CLINICAL EDUCATION INITIATIVE
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE

Clinical Education Initiative
Support@ceitraining.org

MOLECULAR EPIDEMIOLOGY-INFORMED HIV PROGRAMMING IN NYS

James Tesoriero, PhD
Randall Collura, PhD
Mark Rosenthal, MSPH
Thomas Sullivan, MPH
New York State, AIDS Institute

5/13/2019

Molecular Epidemiology-Informed HIV Programming in NYS
[video transcript]

[00:00:04] Good afternoon everyone. My name is Melinda Godfrey, I'm the program manager for The New York State STD Center of Excellence. Thank you for participating in today's webinar. The topic today is Molecular Epidemiology-Informed HIV Programming in New York State. I would like to thank the New York State Department of Health AIDS Institute who allow us to bring you these free Lunch and Learn webinars. Our next Lunch and Learn is on July 9th at 12:00 noon. And that topic will be on EPT, Expedited Partner Therapy, and specifically on a project was run here in New York State. The presenters will be Jenna Slutsker and Julia Schillinger. And then on September 9th, we're going to have the topic of medical care for Gender Diverse Youth and that's going to be with Dr. Karen Teelin.

[00:01:12] So I'd like to introduce our speakers today. But before I do that, I just want to remind everybody that if you want to get CE credit for today's Lunch and Learn we need you to go on the ceitraining.org website and register there, so we can mark you as attended and you'll get an email tomorrow that will tell you what the login information is. So we have four speakers with us today all from the New York State Department of Health AIDS Institute.

[00:01:52] Our first speaker is Dr. James Tesoriero and he is the director of the AIDS Institute Division of HIV STD Epidemiology and Evaluation and Partner Services. He oversees all HIV and STD surveillance and field services within New York State. And then we have Thomas Sullivan, he's a project coordinator for the molecular-informed Project Mas in the AIDS Institute Bureau of HIV STD Field Services and he coordinates all the activities for Project Mas in collaboration with multiple New York State Department of Healths. We also have Dr. Randall Collura. Dr. Collura is currently working in the AIDS Institute, the data analysis unit. He develops methods for detecting Space-Time clusters of HIV diagnoses across New York State. And last but certainly not least, is Mark Rosenthal, he's a research specialist with the AIDS Institute HIV Field Services. And with that I just want to let everybody know if you have any questions, you can type it into the chat box and we will read them at the end. And with that I am very happy to hand it over. Thank you guys.

[00:03:46] Thank you. Actually this is Randall Collura and I'll be speaking first. And we need to advanced the slides here. We have no disclosures.

[00:04:01] Some learning objectives. We are going to describe the importance of HIV drug resistance testing and its role in facilitating public health programming. We're gonna be describing our HIV molecular-informed programming and we're gonna be soliciting clinical and community perceptions concerns and recommendations about the use of HIV molecular surveillance in New York State.

[00:04:28] So to start off with, this is something that everybody should be familiar with. It's the Ending the Epidemic goal for New York State and their three major goals; to identify persons with HIV who remain undiagnosed and to link them to health care, to link and retain persons diagnosed with HIV in health care to maximize virus suppression so that they remain healthy and prevent future transmission, and facilitate access to Pre-Exposure Prophylaxis or PrEP for high-risk persons to keep them HIV negative.

[00:05:10] And I'd like to show how molecular HIV surveillance can support all three of these ETE goals. So what is molecular HIV surveillance and how does it differ from other methods? Non-molecular methods have investigated temporal increases or Space-Time, sometimes called time space clusters of HIV diagnosis. And essentially this is just looking for increases above expectation for a particular region or particular city or area. Molecular HIV surveillance uses viral genome sequence data reported to New York State from drug resistance testing. Individuals with viral sequences that are more similar are clustered together and I go into a little bit greater detail about that later on. These molecular clusters can indicate networks with rapid and active transmission of HIV for intervention. All of these clustering methods are utilized in such a way that allows us to intervene and try to prevent transmission if possible, and actively growing clusters.

[00:06:28] For molecular cluster work, you could think of everybody being connected in one sense because you have to get the virus from someone, so all HIV sequences are therefore related and they form a gigantic transmission network since the first transfer from a simian host. However HIV evolves very quickly. That's one of the reasons why it makes it hard to combat. So in the work that we do, we don't look very far back in the transmission network or the transmission tree.

