

**International AIDS Society
2nd IAS Conference on HIV Pathogenesis and Treatment
Forum: Mother-to-child HIV Transmission
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FEMALE VOICE: (unintelligible)

RUTH NDUATI: mother-to-child to infusion (misspelled?) of HIV and before the primary data in several of the presentations yesterday. (unintelligible) alone does not work and maternal HIV (unintelligible) does have a significant affect on the efficacy of this drug. We also know that short-course regimens can give efficacy levels similar to triple-drug combinations and we are looking forward to the (unintelligible) little to do when we listen to the results from the SIMBA (misspelled?) Study. This is remarkable progress. We know, we've talked about infromproflatus being potent and the (unintelligible) as being critical. This intervention will require a walk-in health service. It requires a mother who can drop in the hospital at the right time for (unintelligible). It requires a mother who can drop at the right time for her delivery and if we miss the delivery, who's there in the post- (unintelligible) for us to be able to give the interventions. Just remember the context in which you do this. Now breastfeeding continues to diminish our efficacy of protocols to administer (unintelligible) period and it is interesting to note that the protocol (unintelligible) is increased efficacy in the distant (misspelled?) studies. A lot of that conservation of that efficacy is that women are breastfeeding for shorter durations of time. Yet we know that breastfeeding will continue to be a reality for many, many women who are HIV-

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infected in our part of the world. You saw this (unintelligible) prevented yesterday when we showed the incidence of breast milk transmission as being (unintelligible) at 5% and that's overall about 44% of the transmission is from breastfeeding. Now I think it is important for us to understand on this plan what are the risk factors around breastfeeding, if we are to improve the performance of our short-course protocols in prevention of mother-to-child transmission. In some of our works that were recently published, we have looked at breast milk for mothers who are HIV-infected and try to look at what are the risk factors for transmission and the first we have found is that 80% of breast milk samples from HIV-infected women have detectible HIV virus and that there is a correlation between the amount of virus in breast milk and mother disease status, so mothers who have high viral load, mothers who are immunosuppressed are more likely to have higher amounts of breast milk virus in their breast milk. Now when we look at the relationship between the breast milk viral load and transmission, we can see a (unintelligible) from this slide that women who have higher amounts of virus in breast milk are more likely to transmit to their infant. What's also interesting is that the amount of virus in breast milk is several amount (misspelled?) lower than that found in plasma. Now everything we have looked at is a pattern of HIV sharing (misspelled?) breast milk and we find that we looked at breast

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milk, over 400 samples of breast milk from our nearly 200 women and we looked at an average of 3-4 samples of breast milk per mother and we found that only 4% of the women in our studies had undetectable virus at all time points when we looked at their breast milk. We found that 56.5% had virus, detectible virus some of the time and nearly 40% had detectible virus all the time, and when we looked at the relationship between when we had virus some of the time or none of the time on transmission, you can see the relationships are very clear, that women who don't have virus in their breast milk at any time point did not transmit to their infant. We also had intermittent shedding transmitted about 20%... there was an overload transmission or 20% of them transmitted to their infants while those who have consistent shedding, over 40% transmitted to their infants. Now this data, I think it will be useful as we look at new ways of increasing the efficacy of our protocols in prevention of mother-to-child transmission of HIV. I believe, for example, the (unintelligible) have studied, which looks at the use of combination ARVs in women who normally not qualify for (unintelligible) therapy would be very important in trying to answer this question. Although we saw a relationship between CD4 count and viral load and the amount of HIV in breast milk, it's not on... a lot of women who were CD4 count about 200 who had detectible virus in their breast milk on sometimes-high viral load, so this study will be very

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important. Now we have focused very much around anti-retroviral therapy and I just want to sort of take us back to ground zero in the health center system, you know in developed country settings. This is different from our (unintelligible). Now in order to deliver this intervention, women must be ready to be tested, they must look at their results and they must come back to the pick up their ARVs. There is data from more than 4000 women who are offered, who presented in health facilities where we were doing PNPTV (misspelled?). The green bar shows all the women who came in for their first-time visit. The blue bar shows the woman who actually, who received one-on-one counseling so that they could make a decision about testing and the last blue bar shows the women who actually accepted testing, while the green bar shows women who are tested and came back and collected their results. Now with this kind of pattern of health seeking data (misspelled?), if you have an intervention that's only 50% efficacious, say like they had nevirapine short protocol, you are unable to prevent 10% of the infant infections in these health facilities. I think we need to keep remembering this, that we should not focus only on the ARVs and how are they working, we also have to devote some energy in how to get this intervention to work within the settings that women present themselves to. This is my last slide and just to remind ourselves that prevention of mother-to-child transmission of HIV, for us to achieve the successes

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that have been seen in the developed countries, we need to do all this, we need to do primary prevention, we need to be very unhappy that 15-20% of (unintelligible) women, young women, age 15-25 are HIV-infected, we are not doing enough primary prevention. We need to (unintelligible) here, there was a discussion about women coming back, subsequent pregnancies for prophylaxis. I think we need to be clear that we don't want HIV exposed babies. We need to see childbirth as not just childbirth, but bringing up a child for 20-years. We need to be courageous to talk about these issues, and then we need to give care and support and I think enough has been discussed about care and support for women and children, as part of the package of care to prevent mother-to-child transmission of HIV. I'd like to stop here and let my colleague, Glenda talk. We have a very, I think and interesting series of abstracts to be presented and we'll defer the questions until the end and I hope there will be some lively discussions around here. Now I'll do like Jim Macintyre (misspelled?) in terms of introduction. Glenda, you all know her. She's here. I think she is one of the leaders in this field of mother-to-child... research on mother-to-child transmission of HIV. She's goes back... she's a veteran of this too and she's an expert in (unintelligible). She works at Wit's (misspelled?) University, she works at Baragwaneth Hospital in Soweto and her current work is not only in this clinical trials around prevention of

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mother-to-child transmission of HIV, but she does work in the field of vaccines and (unintelligible) to prevent the mother-to-child transmission of HIV.

GLENDA GRAY: Good morning everybody. This talk has caused me lots of (unintelligible) and I've changed it about 20 times since I've been here. I've got slides and the interesting things have been incredibly well covered in this conference and I was trying to make sure that what I covered had focused on different things and that we wouldn't repeat a lot of this stuff. I'm also not going to repeat a lot of the late breakers and I'm not going to mention (unintelligible) and the results of his study and so I'm going to focus on where we should be going and I'll look at some of the issues I think that there out there and we try to implement into such programs in the developing world. So I should say that why do we need to look beyond nevirapine or why do we need to maximize nevirapine cover? And I think that it's a failure on inadequate drug level (misspelled?) that by 2002, 3.2 million were infected with HIV and most of these were infected in the developing world and was mostly by mother-to-child transmission and despite this, since 1997, we've seen seven large randomized controlled studies in the developing countries and five of these large trials have involved (unintelligible) populations, and these interventions did affect efficacy and we know that the interventions reduce transmission by about 50%, even in the presence of

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breastfeeding. Sorry I think I lost a slide somewhere. So despite the fact that we do have interventions and I think the most important intervention to mention is the HIVNET 012 study done in Uganda. It set the stage for easy and rapid implementation of programs that could at least halt transmission from mother-to-child and I'm not going to repeat the slides, but just to show you that at six-weeks, a single dose of nevirapine for mother and a single dose for baby who had transmissions around 12.7% and even up to one year, transmission rates of around 19.5 (misspelled?) showing that even with prolonged breastfeeding, the (unintelligible) intervention did work. This study was (unintelligible) study, which modified the 012 nevirapine, gave two doses to the mother and a single dose of nevirapine was completed to the (unintelligible) RMV (misspelled?) study, which was an intrapartum/postpartum regimen of ADP/CTC and there you can see that at eight weeks of age, 9.3% of infants were infected as compared to 12.2% and this was (unintelligible) They sort of demonstrated that ultra-short course regimens and given in labor and post-natal to the infant could reduce infection quite efficiently in (unintelligible) even in the presence of breastfeeding. So what do we need? I'm showing you two studies that show that we can reduce transmission on about 50%. What do we need to do to control and eradicate pediatric HIV-infection in the developing world? I'm going to argue that we need border

