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SEXUAL TRANSMISSION OF HEPATITIS C: INFECTION AND REINFECTION

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5/9/2022

Sexual Transmission of Hepatitis C: Infection and Reinfection

[video transcript]

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Dr. Fierer is a professor of medicine and Infectious Diseases at the Icahn School of Medicine at Mount Sinai. He received his medical degree from Yale University and his infectious diseases training at the National Institutes of Health. In 2006, he and his colleagues at Mount Sinai recognize the presence of an ACC an epidemic of Hepatitis C infection among HIV infected men who have sex with men in New York City. Since then, Dr. Fear has become a leader in the investigation of this emerging epidemic in the US and worldwide. His work in the field has included characterizing the rapid onset of liver fibrosis in these men, the behaviors, molecular epidemiology and bodily fluids associated with the sexual transmission of HCV and reinfection and pioneering the use of direct acting antivirals in the treatment of early Hepatitis C infection. Welcome, Dr Fierer.

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Yes, thank you. Pleasure to be here. And this new hour. I know, it's tricky to join at this time, it's squeezing between my clinics anyway, so I certainly understand. Alright, so there's the title today, my I have disclosure, I have some money from Merck, that goes to an institution that used to try to figure out some of these questions. And so my talk is going to follow along the learning objectives. If you look carefully, previously, I reordered them slightly, but they're the same ones. So we're going to go in this order, and I will be introducing those topics. So today, I actually going to try some, some new slides and new ways of describing some things and some brand new data. Or at least it's brand new analysis of some work that we've done a couple of years ago on reinfection. So this is the inaugural presentation without seeing how that goes. All right. So I will start out with with a patient who I saw early on, in my experience, and give me some clues as to how to think about this whole issue. So 46 year old man who had sex with men and came for first visit for newly diagnosed HIV infection, and the usual tests drawn the CD for kind of viral load, and Hepatitis serology, normal alts came back three months later, for routine checkup, it felt fine and get to know his doctor a little better and said, Well, you know, my sex life has been including unprotected, receptive and inserted and what of course with with mobile called condomless. I'm gonna take it back. typo there, we say condomless. Now, sex with many men and then using in particular crystal meth amphetamines and ecstasy and evil nitrate. And from that, visit the we have a striking difference in liver injury paddler the ELT of 960. Up from 30. And a St. Similarly, alkaline phosphatase up a little bit, not joined us wasn't this wasn't cola static infection. And so this is a pretty classic, new infection. enzyme levels can lots of different things. I'm not going to go into that today. But just to give a flavor of we're looking at now and of course now had seroconversion and has genotype one A, which is we've mentioned is decided by 90% of what we see in New York versus sort of our epidemic genotype. All right, so let's go back in time a little that's my back in time graphic to the first descriptions when I saw this man and a few others went to literature and it turns out that about a year before I saw him in 2004, and five they were for sort of case small case series from England. There'll be a quiz, by the way on the coding put that learning objective the colors of the flags. So this is in the London area, Amsterdam And around Paris in Germany, saying, you know, we think we're seeing sexual transmission sees your men have sex with men with HIV

and thickness and sexual transmission. So just within a few years, certainly less than a decade, we now have reports of MSM with HIV in particular at the time. Who, across four continents, both hemispheres. And you can see many, many locales, and they say, well, what's the extent of this province to introduce this part in the epidemiology, I'd say that the some groups did some nice work, it's not that easy to figure out incidence rate. But you can see that across the cooldown period, the incidence is around, this is about point three 2.9 per 100 person years, that's what the percent is, or some people put it for 1000 person years, but I usually refer to it for 100 person years. And this is a relatively lower rate compared to what we're used to, we may hear about people who inject drugs. But nonetheless, fairly uniform, very broad spread. And so that led me with to think about, well, how we're going to figure out starting at least with behavioral risk factors, a classic place to start. And a number of groups had looked into that over this period of time, we had seven case control studies with multi variable analysis. So this is not case series, this would be higher level. So a few of them are perspective. And so this is sort of higher level data. And there are really quite a number of different finds and some of my favorite things here insects interact. So and just in who, who found these and who didn't and protected now we call condomless Halal intercourse, group sex is found in some fisting was found to be a significant risk factor in the form of the studies that looked at it, but not in New York. Rectal bleeding in particular was a focus of the German publication, and specifically not found in other places, and stiffing drugs, other injection drugs because that was less commonly reported. And that was found in the minority of study. So it's hard to put this together, you want to look at all these and say, well, what's the generalization here? And I would say some that a few SEC's risk factors and a few drug related risk factors. Do those drugs have anything to do with the transmission or not? So always the question. So let me go talk about what we found in our work in New York specifically, because this is course the fluids how I'm going to do more work here. And so we publish them on World Hepatitis Day. It's an updated kind of nicely, this reported with the CDC MWR. And what we found, in our analysis, we wanted to take out the question of, did people just get a projection you'd say Hepatitis C in the field, and immediately thoughts go to needles and needle sharing heroin addiction, largely, and the Hepatitis field has really been very focused on that. And so we decided with the CDC and the encouragement, we're going to look at it and just take that out, really just look at sex, that is, anybody who had injected anything was not part of this analysis. So these were people any injection of substance, testosterone, if it were not medically visit. So what we found was two independent perspectives. One is, this is condomless, receptive anal intercourse with ejaculation of semen into the rectum, as specifically opposed to condomless receptive Badewanne. Of course, without ejaculation, this was a specific report about semen in the rectum, as I've just come to call it and shorthand, and then sex while high on crystal methamphetamine, not another drugs, it was specifically sex while high on methamphetamine in the multivariable analysis, and the odds ratio is very high, very significant P value. So it's pretty striking. That was not good sex knights fisting not. Other things. In people who who were not injection, users did nothing to the stuffing or any of that it's very straightforward semen in the rectum than being high on meth during sex. And so that led reasonably to say, Well, what about Hepatitis C and C? There was a there was something of a literature mostly on interest. Interestingly on the reproductive Health side is there Hep C and semen. And the conclusion was there's very little that was gotten to where it was we in Australia, I'm going to show you our data, went ahead and looked specifically in men who had had recent infection who came to us. So anyway, I saw with a recent infection or somewhat