[00:07:06] The current clustering methods really look at very recent transmission. So in essence, we're looking at the very tips of the branches of the tree. We're only looking at very recent transmission and the reason why that is because changes over time in HIV sequences pretty much obscure the deeper branches of the tree, at least the way that we do the analysis right now.

[00:07:33] We have to think of molecular clusters as part of a larger network. So the molecular cluster, in order to get a molecular cluster with the work that we do, we're going to be including people who have diagnosed HIV infection. They've entered into HIV care. They've had a resistance test done and that sequence that was generated as part of the resistance test has been sent to New York State and processed by our systems. And that's a subset of the individuals that have HIV. It's a subset of the individuals who have been diagnosed with HIV. So you could think of it as like the center of a transmission cluster, the transmission cluster includes people who are both diagnosed and undiagnosed. But the diagnosed individuals, may not have a sequence available. That is to say the physician may never have ordered a resistance test or there's a number of reasons why sequences perhaps might not be

usable to us. And that falls within a larger risk network of individuals who are not HIV infected but they are at risk of infection, through sexual partners or needle sharing partners or they have some sort of a risk factor that are associated with individuals in the transmission cluster and in the molecular cluster.

[00:09:03] There's I think a lot of maybe misconceptions about molecular clusters. We know for instance that they are a subset of individuals. So if you look at the hypothetical molecular cluster that's shown here on the left of four individuals. If we could know the underlying transmission cluster, and we certainly would like to know the underlying transmission cluster, we make efforts to try to find these individuals but a lot of them are hidden. We don't know who they are. But there could be lots of individuals that are part of this transmission cluster that we just don't see. And there's other individuals that are part of the risk network that we may never know about. We try to get information about them, but there's probably a lot of individuals that we're not going to get. And there's a lot of I think misunderstanding about molecular clustering. It can't reveal any direct relationship between the individuals in that cluster. We don't know anything about who may have transmitted the virus to somebody else. We don't have any information about directionality. If you have two people that are in a cluster they may have gotten the virus from a third person that we don't know about. There could be any number of individuals between those in a transmission line, between those two people that we see in a molecular cluster. So we don't know anything about direction and we don't know about other individuals who may be part of the transmission cluster. And so it basically just shows that since the sequences are closely related that there's a likelihood that the transmission occurred relatively recently and that gives us information that we can utilize for intervention and programming.

[00:11:04] We do work with both Space-Time and molecular clusters. I like to think of them as being complementary. Space-Time clusters generally will identify increases more quickly, more rapidly, in part because it takes time to get sequences generated and sent to us. However on the downside Space-Time clusters since the data is very very recent, sometimes and in many cases is subject to revision. That is to say we go out and we get more information about an individual, it may be that someone we thought was a recent diagnosis was actually diagnosed previously in another state. So there's a lot of revisions that occur. And so the data isn't as clean but we want to get the information as quickly as possible, so we use the most recent information. So it identifies clusters more rapidly, but it's subject to revision. Molecular clusters on the other hand, we know if we get a sequence from someone that they're a real case and they're in care. And so that's a certainty. However Space-Time clusters only look at particular regions, molecular clusters can detect clusters that span across geographic regions. Sometimes they may span across states. This information we can't deal with in New York State until we get information from the CDC. The CDC aggregates this information and looks for clusters that span states, which they sometimes do. But even within New York State we can detect clusters that may include individuals from all across the state, which we wouldn't have picked up using Space-Time methodologies because we're only looking at say a county or adjacent counties. The downside of molecular clusters, which have alluded to before, is that it's only a subset of people who have been diagnosed with HIV. We're relying

upon linkage to care ordering of resistance tests and reporting of that sequence to the Department of Health.

[00:13:21] So let's talk a little bit about the clinical guidelines for ordering HIV drug resistance testing. Genotypic resistance testing, that includes the protease and reverse transcriptase gene, is recommended at baseline regardless of whether ART therapy is being initiated. It's recommended for ART naïve patients before the initiation of ART and in patients experiencing treatment failure or incomplete viral suppression. The integrase resistance testing is recommended when integrase resistance is expected.