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access and we need to improve are coverage of nevirapine programs in the developing world. We will need to optimize once we've managed to improve coverage needs after mild (misspelled?) regimens. We need better drugs. We need to individualize prophylaxis and we need to maximize the reduction in transmission rates and not be happy with transmission rates that are around 8-12%. And we need to do this because even though we have these regimens that have been well described, between 1900 and 2000, 200 infants are infected per day by mother-to-child transmission and reach today in 2003, only 3% of HIV-infected women in Africa have access to these programs and there are lots of challenges in terms of coverage and this is one example in (unintelligible) and it shows that of the people that visit the international clinic, 71% accepted testing, of these 97% were tested and of those 14% were HIV-infected and this is the amount that got nevirapine, which is about 20% of those that were eligible for nevirapine. So you can see that we are having trouble in translating our research in interaction and this only happens in the nevirapine programs and this is an example of a program in West Africa where you can see that of the women who were eligible for the program, this is the amount that accepted testing, this is the amount who were HIV-positive. And 30% of women that eligible for the AZT program actually got it and so we obviously need to do a lot more work in making sure that women get the programs that

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they need. There are some successes in terms of operationalizing the nevirapine program and I'd like to report on the success that we've had at our (unintelligible). Last year we screened 50,000 (unintelligible) or which were 30% were positive and we managed to give 72% of women nevirapine at the time of post-test counseling. Obviously, (unintelligible) we need to make sure that the nevirapine intervention is effective and I'm going to show you some effectiveness studies done in some of the spots (misspelled?) in Africa and this is just comments on the transmission of HIV-RC. The first one I'm going to talk about is a study done in Coronation Hospital by Carl Schinman (misspelled?) that showed a transmission rate in an un-breastfed infants in Coronation, which is a little suburb outside Johannesburg, about 8.9% at three-months of age. James showed similar results in a study looking at sites in South Africa in King Edward and Bella (misspelled?), which show transmission rates of around 10% then in predominately formula-fed infants. (unintelligible) transmission rates of 11.2% and again in 12% in Racha (misspelled?) So we are seeing that the nevirapine regimen when translated into action does reduce transmission and continue to do that. But obviously, we need to optimize regimen, so now that we've got down to (unintelligible) developing countries, how to we maximize their transmission? How do we minimize transmission rates and optimize originally? And I won't just talk about one... I want to

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talk about a couple of studies. I won't mention one that has been presented today, but this is one that France ought to be presenting at the retrovirus conference. It showed by adding a single-dose of nevirapine to the mother and infant under a background of AZT, reduced transmission rates were around 5%. So you can maximize transmissions by playing around with nevirapine at the time of delivery and to the infant. Mark Ellimen (misspelled?) presented as his work at this conference, that by adding nevirapine and (unintelligible) and then adding nevirapine to the mother and infant and or maternal (unintelligible) early, you get transmission rates of around 2.1% in un-breastfed populations, but it's possible to take (unintelligible) add nevirapine and reduce transmission's further. Obviously the (unintelligible) are the issues around the (unintelligible) resistance, which I'll deal with later. Other studies that we need to look at in terms of developing country settings are other drugs and almost preventing this day to where... we had D4DDR (misspelled?) hidden in the combination therapy and got transmission rates in numbers where population (unintelligible) to under 5%. Looking at avoiding nevirapine only studies, this study has just started in South Africa. It's a big and extensive study. James is the principle investigator and basically we are looking at a three-arm. The inhibitor one, two arm and I'm looking at adding AZT and 3TC in intrapartum and postpartum period for between three and seven days.

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Hopefully we'll have the results in about a year's time. So I was talking about optimizing regimens and I also think that there is a need, and I heard from the questions yesterday, the need for better drugs, or for exploring other options and I think one of the most exacting options that needs to be explored is the tenofovir or PMPA (unintelligible) and this is an NRTR that (unintelligible) that doesn't have to be phosphorylated to the axis. It has a fairly long half-life and it remains stable, which is very important against the background of drug-resistance HIV strains in vitro and it (unintelligible) in the maternal, future maternal therapeutic options, once these are available to women. And also importantly, it has been shown to prevent or emolliate HIV disease in newborn (unintelligible). So I think we need to look at new drugs that the PAPPG (misspelled?) has been working on the protocol, but anything between two and four years and nothing's happening. I think we need to rapidly translate dispatching new drugs into some kind of intervention. Furthermore, we need to also individualize and (unintelligible) prophylaxis. I think it's time in the developing world to try and make sure that we maximize reductions in transmission by looking at maternal disease. And just to show you this rather hackneyed and (unintelligible) of the world, but to show you the correlation between RNA levels and anti-retroviral use in transmission rates and clearly it's important that the more

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complicated and (unintelligible) and regimens do to reduce transmission rates to the fullest and these irrational individual regimes, if you look at the (unintelligible) and you look at transmission rates of CD4 counts, you can see (unintelligible) CD4 counts of under 200, the intervention had a real impact on transmission and the maximum impact you got from the 012 regime, particularly in the nevirapine arm, was when the CD4 counts were between about 500 over 3 and 350 over 500 and so we need to then look at a further CD4 counts and see whether we can maximize at an individual level interventions which will reduce transmission. Similarly, you see in data from (unintelligible) that the CD4 count is about 500 and you have maximal reductions in transmission rates and as compared to CD4 counts of under 500 would be around 82 (misspelled?) in the placebo arm, so the indications are such, we need to (unintelligible) to maternal disease in the developing world. So what do we need to transfer that? I think that I've showed you (unintelligible) optimize on different drugs. We also, even though we need to improve axis in coverage, we need to maximize reduction in transmission in developing worlds and obviously, we want to mimic the kind of figures seen in the developed world where people (unintelligible) of 1% plus they have access to (unintelligible) anti-retroviral therapy, no breastfeeding and (unintelligible) infection. For the moment we know in the developing world that two drugs are better than one based on

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rates of transmission and you can see that the (unintelligible) regime that AZT was inferior as compared to AZT with single dose nevirapine and in Africa, we've seen that AZT with single dose nevirapine, when compared to AZT 3DC is better and at once you can see that addition of single dose nevirapine minimizes transmission even further. We studied a little bit about post-natal transmission, so I'm not going to do a lot with that, but just to add on the role of HIV vaccine (unintelligible) transmission and the rationale for using HIV vaccination in the post-natal period is because you only need to immunize and in addition is only need for the duration of breastfeeding. And it would be easy to implement a vaccine program because the government vaccine delivery systems are set up for infants. And there are a couple of (unintelligible) which I won't mention too much is the PAPPG (unintelligible) is the promise that was done by (unintelligible) they looked at vaccine induced preproduction of immunized monkeys who received multiple challenges of (unintelligible) and then there is the work by (unintelligible) which is a collaboration between Harvard Medical School and (unintelligible) to do a study of monochrome antibodies to deliver the HIV epitopes and this is for the express purpose of erasing (unintelligible) transmission and they are having some proof of concept (misspelled?) studies that are showing have shown that high doses of monochromic antibodies can protect monkeys against high dose oral