longer infection, longer duration infections, can you provide a semen specimen or two or three. So we collected 123 specimens from 33 men, and did viral load testing and founded in a third of the men, the median viral load is not high, but not high. But the way it's divided, was more interesting in that if you look at people who have an average blood, Hep C, viral load of about six logs, which is actually lower than average, in in men with HIV, you find it's quite a significant proportion now who have detectable in the ceiling, and did a little calculation there, the average jacket would deliver between 50 and 6600 or so international units of Pepsi and so the into the rectum of the receptive partner,

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and which is comparable to a small amount of blood. And so that that makes sense that this is not trivial. This is not an insignificant thing. This is clearly a way the directing is a very absorbing region of ice on debt with the colon and rectum as part of that fluid absorption and quite in your blood vessels. So the other thing we wanted to look at was was, was rectal fluid. So during that this is important sexual body fluids, good five plus MLS, and it is possible to get infected in certain penis or bring it as that I will describe that as I call it penises, fomite, or fists or to another rectum. And so what do we do a simple thing, we insert a swab to the dentate line, rotate around a little bit and then put that in viral transport media and send that to the lab and do virulence and and we saw a pattern that is pretty similar to what I showed you for the semen that is people who had low blood viral load didn't have much of any shedding in the semen. But we had about half men, half of men whom we sample who did have measurable Pepsi. And again, drawing this line here dividing the six logs in blood, and secure that that was actually quite even more impressive than 86% of people who had blood viral at least six logs had detectable Hepatitis C in the rectal fluid. And so putting that in perspective of an inserted penis would be exposed to about 2300 items in the rectal fluid for the duration, the amount of course and the surface area of fists generally larger than that. So fist could be much more exposure to we're not wearing gloves, for instance. So plausible explanation for how the English study had found that tap dancing was a transmission or acquisition was associated with kind of musters, activating force and sending group sex you could have it brought from the coding of the penis, from one man to the man next to him. And interestingly, of course, that wouldn't have anything to do with condom use because the that's the the man with the with the insertion of the penis is not does not have access to the Pepsi isn't relevant to the situation. So two very important things worked for the rectal fluid. And so really to address further some it concerns especially with German colleagues saying, oh, you know, bleeding rectums that has something to do with it while bleeding rectums may open up a portal larger portal of entry, but people don't auto infect from their own bleeding. And so bleeding of itself doesn't really matter so much. And so unless it's detecting that certain cancer and we're talking about infecting not the uncertainties, but the receptor partner, so we want to I chose to collaborate with somebody who had been in the HIV field and coming into the Hepatitis Seafield George Shaw and it's brilliant, very technically challenging. assay called a single genome sequencing and And that hypothesis is show you here that the root of infection that is sex or injection use for HIV is there's a correlation with the number of transmitted viruses and we can measure it. So sexual transmission one of the two viruses for minutes X has been that's all it takes to to establish an HIV infection, and injection dragees associated with multiple viruses. And they've done a preliminary experiments suggesting that Hep C might be similar. They had, although as anonymous blood donors,

