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RAPID ENTRY AND ART INITIATION IN HIV CARE: IMPLEMENTATION OF A NEW PARADIGM

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Rapid Entry and ART Initiation in HIV Care: Implementation of a New Paradigm
[video transcript]

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Good afternoon. Thank you, first of all, to the conference organizers. This is definitely one of my favorite conferences because I think it's so clinically tangible and relevant. And I really want to say thank you to you guys that are all out there. First of all, you've sat through this all day and second of all, you're the ones on the front lines really delivering all this excellent, compassionate care and helping turn the tide of our epidemic in this country.

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After I finish, I hope that you're able to describe some of the rationale and evidence for rapid entry into HIV care, to compare some of the models of rapid entry from around the globe, and then most importantly in my mind, identify some of the challenges with implementation of programs and think about how you might be able to do similar things in your own settings. And I will say, and it's been brought up in both of these previous talks by Judy and David, about whether we're initially starting therapy or changing therapy, despite the term "rapid," it needs to be done with caution and care and we still need to do what's right for the patient and not just throw them on something and send them out to the door.

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So, just curious, and this may be an estimate because you probably don't have the data at your fingertips, but in your clinics, on average, how long after patients enroll in clinic, not necessarily when they see you the provider the first time but when they enroll in your clinic, how long after that are they beginning on antiretrovirals therapy? Same day, within a couple of weeks, within a month, or does it take longer than a month?

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Okay. So, an array of responses and mostly kind of takes a couple of weeks to maybe a month or so.

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So, why are we pushing at this point for earlier anti-retroviral therapy? And you've heard a lot about this throughout the day. First and foremost, our guidelines have shifted, both the DHHS, the WHO, IAS. We all now agree that everybody needs anti-retroviral therapy. What we don't necessarily know is exactly the timeframe. Furthermore, we know largely from studies in the developing world but also here in the U.S., that we have high attrition rates from the time someone has a positive test to when they start anti-retroviral therapy. I'm sure that you all have had the patient who shows up in your clinic, they were diagnosed with HIV 10 years ago, and you ask them why they haven't been in care and they say, "Well, because they told me I didn't need medications." So, by giving that message that you don't really need the medications right now, it does send a bit of a mixed message to our patients. Furthermore, those delays in treatment are associated with increased mortality, diminished CD4 recovery, avoidable hospitalizations, which can lead to increased costs and opportunistic infections. And then the public

health aspect, we definitely know that it leads to increased HIV transmission as well. On the other side of the spectrum, we're able to do it more quickly because of the improved drug tolerability and the durability of our drugs and the lower risk of resistance. It's not that the risk is absent but it's certainly lower than it was 10 or 15 years ago.

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So, Judy kind of asked this question. Similar anyway. Since what year have the DHHS ARV guidelines recommended anti-retroviral therapy for all?

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All right, so I guess it was a decent question.

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So, this kind of shows the evolution of the, specifically the Department of Health and Human Services guidelines, and you can see in the bottom left corner, way back in the 90s, we were only really treating those who had CD4 counts that were less than 200 or they had symptomatic disease. And then as we progress to the right, you notice that treatment kind of moves up the spectrum. And in 2012, for the first time the Department of Health and Human Services recommended starting antiretrovirals for a CD4 count of greater than 500. And then in 2015, the WHO recommended therapy for all as well.

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And I won't mention these studies so this will get through the presentation more quickly because these have all been referenced earlier in the day. So, this study on the left is the HPTN 052 study, which was the landmark study for treatment as prevention. And this study on the right shows the decreased risk of adverse events and death when starting therapy at CD4 counts above 500 as opposed to below 350, and that was the START trial. And another similar trial was the TEMPRANO trial that the guidelines also reference as a reason for recommending therapy for all.

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And so now we're starting to talk about the end of the AIDS epidemic. And UNAIDS has put forth this diagram and this metric to say that if we can achieve this, maybe we'll get to the end of AIDS by 2030. And what they're after is diagnosing 90 percent of people living with HIV around the globe, getting 90 percent of those people on treatment and finally, getting 90 percent of those people are logically suppressed. And I think that's a great target but at the end of the day, even if we do that, that really still leaves less than three quarters of patients living with HIV virologically suppressed. So, I'm always thinking for the patient that's in front of me, what is it that I can do to get them virologically suppressed?