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challenges and this is the way we need to move in terms of post-natal transmission, particularly through the unexposed infants and women who (unintelligible) in the developing world too hot to minimize breastfed transmission. Similarly, the (unintelligible) that looks at an (unintelligible) vaccine and basically looking at (unintelligible) immune responses and infected infants who are born to HIV-infected woman who have CD4 counts over 500, and we need to see the results of the immune (unintelligible) and see how this is tolerated newborns and young infants. So what should we be worried about? And I think that we have heard in the conference that we are worried about nevirapine resistance and we are worried about what nevirapine resistance would do to future maternal... or infant's therapeutic options and to subsequent pregnancies. And just to say that we are seeing quite a high rate of nevirapine resistance in all the studies that are (unintelligible) and in all the nevirapine containing studies. At 20% in the (unintelligible) or similar rates on development studies is reporting similar rates as was previous published studies, (unintelligible) nevirapine and we've got 67% (unintelligible) mutation and the HPT (misspelled?) and the LT3 showed both birthmark and plasma resistant mutation, 65% in birthmark and 24.3% in plasma and we need to worry about these issues around birthmark transmission and what impact this has on future maternal options for therapy. In terms of infants, we see high

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rates of nevirapine resistance, 36% in the 012, and in the (unintelligible) we saw 53% and 53% in mutations and basically some of the (unintelligible) presented an infant where there might have been some birthmark transmission of the nevirapine resistance mutations. In terms of the HPT and LT3, the predominant mutation was the 103, the (unintelligible) and the 109 and as I mentioned before, the presence of (unintelligible) birthmark and it's a bit of a concern that there is increased (unintelligible) mutations in birthmark as compared to plasma and we need to see on what this does and what impact this has on birthmark transmission. (unintelligible) and nevirapine resistance and that is to be one of six new mutations which has been described in (unintelligible) which seems to predisposed to in developing this and this was a study showing, which showed resistance to (unintelligible) but not to nevirapine or the (unintelligible) and this caused high resistance to both nevirapine and the (unintelligible) and our group looked at some of our specimens from pregnant women and we also found of the 161 women at six-weeks, we found 5% having the (unintelligible) mutation. And we just need to know what this means for future options in women. In conclusion I'd like to show you this graph where we've seen escalating and out-of-control pediatric HIV epidemic at a global level and we've described the mode of transmission; we found that the 076 regimen can reduce transmission by about 2/3 in '96. We found

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out in 1998 that the 3DC short course did work. We described how wonderful the nevirapine regimens were in 1999 and we still haven't managed to eradicate or control pediatric HIV in the developing world. And I'm going to finish with a quote from Nelson Mandela, which I (unintelligible). "We have failed to translate HIV progress into action where it is most needed and this is a global injustice." "It's a travesty of human rights." And I think that's part of our work here is to try and make sure that we translate what we learn very quickly in few operational research in the countries where it is most needed. Thanks.

FEMALE VOICE: Am I going to do the next introduction? I think we can carry on now with the extracts and I'm going to introduce our first speaker from Cote d'Ivoire, Dr. Ekouevi, who's going to present hyperlipidemia in (unintelligible) cause of entry to prevent mother-to-child transmission and this is from the ANRS 1209 Study. Thanks.

DIDIER EKOUEVI: Good morning. I'm (unintelligible) Cote d'Ivoire and I'm very pleased to present today the results of the ANRS 1209 Study undertaken at Cote d'Ivoire in (unintelligible) peri-partum to a sharp course of (unintelligible) prevent mother-to-child transmission of HIV. Since 1999, the (unintelligible) toxicity has been discovered in infants. (unintelligible) long-course regimen of (unintelligible) want to activate infected mother

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(unintelligible) dysfunction. This observation was not found in the American infant cord and the recommendation at this moment was to continue to explore this toxic side effect and to (unintelligible) dysfunction (unintelligible) can be used. This (unintelligible) had a good sensitivity, but not specific for me to control dysfunction. There is a (unintelligible) during pregnancy. Our knowledge (unintelligible) presented in the AIDS conference in Barcelona reported that 50% of infants had hyperlipidemia in Spain and 52% in Italia. In Africa, where a short-course regimen of (unintelligible) there has not been yet any study about hyperlipidemia in infants born to HIV-1 infected women and exposed to anti-retroviral. The objective of this study were firstly to estimate the prevalence of hyperlipidemia in infants born to HIV-1 infected women (unintelligible) during pregnancy. Secondly, to determine the risk factor (unintelligible) with hyperlipidemia and finally to study the (unintelligible) and clinical (unintelligible) of infant presenting hyperlipidemia. (unintelligible) study was set up in infants born to HIV-1 infected women between NOS 1201, 1202, (unintelligible) Cote d'Ivoire. All HIV infected pregnant women (unintelligible) of pregnancy and (unintelligible) All children with (unintelligible) one dose every six hours during the first seven days of life and a single dose of (unintelligible) on day two or day three. Concerning laboratory tests, (unintelligible) to determine was

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called into to assay (unintelligible) dysfunction guideline. (unintelligible) level was symptomatic (unintelligible) in children at 4, 6, and 12-weeks of life by (unintelligible). in collaboration with (unintelligible) University Hospital laboratory in France. For this study, we have defined hyperlipidemia as (unintelligible) we consider this follow-up by (unintelligible) infection status (unintelligible) after birth and (unintelligible) treatment. In mother, we have considered only (unintelligible) hyperlipidemia. Now I'm going to present the main results of this study. A total of 140 newborns were included in this study. 350 (unintelligible) 1.2-2.7 minimal, (unintelligible) was 2.0, standard deviation was 1.2 minimal. 54 of 140 (unintelligible) 2.5 minimal. Because we want to confirm the first (unintelligible) 150 infants who, at least (unintelligible) study. So hyperlipidemia defined by true measure (unintelligible) 2.5 minimal or detecting in 17 infants out of 150 in France. So (unintelligible) is estimated at 14.8% (unintelligible) reaching 8.2% to 21.4% difference. (unintelligible) was 3.3 minimal and ran between 2.7 to 6.3 minimal. This table showed that there is no risk factor associated with hyperlipidemia in our study. (unintelligible) hyperlipidemia in our study. However, we found that there was a trend of significance when otherwise (unintelligible) is better. The second table also shows no maternal (unintelligible) hyperlipidemia. The third part of the study

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were (unintelligible) treatment. The duration of maternal (unintelligible) treatment was 33 days and was no difference in the two groups. Concerning clinical manifestation, all hyperlipidemia is (unintelligible) because none of the children were presented (unintelligible) hyperlipidemia (unintelligible) clinical manifestation like abdominal pain, muscular manifestation, or neurological manifestation. What is the (unintelligible)? In forty infants, (unintelligible) to normal (unintelligible) in the first six-months of life except three of these infants who had (unintelligible) of 2.5 minimal after six-months. This figure was on the value of (unintelligible). The (unintelligible) level was no difference between 2.7 and 4.8 minimal at four-weeks. We also show that hyperlipidemia has reversed spontaneously to normal value at (unintelligible) and only three infants had (unintelligible). We show here in (unintelligible) the value of the (unintelligible) level for these three infants who had birth response hyperlipidemia. The value was reaching 3.6 minimal to 5.7 minimal. In conclusion, this study shows that hyperlipidemia can be detected by screening in infants was more than we first short-course (unintelligible) for PMTCT (misspelled?) in Africa. No risk factor was found to be significantly associated with hyperlipidemia. Only (unintelligible) significantly shown if an infant took a high dose of (unintelligible) during the first (unintelligible) of life. Similar observation was found in HIV-

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1 infected infants treated with (unintelligible) to use (unintelligible). There is no need after this stage to take this finding into consideration and (unintelligible) public health accommodation for Africa. To finish my presentation, this study was supported by (unintelligible) and I would like to thank the French (unintelligible) for financial assistance. (unintelligible) for their contribution of design and contents of the study and I would like to thank the (unintelligible) study group. Thank you for your attention.