there's quite a spread here of one to a very large number of transmitted viruses. And so is that well, that we don't know risk factors then. But we have a group, we do it for a sector. So the hypothesis was that sec, we can distinguish sexual transmission from other routes, say bloody sacks, or share needles, actually needle sharing. And using this single genome sequencing technique work, you have the the different viruses in the blood sample that we draw, and you could actually characterize them and enumerate them. And so what we showed here was that we had eight men who had 10 infections to reinfected closely, and in this group, show you some of the basic things we did. But really, the key here is that this aficionados are interested in what single genome sequencing looks like a profile, if you have a single virus, then they're all very closely related. Because they're not very far apart from each other. Just one nucleotide for most cases, and if you had many viruses, you had this complex pattern. And we have to leave it to the experts on this for analysis to say that this is a pattern of many. And so this is this is our actual results that we found that the exposures in most people all women had sex to had. So they injected meth in one was quite sure there was no sharing, but one in particular with a partner, who actually has no nap FC, remembered specifically sharing with the partner. And this really validated, it's not a very large series, but that they had a single transmitted virus associated with sex. Three is sometimes seen in early infection. And then really, I would say clearly distinguish, although of course, there's always statistical variation. But we had really one who said, I know I shared and had exactly what it expect multiple viruses and one who was sure he didn't share and had the profile of a single virus, which was just like sex, so he just really, there was no nothing suggesting a blood exposure here. There are most men who could say with no percutaneous exposures were infected by a single virus into rectal exposure to semen, therefore likely sufficient, good enough. Would you need a semen in the rectum? And conversely, rectal trauma or bleeding or shared injection equipment is not necessary, perhaps, infection? Sure, you can get Hep C by larger exposures. I think this is a really important extra reinforcement of what sexual transmission of this means during sex means that it's not require extraordinary things beyond simply Congress or safe intercourse among men. So with those ideas in mind, that go back to our epidemiology and want to talk about something more that we've learned from simply the observation of reinfection. And that is, first of all, that it happens. So with these incidences, I'm saying the four point 3.9 per 100 person years. What we found was the there was a paper here in 2011. From the Dutch group, alarming incidence of Hepatitis C, reinfection and 15 per 100 person, so for order of magnitude higher, and this is in the context of the of the primary infection rates, first time primary infection. So pretty substantial shortly thereafter, a really nice collaborative study in mostly England and Germany but also so that's why the papers are over this country's there of six 7% incidence reduction. intent for France 2.7%, approximately 10 fold. So pretty striking difference in incidents. But there's really nothing much known here. So across the pond, we usually have not much of an understanding of these things here. They've done so much more work in Europe. So why do we have we had the primary incidents here in the max. It's covered in four cities. And then in New York City, they're the New York City Department of Health Data. So it's not exactly incidents for primary factory but close enough about point five where the person is but we really just had no nothing on reinfection. Although the UCSD folks have been working on this, so this brings us to the work that we did so said we need to look at reinfection in the core event that I had seen and been treating the initial infection. So from my near acute Hepatitis C referral network. We had

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men who had been infections cleared with interferon, the direct acting antivirals, DHEA, and then spontaneous clearance. We have a total of 305. Today in fall, they were in their mid 40s as bad one in five black one in five Hispanic and even split for insurance status for commercial nine. We filed for first reinfection. 836 persons is pretty substantial median of 2.2 years with 33 infections 12% of the group. This looked a lot like what they're seeing in Europe there. And then we followed subsequently. So the incidence there are 4.3 point 2% Or So somewhere between the French in the in the German experience and it was an immediate, it's just 1.9 years. That's when the reinfection happened after the cure. So we were able to follow 32 men for subsequently infections another 62 person years, and found 66 of them got reinfected as well for an incidence rate almost 10 per 100 person years at a median of 1.1, which in this difference is actually statistically significant. I say, here in this Kaplan Meier survival curve showing that first reinfections in blue secondary infections there and then more Cayenne, I think it's what the the app calls it, and the significant one faster, the incidence rate is higher for secondary infection. And so just keep that in mind for first reinfection is incidence is much higher than primary infection and secondary infection somewhat higher than the first and what that's telling us about the biology and behaviors. So obviously, it's a significant problem. And in other things that are worth noting here, although I'm not going to talk about what's called Hepatitis C elimination, there's no time for that, I think given today's talk, but they give trying to the World Health Organization call for the elimination, which does not mean eradication. In medical parlance, apparently, it means a 90% reduction. It but in Hepatitis C and B through treatment. So here's the problem. We looked at did reinfection happen faster? Whether if you retreated initially with the DA or interferon and spontaneous clearance? And the answer is no. So it didn't matter what treatment you had. So some people worry that if you're not sort of neat enough with treatment, that people will just go out and get reinfected the idea that interferon was so painful, that would be a deterrent. And that's just not true. And that's generally just not true for anything. It's a really stigmatizing thing. But but the other implication of this, since it's actually time ordered the DEA is after so after this means that after release of DEA, the reinfection rate was not significantly lower, you just put it by here and interfere on your and then the DEA era, which in New York started about 2014. But if you draw a line in 2015, when Harvoni came out, it's really still the incidence rate, numerically slightly different, but it's not even close to being statistically significant. So basically, treatments in New York has not decreased the incidence of reinfection in this period through the Entity Data, so not so auspicious for treatment alone. But we don't have time to go into that sort of in a whole nother talk. So he asked, well, what are the risk factors? For reinfection? Is it the same and so we looked at back and we were able to locate quite a substantial proportion of people. So looking at that we had the 304 cleared, we didn't have risk factor information Bill 266. Our risk factor CT was 238 they were very closely. Sunset dome, indistinguishable sunset was really random, missing this and so we assessed all visits from the date of cure for the risk factors for primary Hepatitis. And so we we went and although other groups had had multiple other risk factors associated in New York, primary and primary infection is associated with two was the jackers from Siemens into the rectum, and sex wall. Hi, I'm Crystal Meth, no injections. And in this, for this study, though, we added sexual high math, but by injection, we, since we exclude that, and the first one, we want to address what that might be important. Not so much because people share because they actually don't, but because it can be a marker of intensity of nephews, which may pointed to other things and

