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XVII International AIDS Conference Late Breaker Track C August 7, 2008

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[START RECORDING]

JAVIER CABRAL, M.D.: [Speaking in foreign language].

KEVIN DE COCK, M.D.: Colleagues, friends, good afternoon and welcome to the Late Breaker of Track C. My congratulations to all the speakers and their colleagues for getting these important abstracts accepted. Without further ado, let us go to the first presentation. The protective effect of male circumcision is sustained for at least 42 months: Results from the Kisumu, Kenya Trial, presented by Dr. Bob Bailey and colleagues. Welcome, Bob.

ROBERT C. BAILEY, M.D.: Thank you, Kevin. So, I first want to thank the organizers for inviting us to give this presentation. Also, to all my collaborators, just a few of whom are shown in the slide, and of course to many young men who have participated in our studies over the last 6-1/2 years.

In the interest of time, I am going to read my presentation. One of the main concerns that has been expressed about the evidence for male circumcision, its protective effect against HIV acquisition has been that all three trials of circumcision were stopped before planned completion and the study has extended only 18 to 24 months. Skeptics have said that the protective effect of circumcision will likely be eroded after periods of longer than 24 months.

So, here we report extended follow-up from our cohort in Kisumu out to 42 months or three years. So we have previously reported findings from the first 24 months of the kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

trial in Kisumu. We reported a 53-percent protective effect of circumcision in intent-to-treat analysis and a 59-percent protective effect of circumcision in a modified intent-to-treat analysis.

On December 12, 2006, the Data and Safety Monitoring Board, upon review of these results advised NIH and ourselves to un-blind the study. So, in December 2006, we began offering circumcision to controls. We had already circumcised a proportion of men, who had completed their 24 months of participation in the trial. And in March 2006, we reconsented those men who were still remaining in the study, and we will continue to follow up on them until September 2009.

So, the purpose of this presentation is to report, first, the slight modifications to our previous findings based on further laboratory analysis. And second, to report results from continued follow-up of circumcised and uncircumcised men up to 42 months post-randomization.

Initially, 2,784 men ages 18 to 24 years were randomized to circumcision or delayed circumcision. With all the participants, we performed HIV testing, behavioral counseling. We administered behavioral questionnaire, conducted clinical exam, and collected urine and blood for STI testing. We did this at baseline and every six months thereafter and participants also underwent HIV testing and received behavioral counseling at one and three months. And any man who was circumcised was asked to return to the clinic kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

at three, eight, and 30 days post-circumcision in order to check the wound and to counsel them about wound care and abstinence from sex.

Originally, we reported that at un-blinding of the trial in an intent-to-treat analysis, there were 22 HIV seroconversions in the circumcision group and 47 in the controls. This resulted in a risk ratio of 0.47 or 53-percent protective effect of circumcision against HIV acquisition. These are the results that are most often reported for our study.

However, we also reported a modified intent-to-treat analysis in which we excluded four seroconverters whom we found to be HIV positive at baseline. This analysis which is most comparable to the results reported from Rakhi [misspelled?] and Orange Farm, and undoubtedly reflect a more accurate estimate resulted in a relative risk of 0.41 or 59-percent protective effect.

So, subsequent to our publication results in the Lancet, we have sent samples to Tom Quinn's Lab at NIAID for sensitive PCR and I want to thank Oliver Laeyendecker for his assistance with analyzing those samples. His further analyses result in some slight changes to our original findings. Two men in the circumcision group previously considered positive at baseline turned out to be negative. One participant in the circumcision group considered as a seroconverter at three months turned out to be positive at baseline. And one kalsernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded

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participant in the control group previously considered a 12month seroconverter turns out to have been negative throughout follow-up.

So, these modifications result in a revised modified intent-to-treat analysis defines 18 seroconversions over the 24 months of follow-up in the circumcision group and 45 seroconversions in the control group or relative risk of 0.40 or 60-percent protective effect of circumcision. So, the updated HIV testing results in these small changes to our original estimates.

So now, turning to our extended follow-up, of the original 2,784 men randomized at the beginning of the trial, 1,739 were eligible for extended follow-up. Of these, 89percent consented, approximately equal numbers in the two groups and 1,491 or 97-percent of these now remained on study.

So, we looked to see if there were differences between the men in the control group who chose to become circumcised and those who chose to remain uncircumcised. We found there had been no differences at baseline. And this also means that there were no differences at baseline between those controls who became circumcised and those men who were originally randomized to the circumcision group.

So, here is shown a Kaplan-Meier plot of an intent-totreat analysis of data extending to 42 months or 3-1/2 years of follow-up. The analysis is based on 24 seroconversions in the circumcision group representing a cumulative seroincidence of kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

2.6-percent compared to 65 seroconversions in the uncircumcised group representing the cumulative seroincidence of 7.4-percent. The relative risk of circumcision is 0.36 or protective effect of circumcision against HIV acquisition over the 3-1/2 years of follow-up of 64-percent.

When we do an as-treated analysis, the results are same with only slightly wider confidence intervals. It is worth noting that we had some concern when reporting our original trial results that there were almost an equal number of seroconversions during the interval between 18 and 24 months, eight seroconversions in the circumcision group and 10 in the control group. This suggests that the protective effect of circumcision may be declining. These new results, however, dispel those concerns.

We did additional analysis, this Kaplan-Meier plot shows the HIV seroincidence in men circumcised within two weeks of randomization compared to participants in the control group using their follow-up experience up to the time that they were circumcised. In other words, these uncircumcised men are censored when they become circumcised. So, this is purely experience of circumcision versus no circumcision.

The cumulative HIV seroincidence in the circumcised men over the 42 months of follow-up is 2.7-percent versus 8-percent in those who remain uncircumcised. The relative risk of HIV infection for circumcised men is essentially the same as in the

previous analysis whose case is 0.35 or 65-percent protective effect of circumcision against HIV acquisition.

These analyses result in an average annual seroincidence of 0.77 infections per 100 person-years in the circumcised men and 2.37 infections per 100 person-years in the uncircumcised men. Again, this has a relative risk of 0.35 and the difference is highly significant.

So, there are limitations to our study. There are changes to the two groups because of crossovers from control to circumcision. So, men in the control group who have opted for circumcision may be different from the controls who have remained uncircumcised. Although, we have looked at this and found no significant differences in demographic or risk profiles between the two groups.

Extended follow-up beyond 24 months is available on a smaller sample than the original 2,784 participants. And as yet, few person-years of exposure have accrued among those in the delayed circumcision group. We intend to continue following up these men until September 2009 so we will have more data on experiences of both circumcised and uncircumcised men.

So, the conclusions to be garnered from these results are that further laboratory testing of specimens from the original trial result in only small changes to our original findings and the 60-percent protective effect of circumcision against HIV acquisition that we found in sexually active men in kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

Kisumu, Kenya over the first 24 months of study, we now find to be sustained and possibly strengthened to approximately 65percent over 3-1/2 years of follow-up.