FEMALE VOICE: I think we can allow two or three questions before we carry on. Are there any questions? Okay, I think we can continue. Thank you very much. I'm going to introduce Francois Dabis. It gives me great pleasure to introduce him and he is going to present the ANRS 1021 (unintelligible) Cote d'Ivoire. Thanks.

FRANCOIS DABIS: Good morning. This is one of the contributions of the (unintelligible) group, evaluation of combination direct therapy for PNPPT and today I will report the preliminary results of effectiveness of the combination of a short-course of VVD (misspelled?) and 3TC plus periodic nevirapine to prevent transmission, peri-partum transmission in West Africa and in (unintelligible). Just to drive you to the background of where we were about a year ago at the Barcelona conference, you remember that for peri-partum transmission, we suffered (misspelled?) about a rate of 20-25% in most African

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populations with zidovudine alone, we were in the range of 14% with nevirapine alone, (unintelligible) showed us that VVD plus 3TC was possibly lower although it was not specifically different and we showed last year preliminary results in the same program, 1201, (unintelligible) showing that VVD plus nevirapine could reduce this transmission even lower. The final results that I reported in Boston earlier this year giving us a transmission rate of 6.4% with the combination of VVD plus nevirapine. On the top of that, we know from the ANRS 1075 Study in France that the combination of VVD plus 3TC is also quite interesting, so why should we go further down or is it needed to go further down? Yes indeed, if we look at the WHO recommendation for 2000, clearly they... (unintelligible) advertise for using any anti-retroviral regimen of validated efficacy, but still advertising for constantly researching in this area and we believe after the Barcelona Conference that there was still room for looking for more advanced interventions to prevent peri-partum transmission in this context, so our program has been aiming, in fact, to a package of interventions and for the peri-partum phase, as I said, we started with VVD and nevirapine. It looks like a little bit software version, but we call that 1.0 version of our program reported last year in Buffalo, (unintelligible) in Boston and media just reported the results and the possible consequences with hyperlipidemia. So what I will report to you today is the

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version 1.1, so to speak, using VVD, 3TC, and nevirapine in the use of peri-partum. But because we were thinking of leaving a package of information, we have combined this peri-partum interventions to a systematic proposals of post-partum interventions and this is a (unintelligible) compliment of the project and (unintelligible) two days ago presented the presentation number 63, the premium results for this post-partum phase, but in this post-partum phase, they used no additional anti-retroviral exposure, so in this 1.1 trial version, this is really the combination of VVD, 3TC, and nevirapine. We are certainly choosing be efficacy, but also of course by tolerance and when we moved from VVD to (unintelligible) VVD treated with nevirapine, we had the goal to go below 5% and meaning that we will possibly do at least a half better than what we were doing with VVD plus nevirapine. This is again a non-randomized intervention trial. We felt that there was again (unintelligible) continuity of randomized trials in this context and extremely difficult to do. We only work with women who were diagnosed and consent and inform of their studies. From VVD to nevirapine, we decided to move from 36-weeks to 32-weeks. The reason is that in (unintelligible), women tend to come relatively early in their third trimester of pregnancy (unintelligible) or possibly at the end of the second trimester and the experience we have with VVD and nevirapine was that we were reasonably often asked women to wait and to

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come back at least a month later to initiate treatment and felt that there was no good reason to wait when women were already booked and were already in the (unintelligible) system. The other reason is that the VVD treatment combination in France, have been used roughly around the same time period for treatment introduction of 3TC and the comparison would be more interesting in this respect. So the three part and the anti-(unintelligible) regimen is really the use of the Combivir, the Combivir drug, the combination of the three drugs from 32-weeks and then we have this loading dose of Combivir again at the beginning of labor and which is sort of boosted by the dose of nevirapine, which is given at 12 dose of nevirapine. As far as the (unintelligible) accompaniment is concerned, we have remained to what we have learned to use with the version 1.0, which is VVD plus nevirapine, so as you can see there is no nevirapine in the unit or regimen and the reason is that there was a good documentation in France that adding nevirapine to the neonate was creating an environment of anemia and neutropenia and we even felt, we didn't feel that that was very appropriate, to do that for children in this African setting. What you may see also is that the antenatal regimen of the women is continued for about three days post-partum, so basically the nucleoside regimen, the affect of the nucleoside regimen stops at the same time then the boost of nevirapine that has been given during labor considering the different

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half-life of the two-drug regimen. In terms of judgment criteria, we rely now on (unintelligible) viral load, but the big difference with previous work that we are then leveraging on is now that we are using a new technology, the real-time (unintelligible) technology at four-weeks. There is a poster by Francois Wade (misspelled?), poster number 21177 comparing this to commercial VDNA (misspelled?) methods. The beauty of this method is that you get extremely reliable results with the previous ones, but it's about ten times less costly, with a cost by diagnostic of about \$8.00. So we can turn the diagnosis infection at six-weeks or after the four-weeks (unintelligible) tolerance criteria for the neonate and also look at (unintelligible), before there was no clinical rush in these areas (misspelled?). Okay the comparison that we will make is to compare this three-drug regimen to the previous two-drug regimen and also to the single-drug regimen. The three studies have been done in the same population and we have good data of the same quality to compare. So let's look at that and (unintelligible) so this is the last chance for you to compare regimens before I go to the results. In peri-partum, we move from VVD alone to VVD for a longer period than to VVD three (unintelligible) for even a slightly longer period and in (unintelligible), we move from VVD alone to VVD plus nevirapine and now VVD treated nevirapine and in post-partum, we drop the VVD alone to move to neonate, VVD plus nevirapine and now

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neonate VVD plus 3TC for three days and the same thing here for the neonate. Okay, comparisons, all the tables will be presented the same way. Here you will add the first column with the three drugs, then the column with the two drugs, then the column with one drug. Comparison one means three drugs versus two, in comparison here means three drugs versus one and only the significant results will be labeled in white. No difference of hemoglobin at baseline, here significant differences in CD4 and between groups and we will adjust for that in all the comparisons. As far as (unintelligible) is concerned, very comparable results and, as expected, the length of treatment with three drugs has been longer as was part of the design, although no other meaningful difference for a parameter as a follow-up. As far as accessibility is concerned, we've been moving from zidovudine to zidovudine plus nevirapine and now the three drugs, we have (unintelligible) the acceptance of the regimen, however between two drugs and three drugs and the (unintelligible) were roughly the same, we had absolutely identical acceptance of the drug regimen and for the neonatal treatment, we are no different between the two.

