Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Welcome to the Speed to Cure webinar.

Tatyana Kushner, MD, MSCE: Hi everyone. I'm Tatyana Kushner. I am a hepatologist at Weill Cornell Medicine. I'm an associate professor of medicine in the Division of Gastroenterology and Hepatology at Cornell.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Hi everyone. My name is Patrick Horne. I am a nurse practitioner at the University of Florida, UF Health, in Gainesville, Florida. I'm the assistant director of clinical hepatology research and clinical programs coordinator.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: These are our disclosures.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: This program is an educational program being conducted on behalf of AbbVie Medical Affairs and Health Impact. AbbVie Medical Affairs and Health Impact is the sole sponsor of this program and authored and approved all content presented. AbbVie Medical Affairs and Health Impact selected today's presenters and is compensating them for today's presentation. This program is intended for health care professionals practicing within the United States and Puerto Rico only, and it is not medical advice for the care and treatment of actual patients who may be under your care.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Our objectives for this evening are here. The aim of this program is to explore best practices for assessing for and treating the hepatitis C infection in nonspecialist settings. There's four sections. The first is the challenge, gaps in HCV elimination; the path forward: simplifying the care cascade; enabling access: the role of point of care testing; and delivering results, innovative models of care.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: First section is entitled, The Challenge: Gaps in HCV Elimination.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: So, reaching elimination in the US, the WHO or World Health Organization's goal is to eliminate HCV as a major public health threat by the year 2030. On the left-hand side of the screen, you can see the 4 goals outlined by the WHO to achieve this. The first is reducing new HCV infections by 80%. The second is diagnosing 90% of HCV infected populations. The third is treating 80% of the eligible population, and the fourth is reducing HCV related deaths by 65%. On the right hand side of the screen, you can see where the US currently is or is not on track to achieve these goals. So currently the US is on track to deliver one-fourth of these goals. So for the first goal of reducing new HCV infections by 80% within the US, unfortunately, HCV infections have increased approximately 64% between the years of 2016 and 2022. For our second goal of diagnosing 90% of HCV-infected population within the US, only 63% of individuals estimated to have HCV have a recorded diagnosis with a confirmatory RNA testing. For our third goal of 80% of the eligible population being treated within the US, currently, only 21.1% of the diagnosed HCV patients has been treated as of 2021. On a good note, the fourth goal reducing HCV-related deaths, the US is on track and HCV mortality fell 28% between the years 2016 and 2021, putting the US on track to meet this elimination goal. Currently three states are on track to achieve elimination by the year 2030.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: This is a map of the world, excuse me, showing which countries are currently on track and which countries are not. The countries in green, both on the map

and over to the right in the box are the countries that are currently on track to achieve the WHO goal of 2030. Unfortunately, as you can see, there's quite a bit of red on this map, including the United States. And these are countries that are not on track to not only not achieve the goal by 2030, but also not to achieve it by 2050. The US in fact, is currently approximately 20 years off track to achieve HCV elimination.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Why is early elimination– early treatment, excuse me, important? Well, it simplifies the clearance and care cascade. As you can see from this bar graph, specifically highlighting the dashed box to the middle of the slide, there is a significant drop off between those patients who are identified and infected but that never get treated. But we know that if we treat early, whether this be an acute infection or chronic, so immediate treatment, it will go a long way to reducing transmission rates.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Currently, approximately 30% of physicians are almost always conducting a second RNA test to avoid unnecessary treatment. If you look at the pie graph on the left hand side, you can see approximately 30% of physicians are collecting a second RNA test to eliminate unnecessary treatment; so approximately one-third. We also find on the right hand side, the 63% of physicians who conduct the second test in greater than 50% of the patients do so to avoid the unnecessary treatment. Unfortunately, a delay of treatment due to a second RNA test could result in progression from acute to chronic HCV infection. Immediate treatment following HCV diagnosis is needed to prevent patient disengagement and reduce HCV transmission.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: And this is why this is important. So treatment timing that impacts community spread. One untreated PWED or patient who injects drugs with HCV may infect up to 20 others with HCV within the first 3 years of their diagnosis. But we know through modeling that if we treat every three per 100 PWEDs, we can reduce chronic HCV incidents by 27.3% and the acute HCV incidents will decrease by 23.6%.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: And I'd like to turn it over to Dr. Kushner to take us through our second section.

