplements, and my recommendation is to generally avoid supplements, because everything is processed through the liver, but it's definitely worth the discussion and asking people to share what they may be taking that they don't see as medications, but as healthy supplements and natural food supplements. So we're spending some time there. It's also worth understanding and taking a step back and thinking about how the stigma associated and maybe drug use that could be linked to the Hepatitis C is impacting their ability to engage for a Hep C workup, and it definitely can be an impediment to successful Linkage to Care. It could impact a number of different factors, and it's really important, when we're talking about treating people, particularly in this 20 to 40 year old group, to really anyone to think about how the stigma impacts decision making and their ability to engage In the care pathway. So creating a safe environment is really important when you're thinking about a program that may help people with hepatitis C. Now the double SLD IDSA guidance panel, it says updated, what they updated since the they have long said that the guidance panel continues to strongly recommend universal da treatment for all people. Now what they changed here is notice they now say with acute or chronic hepatitis C, I mentioned that the RNA test won't tell you is it acute or chronic, and what the guidance panel is saying is, we don't care if someone has active hepatitis C, that person should be considered for treatment, and part of the logic behind that is that people who are actively affected, particularly with acute Hep C, let's say someone acquired hepatitis C. Through reuse of needles that they may be sharing with other people in their social and injection drug use network, if that person has active FDIC if you're waiting for that virus to clear spontaneously, they could transmit the FDIC virus to other people. So there were so it may very well be in their best interest to not wait for spontaneous clearance, to declare itself yes or no, but rather to treat, prevent chronicity, limit the time that they might transmit to other human beings. So the guidance panel now reflects that. So that is something that is new, not waiting to see whether they spontaneously clear. So the recommendations the WsL, DSA has also provided sort of what I'll call simplify guidance. I'll come back and talk about that a bit more with different figures. But what do you really need on day one, a CBC and a paddock function panel. Now I will state that I prefer to get a comprehensive metabolic panel. It doesn't have a direct bilirubin, but it gives me the albumin, alt, AST, the B U N, the Creatinine,

and I find that much more helpful, since I'm going to want to calculate the GFR anyway. They also say they want a quantitative hepatitis C viral load prior to treatment. They don't say it has to be within 90 days or 60 days. They also want an HIV test and a hep, B surface antigen test. Now I'm going to pause for a minute here to talk about what's not listed here. They do not list HCV genotype. The reason why HCV genotype is not on this list is this same guidance panel is recommending the use of Pan genotypic therapy, treatment that works against genotype 123456, if we there's seven, eight, and some people have identified nine, the treatments we have work against all the dominant genotypes in the United States. So they don't recommend genotype testing. It's expensive and can take long to come back. The caveat to that, at least where I practice, is that some payers still require genotype. So if I'm perfectly transparent in my practice, I actually get a genotype on all my new patients, people I'm working up for treatment. And the reason I get the genotype is I don't want to have to call them back and say, I'm sorry. We need another tube of blood. Your insurance company now wants a genotype. I recognize that may not be evidence based practice, but it's pragmatic that we want to get all the blood when the person's with us, particularly recognizing it may be hard to get a file appointment and for some people, particularly those who have been injecting drugs for a period of time, phlebotomy can be challenging. I also want to spend a minute talking about hepatitis B surface antigen the surface antigen test tells us is hepatitis B, hepatitis B active? Yes or No. Critically important, because early in the release of DAAS, it's recognized that when you cure Hep C, when Hep C, the RNA and replication stops, Pep B can flare. So what's going on there? Well, there's been a nice number of elegant studies that have told us that what was happening is in the liver, where you have both Hep C and hep B Co occupying the liver, maybe even the same liver cell. The C is triggering the immune system, the innate immune system in the liver, it triggers the innate immune system, which then suppresses SEPTA. Is B. We're talking about innate interferon and other cytokines that suppress our replication. So when you cure or reduce the Hep C and Hep C goes away, the hep B can now become active again because you've removed that innate immune reaction. And we have some studies where we did paraglimber biopsies that demonstrate that happens as early as a week into treatment. Now, if a person is s antigen positive and on antiviral therapy for hepatitis B, that flare won't occur. So it is important to identify Hepatitis B active infection. There was initially concern about core antibody positivity, so s anti negative. Core positive means old infection. I think the risk of that person flaring is extremely low based on meta analysis, and that's why the panel here is. Comfortable just checking the s antigen. Now, in reality, I checked for the triple panel, anti HB, the surface surfaced antibody, anti HB, core and s antigen, because that's what's recommended. Now, that's a whole different talk about hep B, but it's recommended screening for most adults, and then talking about the risk of pregnancy during therapy. I will mention there are, there are studies being done of treatment of pregnant people in the third trimester, but not, not some something we prefer to avoid during treatment. Now, what about a fibrosis assessment? I'll talk about this a little bit more, but they recommend calculating the FIB for fib four functions very well. There are now more than 4000 papers that have studied fib for incredible it's a remarkably used tool