[00:14:08] So part of what we want to discuss here is that resistance testing, I mean obviously it has a clear clinical benefit, but it also has public health benefits because of its use in molecular clustering and its utility for showing cases of recent and rapid transmission that we can intervene on. So there are various kinds of resistance testing that can be done. Phenotypic testing typically does not provide a sequence for clustering. So from our perspective it's preferable to do a genotypic test for public health reasons. And also tests that include all three of the major genes, protease, reverse transcriptase, and integrase are of greater utility for clustering because the full sequence can be matched with individuals with only PR-RT or only integrase sequence. And we're finding a growing number of individuals that just have integrase sequence testing done and the current methodologies that we're using actually can't incorporate integrase. We're only using protease and reverse transcriptase. So there is public health utility to genotypic resistance testing and that's what we're trying to encourage providers to do those tests.

[00:15:32] So I guess I want to go into a little bit more detail about how this process works and how the genotype testing is performed and who gets what information from these tests. When a provider orders an HIV genotypic resistance test that sample is sent to a laboratory, the specimen is prepared, typically viral RNA is extracted and converted to DNA and then amplified and sequenced. Although there are other methods that are being used now. The mutations that are identified when compared to a reference sequence are used to construct a report of which drugs the individual might be resistant to and that resistance report is sent to the provider. New York State does not get a copy of the resistance report that the physician gets. We have our own in-house systems to look at these sequences and look for mutations that are involved in resistance and we do our own analysis of resistance in New York State on an aggregate basis, because we get the sequence from the laboratory and there's a number of steps that are involved in that process, which I am not really going to go into.

[00:16:55] But I just do want to talk a little bit about some of the differences in resistance testing that are occurring now. The typical process that has been done for resistance testing, there's an isolation of viral RNA and reverse PCR and then Sanger sequencing, which is at this point I guess it's an older style of

sequencing. Sanger sequencing that's used to identify the sequence and look for areas where you have ambiguities which indicates that there are different versions of the virus within the individual.

[00:17:43] Over the last several years there have been introduced DNA tests which instead of looking at the viral RNA as the source of the genetic material, they actually amplify the proviral DNA in the cells of the individual with HIV and that sequence is done using different sequencing technology. And theoretically you get more information, you can get information about archived versions of the virus. So you can get potential resistance which may not be indicated if you just look at the circulating RNA and it's recommended for individuals whose viral load is very low. You can still get a resistance test done using this methodology. There's not a lot known about how this affects our ability to use these sequences for clustering and we're just now figuring out how these different sequences vary, what differences there are between them, and how we can utilize them.

[00:19:07] So we get these sequences, they're processed using our RAV software. And the CDC has developed a program which clusters sequences and we can use this methodology to look at clusters in lots of different ways. We can set various parameters to look at only very recent clusters, only clusters of very closely related sequences, or we can relax it and look at sequences that are less closely related. And this is all done securely using a website. The program is called Secure HIV-TRACE and we upload a file which contains sequences and demographic information of individuals that we have in New York State, in our surveillance system. And it's processed in a secure server and then we get information back about clusters and we have been doing this since 2017. The CDC has been using similar technology for several years prior to that and then just studying the results to jurisdictions.

[00:20:22] And obviously we want to look at clusters that are rapidly growing. So if you have clusters where there's numerous individuals that have been diagnosed in the last year or the last couple of years and they're very closely related, that's very troubling. We call that recent and rapid clusters. But there are other demographic characteristics that can be used to select high priority clusters or clusters that we are going to flag for further investigation. And an example of that, we can look at the number, it is not circled here, but the number of transgendered individuals in a cluster. I don't know if it's really readable here, but he's pointing to it with the arrow. So there's a cluster that has a high number of transgendered individuals. We might have clusters that include very young individuals that we might find some concern in. So there's a lot of different things that we can look at in a cluster and flag it for further intervention.

[00:21:28] We'll show you what a cluster looks like when it's returned to us from Secure HIV-TRACE. This is a current cluster that we have been investigating for about a year I guess or maybe a little less than a year. It includes individuals from many different areas of New York State, mostly upstate but there are some people from in New York City as well, and from other states. Most of the individuals are from Rochester and Orange County, Erie County so there's a number of number of counties involved. And this

is the way it's typically displayed in Secure HIV-TRACE. There's a cluster, the individuals are linked with lines and the lines indicate that there is a connection between those two sequences, which means that the sequences are similar to each other. And you can color code these individuals by lots of different information, the demographic information that we send to Secure HIV-TRACE. This is by current county.