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One of those things, I think, is to start therapy more quickly. And so I'll go through the evidence. The nice thing is there aren't that many large studies done on this yet looking at rapid initiation of therapy.

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The first study to be published was called the RapIT trial and this was done in South Africa by Rosen and his colleagues. It was an unblinded randomized controlled trial at two public sector clinics in South Africa. One was a hospital-based clinic and the other was a freestanding Primary Health Care Center. And they looked at single visit initiation of ART and on the next slide I'll show you the two arms of randomization. The inclusion criteria were that the patients had to be over 18, non-pregnant, ART naive, and eligible for anti-retroviral therapy in that setting at the time the study was done, and that was CD4 count of less than 350. The primary outcome that they looked at was viral suppression of less than 400 copies per mL within 10 months of study enrollment. That 10-month follow-up time I know is a little quirky but the reason that was done is they kind of wanted to give people on the long end 90 days to get onto therapy and then the standard of care in that setting is to get a repeat viral load at six months. It's very different than the setting that we practice in. But they wanted to be able to capture that because after enrollment in the study, then patients in either arm just kind of continued in care the way they would otherwise. It wasn't like some of the ACTG studies that are done here where patients are brought in for specific study visits. And then you can see the secondary outcomes there.

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So, this is a busy slide and I don't want you to get lost in it but it's really to illustrate how complex, and this may not be very different in some of our own clinics, that the process of getting on antiretrovirals and the standard arm was. And so on the left side, this red shows you the six visits that a patient had to undergo before they were given those magical little pills. So, when we have a patient in our clinic that has a blood pressure of 150 over 100, we don't say do X Y and Z and then I'll give you your chlorthalidone or hydrochlorothiazide. We give it to them. And so that's what we're starting to do with HIV. Previously they had to get a CD4 count, They had to do a TB symptom screen if they were symptomatic, they had to have TB ruled out, come back for their CD4 lab results, get some counseling, get some more counseling, get your results of your labs, and then finally get your antiretrovirals. And the blue side, this was the rapid arm. They just combined all that into one visit. And this actually happened within a matter of three to four hours. So, it's amazing to think that we were doing this over six different visits and then they were able to truncate it, even in a setting difficult to practice in like South Africa, they were able to get it down to three hours or so.

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So, these are the baseline characteristics of the two arms and the standard arm and the rapid arm, and you can see kind of going down the rows that largely they were similar. Average age was about 35. Slightly over half of the patients were female. CD4 counts around 200 in both arms. And then in terms of the purpose of the clinic visit means that these patients could be enrolled in the trial on the day that they actually came in for their HIV test or on the day that they were coming in for CD4 counts or getting their results, so there were kind of a number of visits where they could enroll them. And then reason for their treatment eligibility. So, as you can see they, again, they had to be treatment eligible so there were actually 20 percent in each arm, it just so happened to balance out, that were excluded because they were not eligible for therapy.

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And here are really the take home results. So, the time to initiation of anti-retroviral therapy in the blue line, the median time was zero days or the same day that they were in clinic, as opposed to the standard arm, which is similar to a lot of the clinics that you all practice in it sounds like, which was about 17 days. And furthermore, if you look out to 90 days, in the rapid arm almost 100 percent of people were on therapy compared to the standard arm where only three quarters of the patients had actually gotten on therapy at that point. Again, highlighting the point that when you have the patient in your grasp, you're there talking to them and we don't give them the therapy, what message is that sending? It gives them an opportunity to get lost from care.

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To me, one of the most encouraging things about this trial is the hope for better long-term outcomes and I apologize, it's probably tough to see. But as most of you know as well, our biggest challenge at this point in HIV care delivery is retention in care. And I don't have a slide that shows the HIV care continuum but only about half of patients in the United States that should be engaged in care and retained in care are. And this study suggests that we may have good longer term outcomes if we engage them in care more quickly. So, you can see here this was their primary outcome, those suppressed, virologically suppressed, by 10 months. In the standard arm it was 51 percent, in the rapid arm increased to 64 percent, which is a crude risk difference of 13 percent. And when they did the analyses adjusting for all the covariates it remained significant. And then this was the retention aspect that I was referring to. So, they looked at retention at 10 months so this was did they have a care visit between the 5 month and the 10 month mark. Only 64 percent in the standard arm did while 81 percent in the rapid arm did. Again, suggesting that getting people into care and on therapy more quickly may help retain them in care in the long run.