So these results further support the addition of male circumcision to our existing limited armamentarium of HIV prevention interventions and to provide safe voluntary free medical male circumcision services in appropriate regions as rapidly as possible. Thank you. [Applause]

KEVIN DE COCK, M.D.: Bob, can I suggest, perhaps, that we do both presentations on male circumcision and take questions afterwards. Thank you very much, Bob. That is a very important study.

So, now Dr. Dirk Taljaard will present the Effect of Male Circumcision on Human Papilloma Virus, Neisseria Gonorrhoeae, and Trichomonas Vaginalis Infections in Men: Results from a Randomized Controlled Trial. And this work was done in South Africa. Thank you.

DIRK TALJAARD, M.D.: Good afternoon, ladies and gentlemen, and thank you to the organizers for giving me this opportunity to speak. The title of my story this afternoon is male circumcisions and the effect on HPV, gonorrhoeae, and TB infections in young men.

So, the background is, what do we know about male circumcision in men. We know that male circumcision reduces the HIV infection in men and we have got two randomized controlled trials to show that. We know that male circumcision kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

reduces HSV-2 infection from two randomized controlled trials and we know that many male circumcisions reduces genital ulcer disease in men from two randomized controlled trials.

We also have observational data that tell us that urinary tract infection in babies are reduced and that there is a reduction of syphilis, chancroid, and HPV infection as well as invasive female cancer which is probably due to the effect of HPV. These, however, are conflicting results about none non-ulcerative STIs for instance, gonorrhoeae, chlamydia, and TB.

For women, there are conflicting results about male to female transmission of HIV, but at least, we think that on the population level, women have a rather indirect benefit in the fact that there will less infected men around.

We know that male circumcision reduces TB from one randomized controlled trial. We know that male circumcision reduce the genital ulcer disease in women from one randomized controlled trial and we know that male circumcision reduces the risk of cervical cancer in female partners of circumcised men, also probably due to the link with TB and HPV.

So, the objective of the study was to assess the effect of male circumcision on high risk HPV, gonorrhoeae, and TB infections in young men using the data from the Orange Farm male circumcision randomized controlled trial, the ANRS-1265.

The methods for this trial included a screening

uncircumcised at inclusion. We then sort them at inclusion up to three months, 12 months, and 21 months visits. At each visit, we took a blood sample, we did a clinical examination. We also did behavioral questionnaire, and offered VCT. Shortly, a few days off the screening, participants were randomized into two groups. Intervention group were circumcised straight away and then we followed various groups at up to three months, 12 months, and 21 months. Those of the controlled group opted 21 months were offered circumcision and most of them took it up.

We collected additional samples at the 21-month visit. We collected 318 days worth of urine samples and then we collected urethral swabs for 262 days. The laboratory methods we employed, we tested the urine samples of PCR for gonorrhoeae and for TB. And we use the PCR-based method from Roche for the urethral swabs that identified 13 high risk genotypes of HPV. The most important of these is Type-16 and 18 due to the link with cervical cancer in women.

The statistical methods used, we did a prevalence study on circumcised person versus uncircumcised and an intent-totreat analysis and we did an analysis of intervention versus control in an as-treated analysis. We calculated odds ratios and adjusted odds ratios using logistic regression and control for covariates of ethnic group, education, age, number of lifetime partners, marital status, condom use, and we used HIV

status propensity score.

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So, the results, in gonorrhoeae, we see the intervention and control groups. You can see the difference between the intervention and control as 10-percent versus 10.3. And in the circumcised and uncircumcised, 10.4 versus 10, with odds ratios very close to 1 and these were not significant. This led us to believe that male circumcision had no effect on gonorrhoeae.

Then, for TB, you can see in the intervention group with 1.7-percent prevalence, and in the control, 3.1. And in the circumcised and uncircumcised, we have 1.6-percent versus 3.2-percent prevalence. This gave us odds ratios of 0.49 and you can see a borderline significance. So, we concluded that male circumcision has a borderline protective effect on TB.

And then, for high-risk HPV, you can see again the difference between the intervention and control. In the intervention, we have 15.8-percent prevalence, in the control, 24.8-percent and this was significant. And then, in the circumcision status, we have 15.2-percent for the circumcised and 25.5-percent for the uncircumcised giving us an odds ratio of 0.52 and 0.44 respectively for an adjusted and unadjusted. And you can see that in both instances, this was significant. This led to the conclusion that male circumcision has a protective effect against high-risk HPV with a prevalence rate ratio of 0.64 and a protective effect of about 36-percent.

The male circumcision had a different effect on different HPV genotypes. You can see in the graph that there kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

is quite a lot of variance between the different genotypes. We are not sure whether male circumcision actually affects these genotypes differently whether this could be a random effect due to the sample size which at this level of analysis was quite small.

And then, there are some discussion and some opinions that lowered detection in circumcised men is because of the sample taking. And so, to test this, we took 371 men from the control group, who were circumcised, and we compared the urethral swabs taken before and after circumcision. So, before they were circumcised, we took a urethral swab with a mean of 59 days and a median of 43 days. After their circumcision, we took a urethral swab again. We analyzed these swabs for High-Risk HPV prevalence and in the first instance of prevalence was 26.4-percent and in the second instance, 26.1. So, you can see it was very consistent over the short span of time which led us to believe that the effect on HPV cannot be due to the differential sensitivity of HPV detection between circumcised and uncircumcised men.

Could the effect be due to the effect of male circumcision on HIV? We excluded those who seroconverted for HIV during the follow-up with the same result for HPV and for TB. So, in other words, the effect that male circumcision has on HIV did not influence the effect that male circumcision had on HPV and TB.

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There are some limitations to the study. We have no biological status of the partners, and in fact, a lot of these young men did not have women partners. The status at inclusion was not available and the effect we are looking at is the effect on prevalence and not on incidence.

However, we are confident about the findings because of the following factors. The group was randomized in the beginning which remained that there is no reason to believe that their HPV status at randomization between the two groups would be different. We have analyzed the effect with and without adjustment. We analyzed the effect in the intent-totreat and in as-treated analysis. And we also have to remember that this study was done in young men and prevalence should rise. In fact, the fact that the prevalence was high in the control group than in the intervention group at the end of study means that there was some incidence.

We concluded that lower high-risk HPV and TB prevalence among circumcised men is likely due to a lower incidence which could lead to a lower female to male transmission. These results were explained with several studies including one RCT that have shown that women with circumcised partners are at low risk of TB infection. In fact, the studies suggest that it is the result of lower risk of TB infection in circumcised men as compared to uncircumcised men that could be responsible for this. These results may also explain why several observational studies have shown that women with circumcised partners are at kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We applogize for any inaccuracies.

low risk of cervical cancer, most of them due to high-risk HPV. Indeed, the studies suggest that there is a result of lower risk of HPV infection amongst circumcised men compared to uncircumcised men.

This paper has been accepted by the Journal of Infectious Diseases and is currently in press and should be here shortly.