As far as tolerance is concerned, we had very few severe events have been reported and no statistical difference, again, same thing for the live birth and very comparable neonatal deaths, 28:1000, 16:1000, 21:1000. For now, what are the overall results in terms of transmission, so for the three

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drug combination that's preliminary analysis, however, I (unintelligible) almost 200 children. We have only nine infected children or a transmission rate of 4.5%. In eight of these eight infected children who are positive at day two, the first real time PCR (misspelled?) until we believe we are all (unintelligible) here, out of the 23 that we had positive with 4-6% transmission rate, we had about 14 which (unintelligible) and here you have the reference of the AZT alone, so we do efficacy comparing the three drugs to the two drugs, the advantage to adding the third drug to the two is limited and absolutely not statistically significant and is even when adjusted in CD4, but again you can compare three drugs to one, the advantage has become extraordinary important now and it's even more important when you are just on CD4. Considering the primary data that we have on about 200 children, are scientists here have advised that we should not continue the study much beyond what we are so far, because it would be absolutely impossible to compare these two groups in a statistical fashion unless having more than thousands of (unintelligible) that we are not capable of having, so we will remain in a non-statistical difference here between these two groups. We have broken down our (unintelligible) by CD4 strata and the by breastfeeding exposure. By CD4 strata you can see that below 200 CD4 we have results that look slightly better, however, none of these reach statistical significance. For the other

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strata, by moving from one drug to the two drugs was extremely important, and moving from two drugs to three drugs didn't make any difference. Same thing here and same thing here. Again, we are certainly lacking statistical power, but it becomes extraordinarily difficult to make any conclusions on that. With respect to breastfeeding, now we compare column by column. For the two drugs there was no statistical difference between those who were exposed to breastfeeding and those exposed to formula feeding and here, same thing, very comparable -- very comparable results. But again, we are only talking about four weeks of exposure to breastfeeding in this breastfeeding group. So where do we stand in terms of results? Clearly, we are -- we stand now at the lowest result that has been obtained so far. No -- impossibility for us to demonstrate a statistical difference between the previous regimen and we have also to take into account substantive differences in CD4 and (unintelligible) when we have it. But it's (unintelligible) in all the studies. Our previous study was extremely low in terms of CD4 and just by that (unintelligible) if you could see this one is slightly better and we have also an extremely good efficacy. So, as far as results is concerned for the findings of the study, we can conclude that certainly there is very good (unintelligible), as you can see, of this regimen, that there hasn't been any comparable data so far. We have, as I said, we will stop enrollment again of this month's formerly in this

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scientific trial. The advantage versus (unintelligible) remains uncertain and not necessarily obvious. Certainly, we need to (unintelligible) data and, more importantly, drug resistance data to fully understand the advantage and disadvantages of this new protocol. And again, we have seen that below 200 CD4, certainly we can -- we have to do better and in a different way than this. And the (unintelligible) has been one of the approach, but is a privilege for not using (unintelligible) during pregnancy. So, for (unintelligible), we clearly think of the moment. It's too early to say whether this should be considered as one of the options in the WHO Standards. Certainly, we need to (unintelligible) incidents of viral resistance. We need to consider what the consequences it will be to use this regimen if the woman needs to have later in her life and we need to consider using balance with the use of immediate (unintelligible) between the last trimester of pregnancy. Again, we are moving in the direction with the (unintelligible) drug initiative. In fact, we will start it next month in. So, instead of showing you again the list of members of our team, I would like to just show you a picture of this wonderful group that has been doing all these studies in (unintelligible). Thank you very much.

RUTH NDUATI: Thanks, Francois. Do we have any time for -- oh, we have some time for questions. I see we've got a few there. Can we have the lights on so we can see who's

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asking questions, if there are any. (Unintelligible). Over there?

MALE VOICE: Francois -- over here. Thanks for a lovely study and a very important one. I'm a bit concerned about your ability to draw conclusions. From the beginning, you must have realized you were under powered even if you projected dropping the transmission rate to 3 percent or 2.5 percent to really draw statistical conclusions. So maybe statistical difference wasn't really the end point you were going for. But what's really going to matter, as I'm sure you know, is the difference in resistance. And how are you powered for looking at differences in both Nevirapine and 3TC resistance over time?

FRANCOIS DABIS: As far as the efficacy is concerned, originally when we were advised by our Scientific Board to move from (unintelligible) to the combination -- the (unintelligible) we had, in fact, in the higher estimate of transmission, (unintelligible) plus Nevirapine. In fact, I reported (unintelligible) results let's say in Barcelona which were at least one point higher than that. So, therefore, we felt we were still in the position to statistically demonstrate an advantage of the combination of -- by using (unintelligible). As you have seen now is the final result and the final estimate (unintelligible). We are much lower, 6.4 percent; therefore, it becomes extremely difficult to go lower.

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And, again, we are probably seeing differences that are not extremely important from -- in the public standpoint and adding thousands of observations to demonstrate it was not felt to be necessarily important. But at the beginning, we were empowered to be able to draw the conclusion that (unintelligible) plus (unintelligible) would do half better than the interim estimate of (unintelligible). As far as (unintelligible) is concerned, I am not sure that any of the resistance studies so far have made a serious statistical consideration on different incidents of preventive resistance. This resistance have to do (unintelligible) have to do in African settings. We rule out about one of the observations in our cities when the study is finished. We are talking, according to the French study, to a relatively high frequency of resistance to (unintelligible), at least that's what was done in the (unintelligible). So we may be able to have a reasonable estimate of the prevalence of resistance.

MALE VOICE: (Unintelligible) further about a resistance issue because like in Thailand they will have been containing regimens that we used for (unintelligible). Okay? So my question is could you predict that in a full regimen of SAT, the old 76 regimen, the full regimen, both to the mothers and the infants, whether the (unintelligible) will add any more benefit to the regimen.

FRANCOIS DABIS: It's very hard for us to draw any

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conclusion or really comment on this based on our observation in the sense that as you have seen, women do the first booking sometimes (unintelligible) trimester, beginning of the third trimester. So we are far from the standard of 76 regimen or the regimen that you, I believe, are using in Thailand. We know that there is only one evidence from the 316 trial trying to look at the exact contribution of Nevirapine to long regimens. It's extremely difficult to make these type of conclusions based on their findings. However, I believe that PHPT through trial that was preliminarily reported two days (unintelligible) may answer your question. But I don't think the preliminary finding that we saw two days ago will provide the answer.

RUTH NDUATI: Next question in the middle.

MALE VOICE: Can you tell us -- two questions. Can you tell us anything about adherence in the related study perhaps compared to the earlier ones, and also over time, has there been any discernible change in the background transmission rate for women not included in your intervention studies?

FRANCOIS DABIS: As far as adherence is concerned, we have looked at various -- with a simple social demographic factor that could explain differences in adherence. It's hard to really cite what studies we've (unintelligible) the data and also because we have also a few number of non adherent women. My personal feeling, but it's not really well supported by

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data, is that the big difference between the GDD (misspelled?) and the next stages has been that the GDD was really (unintelligible) control trials where women were faced with completely different setting of explanations and involvement and that makes then why the adherence was more complex for them. But I cannot really make sure -- in the two other phases we were almost in the direction of operational administration of the drug. As far as the background transmission rate is concerned, I'm not aware of any study looking in parallel to groups of women or men exposed to any antiretroviral regimen at the same time that we were conducting the studies. I cannot answer that.

RUTH NDUATI: Next.

MALE VOICE: Thank you very much. (Unintelligible) from Uganda. My question is concerning the management, the (unintelligible) management of this (unintelligible). In an (unintelligible) variable era, sometimes the compliance or the adherence to treatment has not been adequate. What have been this (unintelligible) was (unintelligible) extracted and the (unintelligible) or for that matter, the drugs are not the (unintelligible). We have been accused over many times extracting the data on a (unintelligible). How do you handle the (unintelligible) chance of these resistances and other (unintelligible) as a result of (unintelligible) of moralities of the (unintelligible) has been extracted?

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FRANCOIS DABIS: My answer is that certainly when introducing possibly half as one of the possible strategies for some groups of women, not only transmission will be important but adherence and the true consequences of what has happened up to delivery and (unintelligible) will be critical because we are setting the scene for the future treatment. And I'm sure a lot of data will have to be gathered to understand how easy it is or how difficult it is to initiate half during pregnancy. I believe obstetricians in Europe or in the U.S. find very, very different situations, sometimes easy, sometimes difficult, and we need to learn that and document that before making the new recommendations. So it's not only a matter of eradicating the disease, projecting disease, for a few women. It's a matter of doing this at the same time that we are setting the appropriate scene for continuing half in the same populations.