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So, that's great. But now I'll ask you a simple true false question. So, it seems like same day ART may increase rates of viral suppression but patients are going to be reluctant to start therapy that quickly. They've heard all the horrible things about those antiretrovirals.

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If I was Dr. Saag I feel like I would ask for music up here. Okay, so a three quarter-quarter split.

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Now I'm going to tell you a little bit about the study that Dr. Galant (?) referenced in his talk a little while ago and this was the rapid study that was done in San Francisco's General Hospital on their ward 86. And what I will say this is not a randomized controlled trial. It was a study, a health services study done in the context of the usual practice environment. This graph shows, similar to the South Africa study, what patients had to do before they got in or before they finally got on antiretrovirals and it required three or four visits in their clinic as well. And then finally anti-retroviral therapy was started. So, like they did in South Africa, they truncated that all to a single visit multi-disciplinary care. Everybody in the clinic really has to pull together for this to work. You have to take care of the pharmaceutical, the labs, the social work issues, the insurance, all of the social determinants of health.

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And so this was really a feasibility study as I said, in a health system setting for same day outpatient antiretroviral therapy. And these were, again, newly diagnosed HIV infections. Initially, when they started in July of 2013 they were only doing what they called acute or recent infections. And so, those were people that had a true acute HIV infection that were presenting with retroviral syndrome or patients who had a newly diagnosed infection with a negative antibody within the last six months. As they got rolling, once 2014 hit, they extended that to include those who had active OIs. We have a nice ACTG study that showed that there's benefits for starting again in active OIs, excluding cryptococcal disease, or those with CD4 counts of less than 200. And this was deployed, again, it's not a randomized trial and it was deployed in the context of their already extensive services that they had in their clinic for navigation, linkage and retention. All those were in place for these patients. So, they facilitated same day appointments, they came up with flexible scheduling for providers so they essentially had a on call provider that would be called in to see these patients if one showed up. They had some pre-approved antiretroviral regimens that were used and that were considered safe to use before labs returned and before the genotype results returned. As Dr. Aber (?) pointed out, all these things are still very necessary and are going to inform our decisions. And so, if we're going to start before those results are back, we need to make sure they're sent and we need to make sure that we're starting regimens that are absolutely safe in those contexts. And this was largely tenofovir-based regimens, whether it was TDF or TAF, and dolutegravir or boosted protease inhibitors because of their high barrier to resistance. They had five day starter packs available that they would give to the patients so that this allowed, if they needed health insurance, or they needed a pharmaceutical assistance program, it allowed the paperwork to be processed and they could start taking their pills that day. And then they actually tried to give the patients their first dose in clinic observed to kind of give some extra encouragement.

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And this is what their two arms of their study looked like. Again, this was not randomized. If they came in as an acute infection or met one of those other criteria, they went down the rapid pathway. If they came in otherwise, they went down their usual pathway. But despite the fact that it was not randomized, you see that the two arms were virtually similar in terms of age, sex, ethnicity. And then I highlighted in red these aspects here that we consider sometimes very challenging socially and oftentimes use as an excuse not to start anti-retroviral therapy. So, it's not that they had a pristine population in terms of social determinants to work with. The only difference where these two arms really came out was whether or not the patients had acute or early infection and that's because that was one of the ways they selected the populations. Their patients had much higher CD4 counts by and large to start because they're doing a great job testing early in San Francisco.

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And this gets at that true false question that I was asking. Is this acceptable to patients? So, the blue bar is the rapid, the orange bar is the universal. And these were the percent on antiretrovirals after the day that they came into clinic for the first time. And you see that on day zero, 90 percent had said yes. By the next day, 95 percent were on therapy. And by day seven, 97 percent were on and they were well on their way. So, most patients want this and I'll get into our own clinic's experience and a few slides, but

certainly in my experience with patients, we have patients coming into clinic asking for medications. They do not want to leave without medications.