I would like to thank our sponsors, the ANRS and the Bill & Melinda Gates Foundation who funded the additional testing, and then all our colleagues of INSERM, the National Institute for Communicable Diseases, University of SA. Thank you very much. [Applause]

KEVIN DE COCK, M.D.: Thank you very much, Dirk. I suggest that both these papers be opened for questions. Could you please identify who you are and please keep your questions as succinct as possible?

BRUNO HOEN, M.D.: Okay, my name is Bruno Hoen and I am from France. My question is to Dr. Bailey. I would like to understand why so many uncircumcised men remain so while they were offered to be circumcised and were aware of the protective effect of circumcision from the results of the trial they were enrolled in?

ROBERT C. BAILEY, M.D.: Yes, it is a good question. About 42-percent of the controls have now been circumcised and one of the reasons that there has not been larger uptake is that many of these men have moved away from Kisumu and living kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

in Mombasa, Nairobi, and other cities. So, we have been required by the IRBs and by NIH to continue that follow-up of ensuring that we see them at three, eight, and 30 days postcircumcision. We think that that is a very large deterrent. A lot of them have come to us or called us saying they want circumcision but when we say you are required to stay for a longer period of time, then, they do not come.

KEVIN DE COCK, M.D.: Microphone three, yes?

KELLY KERN: Kelly Kern from Chicago [misspelled?] this is a quick question for Bob Bailey. I was really curious to see the number of men who were initially classified as HIV positive who were then reclassified following the more sensitive testing in Tom Quinn's Lab or vice versa, could you comment on that a little bit and for the implications of those of us that worked in the HIV counseling and testing?

ROBERT C. BAILEY, M.D.: Yes, one thing I have learned during this trial is that the science of determination of HIV is far from a science, actually. And we had a lot of difficulties and I know other groups have as well in actually coming to determinations about definite seroconverters versus borderline or indeterminants. Originally, we used rapid test and ELISA, double ELISAs to determine seroconversion. And then we did LIAs in Canada but we found still there to be conflicting results. So, we believe that Tom Quinn's Lab is probably one of the best if not the best. So, using more sensitive techniques, these are the results that we have kalsemetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

considered to be determinant. But it is never easy and I think people should be skeptical sometimes about determination of seroconversions.

KEVIN DE COCK, M.D.: Microphone two?

GEORGE RUTHERFORD, M.D.: George Rutherford from the United States for Professor Bailey. I think I may have missed it, but was there a relatively parallel incidence between the circumcised and uncircumcised groups after about 2-1/2 years of follow-up? That is, are you starting to see the speculation would be that the incidence rates remain relatively the same in those later years that you might be seeing a community level for benefit of circumcision?

ROBERT C. BAILEY, M.D.: There has not been so much uptake in the community at circumcision that you are going to see a drop in incidence due to circumcision in the community. But the rates are quite consistent across all five years of our study and the relative risk is increasing slightly but it is really within confidence limits. So, we cannot really say that relative risk is changing.

GEORGE RUTHERFORD, M.D.: Thank you.

KEVIN DE COCK, M.D.: Could I ask if there are some questions for Dirk's study? Yes, could you come to the microphone please?

DANIEL HALPERIN, M.D. Actually, mine is partly Kevin. KEVIN DE COCK, M.D.: It is Daniel Halperin Good

Lord. [Laughter]

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DANIEL HALPERIN, M.D. Yes, it is. We are old friends, are we not [Laughter]. I still remember the days when we were not allowed to talk about this subject. [Laughter] Actually, can I ask you a question, Kevin?

KEVIN DE COCK, M.D.: No, let us stick to the speakers. We well got six of the speakers, we will see if there is any time left.

DANIEL HALPERIN, M.D.: Okay, then I will wait because it is a question for WHO.

KEVIN DE COCK, M.D.: They are invisible at this conference. [Laughter]

JEAN SHAPEN: My name is Jean Shapen [misspelled?]. I wonder what kind of consideration has been given to the effect of the intervention itself, the fact that the men who were circumcised were given more attention and more follow-up and whether that was considered particularly in the differential and HPV, were they more likely to use condoms with their partners? I know that according to your studies, you encouraged men to use condoms and one would assume that the people in the experimental group would have had a higher degree of education in condom use, was that considered at all in differential incidence after the study period?

DIRK TALJAARD, M.D.: I think that the condom use was quite consistent between the control and the intervention groups -

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KEVIN DE COCK, M.D.: Please speak at the microphone again.

DIRK TALJAARD, M.D.: I think that the condom use was quite consistent between the control and the intervention groups. And we do not think that this played at all.

KEVIN DE COCK, M.D.: Could I ask you a question, doc? Does that the answer to your question? Is there another question for doc or?

NICOLA LOW, M.D.: Yes, please.

KEVIN DE COCK, M.D.: Okay.

NICOLA LOW, M.D.: Hi, I am Nicola Low from the University of Bern in Switzerland. Question about the STI data, can I ask you very briefly why you did not test for chlamydia? And secondly, what you speculated as being the reason for the lack of effect on gonorrhoeae but effect on trichomonas?

DIRK TALJAARD, M.D.: The short answer is funding, [Laughter] for not testing for chlamydia. And then for gonorrhea, I really do not have an explanation.

KEVIN DE COCK, M.D.: Microphone three.

DR. DR. KUBOTA, M.D.: Kubota from the United States. The HPV data, could it be a matter of persistence as opposed to acquisition? You only tested at one point in time?

DIRK TALJAARD, M.D.: Yes. We only tested at one visit, yes. So, I think it is possible. But for some of the

control, we did test also 21 months, and again, after six weeks. And in that testing, it was quite consistent.

KEVIN DE COCK, M.D.: Daniel?

DANIEL HALPERIN, M.D. Thanks, Kevin. If you can answer it, Dirk can partially answer. Two questions I have are mainly for WHO, one, in the kind of more sophisticated reanalysis that Bob Bailey has talked about, were you looking both at the biology of seroconversions and longer follow-up, as we start to get these from the other trials, the effect size may potentially grow. It looks like they have gone from roughly 55-percent from the published article to now, 65. If we see a similar trend in the other trials, is there any possibility that WHO may up at 60-percent estimate?

That is the one question, estimate for the HIV protective effect may end up being somewhat higher up in the 65 or 70-percent range. Second question may be more importantly is, given the strength of the evidence on cervical cancer in particular or predictors for cervical cancer, and may be will end up getting data on cervical cancer and on TB, is there any possibility that WHO may endorse male circumcision as a holistic reproductive health measure for both men and women and not only as a strictly HIV prevention modality?

KEVIN DE COCK, M.D.: I have got WHO colleagues sitting there itching to comment. [Laughter] Kim, why do not you come to the microphone? Let me answer perhaps with the - I just want to ask another question and then I will comment on what kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

Daniel has just asked. Can I ask, Dirk, what do you think is the biological mechanism of protection against HPV and can you see us getting into a debate internationally about whether it is more important to circumcise men or give HPV vaccine to women?