Tatyana Kushner, MD, MSCE: Thank you so much. And really we've heard the statistics about where we are in our efforts to work towards hepatitis C elimination by the year 2030. So how do we get closer to our goal of hepatitis C elimination? And really a path forward is to make hepatitis C simpler. And so we need to simplify the care cascade in order to optimize the numbers of individuals who can access hepatitis C screening and treatment.

Tatyana Kushner, MD, MSCE: So the first aspect of simplifying the care cascade is really about hepatitis C screening. And now really there's agreement between all the major societies within the US about the importance of universal hepatitis C screening for all adults. There's agreement between the Liver and Infectious Disease Society, AASLD, IDSA, the CDC, and the United States Preventative Services Task Force. And we see here a summary of the current recommendations for hepatitis C screening. So on the left you see that adults should all have one-time universal hepatitis C screening if they are over- age 18 years and over, regardless of any known risk factors. Now, for those individuals who are under 18 years of age, the guidance is not at the moment universal, but a one-time hepatitis C testing is recommended for all people under 18 years of age who have known risks such as exposures or circumstances associated with an increased risk of hepatitis C infection. Importantly, pregnant individuals should also

be screened with each pregnancy. So prenatal hepatitis C testing is part of routine prenatal care and is recommended with each pregnancy in line also with recommendations for hepatitis B screening in each pregnancy. And then on the right you see that in those individuals who are at ongoing risk for hepatitis C infection, periodic repeat hepatitis C testing should be offered to these people with activities, exposures, or circumstances associated with increased risk of hepatitis C infection. This includes individuals who are incarcerated, who have opt out hepatitis C testing and periodic repeat testing, as well as people who inject drugs, HIV positive individuals, men who have sex with men, and men who have sex with men on PrEP. So at least annual hepatitis C testing should be recommended in these groups and more frequently depending on ongoing risk.

Tatyana Kushner, MD, MSCE: Now, in terms of simplifying the aspect of treatment, we now have a clear recommendation that everyone with hepatitis C really should be treated regardless of whether they have acute or chronic hepatitis C infection. So, on the left we see that treatment should be initiated immediately after diagnosis of acute hepatitis C infection with viremia. In the past there was a recommendation to weight and perhaps a weight spontaneous clearance in those individuals with acute hepatitis C. But now our guidance is updated to say that those with acute hepatitis C infection with viremia should be treated immediately. And then on the right, you see that antiviral treatment is really recommended for all adults with chronic hepatitis C infection, except those with a short life expectancy. So, per the AASLD, IDSA guidance, all individuals with at least one year of life expectancy should be offered hepatitis C treatment.

Tatyana Kushner, MD, MSCE: Another aspect of simplifying the care cascade that we've been hearing more and more about over the past year or few years is point-of-care testing. So, this is clinical laboratory testing that is conducted close to the site of patient care by specially trained healthcare professionals. And the goal here is really to obtain accurate hepatitis C test results in a very short period of time at or near the location of the patient, which could be primary care or in the community or secondary care setting. Point of care assays are valuable in community settings where there may not be as easy access to routine testing that we do in the healthcare setting. They allow for finger stick collection rather than phlebotomy results. Reporting from point-of-care assays should be done via the medical record and health authorities and positive point-of-care tests should be followed with immediate hepatitis C RNA confirmatory testing rather than referring a patient to another provider or setting to have that test performed. And availability of tests may help increase the reach to high risk populations and very exciting that the FDA has recently approved point-of-care testing for the diagnosis and screening for hepatitis C infection.