directly. So when we did that, we found that our first read section, looking at the core for first reinfection, we have since 1200 21 visits and 28 re infections among that group. And then information on secondary infection also add 20 people and 166 more visits assessed and found 63 infections in this group. So this is the basis of our risk factor assessment. And we are looking at the ceiling and the rectum sexualized Matthew's and with with or without injection, and so yeah, no, but you said that these were the ones in New York, but what about those others? How do you know you're not missing stuff? And what's interesting is a way of thinking about that, that people 95 People reported none of these three. So it didn't do any of them at any point who whether it was proximal to their infection or not, at any point, only one of those had a reinfection where basically 33 of the rejections occurred in among 121 reporting at least one of those rights factors at any time. So it's very unlikely that we're missing any important risk factor here aside from and what we did there, Stephanie factor, a longtime colleague on this all the way back to the primary infection time, fabulous. Epidemiologists, we've been working very hard on this for a while. But the analysis of this turns out to be quite tricky. And very just recently figured out here that in the multivariable logistic regression, and this is a time dependence analysis. So you're really looking for over time, what are the risk exposures that are related to the reinfection event, and figured out that separate models are necessary specifically for blacks and whites due to a very different magnitude in the risks and I'll show you what that looks like here. And that is that although the risk factors generally qualitatively similar, that semen in the rectum was highly significant in both the magnitude of the odds ratio, the hazard ratio, the association's senior director, wax lights was was even higher and they were both statistically significant and the other interesting differences that that sexualized use of math by the by injection was a very significant risk among blacks but not least sexualized drug use was not at all risk among whites in so so yeah, well, that's interesting in contrast to primary infection where you found that it was highly significantly associated with the was both semen in the rectum and sexualized strategies. And so this is I want to highlight differences and I think an important difference in how to think about this is a lot of information on once I'm going to try to sum it up in a graphic way, and hope that that helps some. But so in the words description, and then I'm going to try out showing this visually. What helps you reinfection tells us about Hepatitis C networks in prevention. complicated set of things, we'll see how this comes across. So thinking about this to start with what we know from experience with people who inject drugs to P. W IDs depreciation, I don't like to say it out loud because it's only a point of not reducing people to just abbreviations. So but people who inject drugs when they encounter very high Hep C prevalence when the initiative objective gets in, in many communities, it's 90% prevalence even among people and the network's probably completely And so the choir the primary infection rate, people who are entering the first year or two is very high by 23 brand new persons after cure and participating in various harm reductions, and so there are important reductions that are there are available and very effective for people who inject drugs. One is opioid agonist therapy is different ways of stating that phraseology. But basically, you can take buprenorphine methadone, and really decreases

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injection use period. And then there's needle exchanges and people who are most are really quite interested in that so. So you get cured interested in some of the programs and those who are participating in the programs are infection rate is, is much lower in order magnitude, than 1.4