DIRK TALJAARD, M.D.: I think as of HIV, the biological mechanism is not yet determined and it is very difficult in this case to say why because you have to keep in mind that these were urethral swabs, not swabs taken on the outside or in the inside of the foreskin. So, we have speculated a lot about the biological mechanism but it is not clear and I really do not know.

KEVIN DE COCK, M.D.: Let us close this down and let me just quickly comment on Daniel's question. I think, Daniel, trying to get a point estimate of efficacy, I think, is somewhat artificial and I think that the qualitative description that is out there from WHO and UNAIDS is adequate for the public health message to get across. As far as your second point is concerned, I mean, yes, I do certainly see, you know how global norms and standards get made. I do see that there will be future discussions and consultations and so on about the broader aspects of male circumcision especially as there is more data of this kind of nature become available.

So, let me thank both speakers for being so collaborative also in answering questions together. Let us move on, we are a little bit behind time. I will introduce the kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

next speaker and then I am going to hand the chair over to my colleague, Dr. Cabral.

So the third presentation which is being presented by my friend and colleague from CDC, Dr. Walid Heneine, is entitled Complete Protection Against Repeated Vaginal SHIV Exposures in Macaques by a Combination Emtricitabine and Tenofovir Topical Gel.

WALID HENEINE, M.D.: Thank you, Kevin. It is a pleasure to be here to present this data on behalf of our group in the Lab Branch at CDC. So, we will move to the cousin species of ours, the pigtail macaques here to evaluate this particular strategy of microbicides.

As you may have all heard in this meeting, HIV continues to spread globally mainly through heterosexual sex and in many parts of the world, women are disproportionately affected by HIV. And obviously in the absence of HIV vaccine, alternative by medical interventions are critically needed.

Vaginal microbicide gels can provide a female controlled prevention strategy. However, the microbicide gels tested thus far that contained the first generation products like surfactants and polyions have been ineffective. However, the retroviral drug-based gels, as you probably have heard in this meeting, maybe more promising and can deliver potent drugs at the virus point of entry.

So, the question with these gels is what modality is productive, is it gels containing single or combination antiretroviral drugs will likely be more effective? We have ongoing trials now with 1-percent tenofovir which is a nucleotide RT inhibitor. Data reported actually this week by Cranage et al. in Plos Medicine showed that this gel is protective against rectal transmission in a macaque model.

However, a combination in nucleotide gels may be more protective than gels with single NRTIs because of the higher antiviral potency. They can also be more effective against circulating drug-resistant viruses.

And we already know from monkey work done in our lab and others that in oral pre-exposure prophylaxis combination in NRTIs such as Truvada was more protective than single drugs alone.

So, our study goals were three-fold. First, can a tenofovir and an FTC be co-formulated into a topical gel? And, can this drug combination protect female victim macaques from vaginal SHIV infection? And, which modality is protective, single application before virus exposure or daily application?

First, regarding co-formulation, we were able to successfully formulate 1-percent tenofovir plus 5-percent FTC and the higher dose of FTC was possible because of the highwater solubility of this drug. These were formulated in what is known as universal placebo, hydroxyethyl cellulose or HEC, kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

2-percent. And to provide a clear odorless and viscous gel, we have tested stability over time at different temperature including 37-degrees and this gel was stable for up to six months.

So, regarding evaluating the efficacy of gel in a monkey model, we device a study with three arms. First one, containing no gel armed with two animals, placebo gel that has no drugs with six animals, and the gel with the combination drugs, again, with six animals.

What kind of macaque model reviews for our study, this is reviews that are repeated low dose vaginal model originally develop by Ron Otten and Tom Folks in our lab. And this model closely resembles human transmission in many ways. First, the virus challenge contains which is SHIV-SF162p3 strain contains an R5 tropic HIV-1 envelope similar to most transmitted viruses. The inoculum is more physiologic. It is lower dose than the classical single high dose challenge models. And more importantly, virus inoculations are repeated in the animals; in this study, it was twice weekly so that we can assess protection over several exposure and repeated exposure. Protection was measured by the degree infection is prevented or delayed relative to controls.

So, this is the detail of the applications of gels and challenge. So, twice weekly each time, we apply three milliliters of the gel followed 30 minutes later by a blood kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

collection and then immediately a challenge with the virus. And, as I said, this was done twice weekly for up to 10 weeks. Animals, therefore, that did not show any sign of infection were followed for an additional 10 weeks by diagnostic testing for evidence of infection.

Monitoring of infection was done in real time twice weekly on each of the blood sample that was collected and samples were tested for RNA, PCR followed by proviral DNA, PCR, and antibody testing. So, an animal is considered positive is that shows these diagnostic markers. Animals are considered negative if all these three tests were consistently negative in real time and after 10 weeks of follow-up.

So, here are the results of the study. First, in white, you see the two controls that received no gel, both of them got infected early on. And then, in blue, you see the six animals that received the placebo gel, again, getting infected around the same time. We have one late infection here but one of the six animals remained resistant after 20 challenges. The median to infection in this group is about 3.5 challenges.

In contrast, all animals that received the tenofovir FTC gel remained uninfected after 20 challenges. Of note, here says the median to infection is 3.5 in the controls, so an animal that was remained protected after 20 challenges

would have been protected against a median of around six transmission events.

This is the acute viremia in the controls that are typical with this virus in this model that show similar to what you see in the humans at peak of six to seven logs of RNA that goes down over time.

All the placebo and the control gels showed virus RNA followed by seroconversion and proviral DNA. Detection in the peripheral blood lymphocytes, and contrast, all the protected animals had negative results in these tests.

We also, from that sample, collected 30 minutes after gel application, we measured the plasma levels of FTC tenofovir to get an idea about the systemic drug exposures in these animals and consistent of what you see in human studies, we see where both drugs were detectable and that the majority were at low levels including a median of 67 nanograms for FTC and a median of 23 nanograms per mL for tenofovir.

So, in conclusions, an FTC-tenofovir combination gel conferred complete protection against repeated vaginal exposures in pigtail macaques. The low levels of both FTC and tenofovir in plasma 30 minutes after application suggest rapid drug absorption with relatively higher levels of drug remaining in vaginal tissue. The single gel application before virus exposure in this model is sufficient for high protection. Daily gel application is, therefore, not needed. kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We applogize for any inaccuracies.

This model identified a highly effective strategy and does support further evaluation of FTC-tenofovir gel in human clinical trials.

I would like to finish by acknowledging the tremendous amount of work done by our group, in particular Urvi Parikh, who is the postdoc that led this work and had got a lot of help from Sumida and Mier, Charles who were helping with this brief time diagnostic testing and all the logistics, obviously, a lot of help from gel formulation of Hunguay, the protocols, drug levels as well, and the statistics, and Yerkes Investigators, Frank Novembre School for their help in the animal testing. And, I would like to also thank Jim Rooney and colleagues from Guillard who provided the drugs with the part of material transport agreement with the CDC. Thank you. [Applause]]

KEVIN DE COCK, M.D.: Thank you, Walid. This paper is open for questions. Microphone four.