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This is a similar slide to what Dr. Galant (?) showed, just in a different format, showing the changing time to viral suppression as they began to start antiretroviral therapy at different points. So, on the far right, the curve on the far right is from 2006 to 2009 when they were using CD4 guided therapy and again San Francisco is well ahead of the curve and at this point was offering antiretrovirals to CD4 counts at 500. And then universal anti-retroviral therapy was being offered in 2009 to 2013. That truncated the days to viral suppression to 126. And then finally, in this rapid arm in this study, all the way down to less than two months, which is I think a huge win, again on the public health side of things when thinking about treatment as prevention out in the community.

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Safety has been brought up and making sure that we're doing this carefully and so the nice thing about this study is they reported out a lot of their safety data. As you would expect, most patients in these trials were being started on integrase inhibitors, so 87 percent, and the most common one was tenofovir/FTC dolutegravir. There were indeed more antiretroviral therapy modifications in the rapid arm compared to the universal arm. However, it wasn't happening because the patients were failing therapy. So, a couple of patients had a rash but the majority, ten of those changes, were due to simplification. So, once the genotype came back or one set of HLA B5701 tests came back, then you could simplify the patient's regimen to something if they really wanted a single tablet regimen. Importantly, there were, again, there were no changes for virologic failure. And even after those genotypes came back, it's not like any provider had to go back and change a regimen because of resistance that they saw and they were nervous about. In terms of the transmitted drug resistance that was seen, there were 75 folks in this cohort that had genotype results, 82 percent in the rapid arm versus 92 percent in the non-rapid arm. Now, that difference was non-significant but I'm not quite sure what to make of that, if that's hinting at when people are starting quickly, we're getting careless with labs and we need to be really careful about that and still order the genotype. 35 percent had any major resistance mutation and most of those-- so this is 24 percent of the total, not 24 percent of 35 percent-- had NNRTI mutations, as we would expect. So, they had the K103N since that's the most common transmitted mutation.

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And then the last study that's really demonstrated this, and this was in a randomized controlled trial, is the same day ART study, or the SDART study, that was done by Serena Koenig and her colleagues down at GHESKIO in Haiti. It was presented at IAS and she's working on getting the paper out now. So, she did a randomized controlled trial to compare against same day versus standard therapy. Their inclusion criteria are a little bit different. These were adults, they were ART naive, but they were actually early stage WHO criteria and had a CD4 count of less than 500 because this was standard of care at the time that she did this therapy, or this trial. Her exclusion criteria was anybody that they thought might have active TB essentially they wanted to hold off on. And now they're looking to see if they can start them

rapidly as well. And then they also did a antiretroviral readiness survey that had a handful of questions to kind of assess did the patient really want this? Were they ready? And only two patients in the trial failed that survey and did not get included because of that. Her primary outcome was retention and care with viral load less than 50 at 12 months and then had secondary outcomes of starting antiretroviral therapy and survival.

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In her standard group, this was standard at the GHESKIO clinic, on days 7, 14, and 21, they saw a physician or provider, had some social worker visits, and then on day 21, they got their antiretroviral therapy and came back another week or two later again for a medical and social assessment. In the same day group, the only thing that changed was the timing of antiretroviral therapy. So, they were given it up front but then still went through the same process of seeing the providers, the social workers, and all the wraparound services in their clinic. Ultimately, they enrolled 762 patients but then the data safety monitoring board stopped the study and recommended publication in April 2016 because of the results. And so, they only analyzed 564 because those are the ones that had the follow-up data at the time.

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And here's just a summary slide of her results. I didn't break them all down but you can see that in both arms they completed CD4 counts at the same rates. They do a tremendous job there of getting folks on antiretroviral therapy regardless, which is wonderful, but 100 percent in the rapid arm started, compared to 92 percent in the standard arm and that was statistically significant. And then more importantly, those who were alive and in care at 12 months, so another kind of metric of retention, was 80 percent compared with 71 percent. And then finally, alive with an undetectable viral load, 61 percent compared to 50 percent. And these were all statistically significant findings, which is why the DSMB said this should really be offered to the rest of the folks.

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So, for the last few minutes I'm going to shift our clinic's experience down in the south where you heard this morning that is really the epicenter of our domestic epidemic. All the deep red colors on Dr. Brito's (?) slide were in the Deep South and unfortunately, my state of Georgia has been in the top few states in the country in terms of HIV incidence for the past few years, so we really do have what we are considering an emergency that we need to respond to.