[00:22:37] This shows individuals that have been diagnosed in the last 12 months, in the last 36 months. Color coded red is last 12 months. And it also highlights individuals that form clusters of very close relatedness. The CDC believes that this indicates recent and rapid transmission, and if you have five or more individuals that are in a cluster that meet certain criteria diagnosed in the last 12 months, this is considered to be a national priority cluster. We have several of those that we are looking at right now.

[00:23:14] Because we upload demographic information we can look at clusters using this information. In this case, we have racial information that's shown. And we can also zoom in. We can look at the viral load status. This is a very important thing for us, how many individuals in this cluster are unsuppressed? And that's a reason why we might go out and talk to those individuals or their physicians and try to see what's going on. Are they currently in care? Why is their viral load not suppressed? And we can also zoom in and look at the sub-clusters or the clusters of very closely related individuals. This is a sub-cluster which actually the CDC designated a national priority cluster within this larger cluster, and indicates individuals in red that are not virally suppressed.

[00:24:25] So moving forward with molecular HIV surveillance in New York State. Some of the issues that we're confronted with are resistance testing is recommended at entry to care, but we have a good number of individuals who we know are diagnosed and we know that they're in care and they have not been given resistance tests, so we'd like to increase that number of individuals who are getting resistance tests. There is some regional differences that is to say that certain parts of the state are better, have a higher percentage of individuals that have resistance tests than others. We we still have to deal with the fact that some individuals are in multiple states and we only get that information from CDC. Typically we don't get that. And we are using this for routine looks at cluster molecular clusters within New York State. We also are looking at specific, we have a grant that we're looking specifically at Hispanic and Latino men with a history of male to male sexual contact. And that's a special grant that we are working on. And I think that's my part. I'll turn it over to Thomas.

[00:25:47] Okay so thanks Randall, and Randall gave kind of a good intro into this and so I'm going to talk a little bit about two molecular epi-informed projects that we have at New York State currently. So just a little bit about definitions, these numbers are given by CDC but we have two focuses. One is 1802 and one is 1711. 1802 is really focused on rapid and recent molecular clusters meeting national priority, which is five or more new diagnoses in the last 12 months for New York State. So that's for 1802. And then we have a another project that Randall had mentioned, which is 1711 and that's focused on rapid

and recent molecular clusters with Hispanic and Latino gay, bi, or other men who have sex with men. So it's really a subset of that larger 1802, some could be actually in both. And this slide just represents that we are covering the entire state and for 1711 we also collaborate with New York City. And it's also allowed us to hire 8 new partner services or disease intervention specialist staff out in the region to conduct these investigations.

[00:27:12] So to oversimplify, we have a two step process. So when Randall mentioned about Secure HIV-TRACE and he runs that file. We have clusters, many many clusters, and based on resources as well as public health reasons to contact individuals. We go through the entire list and we apply criteria to select specific clusters and so the first part is selecting the molecular clusters, which are a group with related infection. And we do that currently using timeframes. So that's both new diagnoses in the last 12 months, but sometimes we also limit it by the diagnoses of when they were actually diagnosed. In some cases we've used three years. And then we also use what's called the Genetic Distance Threshold, but that's the relatedness that Randall was talking about, and how related are the sequences to each other. Once we've selected, let's say if we had 80 clusters, and out of those 80 we selected 3. So now we go down to those 3 molecular clusters, from there then we're also not going to be sending out every single individual for investigation. And so we really do a deeper dive into those 3 selected molecular clusters and we prioritize their cases by current things that we currently do with our partner services. So looking at people at their care status, who may be presumably out of care mostly as a proxy using lab tests because we haven't received a lab test in a certain amount of time, individuals who are currently viremic. Have they ever received partner services before? Which can be for many different reasons, but most cases they've recently moved to the state but were already diagnosed or have already been investigated at least once. Co-infection, so current co-infections with either syphilis, gonorrhea, and/or chlamydia. And then also if there's drug resistance present or no resistance test result was available for individuals that were at the transmission cluster. And these also vary in terms of how we respond to the individuals, in some cases we may not even contact the individual patient. Sometimes it's a discussion with the provider. For instance the last piece with the drug resistance present, sometimes we'll reach out in collaboration with the medical director to reach out and see if they need any assistance in terms of interpreting the results because sometimes they're a little complex.