around the world, not just in Hep C, but in hep B and metabolic liver disease. It includes AST alt, platelet count and age, and I'll show you my formula in a minute. I use the University of Washington website to calculate it. I do this in clinic at times. I'll copy the result and paste it into my uh EMR note. Cirrhosis is generally considered a score of greater than 3.25

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other important issues listed here. I'll come back to cirrhosis. I hope you labor that point here. Medication reconciliation, asking people what they're taking also, including non prescribed medications, are important to understand a drug interaction assessment. This is certainly important, particularly people taking anti seizure medications that may have interactions, and some of these medications may be used as mood stabilizers. And then really talking about adherence, what I tell people is, if they take their medication daily for 56 or 84 consecutive days, take their pills every day. There is an extremely high probability that they will achieve eradication or cure of the virus. So incredibly important to talk about that now, at the same time, I tell people that I don't want them to stop therapy if they miss a dose, pause here and take a quick drink.

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Because we do know, from our own experience and that of many people in the published literature, that while medication adherence is the optimal is daily pill taking for 56 or 84 days, patients can be cured with sub optimal adherence. And many people who practice in the hepatitis C field have stories of people being cured with relatively short durations of treatment, not optimal, but encourage people to continue to engage and talk and persist with the treatment. So I want to go back to fibrosis. Why does it matter? Because it really it determines their prognosis. Multiple studies show with liver disease, people with cirrhosis, even when they're cured, have a greater risk of liver cancer, and surveillance is recommended after cure. So in this sense, I tell patients that I want to know their fibrosis score, and I equate it to miles on a car, so a brand new car, fresh off a lot is a zero fibrosis score. And a car with 150,000 miles on it is cirrhosis. Now that car with 150,000 miles on it could be running beautifully. It could be running great. It could have been cared for, working perfectly, no problems at all. But we also know that if you look at those two automobiles, the one with more miles on it is more likely to fall apart and cause problems. So maybe it's not 150,000 I used to say 100,000 but somewhere in that range where you really have to worry. And I have found that using that comparison to a car with miles on it, most people can relate to that in terms of why cirrhosis matters. The key point, though, is they don't know how many miles are on their liver. You really can't tell until the patient decompensates, and then it's obvious. Everyone can see the problem and they can feel the symptoms, but you have to go looking for trouble. So we used to look for trouble with biopsy, and it's important to recognize that biopsy actually does measure fibrosis. So shown here is these thick bands of scar tissue. Issue in the stage four cirrhotic liver, and in a stage one, there's just a little bit of scar tissue on the portal tracks. So we when we talk about staging, we