Tatyana Kushner, MD, MSCE: So, the AASLD and IDSA provide guidance on hepatitis C point of care testing and treatment, and how to move through the cascade in a more rapid way from point of care testing to treatment. So here you see this depicted. On the left, you start with point of care testing, and if an individual is found to be hepatitis C RNA positive and they do not meet any of the criteria in the dark blue box which are listed, and include either clinical evidence or history of decompensated cirrhosis, advanced liver disease, or known liver cancer, or known positive hepatitis B status, or prior DAA treatment, if they do not meet any of those criteria, then they can move forward with this hepatitis C point of care testing and treatment cascade. And what you would do is, once they are hepatitis C RNA positive, you can initiate treatment with approved DAAs for hepatitis C, you can perform medication reconciliation, draw labs, and discuss the risks of hepatitis B coinfection. You will then test for hepatitis B surface antigen, because if they are found to be positive, there is a potential risk for hepatitis B reactivation in the setting of hepatitis C treatment. And in that setting, you would continue hepatitis C

therapy but speak with the patient about either initiating hepatitis B therapy or monitoring for AASLD/IDSA guidance. If they are hepatitis B surface antigen negative, which the vast majority of individuals in the US will be, then you can just continue hepatitis C therapy without the need for ongoing monitoring for the hepatitis B surface antigen status.

Tatyana Kushner, MD, MSCE: So when we think about ways in which we can further shorten the care cascade and achieve a test and treat paradigm, we need to think about this aspect from the initial diagnosis to the pre-treatment to the treatment phase, and how we can really shorten each stage within the care cascade. So previously, when we thought about our initial diagnosis that we needed to make prior to hepatitis C treatment, we would often have to wait for 24 weeks in order to confirm chronic hepatitis C infection. And then when we moved to the pre-treatment phase, it was often a requirement to after putting in a prescription for hepatitis C treatment to obtain prior authorization and await medication approval and delivery. And only then were we able to start treatment for eight to 12 week treatment duration followed by an SVR12 check. So, as you see here, there's really a huge potential to shorten the care cascade in order to achieve each of these steps much more efficiently. So looking at initial diagnosis, we no longer require that 24 week period to confirm chronic hepatitis C treatment– a chronic hepatitis C status, because we now recommend offering treatment to any individual with active hepatitis C, whether it's acute or chronic. So we can cut down that waiting period to confirm that initial diagnosis. And then in the testing phase, we can perform point-of-care testing, which can lead to more rapid test results, as well as if point-of-care testing is not being used, reflex testing where we directly test HCV RNA as a reflex from hepatitis C antibody. And then after we have these more rapid test results, we can link to care those individuals who require specialty care or we can treat in the primary care setting if they are not complex or require specialty care for their liver disease.

Tatyana Kushner, MD, MSCE: Now in regards to the pre-treatment phase, previously, often prior authorization was required, which delayed the ability to obtain the medication. But now really the goal is to eliminate any restrictions on treatment that require prior authorization in order to be able to start treatment really very quickly after the prescription is placed. And again, this can be done in the primary care setting and there should be no restrictions and prior authorizations that delay the ability to start treatment.

Tatyana Kushner, MD, MSCE: And then finally, when we look at the cascade overall we can see that the time to treatment, time to diagnosis to pre-treatment evaluation and to treatment initiation should really be cut down significantly. And even we can aim for same day test and treat paradigms, which are already being done in different practice settings where we don't need to delay obtaining medications, but rather we can efficiently screen individuals obtain the test results and then quickly move to treatment initiation, and of course, lead to treatment with 8 to 12 weeks treatment duration, and then the SVR12, putting it all together, making this a much shorter care cascade, which simplifies our ability to offer treatment to many more individuals.