GUS CAIRNS: A couple of questions -

KEVIN DE COCK, M.D.: Could you say who you are?

GUS CAIRNS: Yes, Gus Cairns, UK. Firstly, how does the systemic levels of FTC and tenofovir compared with what you would see after a normal dose?

WALID HENEINE, M.D.: Well, we measured the 30 minutes, obviously, here only. But from additional data we have, we are looking over a 24 period of time. Those levels are

substantially lower than what you see in oral TDF treatment, at kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

least, 10-fold or more lower. So, the systemic drug exposure from these topical applications would, in fact, lead to very low systemic exposure which I guess probably for less drug toxicity.

GUS CAIRNS: Is not that, therefore, and if it is only 10-fold, would not that be possibly caused resistance if somebody was seroconverting if they have kind of level in their blood?

WALID HENEINE, M.D.: In fact, the low systemic drug exposure would not promote a drug selection. In fact, from all the data we have from treatment, you really need a higher drug levels to sustain drug selection against persistent viruses. So, this would argue actually the opposite way.

GUS CAIRNS: Okay, I have got one more, there is nobody else.

KEVIN DE COCK, M.D: I think, Gus, there is actually at the back, microphone one.

GRAHAM VALDEZ: Hi, my name is Graham Valdez and from here. I just have a quick question. What do you think caused that one monkey to be resistant to 20 challenges?

WALID HENEINE PH.D.: We have these out layers even with our rectal model usually there are at the frequency of 1 and 30 animals or so. This happened to be in the first eight we have tested. We have now additional controls that they are all getting infected again within the median. No clue, we are looking at some resistance factors and innate factors. But it kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

is very interesting and this would be actually some material to look at natural resistance to infection.

GRAHAM VALDEZ: Thanks.

KEVIN DE COCK, M.D: Dr. Kens.

DR. KENS: Thanks for the doctor, I am a mister. The other question was exactly how do you do the inoculation with the SHIV and have you considered developing models which mimic sexual trauma and/or STI infection?

WALID HENEINE PH.D.: The virus is titrated and is put in buffer and is applied in the vaginal cavity with no trauma. So, obviously there are the other issues of whether you can do those efficacies studies in the background of STIs, but at this point, this is the first set of studies where we want to do it in a very clean manner to get a sense of the efficacy of these drugs and these gels.

KEVIN DE COCK, M.D.: Walid, can I ask you, how do you decide how many monkeys to use? I think, these are extremely impressive data and I think actually your group, needs a lot of congratulations for giving such biological plausibility in your various work to the human trials that are going on. But, I mean, if we said when we protected six humans, everybody would say, well, go home. How do you decide how many monkeys to use and do you apply any statistical analysis to any of these observations or?

monkeys because of cost and logistics, you are always going to kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

WALID HENEINE PH.D.: Yes, I mean, obviously with

be limited with the numbers, so you develop a model that simulates as close as possible to human transmission or main conditions of human transmission.

However, we have tried to work around that in this model by doing repeated exposures. So, each animal, the end statistics you will get will be a very strong measure of efficacy of your product because the protected animals in this case would avert six transmission events. So, yes, it is six but it is in fact a large number of transmissions that you have averted with your product if you seek protection.

The small number is inherent limitation of monkey models. Unfortunately, we cannot do 20-end and 20-end because of cost effectiveness but these are proof of principle experiments that come very close to address specific questions about potency of the product, role of two drugs versus one drug under identical conditions. So, you can get useful information that help and control this one.

KEVIN DE COCK, M.D.: If somebody said to you, what is the difference between using a product rectally or orally when it is the same compound, the same drug? What would you say the biological difference is?

WALID HENEINE PH.D.: Yes. There are big differences in the dosage which was the first question and today, after all the formulation it is very different that the tenofovir, that this formulate in the gel. So, the PK studies that now have been done in humans as well as we are doing them in the monkeys kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

which shed light on the differences between oral versus topical with two versions of the same drug and what are the intracellular actually concentrations of these drugs from oral versus topical application. But there are distinct differences.

KEVIN DE COCK, M.D.: I am sorry I took up time. Could we take very quick, final question?

EMILY BASS: Sure. Emily Bass from AVAC, the AIDS Vaccine Advocacy Coalition. So, the ARV-based prophylaxis field has already once reacted to data from animal study showing more efficacy with the combination drug and has switched the drug in human trials, based on this trial, what is your feeling given that there is a single drug topical gel going into efficacy studies, what is your feeling about how to proceed?

WALID HENEINE PH.D.: Yes, I mean this is the first study in the series of investigation we were doing. Right now, we have started a similar study with tenofovir, 1-percent tenofovir only to address the question that you have raised. Do we really need if we are delivering a lot of drug topically, do we really need two or one is enough? So, we hope the second study will address this question.

KEVIN DE COCK, M.D: Okay, thank you very much, Walid. [Applause] And I would like to give the chair to Jose. Thank you.

JAVIER CABRAL, M.D.: [Speaking in a foreign language] kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

SUZANNA ATTIA, M.D.: Good afternoon, ladies and gentlemen. [Speaking in a foreign language]. It is a pleasure to speak here at my first International AIDS Conference. So, can unsafe sex be safe? Today, we will discuss current evidence on HIV-1 transmission rates according to viral load and under the influence of highly active antiretroviral treatment and sexually transmitted infections.

To give you some context, our research is in response to a statement published in January of this year by the Swiss National AIDS Commission. This statement declared that the risk for an HIV positive person to transmit HIV through unprotected sex is less than 1 in 100,000 if that individual has a blood viral load less than 40 copies/mL for at least six months, is fully adherent to antiretroviral therapy with regular follow-up by a physician, and does not have any other sexually transmitted infections. As you may know, this statement created a large amount of controversy nationally and internationally among physicians and community alike. If you are interested, the transcript and video of a satellite session on this statement at this year's conference are available.

Our objectives: We at the Institute of Social and Preventive Medicine of the University of Bern believe that such a statement, indeed, any public health statement with such farreaching consequences demands a thorough and statisticallybased evaluation of current literature. Therefore, our

objectives were to conduct a systematic review of longitudinal kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

studies on HIV transmission in serodiscordant couples and where possible to perform a meta-analysis of HIV transmission rates in those with undetectable viral load without sexually transmitted infections and with and without HAART.

Our systematic review began with the search of literature from 1996 when viral load testing became widely available. We included full-length articles, citations from those articles, and abstracts of HIV discordant couples which documented HIV transmissions and viral loads in the HIV positive partner. We conducted the review according to recommended standards with two reviewers accessing eligibility and extracting data independently.

We are currently collecting additional data from authors. For studies awaiting follow-up times, we have estimated the follow-up time from the published mean or median follow-up time. Where data were available, we used a random effect model to combine results and estimate the HIV transmission rate. This method takes into accounts statistical heterogeneity in results from different studies and study populations.