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So, this is our clinic just to give you a general overview of the population that we're serving and the scale that we're doing it on because that's been one of the biggest challenges is figuring out how to do rapid entry when you're dealing on a large scale. So, we have over 6,000 patients in our clinic and these are primarily patients that are diagnosed with AIDS. I'll go through in a few minutes, but up until we did this intervention, this program in our clinic, the way patients were triaged in Atlanta, as crazy as this is, to get their HIV care was based on their CD4 count. And so, if patients who are uninsured they had to know their CD4 count before we could tell them where to get their HIV care. If it was less than 200, they

would come to our clinic. If it was more than 200, they would go to the health department. And so, these patients were getting diagnosed at Grady Memorial Hospital in the ED. The social workers were telling them, "You have HIV. This is a disease that we need to treat. But we've got to send this lab. It's not going to be back for a couple of days. Then we can tell you where you're going to get your care." You can imagine in a hectic emergency room with the types of patients that are coming through a tertiary care hospital, you're not going to get back in touch with those patients to tell them where to follow up. And we have no strong public health safety net like they do in San Francisco to kind of follow up on all the patients, and in New York, who are being diagnosed and assure that they're linked to care. Three quarters of the patients are male. The vast majority are African-American with a much smaller proportion of Latinos. And you can see with the age breakdown that we still have a very young clinic population compared to a lot of other settings in the United States, so half of our patients are less than the age of 45. 90 percent are two times the federal poverty limit. So, a very impoverished and socially challenged population. 46 percent are uninsured with about equal proportions with Medicaid and Medicare. And a very small proportion with private insurance. And you can see the risk factor breakdown for HIV there. We still do have a large number of perinatal patients in our clinic. Thankfully, those are not happening within our health system, but any patient that does get HIV transmitted in the perinatal fashion tends to follow up in our clinic. And as of right now, we have a fairly small proportion of folks who inject drugs as their risk factor, but like the rest of the country, that's increasing if we don't get on top of things, like John Brooks suggested.

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So, these were all the barriers that we were facing when we were thinking about implementing this program. And to me, the toughest ones are always the structural barriers and the systematic barriers. So, as I said, HIV testing was done off site. We're just a Ryan White funded clinic so we don't do HIV testing, we don't have any HIP funds. And so, they were all coming from outside our clinic. We had complex eligibility. Like I said, they had to know their CD4 count. Not to mention to enroll in our clinic, they needed to have income documentation, proof of residence, lots of paperwork that can be very challenging to come by if you're homeless, have a substance abuse problem, have six kids that you're worried about feeding. How to access medications without a payer source so how were we going to do that quickly? How to get these folks scheduled. Again, in a clinic with six thousand patients, that was going to be challenging. Also how to deal with with providers. We've always done it one way. Why are we going to make this change? It's been working pretty well the way we've been doing it. But what we said is it hasn't been working quite well enough based on the epidemic that we have in the south. The other thing was the labs that have to be ordered up front. Working with minimal labs can be very uncomfortable when we're used to patients getting labs a week or two in advance and coming in with all the data at our fingertips, so we have to think a little bit more critically about the decisions we're making. And then in our clinic in particular, and I'll show you a slide in a second, PPDs were a huge barrier to getting folks into care. Not to say that we shouldn't be screening for TB but we always doing active screening and patients were being forced to come back for PPD readings before they'd even get an appointment. There was fears about the patients' attitudes. Would they want this? Would they want to be offered antiretroviral therapy so quickly? I think the San Francisco data is pretty powerful along those lines. And then of course, those social barriers that I mentioned before.

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So, this is-- I don't want you to get lost in this flowchart because it's busy and that's the whole point of it. But in July 2015, when I started as the associate medical director, this is what it looked like for a patient just to try to get an appointment. So, the green circle at the top left is when the patient would come to the enrollment portion of our clinic and say I want to get an appointment here. And this green dot over here was not when they're seeing the provider but just when they're walking out that day with their provider appointment. All the red stop signs were points along the way where someone would tell them you need another piece of documentation, come back when you have it. And this down here, this little circular mess, was the PPD issue. In our health system we don't have the resources right now to do the Quantiferons and so it was requiring patients to get a PPD placed, come back three days later, get it read, and then they were given their appointment. Well, we know that PPDs are very very poor marker of TB in a significantly immunosuppressed population. So, we felt it was much better to be focusing our efforts on the active TB screen. Now we still require PPDs of course, but it's not going to be a barrier to getting them an appointment.