Tatyana Kushner, MD, MSCE: So, I'll turn it back to Patrick, where now we'll talk more in depth about the role of point-of-care testing as a way to enable access to hepatitis C treatment.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: So, point-of-care testing provides quite a few opportunities actually. It allows for screening and diagnosis in a decentralized setting. It allows us to scale up the access of care and treatment, including decentralizing it, and it allows for immediate linkage

to care. Linking to care the time of diagnosis then will enhance treatment uptake, as you can imagine, and provides the opportunity to accelerate HCV elimination.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: So where can point-of-care testing be done? Well, I would say it could be done really anywhere. Here are some examples: mobile van, a retail clinic, traditional medical office, the emergency department bedside, even in the home in other areas like correctional facilities.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: Current point of care options for HCV are listed here. There are three FDA-approved options, from left to right, the first being the OraSure OraQuick HCV rapid antibody test. This detects an HCV antibody from a finger stick or a venipuncture blood sample, and you get results within 20 minutes. The second one is the DBS testing. This detects both a hepatitis C antibody and/or an HCV RNA from a dried blood spot sample. It is shipped to a central lab to obtain the HCV RNA testing, but you are able to detect both the antibody and/or the HCV RNA if needed. And our third is the Cepheid Xpert HCV finger test. This detects just an HCV antibody from a finger stick blood sample. Results take about 40 to 60 minutes. But all of these can be done pretty much real time, in the setting, point of care, as I mentioned.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: What about point-of-care fibrosis assessment? So if we identify a patient who has chronic or acute hepatitis C for that matter, we need to assess their fibrosis stage. So, we do have some tools available for us as a point-of-care fibrosis testing as well. Transient elastography, better known as fiber scan, is a non-invasive test that measures liver stiffness and elasticity. This is something that can be done in an office, can also be done in a mobile setting. And then we also have laboratory calculations that are very easy to do as well. So, we have the APRI which uses laboratory data to predict the presence of significant fibrosis or cirrhosis, as well as the FIB4, which is a method of estimating the amount of scarring in the liver. So, both of those are very easy, mostly accessible testing that can be done pretty much anywhere as a point of care.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: So we really need this test and treat approach to achieve our HCV elimination goals. Again, HCV is a major public health threat, and so in order to eliminate it by 2030, we need some things. Here's what we have so far. So, we have very simple and effective DAAs, 8 to 12 weeks of therapy. We do have simple and effective point of care testing available to us, but what are we still missing? What are we working towards? We still need simple, decentralized, and integrated care. So again, we need a test and treat care model because that is important to reach key patient populations, promote engagement in care, reduce HCV incidents and risk of transmission, and reduce the long-term healthcare resource utilization of these patients.

Patrick Horne, MSN, APRN, FNP-BC, AF-AASLD: And with this, I will turn it back over to Dr. Kushner, who will take us through some innovative care models.

Tatyana Kushner, MD, MSCE: Great. Thanks so much. And I think a bit of what you touched on is this idea of decentralized care. And as we'll see, the theme here is really finding innovative models to decentralize care. So we're no longer just treating in a healthcare setting, but we're bringing hepatitis C treatment to settings, which perhaps in the past, we did not think we would be able to do.

Tatyana Kushner, MD, MSCE: So again, some of the models of care that I will share examples of the goal is to improve diagnosis, treatment, and cure rates in key patient populations, which are decentralized

and which also have high prevalence of hepatitis C infection. And the innovative models that I'll touch on really look at many different healthcare and non-healthcare settings, and they incorporate the use of telehealth, mobile van housing services, bringing treatment to housing services bringing treatment to addiction treatment settings and to correctional facilities.