[00:30:16] Like I said we were using mostly previous used public health messages, but some of them are new and it has moved us to develop new messaging and protocols to respond to these particular cases. And so some of these you see on the screen, as well as individuals who may not have been maybe diagnosed several years ago, and how does that conversation go about? Which is a slight departure from our traditional partners services that goes out on newly diagnosed individuals both for HIV, syphilis, gonorrhea, and/or chlamydia.

[00:31:00] So along with these projects, we have several different activity strategies to assist. So I will start with the first one, so clinical education and detailing. So these are really targeting the clinical

providers across New York State, outside of New York City, that are serving molecular and transmission cluster members. It's also tied with our University of Rochester grant related to rapid initiation of ART. And those will be starting soon and we get that information both from our cluster investigations, in terms of what happened in the past as well as reaching out to clinical providers who may be requesting additional education or detailing related to this. Social network strategy is targeting the larger risk network. And so that's asking potential individuals within these molecular transmission clusters to see if they would like to become, they're called recruiters, will actually be given coupon codes to go out into the community to reach out to friends or other people that they may know in the community who may benefit from an HIV test. The HIV Home Test Giveaway which we have been doing in New York State along with New York City for several rounds. This one we are still continuing the same methodology, however we have shifted in terms of where we target the advertising. Mostly on our social media, so that is Facebook as well as the apps that are used by the target population such as Grindr, Scruff, Jack'd, etc. And so we set the geofence for advertising based on some of our current rapid and recent molecular clusters. And the next is Social-Structural Factors, so a big piece actually of the 1711 projects that focuses on Hispanic and Latino gay, bi, and other men who have sex with men, is to really look at the barriers both to HIV care as well as the prevention services for the risk network. So we've been conducting focus groups for the last month as to better inform our processes, as well as we begin to conduct some of the investigation we'll be soliciting some of these factors. And then in turn, bringing them back to message out to the community to find better ways to address potential gaps in our region. And the final is Collaboration, so this involves big collaboration which will be on the next slide. But in addition is working closely with many of our local health departments, both the funded ones who provide partner services as well as the non-funded, based on resources. And we collaborate very closely with New York City and as well as a community based organization that serve the population.

[00:34:23] So this is just a representation of our internal collaboration. So we all sit underneath the Division of Epidemiology, Evaluation and Partner Services and then we have several units in both the Bureau of HIV STD Field Services, which oversees our partner services out in the field, as well as the Bureau of HIV AIDS EPI where the molecular cluster information is coming from for our HIV surveillance, and the Bureau of STD Prevention and Epidemiology which is where the partner services information is actually housed, as well as incorporating some of our STI information. And then in addition, we're collaborating with other offices, Office the Medical Director to inform some of our clinical detailing as well as potential information for providers and resources, the Division of HIV Prevention and the Division of HIV/HCV Healthcare.

[00:35:30] Okay, Thomas you're going to turn it over to me. This is Jim Tesoriero. Just one slide left before we look at the questions that relate to this overall presentation. So is molecular epi worth it? The answer is we don't know right now. The Centers for Disease Control is all in on molecular epidemiology, they have seen potential as it relates theoretically to this newish technology and have required all funded jurisdictions to engage in some form of molecular epi. So that's the entire country has to be doing something around molecular epidemiology. We are proceeding with caution. We're doing what's