really are talking about scar tissue or excess collagen the liver. That's not what we're measuring with the FIB four or the liver elastography. We're estimating what we may see. It's important to recognize that they can be thrown off. A great example with the FIB four. If you look at age older, someone is the it's on the numerator. AST is on the numerator as well, whereas platelet counts on the denominator now, so the higher the AST and the lower the platelet count, the higher the score. Well, if someone is actively consuming alcohol to the point it's causing liver damage, they're likely going to have a low platelet count due to direct toxic effects of alcohol and a high AST, and it may not truly be reflecting fibrosis that said that person needs care, so I'm not concerned about the over diagnosis. Now you'll note this has a square root in it, so I definitely use the calculator. The deliberate E can also be thrown off by eating, so people need to be fasting, and sometimes it can be thrown off by things like right sided heart failure. So remember, we're estimating fibrosis, and even a liver biopsy is just an estimate. So I'll mention just one thing about drug interactions. We could manage most of these. I personally use the Liverpool drug interaction website, I find that to be the most readily accessible to me. There are many others out there that one can think about in terms of using I mentioned the seizure medication used as mood stabilizers, and some concern about acid reduction with all the therapies. So let's talk a little bit more about the simplified guidelines and putting this all together. So the C, the wsld IDSA actually published this in Clinical Infectious Diseases. The reference is there. So they talk about a simplified algorithm. So who is eligible adults with chronic hep C, including people with HIV. Some of you may recall that when they first released the simplified guidance, they said people with HIV, nope, they should be treated to simplify guidance. They changed that because of data from the min study led by Sunil Solomon, my colleague at Johns Hopkins and the AIDS clinical trials group or ACTG that enrolled 40% of the people, 140 people with HIV, and treated them with a simplified algorithm, so any genotype treatment, ie being not previously treated with cirrhosis or without cirrhosis has to be compensated, and this is how they're defining cirrhosis. Liver stiffness greater than 12 on the FibroScan a fib four greater than 3.25 or imaging studies showing nodularity or spin omega. And they also go to say, you know, anyone with a plate account less than 150 be concerned about that. If you think someone may have cirrhosis, you need to think about whether or not they're compensated. We'll talk a bit more about that in terms of calculating the child Pugh score. So who's excluded prior treatment, Hep B surface to antigen positive. It doesn't mean it's complicated. It just means you as a clinician, need to do a little bit more. People with decompensated cirrhosis, defined as the child Pugh, scored greater than seven current pregnancy, known cancer or prior transplantation. Now they also say prior decompensation, someone may have been decompensated in the past to be doing better. Now that's still a person you need to worry about, and this is a key recommendation. So now you can see how we're applying the pre treatment evaluation in terms of moving forward. So putting this all together before initial antiviral therapy, calculate the FIB four, assess for cirrhosis. CBC, I like to see MP, but they recommend hepatic function panel, GFR, medication reconciliation, drug drug interactions, measure hcbrna, for pragmatic reasons, I still do genotype. Check for anti HIV,

check for surface antigen. I check for the triple panel, antibody against surface, antibody against core NS antigen, pregnancy test and counselor pregnancy, and then talk about adherence, prevention, reinfection, that is harm reduction and avoidance of excess alcohol. I'll add that someone with an active. Of substance use disorder. Great time to think about linking someone to treatment for that active substance use disorder. I'll mention that extends to tobacco use. It's a good time to talk about smoking cessation as well, when you're about to launch into one of the most powerful interventions we have, hep, C cured on treatment, some discussion about monitoring people with diabetes, fibroglycemia, but no laboratory testing. Mod required. In person, visits are optional. Phone visits are optional if needed. That's really pretty remarkable, and this is what was studied in the mid mod study, where that's exactly what was done, and people did very well with safety, tolerability, efficacy. They recommend RNA testing after completing treatment. I just wanted to mention a couple other things that you really do want to continue about liver harm reduction messages, particularly in someone with cirrhosis, if cure is not achieved, or if reinfection occurs, really important to treat that in a non judgmental, safe atmosphere where you're just going to talk about, what can we do to make Sure the next round of treatment is effective? Now in this one with cirrhosis, the biggest issue here is that HCC monitoring, or liver cancer monitoring, is needed. I mentioned a couple times child or cough Pugh scoring, this is an old system, but again, I wanted to show just kind of how the laboratory tests get factored in, bilirubin, albumin, INR and people with cirrhosis, is used to calculate. The child Pugh, and a score of five to six is compensated. Anything above seven is decompensated. So you're going to apply these. And there are calculators I like the University of Washington website to calculate accessible to me, so I'm going to stop there, and I'm happy to take any questions or further discussion. And I did add my email, but I'm happy to provide that.