RUTH NDUATI: I don't think there's any more questions. No, okay. Thanks, Francois.

RUTH NDUATI: Thank you very much, Francois. You're, as always, very stimulating presentations. We now move to the next speaker which is (unintelligible). And this is being presented by (unintelligible). This is a study done out of the School of Public Health and Primary Healthcare in (Unintelligible), (unintelligible) Institute of Topical Medicine, Antwerp.

DAVID COETZEE: Just waiting for it to come onto the

screen. Here you go. Okay. Thank you. This study was conducted by Catherine Hildebrand (misspelled?) in Kiucha (misspelled?) which is a township close to the (unintelligible) of Capetown to look at the feeding practices of mothers who enrolled in the Mother to Child Transmission Project. Ever since the first cases of HIV transmission through breastfeeding were acknowledged, there's been a fierce debate on guidelines for infant feeding in (unintelligible) setting such as Kiucha. And the question being when is it safe and feasible to formula feed as breastfeeding protects against other diseases. Kiucha is an urban township with approximately 500,000 inhabitants and we estimated that about 10 percent, or 50,000, are HIV positive. These show quarter by quarter the mothers, the pregnant mothers, who are enrolled in the anti natal program and it shows you how from 1999 the prevalence of HIV amongst mothers is increased from about 14 percent to 25 percent in January to March 2003. The DODCT program was started in 1999 in midwife obstetric units where approximately 7,000 women deliver each year. And today it's more than 4,000 women have been diagnosed and treated as part of this program. At the time of this study, AZT only was used and given at 34 weeks and during delivery. Mothers attend the service weekly after the child is born in order to obtain free formula for nine months. Support groups are also very important part of the program and this is both inter natal and postnatal. (Unintelligible) is

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provided from six weeks of age. In terms of the program, 96 percent of mothers accept testing, accept HIV testing, and of the mothers who are HIV positive, approximately 78 percent actually enroll in the PNTCT program. Other aspects of the HIV program in Kiucha, public services for HIV infected persons were opened within the primary healthcare services in Kiucha in February 2002 and (unintelligible) was introduced in May 2001. To date, approximately 25 percent of the persons on (unintelligible) have come from the Prevention of Mother to Child Transmission Program. What are the major issues relating to formula feeding, which is breastfeeding in this setting? As I said, the risk of HIV transmission versus the risk of death from other causes, the problem of stigma and discrimination which may prevent women from formula feeding and a third issue is that mothers may leave the area and move to other areas, particularly more rural areas, where the risks of death from other causes are greater. So the objectives of the study were to identify the proportion of HIV infected women who are breastfeeding and who are formula feeding, and I'll define these in a minute, to identify women who made the choice themselves, so was it their own choice to formula feed or not, to identify the constraints which women faced in implementing their choice and then to identify episodes of diarrhea in their child. So there's a (unintelligible) survey of women attending the postnatal clinics where the mothers come who are enrolled

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in the Prevention of Mother to Child Program, a sample of consecutive women and the women were interviewed at the clinics by trained interviewers who were not nurses and they were not linked to the clinics in any way in the language of the women. In addition, six focus groups were held with 38 of the women. Exclusive breastfeeding was defined as only breast milk taken and no other solids or liquids, including water and herbal teas and formula feeding was defined as formula and no breast milk, but other liquids not contraindicated. 113 women were included in the analysis and the median age of the infants was 8.5 weeks. And 96 percent of the women said that they did not breastfeed at all. Four women breastfed only and one woman breastfed and formula fed. The reasons given for choosing this method of feeding, and this is an open question, 65 percent of women said that they themselves had made that decision in order to prevent transmission to their child, whereas 35 percent said that they were advised or told by the clinic to breastfeed or not to breastfeed and that's why they did so. The reason why the other women breastfed and didn't formula feed was that they did not want to disclose their status or had difficulty in not breastfeeding because that would disclose their status. Women were asked about disclosure of HIV status and two different questions were asked. One was about disclosure in general and the other about disclosure to members of their household. 69 percent of women had disclosed to someone else, but only 57

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percent had disclosed to someone in the household. Almost 10 percent had disclosed to everyone in the household, approximately 50 percent to some members and 43 percent to no one else in the household. As to whether women would stay in the area or move out of the area, the median time they had lived in the area was six years. 88 percent of women said they intended to stay for a long time, 8 percent said that they would leave very soon and we wonder if these women didn't specifically come to the area because of the PNTCT program, and 4 percent did not know how long they would stay. 71 percent of women said they had access to safe tap water, portable water, at their house. It wasn't necessarily in the house, but it was at the house. And approximately 30 percent had to walk to fetch water with the median time to fetch water being five minutes. And 75 percent of women have electricity at their house. Asking mother about episodes of diarrhea, 70 percent said their child had not had diarrhea, 27 percent said there was one episode and 3 percent said that their child had two episodes. However, none of the children were admitted to hospital for these episodes of diarrhea. In terms of the focus groups, it was obvious that stigma is still very high and women actually lie to their friends and family about their HIV status because if they don't breastfeed it's viewed as being HIV positive. So the reasons given are that they have TB, chronic diseases such as hypertension, they have bad milk, problems

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with feeding previous child or that they had had a cesarean section. So women felt that the stigma related to not breastfeeding was mostly linked to HIV. And a common quote was that, "When people ask me why I'm formula feeding, what they're really asking is am I HIV positive." Yet, most women acknowledge that in the community breast and formula feeding is common and acceptable. They also indicated that support groups were very valuable in deciding not to breastfeed and the reason for this was that they could share stories and give mutual support to each other so that they could breast -- so that they could formula feed. Many women said it was the only time to talk about their status and to ask questions and they appreciated the talks and information that was distributed at support groups. Most HIV infected women do not breastfeed in Kiucha and this setting is similar to many other urban areas in South Africa. Approximately 60 percent of the population of South Africa live in urban areas. The majority of the women chose not to breastfeed. They made the decision themselves, although they had this behind other reasons because stigma is still present. But women find ways and -- to counter this. The women found support groups very helpful in (Unintelligible). In addition, data from the Health Information System (audio out) in the city accepting (audio out). Thank you.

RUTH NDUATI: Thank you very much for that

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presentation. The (unintelligible) is open for discussion.

Yes, I can see there's some questions.

MALE VOICE: I think this study is an excellent study. I would strongly recommend that this study should be kept as a best practice example by (unintelligible). I think (unintelligible) that breastfeeding is not possible in poor countries, so I really admire this one. My question is who else (unintelligible) for the formula feedings, the government or (unintelligible) or the government pays for them? Who pays for the (unintelligible)?

DAVID COETZEE: It is paid by the provincial governments of Lewistown Cape, so it's paid by the government.

MALE VOICE: Okay. So if you present this to the South African government, will they accept the fact that, you know, from now on there should not be any breastfeeding in South Africa? Do you think that will be status for doing that?

DAVID COETZEE: Certainly the provincial government of the Western Cape I think accepts that, but I can't say the whole country, and (Unintelligible).

RUTH NDUATI: Yes, there's another question there.

MALE VOICE: Hi. A nice study, but do you have any information on how many women were approached to answer whether -- and how many agreed to actually -- what percentage of women who were approached to be interviewed agreed because of course if -- depending on that percentage depends on how

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representative of the total sample.

DAVID COETZEE: Katherine wanted 120 women in the study and she got 113. I think two were also excluded for other reasons. So it was a small number actually refused to participate.

RUTH NDUATI: Yes, far corner. And please say who you are and where you're from.

FEMALE VOICE I'm Dr. (Unintelligible) from Kenya. Can you hear me?

RUTH NDUATI: Yes.