required. Clearly there are costs and risks associated with molecular epidemiology. The biggest now that we're really almost two years in, the biggest cost is the time and systems requirements that it requires us to do. To do a molecular epi it isn't just about identifying the sequences, that's actually as Randall tells me, the easy part. The hard part is figuring out what to do with those sequences and the way that the data are required to be reported and collected and for programmatic purposes, requires us to match data from our HIV surveillance system with data from our partner notification and tracking systems with most recently, data from our agents to reporting systems. Things like social network strategy is being accommodated, in part any way, through relationships we have with funded providers. So we start with a cluster member, ultimately we engage in some sort of additional field work as it relates to partner services. And then in some cases, these individuals are being recruited as social network strategy-testers or recruiters, and they're being handed off to community based organizations. And so to track all of this requires system operability that we don't have right now. So we've never had to do programming like this across this many systems before. So the cost associated with this, just from the staffing and systems level, is really unprecedented and came with no additional funding. So definitely a lot of work associated with this. Also although Randall definitely and correctly indicated that there's no way to to identify directionality with molecular epidemiology, I don't know that because two sequences are related to one another that there's any that those individuals even know each other. When you combine molecular epidemiology with partner services work, it brings you closer to directionality. Now to be honest we've always had that possibility, just with partner services all by itself. When we are out notifying partners and if someone has only had one partner and they've been notified that they've been exposed, then for all intents and purposes you are identifying where that transmission came from. So that's just something that we're aware of and which is why the data do need to be highly secured. So there are costs associated with molecular epi, the benefits on this slide are at this point all potential and none have been realized. So again this allows us to focus in a more effective and efficient way. We have the capability in New York State to do about 10,000 partner services interviews a year with what we have in terms of staffing. There are currently tens of thousands of cases of chlamydia outside New York City every year. There's over 10,000 cases of gonorrhea, 3000 cases of syphilis and HIV combined outside the city, so we have limited capacity. So for every staff person's time and effort that gets associated or put toward this effort it's less time and effort that we have to do other forms of traditional partner services. And so we need to make sure that this is actually yielding benefits before we jump in with both feet on this. So the potential is there, clearly, to target individuals who are most at risk and to target networks that are rapidly increasing. Again if some of these partnership projects work, then we'll have the potential to identify individuals through partnerships with community based organizations in better ways. And certainly we have proven through our Data to Care programming which has been up and running now for over five years, that that's been an effective method for relinking persons back to care. So there is a lot of potential with molecular epi, but that potential to this point has not been proven anywhere in the country and so we have to keep our eyes on this to make sure that potential is realized and that it's worth it, relative to what we're giving up in terms of working on traditional partner services activities. I think that's what I wanted to say about that slide.

[00:40:22] So I'm actually going to pass it back to Melinda, who may be reading the questions. So that is the end of our presentation and we're going to lead into some of the questions, and then I believe open it up for discussions that can be sent in via the chat.

[00:40:42] Absolutely. Thank you very much. So these are questions that when we put the Lunch and Learn up on the CEItraining.org, these were the questions that get asked at the end. And I thought it would be a good idea to kind of go through these. So number one, true or false, HIV surveillance data can not reveal which cases are directly related by transmission. If anybody would like to type in what they think that answer is, that'd be awesome.

[00:41:30] The answer is true. And I'll go to number two. True or false, HIV molecular surveillance data can not determine the direction of transmission.

[00:41:46] And that is true as well.

[00:41:50] The third question. True or false, HIV molecular surveillance uses viral genome sequence data reported to New York State from antiretroviral drug resistance testing. And that is true as well. Do you guys want to say anything about these questions or review at all?

[00:42:19] Hi. No, I think if we tried to make them fairly straightforward from the slide so I think we're good.

[00:42:31] And question number four, which of the following scenarios should a clinician order HIV drug resistant testing? And I'll let everybody read them. So the answer is all of the above. So at baseline in antiretroviral therapy, and patients experiencing treatment failure, and patients with incomplete viral suppression. And then number five is which of the following is a disadvantage of molecular cluster investigations? A is individuals with a sequence may not be real HIV cases. B is limited to individuals with a genotype sequence reported to the New York State Department of Health. C is individuals in the molecular cluster may be HIV negative. And D, cannot detect clusters that span the geographic boundaries. And the answer to that one is B, limited to individuals with a genotype reported to New York State.

[00:44:03] So I do have a couple questions that have come in since I've been reading those questions. This one is since HIV is an RNA virus, how does DNA sequencing help?