Tatyana Kushner, MD, MSCE: So, I'll start by sharing a few different examples here. So, this was a program that was conducted in prisons in England, and this was a nurse led test and treat model in 47 English prisons. And this was a partnership that was done between the Practice Plus Group, the Hepatitis C Trust, and industry that supported this in order to increase hepatitis C screening and linkage to care in the prison setting. And so, the sequence of steps that it entailed are summarized here. It started with an opt-out screening for hepatitis C for people who are entering prison less than seven days before they enter prison. And point of care testing was offered in the setting with follow-up blood tests thereafter. And then after that, within less than 5 days of the initial Hepatitis C testing, the patient was informed of their results and treatment options and were referred to treatment. And then they accessed the specialist clinic where they were able to do a more in-depth liver assessment and make a decision about treatments. They started on treatment and follow up, really required minimal monitoring. They also leveraged peer support to assist people in completing their treatment and made sure that people, when at all possible, came to their SVR 12 appointment to assess SVR 12. And they also acknowledged that there may be early release or transfer between prisons. So the prison ensured that the resident left with their medicine if they did not complete their Hepatitis C treatment while they were at that prison site. And on the right, you see a summary of their screening and treatment results. Over 5% of new arrivals to the prison that were tested were indeed hepatitis C positive. And of all of the individuals that entered prison, 91% were offered hepatitis C testing. And 53% had hepatitis C testing within 7 days. So again, this is an example of bringing a screening program to a prison system in order to optimize rapid screening and treatment initiation on site.

Tatyana Kushner, MD, MSCE: This is an example of another decentralized hepatitis C model of care for people who inject drugs. This was implemented in 21 centers in the Balearic Islands in Spain. And here among over a thousand participants recruited, there was a 12% prevalence of active hepatitis C infection. Again, emphasizing that in some of these settings where people are not accessing healthcare per se, there's really a high prevalence of hepatitis C infection. So in this program, phase 1 involved screening and enrollment. So, people were screened with or a quick test that Patrick mentioned, or phlebotomy for hepatitis C antibody. And then if they were negative, they were provided education on hepatitis C. If they were positive, they then underwent confirmatory testing and were tested for hepatitis C RNA. If they were positive at that point, a hepatologist was able to prescribe the hepatitis C medication remotely. So, the hepatologist was in the clinical care setting, but they were able to prescribe remotely, and the medication was actually delivered to the study centers via the hospital pharmacy, and the treatment was dispensed to the patient on site. And then the last phase was post-treatment and follow-up where individuals were assessed for SVR4 and SVR12. And on the right we see the results. So, there was very high acceptability among participant to receive this decentralized screening and treatments. And in regards to the results, 86% of the people who were found to be infected did initiate treatment. And of the 95 individuals who presented for their SVR12 visit, 93% were cured. So not too surprising, but again a novel treatment setting where we see very high cure rates for hepatitis C.

Tatyana Kushner, MD, MSCE: Another important patient population is people that are being seen in homeless clinics. And this was a program in Oregon where over 3000 patients were screened. And in this

particular program, what they did is that they implemented a reflex laboratory bundle. So previously when people were screened, they had to come back to obtain further laboratory testing to evaluate their liver disease. But in this program, they implemented a reflex laboratory bundle. So if someone screamed positive for hepatitis C, then they would reflex to the further testing without having to have the patient come back for another blood draw. And they found that those people who actually did receive the reflex laboratory bundle were much more likely to receive DAA direct acting antiviral treatment sooner. So it decreased the time to treatment, and then increase the likelihood of cure as well.

Tatyana Kushner, MD, MSCE: Another innovative program that has been published and has been very effective is from San Francisco, California, where a mobile clinic van was developed. It's called the DeLiver Care mobile van. And the goal here is to really bring mobile hepatitis C screening and treatment to people who currently or previously used drugs. And so, this mobile van would be parked in settings where there was there were either next to addiction treatment services or other settings where there were people who currently or previously used drugs. And on this van, they were able to offer free screening for Hepatitis C, and they were able to actually initiate treatment within one week of hepatitis C testing. And what they found is that in over 1,000 individuals who were screened for hepatitis C, there were about 38% of the Hepatitis C antibody positive people who were still actively viremic. And of those about half initiated treatment within the delivery care van. And what they found is that among those who successfully initiated treatment, they were able to complete treatment in 79%. There was a drop off in those individuals who actually showed up for an SVR12 check. But nonetheless, the fact that a vast majority were able to complete treatment in this setting was very encouraging to see.