In the absence of HIV transmissions, we obtained an estimate of the upper 95-percent confidence interval using an approximate method. We defined STIs as syphilis, Chlamydia, gonorrhea, or genital herpes and classified studies as STI status unclear if study authors either did not stratify their data according to the presence or absence of STIs or did not kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

performed diagnostic tests for these infections. Our transmission rates are measured in rate per 100 person-years and not per coital act as that assessment were not extractable.

In addition, we used a limit of detection of 400 not 40 copies/mL of blood viral load as this was the limit reported in most studies. Our systematic literature search yielded 252 publications of which 241 studies were excluded due to duplication, irrelevant topic, or study design, or refusal of additional data from study authors. We were left with 14 potential cohorts comprised of seven published or in-press papers and seven studies published as abstracts.

We are still awaiting some study information and may be forced to exclude additional cohorts in our final analysis due to incomplete information.

This slide summarizes studies which we have included so far. By region, the greatest number of discordant couples and transmissions came from Africa with only 424 from Europe. Only one study noted the inclusion of men having sex with men. All other studies reported heterosexual relationships without conclusive information about the types of sexual acts. Most importantly, nine cohorts reported used of HAART in the HIV positive partner in 428 couples. In addition, eight cohorts reported some information on sexually transmitted infections among a total of 1,056 couples. We are currently awaiting clarification on these numbers.

We were able to conduct a meta-analysis to combine available data in the groups that are presented on this slide. Our systematic review did not identify any studies which fulfilled the Swiss statement criteria, that is, having individuals on HAART with an undetectable viral load and no other sexually transmitted infections. In this group, we did not include one study of 22 couples because the HIV negative partners received pre-exposure prophylaxis. Only one other study contained HIV positive individuals on HAART with undetectable viral load. However, the STI status of these individuals remains unclear.

The transmission rate in this study was 0 per 100 person-years from 283.2 person-years of follow-up. This gives an upper confidence interval of 1.06 transmissions per 100 person-year. All other studies were in HAART naive individuals. Only one transmission occurred within these groups at a level of 362 copies/mL of blood viral load.

Can unsafe sex be safe? In summary, we have not yet identified any studies which directly quantify the transmission risk of HIV positive individuals on HAART with consistently undetectable viral load and no other STIS. However, a body of indirect evidence suggests that transmission of HIV infection at low viral load levels is very rare. We did not identify any studies or case reports in which HIV transmission occurred at a viral load below 40 copies/mL.

Some limitations of our study include a lack of data on types of sexual acts and as a comment on this, a recent modeling study from Australia available on Lancet, July 26 to August 1 edition of this year, suggest that the Swiss statement may not be generalizable to men having sex with men engaging an unprotected anal sex.

In addition, we have a lack of complete data in our studies on protected and unprotected sex within our couples. Other limitations include a minimal detection of viral load assays at 400 copies/mL, as I said before, and an inability to determine the duration of viral suppression.

It is also difficult to know about the importance of STIs to HIV transmission risks in individuals on HAART because of a lack of consistent measurement of STIs significant to HIV transmission especially genital herpes and a lack of numbers on those with STI diagnoses.

It is important to note that this review is ongoing. We hope that incoming data will allow us to increase the precision of our estimates. So, is it possible for an empirical study to estimate a transmission risk of less than 1 and 100,000?

In a very simplistic calculation, if we assume a coital frequency of eight per month, it turns out that in order achieve an upper 95-percent confidence interval of 1 in 100,000, only one transmission can occur in 550,000 coital

acts.

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Amassing this number of coital act with the frequency of eight coital acts per month would require 1,145 couples followed for five years. We are aware of at least one study of heterosexual HIV transmission in serodiscordant couples with HAART use in the HIV positive partner. This study approaches the levels of couples in follow-up time estimated by the calculations I just mentioned and has an expected finished time of 2016.

We hope that it would, therefore, more precisely established transmission risks per coital act for the growing number of couples reaching undetectable viral loads under HAART.

It is now the accepted standard of practice to perform systematic reviews and meta-analysis in the development of statements which are intended to guide clinical decisions or public health recommendations. In addition, authors of such statements must always clarify the source, the quality, and the direct applicability of supporting evidence to the study topic.

We recommend an increase in research on HIV transmission in serodiscordant couples with the HIV positive partner on HAART and a specific investigation of the effects of different types of sexual acts symptomatic as well as asymptomatic and intermittent sexually transmitted infections as well as reproductive infections and the influence of viral load dynamics in blood and genital secretions.

We are very grateful to the study authors who actually were able to give us additional data and to those who hopefully will provide us some after their publications are done and I would personally like to thank my co-authors Matthias Egger and especially Nicola Low who is also here in the audience. Thank you for your attention. Nicola and I will be more than happy to take your questions. [Applause]

JAVIER CABRAL, M.D.: [Speaking in a foreign language]

EDWIN BERNARD: Oh, hello! Edwin Bernard from the UK reporting for Aidsmap.

SUZANNA ATTIA, M.D.: How are you?

EDWIN BERNARD: Hi. I was at the Sunday's Satellite and I remember you actually stood up and talked about how you identified the threshold of transmission being 362 copies/mL and can you tell me where that study was from and what was the next level after 362?

SUZANNA ATTIA, M.D.: Sure. So, yes. So, the lowest detectable transmission was in 362 copies/mL as you said. This is in a study performed by Jesus Castilla in 2005 and he did the study in Spain. And I believe the next - I do not want to give you the wrong number but I believe the next viral load was around 1,479 but I would like to just check my data and give you an accurate number.

DR. KUBOTA, M.D.: Kubota from United States. What do you think the implications of the study is for seroconcordant couples who are persistently perhaps untreated persistently kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

with negative viral loads and potentially even with same resistance backgrounds?

SUZANNA ATTIA, M.D.: Could you please speak louder? I actually did not hear your question.

DR. KUBOTA, M.D.: What are the implications for seroconcordant couples with persistently undetectable viral loads on treatment with, say for instance, the same resistance background with their viruses? Seroconcordant couples.

SUZANNA ATTIA, M.D.: So, your question is what is the implications for seroconcordant couples? Right now, I mean, our study is focusing only serodiscordant couples and I actually cannot tell you the implications for seroconcordant. I do not know if Nicola has anything to add to that [Laughter]. No, not really. Yes, sorry. It is an excellent question, one that should be addressed by our scientific community.

TIM FARLEY, M.D.: Tim Farley from WHO. I much enjoyed your analysis.

SUZANNA ATTIA, M.D.: Thank you.

JIM FARLEY: And I agree. The Swiss National AIDS Commission was probably a bit naughty in not doing the metaanalysis before making their recommendations and you have shown us the sort of data that would need to be there for them to make an evidence-based recommendation. However, the recommendation is out there now and I just like you to speculate what information would you have to say that their

recommendation is wrong?