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The reason we were able to do this was for some political will that took place in our county and I know Judy brought up Ryan White and I bring this up. Still to this day in HIV care, advocacy is just as important as it was in the 80s in the 90s and is still what we're having to do to advance the needle forward. So, actually in 2014, when our county commissioners heard the local data of what was going on with HIV, they said something's got to happen. Something's got to be done. And so they formed a task force on HIV to say let's think differently about HIV. Tell us what we need to do to change things. And we as a task force came up with a strategy, a document that we based off of San Francisco's and New York's documents to end AIDS in Fulton County. And one of the objectives was to increase the proportion of those diagnosed to care within three days to 85 percent. So, we've seen the national HIV strategy go from a goal of 90 days to 30 days. And based on some of these more recent data, our county said well let's really shoot for the stars and try to get these people into care within a couple of days.

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Having this document really allowed me to work with our clinic administration and leverage that and say there's will here. This is what the county wants to see. We need to change the way we're doing things. So, we completely revamped the CD4 criteria. It required discussions with our Ryan White planning council in Fulton County and the Atlanta metro area to say can we rethink how patients are being referred to care? Now granted, our clinic can't handle every single new HIV patient. So at this point, what we're at least saying is those who are diagnosed within the Grady Health System can just walk in our door. They don't have to wait for that CD4 count to come back. Additionally, partners who come in with their patients can be seen in our clinic. Previously they were being told go to the health department, get an HIV test, then figure out where to get your care. Documents, we've softened the requirements on documents. Patients still need all these documents: an I.D., proof of income, proof of residence to officially enroll in Ryan White and to enroll in our health system in the Grady Health System. But we were able to get some grace period of about 30 days to say we can enroll them in care. we can start their primary visit, we can get them medications and then link them up to a peer counselor

who will help them get those difficult to access pieces of paperwork. I talked about the PPD. We removed it as a hard stop. It's still a requirement and it's still a metric that we measure in our clinic but we're relying much more on our active TB screen to pick up patients who may be infectious to others. We had to completely revamp the way that our provider template was structured. So, a lot of clinics with smaller volumes have done a single provider may be seeing these patients or they have an on call doc, but that's really tough when there may be three or four new patients coming in in a day. And so, we just restructured our templates to have visits blocked on different providers' schedules on different days of the week so that there should always be an open visit if someone walks into the clinic and if it's not today, hopefully it's at least in those next 72 hours. And then most importantly, probably, was improved communication across our multi-disciplinary team to assure that someone is helping the patient access their medications quickly, complete their paperwork, access health insurance if they're able to do that.

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And then this is what that ugly flow chart looked like after we made all those changes. You notice that there are no quote unquote hard stops for patients. They're going to walk in, they're going to get an appointment, ideally the same day, but if not at least within the next couple of days, to see a provider and to begin a discussion about antiretroviral therapy.

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And I say begin a discussion because in this cohort, and I'll go through the data we have, first and foremost, these are preliminary data so take them with a grain of salt. They're not perfect. Secondly, we took all new patients that were patients that were new to our clinic, were going through this process. They weren't necessarily new HIV infections. They may have been antidretroviral experienced and so we did not have a requirement to say we got to start these patients on therapy the same day you see them. But we wanted to ensure that they were warmly getting into care, that they were being received and given that message that we want to engage with you, we want you to be in care here. So, you can see the difference between the San Francisco volume and our volume. This was over the course of two months from May 15 to July 15, 2016. We had 100 new patients to our clinic whereas San Francisco at a year and a half had about 36 that went through their rapid arm. So, it's a much different scale. The numbers on the left, in terms of demographics, were very similar to our general clinic population. You can see that despite the changes in our CD4 criteria, the vast majority still have pretty low CD4 counts. We have higher CD4 counts and we've always had higher CD4 counts in our clinic because outside the CD4 criteria all those who are under the age of 25 who have severe substance use, mental health disorders, or who are pregnant can be seen in our clinic because of the types of funding we have. And you'll notice that even some of these patients that were coming in new to our clinic were actually virally suppressed at that initial visit. And so, we excluded them from any time to viral suppression outcomes and that's because they were either transferring care or they came from the hospital on antiretroviral therapy.