Tatyana Kushner, MD, MSCE: And then another treatment setting that has gained a little bit more traction and attention is treatment in the obstetric care setting. So we do have recently more data on the safety and efficacy of hepatitis C treatment during pregnancy. And currently the AASLD/IDSA guidance suggests that treatment can be offered on a case-by-case basis in pregnant individuals after discussion of the potential risks and benefits of treatment in the pregnancy care setting. So we implemented a program where we co-located in an obstetrics practice within our health system, but again in an atypical setting, this was an obstetrics clinic, and we did offer treatment on a case-by-case basis to people during pregnancy. And what we found is that among those who actually received and completed treatment, there were very high SVR rates. And similarly to some of the other care settings, one of the challenges was having people come back for the SVR 12 check to make sure that they actually had official cure. That being said, I think this is a setting that can be really thought about more as a potential place that hepatitis C treatment can be offered because oftentimes women only access healthcare during their pregnancy care may not be seen in the healthcare setting at other times during their lives.

Tatyana Kushner, MD, MSCE: And then another very important program and tool that we're using more and more is telehealth in order to facilitate treatment of hepatitis C. This is a program called TeleHCV and this was a randomized study comparing peer facilitated telehealth with referral to local prescribers among people who inject drugs in rural Oregon with the aim of really streamlining hepatitis C treatment, saving costs, and promoting engagement and retainment in the care cascade. And this was a trial that was conducted for 9 months. And what they found is that among 29 patients who were randomized to either receive the TeleHCV intervention compared to the more standard practice, those who were referred to that TeleHCV option were much more likely to initiate treatment with 87% compared to 7%.

Again, really emphasizing the importance of bringing treatment to where people are as opposed to waiting for people to show up to the more traditional healthcare setting to seek treatment.

Tatyana Kushner, MD, MSCE: So, I'll summarize our talk here. So currently, we are not on track to achieve hepatitis C elimination by 2030, and we really need to be thoughtful about what we can do better in order to get closer to achieving this goal. Simplifying the care cascade and introducing rapid test and treat approaches will really be essential to make elimination a possibility. Point of care testing can help simplify and speed up the diagnosis of hepatitis C infection and opportunities exist to incorporate point of care testing into different settings using unique modalities to reach key patient populations with high prevalence of hepatitis C infection.

Tatyana Kushner, MD, MSCE: How can you help? Well, you play a critical role in hepatitis C screening and diagnosis in order to provide timely treatment or referral to a specialist. So this is really a call to action that all of us should really work together in order to screen all adults at least once, and patients with risk behaviors or risk exposures routinely, and to consider incorporation of point of care testing for rapid diagnosis in both the community and primary care settings; to evaluate liver health, so assess liver fibrosis, and this can be done also with point of care testing and done with common lab values that we have accessible routinely to treat patients with minimal or no fibrosis, which can be managed by non-live specialists, so primary care providers can and should be included in our efforts to offer treatment to more individuals with hepatitis C. And there are treatment options for patients with all major hepatitis C genotypes. So, treatment has become very simple. And so we can offer a treatment to really the vast majority of people living with hepatitis C. And when needed to refer or work with a specialist. So, patients with advanced fibrosis can be referred to a specialist for cirrhosis assessment, hepatitis C treatment, liver cancer screening, and long-term monitoring of liver health.

Tatyana Kushner, MD, MSCE: We'll also provide you with some resources to help you on your journey to hepatitis C management, which will be included in the deck. And I'd like to thank you for listening and participating in this session. Thank you.