FEMALE VOICE: I'm Dr. (Unintelligible) from Kenya. I'm glad about your findings. The only problem I have is you are (unintelligible). Because I do have a feeling that the (unintelligible) that you present is the same (unintelligible) that is being followed for the other studies, and I wish you could have presented more of the perspective data rather than having a cross section of data. Some of the things that weren't clear from these kind of a study design was when you talk of diarrhea was it, like, every day or rare or was it within the last so many days or when you talk of exclusive breastfeeding was it over this last 24 hours or ever, you know, within and then kind of do (unintelligible) your children into the (unintelligible) and the like so that when you present it, it has more strength in it. We do also have a similar experience in Kenya, although most of our women actually choose

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to breastfeed regardless of all the effort and even provision of pre-formula. They still choose to breastfeed. But to get a mother to actually accept to formula feed, we invest a lot in counseling them and getting them ready. So I don't know what kind of experience you have in this group that you're dealing with. Do you invest a lot in terms of counseling, demonstrating the formula feeding preparation so that by the time they get to actually give the formula, they can give it safely within this kind of setup? Thank you.

DAVID COETZEE: I can't remember all the questions. It was asked if they ever breastfed, yes, so it was from this. They were asked if the child had diarrhea in the last month. In fact, data shows that it's best to ask in the last two weeks and that's the best recall. But, in fact, they were asked here in the previous two months or in the previous month. And the other question relating to support groups and counseling, yes, a large emphasis is placed on talking to the mothers about breast and formula feeding and the risks and supporting the mothers in their choice.

RUTH NDUATI: Okay. (Unintelligible).

MALE VOICE: I agree that it's a nice study. But, this whole area has been asked already so I won't repeat that question. But the issue I think that the issue of formula feed or breastfeed, breastfeeding in HIV women in developing countries, I think it's (unintelligible) in addition to the

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(unintelligible) that would come with it. Also I think the issue of cost is one very important factor. It would be interesting to know the income levels of the women who were in your cohorts. It also have been (unintelligible) to know the outcome of the babies of these children. Because of costs we know that's not (unintelligible) women who breast and formula feed just to save some costs. So the first one is what are the income levels of these women? And the second one, do you have any plans to (unintelligible) to know the outcome of being formula fed?

DAVID COETZEE: Okay. The women don't pay for the formula. I would -- the majority of women are, in fact, unemployed and they don't pay for the formula. The formula is given to them free. In terms of -- it would be ideal to do an longitudinal study and to follow our cohorts. In terms of transmission rates, at the time that this study was done the transmission rate was 11.9. Since then, Nevirapine has been added as well. So -- and we are doing a (unintelligible) at the moment. Unfortunately, our members are still under 100. They're around 90. And the transmission rate is 8 percent. Obviously that's a very wide confidence interval and we will only have that information in the next probably three or four months.

MODERATOR: I think there's one more question there.

DAVID COETZEE: But the regimen has changed.

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MALE SPEAKER: (Unintelligible), Uganda. Mine was to do, again, relate -- something related to the study design. What's the underlying infection rate of the area and the population? Again, our experience has been that in the natural history studies that people who are involved in such studies in fact even have the children who are involved in these studies have much lower infect without anything being done, anything different being done, but because they're in the study then they're accessing the healthcare -- a much better healthcare system of low infant mortality rates than, in fact, the rest of the population. And again, related to that, you might be in a setting where the area infection is (unintelligible). The other issue is regarding that you had only about 113 and probably you say there were only four who were exclusively breastfeeding. That -- I don't see how you can actually make a comparison in terms of infections when one group has only four individuals. So in terms of determining (unintelligible) those who are breastfeeding versus those who are not breastfeeding I think might be different. I don't see how you can do that with that sample size.

DAVID COETZEE: We don't know the HIV status of these children. But I agree, we would have to look also at the spillover effect in terms of other women who HI -- who are not HIV positive, not breastfeeding their child.

MODERATOR: Thank you for all these wonderful -- yes,

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one more. I think we have time for that.

MALE VOICE: Thank you very much. I'd like to thank you for a nice presentation. I'm impressed with the support group. How far were the husbands involved in this program? Because none of the problems of stigma in the family, it's important the father of the child. Are these women all married or what were the (unintelligible) of the husbands? Too, the other thing is that you look at that data, what happens to the acute respiratory infections in these children on formula? Are there any allergies, things (unintelligible)? (Unintelligible) the (unintelligible) about allergies in breastfeeding versus formula?

DAVID COETZEE: Okay. Unfortunately, the fathers were not involved. And often, the mother had not disclosed to the father of the child. In terms -- we only looked at diarrhea. We didn't look at any other diseases.

MODERATOR: Thank you very much. I have one question for you and also (unintelligible) this is, I think, an excellent example of government's commitment, original government's commitment to prevention. I think the fact that they provided the formula is part of the step towards that. My question is about this peer groups, the support groups. To what extent is support to choose formula support and not peer pressure?

DAVID COETZEE: Well, as you see, also 30 percent of

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the mothers actually did it because the clinic said that they should be. So I'm sure there is a degree of peer pressure and there is a degree of being told by the health service that's what you should do. But by far the majority of women made the choice themselves. But I'm sure the support groups do have an influence on their decision.

MODERATOR: Okay. Thank you very much. I will call the next speaker. I just want to say South Africa is not the rest of Africa. And 35 percent of women have no access to electricity is not the norm in many African cities. I think there still is some (unintelligible). It shows what you can do when we have a little more resources. But the question (unintelligible) are very valid for the rest of us in the continent. Now, the next presenter is Marie Newell, a dear friend of mine for many years and she's presenting what's carried out actually by many of you who are here, you know, and this is the (unintelligible), which as she'll tell you, is a contribution of work from many, many studies within South Africa. So sit back and enjoy your own work and ask many questions.

MARIE NEWELL: Thanks very much, Ruth. I hope you weren't looking at my face when you said that I'd been around for a long time. I do (unintelligible) in presenting the data on longevity amongst HIV infected mothers and children's feeding modality. And I present this data on behalf of the

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Breastfeeding and HIV International Transmission Study Group.

We know that breastfeeding is a general benefit to both infants and maternal health improving infant and child mortality and making child spacing more favorable to maternal health, and also having psychological benefits for both infants and mothers. Breastfeeding, however, substantially increases the risk of HIV infection in infants as we have heard both this morning and yesterday in several presentations. We know very little about the effect that breastfeeding has on the health of HIV infected women themselves. But limited evidence from two studies in Africa regarding the association between breastfeeding and mortality amongst HIV infected mothers gave conflicting results. One study in Nairobi and Kenya suggested that the mortality in breastfeeding women was substantially higher than in non-breastfeeding women in the two years following delivery whereas a study in Durban in South Africa suggested that there was no evidence of any effect on mortality and mortality in exquisitely breastfeeding women. We both aimed to estimate the rate of mortality amongst HIV infected breastfeeding women over an 18-month period following delivery. We wanted also to identify any factors that could possibly be associated with mortality amongst HIV infected breastfeeding women and we wanted to compare mortality among breastfeeding and non-breastfeeding women in (Unintelligible) in Africa. There were in a full data set from nine mother to child