100, prisoners relatively low rate, most of those are in folks who didn't stay in the pocket. And that's despite reentering the same objection network people stay in networks, it's not so much people stay in networks, it's almost definitional. Fact. You are part of the network, you are part of that unless you move to another city. Network is is a bit of a sort of circular definition sets because people don't shift. So much, it's almost not possible. So we'll think about that in the second year. Now in contrast in two, because I'm going to really say in contrast in men have sex with men. We know most about those with HIV, but that was in practice from managing risk and getting Hepatitis C. So they encounter a much lower Hep C prevalence overall, I'm going to be more specific about that. But clearly, the prevalence is quite a bit lower than the networks of people who are dangerous. And so there's a much lower I would say, so therefore a much lower primary infection, a half or so in New York, half per 100 person, because it's supposed to say 23, grinders. Why after cure, as it turns out, there's really no there No, I'm gonna call it acceptable to men. Risk Reduction possible. Getting it from semen in the rectum. There's no increase in condom use. There's overall Secretary trade, decreasing honeymoon significant over the years, and then the reinfection rate is an order of magnitude higher than the primary are finding there. It's basically very close in order to make to hire units in New York, despite overall the overall low prevalence. And so what this suggests and I'm going to show a little bit more about this, that it's there's a real difference in the Hep C prevalence among the networks among intersections. And so, there are two factors on the technical one is that sexual risk factors for primary and reinfection of the same drug use is different from the primary and Hep C, reinfection. And its primary infection, we talked about seeming in the rectum and sexualized during use non injection drug use Neph, reinfection, semen in the rectum, and many blacks, the whites sexually strike us with, with injection, it's really a very different result, it's much clearer, assuming the rectum much less clear what drug use has to do with it. And that makes a lot of sense, because it's not the meth doesn't, I would have seen. And the second point here to, in thinking about this is that the reinfection rate, as we talked about that segment is an order of magnitude higher than the primary infection. And so taking these together that suggest that there's a heterogeneous distribution of hep C among sexual networks. So among the network's some had most little or no prevalence and most networks high prevalence in some way to say about a 10th, maybe corresponding to about the tenfold difference, that's it, back of the envelope, kind of guess, and that we're going to suggest to you that the drug use is a surrogate marker, perhaps the prevalence in sexual death, said the folks who are in networks where there's sexualized drug use that may be these are older descendents from older perhaps heroin networks in the 70s. I don't have a file genetics of the viruses to prove that this point, but it this is my hypothesis here, but that's how you explained the difference. And you'll see a little bit more here. So I'm going to I'm going to make now do this sort of figuratively. So starting again, when people inject, right, so what we have here is, this is sort of a bird's eye view. And nobody knows what a network will actually look like. So This is we are the admission viewer. And in this particular schema, the orange denote somebody who is Hepatitis see, the black figures don't. And that, of course, people don't wear their color. So we don't know. So so when a person enters, starts, injecting begins, injection currents enters then a network, this is going to be his network. And so just sort of zooming in on that. When you start injecting and sharing, heroin, people quickly become infected. Fortunately, we have treatments, and they're really VA so come off to treatment and get and get treated. And now, the person who is now no longer has Hep C, comes back out is thinking about returning or not returning to, to the Jackson network

and is in a program to help and then the reinfection rate is quite low, despite having the same overall we haven't treated the other folks in the network at all, under this premise, but certainly, that's we're trying, and that's good, I get that now, in gotta say, similar contrasts, now we have sexual networks, among NSM. And you'll notice here that the ones with blue figure have no Hep C in them, and the ones that are orange, of course, do and but that the so that the prevalence among the network sniffing ICU is very low. And the prevalence in the network itself is also lower. And in just three year 10 or so and there's much less lower prevalence and so now a person then who is then entering the sexual network, in this case, for our purposes, as introduced network that has the highest Hepatitis C prevalence in in the groups that we have here, this is a sexual network now. So again, kind of zooming in on that network. With this high prevalence in having sex, he becomes Hepatitis C affected, and but we have our nice bag of DHEA and cure him. Then, as he returns now to without Hepatitis C, and back and is looking into essential network again, say, Well, how are we going to prevent that? Well, Mr. Condon will fight fight off Hepatitis C. But in fact, that is not what is Gordon's take it up. And so the reinfection rate is quite high reentry network. So that's my sort of graphical overview on how to think about the differences and the problems that we have. And in particular, if you don't have a plausible harm reduction strategy. So we're going to make a shift here to a away from sort of idea and this picture, just to say, What's practically speaking, how do we do this? I think it's important in some, many will find itself, just pretty straightforward. If you're testing for primary infection, that is people who haven't had it before. There's their antibody, negative serum. So you're tasked with an antibody test. And everybody needs to make sure that that test that particular one, as a reflex the viral and see that they're there are still available recently. And I still see people coming in just had an antibody without reflex, the viral load. And that's a problem on many levels and loss to follow up and having to bring people back. So we just got to make sure that that test didn't it specified and if you're using a computer, the autofill could really mess you up and get the wrong testing. So you monitor within and find this in the reflex the viral is also important because some people may have had previous infections spontaneously clear they may not have been treated. They come in sick the doc I never had it before. They have a positive antibody test, but their virus negative so they've probably already spontaneously. They may not have spontaneous has really got to keep following up. That's a different issue, but that's an important thing to know. I also highly recommend the car against metabolic panel or some equivalent that is a LT and ASD. And reason is that the LT is actually more sensitive. But it's obviously not specific to Hepatitis, but it's more sensitive that the ALP will be elevated, it may not be a lot elevated, but it can definitely elevated weeks before seroconversion.