47:12

Dr Sulkowski, thank you for that excellent presentation. I received an email from a mutual colleague talking about the fact that there are no Rapid Start models, and, you know, low threshold harm reduction settings that do not require fib four. What are your thoughts about that? You know, many settings, it's not possible to do phlebotomy, it's not possible to get blood, but you might have a dry blood spot for HCB, RNA,

47:40

yeah. Yeah. I think there, there are some real challenges to Rapid Start, even with the simplified algorithm, which is, you know, what you're what you're posing, which is, you know, I think that it requires phlebotomy and tests that come back several days later when that opportunity is gone. So there were, there's a couple ways to potentially tackle this. There are point of care tests that may be available, but those are expensive and not widely distributed around the US. The most effective models. There's two ways to go about it. One is if there is access to mobile elastography. And if you're able to test antibody, record a dry blood spot and send that up for the RNA testing and perform elastography in a mobile setting, so for example, on a van or even

the clinic, if their score is less than 12.5 you've identified someone no matter what their labs show, there's nothing in the labs that is going to be a problem for treatment. The other debate that we've had is, so what if we expose someone to a week of therapy that was unnecessary while we're waiting for that dried blood spot to be tested. You know, in other words, we go ahead and treat based on the positive antibody and perhaps a low elastography score with a one or two week starter pack. So this notion of a starter pack, I think, is gaining some enthusiasm among people who are interested in Rapid Start. I could say it is not gained enthusiasm with the third party payers that I work with, and we haven't had a mechanism for a start pack quite yet. But it would make a lot of sense. So that's another way to tackle it. The other comment I'll make is that there is this is not related to the Fit For Question, but there is a push with to get the Hep C antigen test approved. The antigen test performs extremely well, very linear performance. Care. Risk with RNA, except at low viral loads. So it you may have a negative antigen with a viral load of, say, 200 or even lower than that, but if your viral loads above, say 200 you know you're gonna the antigen performs very well. So could we get the antigen test number one approved by the FDA, and number two, available for point of care testing, where you've now been able to confirm active infection. If you have that mobile fiber scan, you now know that they're not decompensated, because anyone less than 12.5 is not decompensated, and there's nothing on the labs that are going to steer me away from treatment. Now, I do want the labs back, but I can get the back next week, so I think we can move to the model with rapid start. I think it's essential. I mean, I can't, you know, the number of people I've seen once, and the good news is we eventually get them back. But literally, years have gone by, sometimes where they come back. So I do think Rapid Start needs the attention of the Hep C elimination plan. And like many, I am hopeful that we'll see Congress act on this it. I like to joke it'll just take an act of Congress, but literally anyway, thank you for the question. I'll pause there and see if there's other comments.

51:30

We do have a question that just came in through the chat, thank you. It starts with some kind words. Thank you for the great presentation working with underserved communities. Are you aware of any programs that support costs related to hepatitis C treatment?

51:45

Yeah, there, there's some challenges there. The medications could typically be achieved, be acquired free through either through company support programs, where you really get a bit of trouble is with the HCV RNA testing, the cost for some of the other interventions is relatively low, the CBC, the hepatic function panel, and I will comment the hepatic function panel costs less than the CMP, but where I've seen a lot of community based programs struggle is how to Cover the RNA testing that needs to be done. And I don't have a great answer for that, other than to say that where we've been fortunate. I practice in the state of Maryland, and our Hep C team has been very fortunate to work with, and I see that Jeff has put a comment up. I'll point

your attention to that. But we've been fortunate that we work very hard to transition people who may not be covered by Medicaid to our state Medicaid program, and that's something we could do. So the most important people on our team are really not well, certainly not me, that's for sure. It's our case managers and our nurses are the most important people on our team. And Jeffrey put it into the chat for those of you in New York, there's a program called Hepcat that covers the cost of labs visits and HCV for anyone not eligible for insurance. We need a hep cap here around the country, so hopefully Congress will model the New York plan. We oftentimes are envious of New York, and consider New York to be the leaders in how we'd be thinking about hep C elimination.

53:35

We are certainly lucky. Sorry, I'm trying to copy a link into the chat with a little bit more detail from our colleagues at hepfree NYC on the hep CAP program. So anyone who's interested in learning more about that, please feel free to check it out. In the meantime, please join me in thanking Dr. Sulkowski for an amazing presentation today.

[End Transcript]