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transmission and prevention trials that have been carried out in mainly breastfeeding populations in (Unintelligible) and Africa where the children's feeding modality had been regularly assessed provided 4,237 mothers that could be evaluated in this analysis. This data set was collated to estimate the risk of postnatal transmission through breastfeeding, but provided a unique opportunity for these additional analysis on the mortality in the women -- in the mothers. In the 18 months following delivery, a total of 162 mothers died. The median time to death was 9.8 months. The median CD4 count assessed around the time of delivery was 464 cells a milliliter. 11 percent of these women had a CD4 count of less than 200 cells, 45 percent had CD4 counts between 200 and 500 and 44 percent of women had CD4 counts of 500 or more. 3,717 women, or 88 percent, ever breastfed and the median duration of breastfeeding in this group was 8.8 months. 40 percent of women were still breastfeeding at 18 months. So what we are talking about really is a population where breastfeeding is very common and prolonged, but where overall the HIV related health status was not so bad. 362 deaths in the 18-month period translates in an overall mortality rate of (unintelligible) years of follow-up. The (unintelligible) analyses infant feeding modality defined as ever versus never breastfeeding was not associated with mothers' mortality in this 18-month period. However, in multivariate analysis where

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we adjusted for geographical location of the child, factors associated with maternal -- with mothers' mortality in the 18 months period were the duration of breastfeeding and the median CD4 count around the time of delivery. In these multivariate models, mortality was lower in women who ever breastfed than in those who never breastfed, but the statistical significance was of borderline. Mothers who breastfed for nine months or longer had a lower risk of mortality than those who breastfed for a shorter period. And in CD4 stratified analysis, the association between duration of breastfeeding and mortality was apparent for women with counts of less than 200 cells per milliliter, but not for those with CD4 cell counts above their (unintelligible). When we looked at the breastfeeding variable in a slightly different way, in a more dynamic way, and where we categorized the experience of each point in time whether the women were still breastfeeding or whether they had ceased breastfeeding either less than three months previously or more than three months before the last visit or before they died. And in a proportional (unintelligible) where this variable was allowed for in a time dependent manner we saw it as looking in a model, in the first model, where we just allowed for the infant feeding variable we saw substantial and significant differences between the reference group that never breastfed and the different categories of breastfeeding in terms of the mortality, but that the direction of the association went in

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opposite ways. However, it's very important to allow for the geographical location of the trial setting because not only is the (unintelligible) mortality different -- very different when you compare West Africa, East Africa or South Africa, but also the -- whether or not the child was breastfed varies by these locations. And if they are breastfed, there are very large differences in the duration of breastfeeding. So when we allowed for geographical locations in model two, as well as the breastfeeding variable, the only significant difference was the substantially decreased mortality in women who still breastfed at their last assessment. The formal CD4 information -- count information was available for about 80 percent of the women that were involved in these trials and we had -- we did a sub analysis on 3,240 women and included maternal CD4 counts in this proportional (unintelligible) analysis with the breastfeeding variable, in a time dependent manner. The only significant results were again the substantially lower risk of mortality in women who were still breastfed at the last assessment versus those who had never breastfed and (unintelligible) that was virtually the same as the one that I showed in the previous slide. There was a (unintelligible) of increased risk of dying in women who had a CD4 count around the time of delivery of less than 200 cells and a substantially lower mortality in South Africa. So, in conclusion, women who have advanced disease, as indicated by a low CD4 account around

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the time of delivery, had a greatly increased risk of dying in the months following delivery. Although mortality rates in the first 18 months postpartum was lower in women who ever than in those who never breastfed, this was not statistically significant. Amongst the breastfeeders, mortality was higher in the group with the shortest duration and it was lower in those who were still breastfeeding at the time of last assessment. And this would suggest that those -- that we are dealing here with reverse (unintelligible) with women who are well and healthy and are able to continue breastfeeding for longer periods. This association is likely to be very complex and very difficult to evaluate in observational data, but we are trying our best to investigate this further. Thank you. I said that I was presenting this data on behalf of a large group of people, some of which -- some of whom have been listed in the slides, but who should also be recognized that each of these principle investigators of the various trials depends on a large team of local people that helped them with the support and care for these women and their children. The (Unintelligible) HIV transmission study is a collaboration between the (Unintelligible) working group on Mother to Child Transmission and NICHD. Financial support for the data analysis came from NICHD with a contract with the Data Management Center at (Unintelligible). And additional financial support specifically for this analysis on maternal

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mortality was provided by WHO/UNH and special thanks to
(Unintelligible). Thank you.

RUTH NDUATI: Thank you very much for that
presentation. That presentation is now open for discussion,
questions. Yes?

MALE SPEAKER: Hi. Thank you. Mike Silverman from
Canada, a nice study. Do you feel that this resolves the
question at all or do you feel because the women seem to be
self-selecting, that the sick women are not -- are stopping
breastfeeding when they get sick that this is evidence that we
should do a randomized trial as much as we can do a randomized
trial encouraging women to breastfeed and not breastfeed to
answer the question?

MARIE NEWELL: I don't think I would want to repeat the
experience that (unintelligible) having a randomized trial of
infant feeding to investigate the mortality experience of the
mothers. I think that the results from this trial, from this
(unintelligible) suggests that the mortality in these women is
associated with HIV status, that women who have advanced
disease are more likely to die and these women can -- what
seems to be happening is that these women become ill and are no
longer able to breastfeed and then they die. So you get a bit
of a (unintelligible) reverse causality. I think that for me,
the very big evidence, the big results from this is the large
differences in mortality by geographical location and it

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highlights the issue that it is very difficult to compare individual study results if you don't take into account the background (unintelligible) where these studies have been carried out. I do think that, to come back, I do think that it would be very interesting to see the results from the various trials that are about to start where nutritional supplementation to breastfeeding women is being evaluated. And I think that that will sort of contribute to the information that we have here.

RUTH NDUATI: We have a question here and then --

MALE VOICE: (Unintelligible), United States. Thank you for a very ambitious attempt to take on a very difficult question. But I think as you just pointed out with the huge heterogeneity, it kind of renders med analysis not a very useful tool to answer the question. But my question is can you look at the strata in which we would be most likely to see an effect, that is women from high mortality locations with low CD4 counts, pool those women and see if within that group who are likely to have an equal possibility of breastfeeding, whether or not there's a difference in mortality?

MARIE NEWELL: That's the first (unintelligible) waiting for and I haven't got that at the moment. And (unintelligible) the data sets are the background the person who has that analysis because it's (unintelligible) available. And the -- however, if you look at the strata sites or the sort

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of frequency tables mainly and by duration of breastfeeding by the different locations and by the different CD4 counts, it does look like the different occasions to give the same results, that the mortality is very high wherever you are if your CD4 count is low and that the differences between ever and never breastfeeders are not statistically significant, but that's probably due to a lack of power and that if there is any difference it's just not large enough to show up. Actually what I want to say is that in this trial because the -- in this (unintelligible) analysis both the Nairobi trial that showed the original results and the vitamin A trial which showed the opposite results, I included and what it is interesting is that the CD4 counts in the women from the -- the breastfeeding women from the Nairobi trial is substantially lower than the CD4 count from the women from (unintelligible) which partly helps in explaining the contradictory results.

MALE VOICE: (Unintelligible) I've probably forgotten it if you told me before. But the third difference, if you exclude maternal mortality in the first six weeks of the (unintelligible) causes because we know that we've seen (unintelligible) mortality in HIV infected women and that that differs dramatically also between (unintelligible) and the other areas. And it seems unlikely that breastfeeding is going to impact in those obstetric, (unintelligible) obstetric causes those first few weeks. Would that make any difference if you

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MARIE NEWELL: That's a very good question, James. You haven't asked me that before and the (unintelligible). I don't know whether the numbers are large enough. We had 162 deaths before 18 months. We had 128 deaths before -- 142 deaths before 12 months, so there may not actually be enough deaths in the first six weeks. But I could certainly ask the strata stations to have a look at that.

RUTH NDUATI: It looks like there are no other questions. Thank you very much for the presentation and (unintelligible). And then I would like to take the opportunity to wish you a safe journey as you go back home to wherever you come from.

[END OF RECORDING]