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So it's interesting version to thinking about comparisons to the the HIV test that has now antigen, and antibody, or less specific than that, but it's an early early one at first. So if you see an ELT, that's a couple 100 And then the antibodies negative, you got to bring that person back into viral testing, because the reflex for the antibody test is only with a positive antibody test. So and I see that the same thing, too, and the practice is, especially if you're not drawing antibodies often. And so what do we do for reinfection? Well, people are already surprised. So you don't send an antibody test. I see a lot of adults lot of antibody testing happening. I think some of it is using epic. When you type in the order for Hepatitis C, it sort of auto populates with your antibody tests because it's more popular, it's hierarchically chosen or something like that. And

the only good news about that sort of is that if you had a positive test, and then you'd have a reflex, the viral load, then you'll actually get the viral load test. But so the error is compensated for by reflex bar. So you got to remember to have CRNA. Another problem with that, though? Well, I get back a second and I do the comprehensive metabolic panel on this. Also, it helps if you didn't draw the viral load. And so they say how often so I collaborated with Natasha Martin in her mathematical modeling group at UCSD. And they've done a lot of work internationally to try to understand what we need to do to decrease the incidence of Hepatitis C. So we'd look to see how often to screen and thinking as a cost effectiveness analysis and, and so with all this, there's various strategies here and the one that we came to this is our latest iteration, it's not published yet, we're still working on crunching the last bit of numbers here. But it looks like what we have now is that that if you test in this is all MSM, so those with HIV every six months or PrEP every six months, and PrEP nonusers, whenever you get an HIV test that that's a very reasonable amount of $80,000. For for the quality of it, such as the quality adjusted life years is considered cost effective thing. Try to look at HIV, those with HIV every three months, it gets much more expensive when you go to decreased intervals further out, for instance, by testing those with PrEP for three months. So it's a it's a reasonable thing to step for infection for primary infection infection, we can only take this as basically the same this is mostly for primary infection, but how often do you do it? Twice a year. So that brings us now to just finish. That's our that was our last objective. So I'm going to go through and summarize so we hopefully have time for some questions. So in summary, the first objective discuss the epidemiology of sexually transmitted C. So MSM acquire Hepatitis C, during sex across four continents, both hemispheres. reinfection rate is much higher than the primary initial infection rate, which tells us that sexual networks are innocent of overall low prevalence, but those who acquire Hepatitis C are by definition part of a high prevalence sexual and so Once cured, then re enter it is that work. So unless you're protecting against receiving semen in the rectum, reinfection is common. And we don't have a good alternative so far to Congress in a novel, novel way. The main behavioral risk factors described there multiple risk factors is done across US and Europe, that sex various names of my friends sex and and drug use. But I think that we've started distilling that our goal here is not so much to find all associations but to find the ones that are actually necessary for for transmission. So risk factor is less interested in what are you going to tell your person is really the thing that's transmitted? So in New York City primary Hepatitis C independently associated with semen in the rectum and sexualized now injection drug use meth use specifically And the reinfection again, semen in the rectum and black for Black MSM that it was a sexualized drug use. Objection, you said I think that what that says here today, again, what I mentioned, to think that that sexualized drug use is surrogate for higher Hep C prevalence of network. And it may say that the prevalence of hep C may be higher in networks in which Black MSM participate. There are other lines of reasoning that would suggest that to be the case and would result in a higher infection rate. We didn't see that per se. But that's my hypothesis, it's the semen that is carrying Hepatitis see some cases that can be record fluid, but largely it's semen. And that drug use has something to do with what your environment is. The bodily fluids, it's talked about seeming to the rectum, very strongly associated epidemiologically. So we found that it was in the semen of a third of MSM group, C, of course, and the average Jacqueline has enough Hepatitis C if rubbed into the vascular area, the included serving area of the rectum, could enter the foreign system and particularly go straight to the liver. And that it's found Hep C is found in the rectal fluid of half read Hepatitis C as well as love that could