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This is kind of just the timeline of of folks enrolling in our clinic in the blue bars and then the days to the provider visit. So, in March is when we loosened our CD4 criteria. So you see a slight uptick in the

number of patients that were coming in per month, about 45. In the orange was the days to that initial provider visit. So, prior to this program, it was more along the lines of a two week wait for the for the patients to get their visit. And then in May, this portion of May when we started the program, that decreased to 72 hours. And then as we got rolling, it improved down to pretty much the same day.

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And so, of those that were initiated on anti-retroviral therapy, 69 of them were prescribed antiretrovirals in our clinic through this program. Thirteen came into the clinic on antiretrovirals so I excluded them from the rest of these data then I'll show you. Five were from hospital discharge and eight were transfers. Eleven patients didn't actually come to their first provider visit so, as a clinic, this showed us I think the importance of that same day visit rather than even the small gap of 72 hours. And seven patients, their provider and the patient decided it was not the right time to start their therapy. Some were in a research study, there were some complicated social situations, and one patient in particular was having really bad reactions to Bactrim that had been started in the hospital. So ultimately, we had 69 patients that we newly started.

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And again, I emphasize this was a patient-provider decision, with guidance from the medical leadership on regimens to start and how to do it safely, but this was not a one size fits all approach. So, of those 69 patients, three quarters of them were indeed prescribed therapy on that initial visit. So, the median time was on the same day. I did time to prescription and time to start because obviously we all we all experience the delays between the time we tell the patient we're going to give them meds and when they actually get them. In our case, they were very similar. Most patients did not experience any delays in picking up their medications, despite the vast majority being uninsured.

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And this is just an overview of the regimens that were started. Very similar to what you would expect and what was seen in San Francisco. The vast majority were on one form of another of tenofovir and one of the integrase inhibitors. Now Abacavir is on here, but remember some of these patients were treatment experienced, some were already coming in with medical records. We made sure that providers were not starting Abacavir without an HLAB5701 being being ordered and the results being known.

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And then this, I would say, is the biggest cautionary slide in terms of the data. Please don't think this is absolute because it's, again, very preliminary but we looked at time to viral suppression just to get a sense of how things were going, and we used a viral load of less than 1,000 because we really had essentially one month of follow up at the time that these data were being looked at. And just for comparison, I looked at a cohort from our clinic in 2010 of 177 patients who were virologically suppressed at their first time that their viral load was rechecked to try to make the arms somewhat comparable. And at that time it was still 73 days in terms of median time to viral suppression. And then looking at 25 patients who were not already on therapy and virologically suppressed when they came

into clinic and had at least one month of follow up. These folks had a median starting load of 115,000 and their time to viral suppression was less than one month. It was 21 days. And again this is comparable to what we're seeing in clinical trials now with these integrase inhibitors with how potent they are. So, I think it emphasizes the impact that we can potentially have in our communities with transmission by getting folks on therapy more quickly and supporting them through that, we can get them virologically suppressed.

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And I'll end by just saying that rapid entry is really one tool, I think among many, that we're really going to need to ultimately get to some of our goals such as declining time to viral suppression and increasing retention in care and durable viral suppression. And so, these are a lot of the different programs we have initiated around our clinic to try to target these very difficult to obtain outcomes.

00:38:06

So, the last question for you guys, or I should say statement of true false, is same day antiretroviral therapy decreases time to viral suppression, but has no impact on mortality.

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Is that true or false based on the data that I showed you? This means that in a way that's perfect perfectly good.

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So, that was the study from Haiti that, and again, these are these are smallish studies that are statistically significant. We don't have as robust of data as we have for some of the other conclusions we've been drawing today, but I think it at least suggests that there may be a mortality benefit. And so in conclusion, just remember that our guidelines support recommending antiretroviral therapy for all. Starting antiretrovirals as early as the same day of diagnosis seems to be safe and efficacious. In particular, we can say with certainty that it decreases time to viral suppression. And I'll say that I think we can at least have a glimmer of hope that it may improve retention in care and decrease mortality. And then finally, that it is possible to create systems for rapid entry even in a difficult to reach clinic population like our Ryan White clinic. And so, think about this in your own populations.

00:39:23

And with that, I'll finish and say thank you to all those who helped.

[Video End]