[00:44:27] Hi this is Randall. To answer that question. So part of the process in the standard way that the sequencing is done, is that the RNA is isolated from the circulating virus in a person's blood. And then what's done is something called rtPCR or reverse transcriptase PCR. So the RNA is converted to DNA and then it's amplified using polymerase chain reaction and then sequenced. So in a typical resistance test using RNA, there's a reverse transcription reaction which changes it to DNA. In the newer kinds of tests that target the DNA within the white blood cells or other cells, then you don't have to do that step because you're actually amplifying the DNA directly from the cells.

[00:45:29] I think that was the question, for the person that asked the question if you have additional questions related feel free to add them to the chat and we can respond if you have further questions and then it looks like we have another question as well.

[00:45:46] Yeah we do. If an individual is already HIV positive and exposed to another strand of the virus through sexual exposure/needle-use partner well they potentially develop an additional resistance?

[00:46:10] This is sort of out of my area of expertise, but I think that that's a very reasonable assumption. Is that if you get exposed to another version of the virus, the version of the virus that is resistant by virtue of various mutations that have already occurred in that virus, then you are exposed to that virus then yes you will. Those versions will then multiply in an individual and in response to the drugs that they're taking. And so yeah that is, that is a possibility.

[00:46:49] And I guess maybe leading off to that, unless if I don't see any questions at least on our end. But this is to Randall, is so going on what this individual had to ask. If someone had multiple strains and they did a resistance test and for HIV 1 and they start to become suppressed, and then they don't become fully suppressed, could that also be due to multiple different strains that there's one that's kind of a lesser variant that ends up when you treat the more common one that the other one starts increasing?

[00:47:29] Good question. I guess there's all kinds of scenarios that can occur. I think typically resistance to antiretroviral drugs occurs within an individual just by the process of mutation. The virus mutates very rapidly, in part because of the way that it replicates. There are mutations introduced during the process of reverse transcription and replication of the virus. And so I think this is the reason why most resistance develops, you have perhaps some variation in an individual taking ARVs, they may skip some time or have some other reason why they're not taking there ARVs and resistance can develop from not taking the ARVs properly. The scenario that was asked about, about being exposed to a different strand, I think that can occur. I don't I don't know how frequently it occurs. But typically what happens is that all

the different strains of the virus are incorporated into the cells that are in that individual. And so if you're on a certain group ARVs and you switch ARVs, you can have a situation where archived or latent versions of the virus in various cells can become active and start replicating. And that's one of the reasons why they do that the DNA based test, because it will look at all the different versions of the virus that you have archived in your cells and you can highlight potential resistance which may not show up if you're just doing a test that's based upon the circulating RNA viruses that are present. And I think that answers the question.

[00:49:38] There was another comment on the question about developing an additional resistance. The person wrote, 'as a follow up, is that potentially seen an HIV 1 and HIV 2?'

[00:49:59] I know very little about HIV 2. Most of the of the individuals in New York State are HIV 1. I'm not sure if that person is asking whether you can have a co-infection with both HIV 1 and HIV 2, or both HIV 1 and HIV 2 react similarly to resistance? I think there is potential that you can have confection I don't know how often that occurs, I think it's extremely rare. At least I've not seen any evidence of it in the sequences that we have. But I don't know how HIV 2 reacts to resistance. I'm assuming that it's similar the way HIV 1 reacts.

[00:50:41] There is a clarification, so yes co-infection with HIV 1 and HIV 2.

[00:50:47] I think that that's a possibility. I think it's out of my area of expertise. I think that the likelihood is extremely low in New York State, just because almost all of our sequences are HIV 1. But I think it is a potential, I think it can occur. We have various subtypes of HIV 1 and you can get co-infection with different subtypes of HIV 1. And so if the population of individuals that are in your risk network have both HIV 1 and HIV 2, then I would assume that that is also a possibility. But again that's that's out of my area of expertise.

[00:51:29] Thank you very much. I don't see any other questions coming in at this time. So we can wrap up a little bit early today. I want to thank our speakers for coming on today and just remind everyone that if you did register online and you want to get CE credits, we will send an email out tomorrow with the code that you need to collect them. If you want to jot down the code right now it'll be 0 5 1 3. And our next speaker will be Jenna Slutsker and Julia Schillinger and they're going to be talking about EPT. Again, thank you everybody for coming and I thank you very much to New York State Department of Health for helping us put this on.

[00:52:33] Have a good afternoon.

[Video End]