plausibly infected a penis or if carried on the penis fist or toy to the man next to him could then bring Hepatitis C that way. So inserted penis would be exposed to a plausible amount of Pepsi for the duration of EPs, and I've had people say, Well, that doesn't sound like very much. And I've asked for volunteers says, Okay, well, why don't we just do the experiment? Because we'll just put some FC 2300 units of Pepsi and we'll just rub it in your penis for 10 minutes, and we'll see what what happens there. So far. Nobody's is volunteered for that. So Well, we'll see. You don't have we don't have a proof of that yet. And finally, optimal test types to monitor for hep C primary and reinfection. primary infection. If you haven't had an antibody with reflux to viral load, comprehensive metabolic gets the sensitivity and specificity and reinfection, draw the viral load and you just have to order that. And I would say that it's actually really important to do this. And one of the things that that I didn't emphasize about the reinfections, if you remember, back to the Kaplan Meier curve, reinfections, were the median time is about two years, if you all comers, if you do first and second together, yeah, it's a little under under two years, but they continue to happen for up to 11 years. And so don't stop monitoring. Particularly, there's a certain amount of fatigue, go viral is expensive, and just don't want to do it. It's really important to continue to monitor people reporting any sex, you know, see your back, perhaps ask them about sex. And the particular about doing that I think most of us think about sexual health, but well, but you know, age can be quite broad. And really just, if you're feeling like you're testing for syphilis, or gonorrhea and chlamydia, and certainly anyone that has had it, then you should be testing for that symptom reduction, really important to not stop testing, and don't test people with the antibody, you've already had infection because this happens all the time. Because there's a lot of anxiety there. Oh my god, I've got it again, people come back to me from their programs that only have a antibody test and see DACA a positive test. If I read effective and it was just an antibody test, it was positive and they're not reading the virus is negative. And then also absolutely important to test men on PrEP. I didn't show you the date on that. But this is well, well shown. Europe and we also here in the US that the PrEP get started having sex condomless sex with with the men who had been reservoir so there's, there's plenty out there. And the testing frequencies is the same, at least nominally twice here with you the test. And that is the talk for today. I do put this up about the the updates and the website, you can scan this code will take you to the directly to the website. And that is I think, where we leave it up, no questions. Write to me. And here. Here's the hotline for other things. I hope I've left a couple of minutes here.

49:47
Okay, thanks very much. That was that was really a terrific presentation. There. There are a couple of questions that have come through the chat, one of one of which I think you answered like almost immediately after the call Question was put in, but one was addressing? Could you Could you comment on Hep C viral loads in vaginal fluids? With with the team and similar?

50:14
Yeah, I haven't. Haven't done that. That's not not my field. The there's there was not much I was surprised actually how little had been looked at for given rectal fluid. So it even Hepatitis B, which had been long accepted as a sexually transmitted virus, there's there was very little on it. The we do know, though, from I would say actually pretty good studies, that that's a high standard for me just say that people who know me say, Wow, all right, that they must have

really been good. They're generally referred to as discordant couples study. So prospectively enrolling men and women. So these we heterosexual couples who keep a sex diary, what did you do? How'd you do it? How often when and would follow, one would have have seen one would not man woman either way, and then would have follow up with testing. And there's even done fairly recently, or at least for a very large studies, and essentially, nobody, no man or woman got your hep seen from your partner there, people got Hep C, but it wasn't a partnership. So and this is really been part of why the CDC says that it says Hepatitis C isn't sexually transmitted or has it modified it a little since I you know, they've published in this country with with the DEA and it's clear from lots of European evidence that it sexually transmitted among men and sex with men. So it appears that the inserted penis in the vagina is not acquiring si si it's mostly stratified tofu. And so, it getting into the urethral meatus may not be such a an issue for for that and there may be just a differences, behavioral differences that are really hard to control for the ASX was not uncommon in the studies, among heterosexuals, but it may be done differently to men, the men and women are no. Without doing that as a real control, we need a Modern Masters and Johnson to look at that. And so what I'd say is that I don't have much for her data on on Hepatitis C and natural fluid, I actually would expect it to be there at levels similar to what we see in the other in safe, direct or fluid receiving as a similar kind of fluid sources. But it does not appear to likely to be a significant factor in infecting a partner. And so condom use is not actually recommended, specifically in that circumstance. And I don't have independent data of that address. It

53:29
was two or three more questions. And so one is to sort of clarify when screening men who have sex with other men who are on PrEP, what tests should you order? Was, were you saying is just an asp or al t? So no,

53:46
it was the same at the same testing fermentum PrEP is Hepatitis, Hepatitis C PrEP is no different than men and sex with men. So that was the what that from the curve, their cost effectiveness analysis is every six months. Man with HIV and PrEP. So you ain't gonna do

54:09
antibody testing if never infected. PVS previously infected with voodoo virus and ASP.