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SUZANNA ATTIA, M.D.: Okay, so the question is what information do we have to say that the Swiss statement is wrong?

TIM FARLEY, M.D.: No, I mean you do not have information to say the Swiss statement is wrong at the moment but what sort of information -

SUZANNA ATTIA, M.D.: Do we need?

TIM FARLEY, M.D.: — would you need to say that the Swiss information is wrong and how we are ever going to get that?

SUZANNA ATTIA, M.D.: So, to make matters simple, we would need to see transmissions under 40 copies/mL. We also need a more adequate understanding of how STIs affect transmission rate because I do not think you can make a statement saying that if the partner is STI free, you will not have any transmission with undetectable viral load on HAART because we do not fully understand how frequently asymptomatic STIs for instance could happen, what the effect is on viral load and how that could actually cause a transmission over a certain period of time and not just set the point that the low viral load was measured.

TIM FARLEY, M.D.: Yes, okay. I mean so you are just saying that one transmission at less than 40 copies would be enough to say that the Swiss statement was wrong. Would that be enough? SUZANNA ATTIA, M.D.: From a logical point, that would be enough. From a statistical point, I do not think that is an accurate assessment.

TIM FARLEY, M.D.: Yes. The point I am getting here is we would probably never have data that would say that that statement is wrong.

SUZANNA ATTIA, M.D.: I am sorry?

TIM FARLEY, M.D.: We would probably never have data to say that that statement is wrong? Unfortunately.

SUZANNA ATTIA, M.D.: Well, hopefully, we should have a pretty accurate estimate of transmission risk in this group after the Myron Cohen Study which is the one that is finishing in 2016 is done. So, we should be able to get closer to defining, actually, how many transmissions would occur, what the risk is in that population but - please go ahead.

JAVIER CABRAL, M.D.: [Speaking in a foreign language] MARSHALL D'SOUZA, M.D.: Hello. I am Dr. Marshall

D'souza from Fort Myers Florida, United States. Mine is rather a comment rather than a question. I follow a large number of patients and I always tell them to practice safe sex but in real life, what we preach and what goes on is quite different.

SUZANNA ATTIA, M.D.: Yes.

MARSHALL D'SOUZA, M.D.: I have serodiscordant couples wherein the man is negative and the wife or the partner is positive and the wife is doing fine on HAART, CD4 count is high, viral load is low. In spite of telling them repeatedly kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

to practice safe sex, several of them have told me they are not practicing safe sex and the man is doing well. Some of them have come for testing and they are negative and some of them have not come for testing. So, in real life, this thing goes on what you just now discussed -

SUZANNA ATTIA, M.D.: Yes.

MARSHALL D'SOUZA, M.D.: - in a big way. Thank you. SUZANNA ATTIA, M.D.: That is a very important point. Thank you very much.

JAVIER CABRAL, M.D.: [Speaking in a foreign language] SUZANNA ATTIA: Thank you. [Speaking in a foreign language] [Applause]

JAVIER CABRAL, M.D.: Dr. Ayisi?

ROBERT AYISI M.D.: Thank you very much ladies and gentlemen. I feel very much honored and privileged to stand before you and make a presentation on what we have done in Kenya on integrating counseling and testing for HIV into family planning services and I thank this panel for this great honor and privilege.

The background of my feasibility are outlined in background, methodologies that we used, what are the findings, lesson learnt, conclusion, and way forward.

Kenya is a country in Eastern Central Africa. Important demographic data is that it has population of 34 million, conservative population rate of 39-percent. We just plateaud for the last two digits [misspelled?] and total kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

fertility rate of 4.9. Family planning unmet needs of 24, HIV prevalence of 7.4 as per KAIS 2007 and prevalence among women is 9.2-percent. There low VCT coverage and low condom rate usage. 50-percent of the new infections are found within the youth 15 to 24 years of age.

Integration of counseling for HIV and family planning services, particularly in research, the range of services are available for family planning clients many of whom are at risks of STDs including HIV in a high prevalence setting. Systematic evidence about offering family planning VCT has been made extremely limited despite widespread interest in this model of family planning HIV integration.

Why integrate HIV services? The government policies support integration of services within National Health Sector Strategic Plan II, clients seeking family planning and HIV share common needs. Most clients are sexually active and fall within the reproductive age bracket of 15 to 45 years. They are at risk of HIV infection or might be infected and they need access to contraceptives. They need to know how HIV affects contraceptive options like interaction between hormonal contraceptive and HIV regimens.

Prevention of unwanted pregnancies is a key point to VCT strategy that has received various attentions which can be addressed through integration of services.

Our study objective is to develop and implement two methods of integration, one was for Testing model and Referral kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

and evaluate the models in terms of feasibility of implementation, acceptability to both client and providers, effect on the quality of family planning services, effectiveness in increasing uptake, incremental cost that is required on this addition of services and to disseminate and utilize results to create conditions for scale up of integration services provision nationally.

Our methodology: We used pre and post intervention design to obtain information. Thus, measurements were conducted at both baseline and endline. Our participants were family planning clients and their providers.

The sites used were in two in central provinces, Nyeri, which have 9 facilities where there were [inaudible] were done and had low counseling and testing services, and Thika had 14 facilities, the fertility who had high family planning, high counseling and testing availability.

A health facility assessment of the readiness of facility to offer counseling and testing for HIV within family planning service was conducted. Data were collected through provider client observations and exit interviews for the clients. Pre and post intervention, focus group discussion with health providers and the clients were conducted to collect the relevant information.

Two models of integrations were piloted, the Referral model where our clients are educated in family planning, or educating family planning clients who were educated about kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

counseling and testing and referred for testing a post test counseling to other sites within the facility or elsewhere where even to stand alone VCT site. And the Testing model involved in educating family planning clients about counseling and testing and offering them counseling and testing for HIV within their routine visit by family planning providers as well as post testing and counseling. This means that HIV and family planning services are given by one provider in the same clinic at the same time.

The interventions to different place was sensitization of provincial and district teams about integration, process, developing training material and really [inaudible] integration of services, adaptation of balanced counseling strategy from the [inaudible] that are better than to be used for counseling clients on family planning and STDs.

We modified the family planning registers to allow routine collection of information of counseling and testing services. In this way, we added one column to collect counseling and testing information.

MOH supplied basic commodities including test kits and family planning methods. The health workers, who are trained on provision of family planning, balanced counseling strategy and counseling and testing.

Results: Most facilities which are ready to offer HIV/family planning integrated services. At least 70-percent of them have basic supplies, equipment and appropriate kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

infrastructure in place. Integrated approach was acceptable to providers and clients. In some focus group discussion, this is more [inaudible] report. We now encourage our clients to use dual protection and know their HIV status. These are information gotten from a source provider and it is better for myself family planning provider to test me and know my status, the information from a focus group discussion by a client.

Overall quality of family planning services improved. The quality of family planning and counseling improved where provider has discussed at least two or more family planning methods instead of [inaudible] counseling at endline compared to the baseline.