54:18
I do I do comprehensive metabolic panels. When I draw my levels, they're cheap. And so I do that then one of my colleagues in San Francisco said he was picking up too much alcohol at brunch, but the magnitude of changes from alcohol are very small, even relatively compared to Hepatitis C peyote is at an krytus. Whereas if your It is 400 That better not be you're not going to last long. So that's going to be updated. See? So to be clear, when I go at least six months it's to get out of people who've had primary infection. If I can show this again, I'm just going to go ahead and go back to this slide. So this is this one here, this this particular thing. It says that if HIV PrEP and PrEP nonusers, six months, every six months, I get a comprehensive metabolic panel when I draw this, this is true for antibody for people who have not had Hepatitis C, viral load for people who have it's actually very straightforward in that sense that they are this is just

the same and simple. It's not fancy this, this shouldn't be there. This is not a complicated algorithms, get the Hep C testing and to get a cause I just get the comprehensive metabolic panel, you really aren't doing that with PrEP a couple times a year anyway. In addition, you gotta get the credit. And I do that in men think of any in any seam in the rectum? No, no, there's, there's, you could do it more if you think that certainly if this is just everybody, this is modeling based on just absolutely everything. And so it allows for screening people who have more intensive exposures more often. But this is this is assuming just average risk. And so we recommend don't do less than this is cost effective. Okay, then guidelines yet, maybe not quite we work on that takes a while to get that stuff updated.

56:44
And one of the you've addressed, really behavioral risk factors, but you didn't really talk about non behavioral risk factors. And I know back in the sort of when this was all starting in the early 2000s, there were reports about outbreaks of LGV, which were just then being described as rectal outbreaks, and strong associations with hep C. So you know, whether that's the same population with the subset with higher risk, or is there some more complicated interaction there? If you could comment on that or other guys?

57:18
Yeah, the bacterial STIs are much more common. They're much more prevalent. LGV happened to be the strain committee, the causes are episodically present in communities. But they're, they're much more common. So it's extremely unusual to not have had a bacterial STI, before getting Hepatitis C, but it's stochastic. So if you have something that's 10 times the prevalence, you are extremely more likely to get that thing that's high, or highly prevalent. But if you're doing coin flipping, for instance, just as an example, it doesn't go heads, tails, heads, tails, sometimes you get run to 10 heads. So, for instance, so there is no connection. I mean, there's no, I mean, there's nothing to do with another STI. People positive, you know, if you have a breakdown and barriers, and would you be more susceptible? Sure, if you have large, ulcerating regions, other things can get in more easily. That's not, but it's not necessary. I think one of the key things is what is it's, it's not necessary for gap. It's sufficient to just have virus in the rectum with seeming without other things. So while things may make it worse, if you have big holes in the rectum for various reasons, is it from syphilis? Shankar is is it LGV with wild inflammation? Is it some bleeding, you know, so much to the rectum is bleeding? Sure, but it's sort of not the point, the point that I'm making is that that's to me just fuzzy around the edges. Because the question is, how does it happen? And that's really what you want to get, of course, you're going to treat someone's LTV you're trying to protect them against it's the same kind of thing with US economy. So the real issue is what is actually what's the biology, that's what sort of getting it in, so you don't need any of these other things. The Dutch did, actually, they found that in retrospect, they just noticed that they that actually, they had a big LGB outbreak, and then they Rotterdam, and then they noticed that some of them had Hepatitis C, and that's what led to their first observation on it. But, again, it's not there's a very important difference if necessary. And sufficient and that sufficient is really, I think, what I'm trying to get at what is it that nominal you need to have, and so sure, is there an association with syphilis possibly how but it's very hard to do that, you know, you'd have to do the experiments specifically. So again, focus on what's really important, which is I think semen really mediates most of it and these

other things kind of are distractions. Um, And so I really want to say it's seeming to direct. And that's that's what's happening. There are other circumstances if you do other things you group sex, it's very hard to control that. I hope that address that. Yeah, yeah.

1:00:12
So I think we're out of time. It's 102. We have one last comment Zika and Hep C and semen. What's next? Yeah, well, yeah.

1:00:22
Those are those are related viruses. So the we've been talking about hep C for a long time, and then all of a sudden, everybody accepted him, the hardest time trying to send it Hep C is an important way of transmitting, then we found this in the Ebola and Zika and semen networks. Okay, that makes sense. You know that what do you mean, we've been talking about Hepatitis C and sexual transmission and explaining it for a decade or more, and then just a couple of reports come out, and they just say, oh, yeah, these people got it, and it's suddenly accepted. So I think that this is a problem with the Hep C field that everyone is so used to thinking of it is it has to be blood borne. It has to be blood borne, and just, it's a, it's an old mindset that just absolutely needs to be removed, because it it's a, it's a scotoma, it interferes with, with making an understanding of the diagnosis. And so just, you know, it's important thing we clearly accepted Zika. So, is that what's wrong with you know, why we do not think about Hepatitis C? I mean, these are both even related viruses. So, yeah, what's next? Well, I don't know things in the semen. You got to think about that. And so Congress or safety data are of course carries, carries with it the pathogens that may come into blood, and we may exactly find, at least it doesn't appear to be way you get cold, you get the hit COVID by breathing right on that person for about 1015 minutes. Having sex, that's probably the root of COVID and Hep C.

1:01:48
All right. Well, with that, I think we'll end Alright, thanks very much. And thanks.

[End Transcript]