And quality of counseling for STI/HIV issues improved where providers discussed an 80-percent of the counseling at endline compared to 37-percent at baseline. Providers explained that condom protects against STI and HIV as well as pregnancy emphasizing the dual function of the condom and 48percent of the consultation at endline compared to 16 at the baseline.

The information I just show you that on the baseline, the services who are low compared to the endline in both Testing and Referral show you that integration of services is very important and improves the service provision.

This shows effectiveness of uptake of services in comparing the baseline and endline. Integration works in both

but it is better in the testing way of services were offered in the same clinic by the same provider at the same time.

We look at the cost analysis of the testing model and we found that the incremental average cost per family planning client tested for HIV is about US\$2.5 and this includes labor, test kits, gloves and provision. This [inaudible] that was done. Again, in the year 2000, where estimated cost of offering the client services at the stand alone VCT site cost US\$27.

What are the lessons learnt from this? The supportive services delivery guideline and MOH leadership is very important if we have to achieve a lot with integration of services. Advocacy is key at all levels including national level, the provincial level, and the district level. We have to build consensus amongst stakeholders for buy-in and ownership of integration services. Ensuring commodity security is important for continuity of services and sustainability.

After the information to the clients, clients are now demanding testing services due to increased knowledge within the family planning at clinics. There is reduction in stigma because of good rapport that has been established between clients and service providers.

The enabling factors for this success was conducive policy involvements, environment that allowed integration to be compared within services and existence of a technical committee on integration that advice the government on integration of kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

national level and at provincial levels. Availability of suitable trading materials that were used to impart knowledge to the health workers. There were ready available trained service providers and ready infrastructure where family planning services are already been offered, the strong and willing partner support.

Challenges: Human resource shortage, weak logistic management system for commodities and supplies that led to occasional stock-outs, inadequate equipment in some facilities, lack of space in some facilities that compromised confidentiality in the counseling and testing and the clients exerting pressure on need of service.

In conclusion, integration is feasible without compromising coverage or quality of existing family planning services. Provider initiated counseling and testing on HIV/FP integration is acceptable to both clients and providers and access quality and uptake of HIV counseling and testing improved integration of services. Use of balance counterstrategy tools facilitated integration.

Way forward: Intensity national scale up for counseling, testing integration, ensure counseling and family planning services is captured in the national reporting tools and ensure that this approach is factored in the pre-service treatment to produce workers that are able to offer these services. Supplies and commodities need to be sustained.

I acknowledge all of my colleagues that worked together on this work one no missed opportunities, we have integrated family planning with HIV services. Thank you. [Applause]

JAVIER CABRAL, M.D.: [Speaking in a foreign language]

TIM FARLEY, M.D.: Hi! I am Tim Farley from WHO. Thank you very much for that. I think that it is very useful to get information on the practicality of integrating services in this way. There is one whole aspect which is a potential downside that you have not looked at and maybe you have some qualitative information on this, but maybe it needs to be collected as you go further on which is, was there any adverse effect on the quality of the family planning service that was provided?

You have only given us measures of the acceptability of the testing and you have given us measures of the incremental cost of providing and testing. But you also want to make sure as this program is rolled out that you are not having an adverse effect on the quality of the family planning services or maybe in fact driving people away from the planning services. They choose not to come to the clinics where the HIV testing is being routinely offered.

ROBERT AYISI M.D.: Thank you. What I have shown you that the side effects where integration services actually improved the family planning services and we did not note anybody running away from the clinic where counseling and testing was being offered. The referral clients who are given a voucher to report with the next visit are going to be tested kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

and would not report many people who will start to accept the services.

TIM FARLEY, M.D.: Robert, can I ask specifically what reproductive health services were provided?

ROBERT AYISI M.D.: Pardon me?

TIM FARLEY, M.D.: Specifically, what reproductive health services were provided? What do they entail?

ROBERT AYISI M.D.: In this study, we only give - it was family planning service and we are integrating counseling and testing for HIV. That is the only service as an endpoint for integration of services.

JAVIER CABRAL, M.D.: [Speaking in a foreign language] Next.

KELLY KERN: Thanks, Kelly Kern, from Chicago [misspelled?] again. I applaud your efforts to integrate HIV and family planning services. I very much agree with you that family planning has been very much overlooked in the response. I am curious, are their any efforts underway to integrate family planning into HIV clinical care? When I hear about FP-HIV integration, it seems that so often HIV is being integrated into family planning, but family planning is not being integrated into HIV. Thank you.

ROBERT AYISI M.D.: Thank you. We have looked at the model we are actually not clear. We have already integrated family planning within counseling and testing in clinical care. It is already done as the second strategy. And we are into kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

integrating other services with HIVs including TB and the CCC or community care centers and the STIs in community care centers. So, we are looking at the integration of services to offer treatment [misspelled?] or care for HIV/AIDS clients.

DVORA JOSEPH: Dvora Joseph from PSI. Thank you for your presentation. I think it is interesting to see how it is being operationalized in Kenya. My question is about HIV positive women. I think another thing that you missed in your presentation is the reductions of vertical transmission.

One of the key things we are trying to do is try to prevent unwanted pregnancies among HIV positive women so that we can reduce mother-to-child transmission. I am wondering what kind of prevalence you had in your site in terms of HIV positive women and what kind of uptake was continued in terms of family planning methods and if there was a change in that method. Another thing we have seen is also among a change of provider, behaviors of really encouraging condom use rather than family planning or contraceptive use once they find out the woman is HIV positive and I am wondering if you saw any of that also. Thank you.

ROBERT AYISI M.D.: Thank you very much for those concerns. I have said in the [inaudible] in Kenya that HIV prevalence was higher in women in a rather age and they are much we have done on the prevention of mother-to-child transmission. We achieved quite a lot from three and from four but various has been done from one and two. I hear from two kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

where we have to prevent unwanted pregnancies in HIV positive women. So, we think within the clinical services, we can be able to cover this and get it all ourselves. In the case reported that we had just a few weeks ago, it is showing 50percent immediate needs of family planning among HIV positive women. I think integration is going to have to pass to achieve that.

JAVIER CABRAL, M.D.: [Speaking in a foreign language]

FEMALE QUESTIONER: Just a very short question. The women who tested HIV positive in your integration trial, how were they referred and was there a possibility to continue treatment within the family planning clinics? Were you also starting to train providers to keep them in care in that trusted facility that they were accessing already?

ROBERT AYISI M.D.: The positive women in the [inaudible].

FEMALE SPEAKER 1: They were sent to different facilities?

ROBERT AYISI M.D.: Yes. Every facility has some accommodative care center so the effort will be, do I able to a part for care and treatment within the facilities.

JAVIER CARBAL, M.D.: [Speaking in a foreign language] [Applause] [Speaking in a foreign language]

KEVIN DE COCK, M.D: Thank you very much to all the presenters, really excellent presentations and to the audience for staying throughout. Thanks. Have a good evening. kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

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