National Institute of Allergy and Infectious Diseases
National Institutes of Health

Telebriefing: Update on NIAID-Sponsored Adult Male Circumcision Clinical Trials

Moderator: Laurie Doepel
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Operator: Good day and welcome to the National Institute of Allergy and Infectious Diseases Telebriefing on adult male circumcision. Today's call is being recorded.

At this time, I would like to turn the call over to Ms. Laurie Doepel, Chief of the News and Public Information's Branch at the National Institute of Allergy and Infectious Diseases, which is part of the U.S. National Institutes of Health. Please go ahead ma'am.

Laurie Doepel: Good afternoon and welcome to our telebriefing, an update on the adult male circumcision trials in Kenya and Uganda.

I would like now to introduce Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases who will present opening remarks and introduce the speakers on the call.

Dr. Anthony Fauci: Thank you, Laurie. Good afternoon. My name is Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases of the United States National Institutes of Health.

NIAID, which is the National Institute of Allergy and Infectious Diseases is pleased to announce today the results of two randomized control trials of adult male circumcisions to reduce HIV infections that were conducted in Rakai, Uganda and Kisumu, Kenya.

I am joined today either in, physically in the room or by call by members of the investigative teams and they include Drs. Ron Gray and Maria Wawer of the Johns Hopkins Bloomberg School of Public Health and Dr. David Serwadda of the Institute of Public Health of Makerere University Kumpala, Uganda, representing the Ugandan trial.

Also, Drs Bob Bailey of the University of Illinois Chicago, Stephen Moses of the University of Manitoba and Jeckoniah Ndinya-Achola of the University of Nairobi and (Corrette Parker) of RTI International, all representing the Kenyan trials.

Also Dr. Carolyn Williams, chief of the Epidemiology Branch at NIAID's Division of AIDS and Project Officer for these grants. And also joining us on the call today is Dr. Kevin De Cock, Director of the Department of HIV/AIDS the World Health Organization and his colleagues at WHO, Drs. Kim Dickson and Cate Hankins [from UNAIDS].

Yesterday, Tuesday, December 12, 2006, the NIAID Data and Safety Monitoring Board, the DSMB, reviewed the interim data from these two ongoing trials. The results demonstrated that adult male circumcision performed by trained medical providers with adequate supervision is both safe and effective at reducing the risk of HIV infection.

The setting of the Rakai district in Uganda based on study results from 4,996 HIV negative men aged 15 to 49, there was a 48 percent reduction in HIV infections. The trial in Kisumu, Kenya, where 2,784 HIV negative men ages 18 to 24 were enrolled found a 53 percent reduction in HIV transmission.

Based on these data, NIAID has concurred with the recommendation of the DSMB to end both trials early and offer male circumcision to all trial participants. These results indicate that adult male circumcision could be an important addition to an HIV prevention strategy for men.

Male circumcision can lower both an individual's risk of infection and hopefully the rate of HIV spread through the community. However, adult male circumcision is not completely protective and must be seen as a powerful addition to, not a replacement for, other HIV prevention methods.

It is possible that the 48 to 53 percent reduction in HIV transmission could be negated by small decreases in condom use or the addition of more sexual partners. Both studies evaluated adult male circumcision performed in a clinic by trained medical personnel. Men were also seen several times shortly after surgery and had ready access to care if they had any medical difficulties.

It should be noted that even in this setting there were mild, moderate and a very few severe adverse events. In the setting of the trial these events could be managed without additional complications. But this reminds us that those seeking circumcision services should choose only qualified providers who can administer adequate post surgical care should the need arise.

Furthermore, these results only apply to men where the risk of HIV transmission is though the penis. Transmission by injection drug use or receptive anal intercourse will not be affected by adult male circumcision. Additionally, a study funded by the Gate's Foundation of the risk of HIV infection for women whose partners are circumcised is currently ongoing.

The research teams will now evaluate in depth the data collected during the two trials and we anticipate additional information on HIV risk related behaviors and attitudes of enrolled men. Also, the studies will continue to follow men enrolled in the trials to evaluate the long-term effect of male circumcision on HIV transmission as well as on HIV related risk behavior.

It is important to note that the Kenyan and Ugandan trials concerned the early results of the Orange Farm trial in South Africa conducted by Bertran Auvert and colleagues, funded by the (Agent National de Research de la SIDA), known as ANRS, which demonstrated 60 percent reduction in HIV transmission among 18 to 23 year old men who under went circumcision.

In summary, we are pleased to announce that adult circumcision is effective at reducing the risk of HIV transmission by 48 to 653 percent in these studies conducted in Uganda and Kenya. While the HIV Aids research community will continue to strive for a prevention technique that safely protects everyone all the time, we are pleased to find a strategy that has the potential to significantly reduce new HIV infections in Sub-Saharan Africa.

We would like finally to take this opportunity to thank the study members and the institutions that support them, in addition to the investigators participating in today's call, Dr. Godfrey Kigozi, in Uganda and Dr. Kawango Agot in Kenya who were both instrumental in the successful completion of this trial and their leadership and responsible for a high standard of research achieved by these studies is appreciated.

NIAID also would like to acknowledge the contribution of the statistical teams for both studies led by Drs. (Larry Molton, Astrof Calsey) and (Fred Lacumbi) for the Ugandan Trial. The surgical teams were led by Dr. Stephen Watya in Uganda and (John Creega) and (John Ocheya) in the Kenyan trial should also be recognized.

And finally, the NIAD appreciates the contribution of the Canadian Institute for Health Research which supported the University of Manitoba in the collaboration of the Kenyan Trial. We will now be happy to take your questions. If you have a general question, I will answer it and/or refer it to the appropriate participant on the call. If you would like to address your question directly to a specific person, please do so.

Female: The operator please join us to provide instructions for the question and answer period.

Operator: Yes, ma'am. The question and answer session will be conducted electronically. If you would like to ask a question, please do so by pressing the star key followed by the digit one on your touch ton telephone. If you are using a speakerphone, please make sure that your mute function is turned off to allow your signal to reach our equipment. We will proceed in the order that you signal us and we will take as many questions as time permits. Once again, ladies and gentlemen, that is star one on your touch tone phone to ask a question at this time.

We will take our first question from Brenda Wilson with NPR.

Brenda Wilson: Thank you. I just, for this press conference, I just would like to know the practical application of this in the sense of how readily available there are facilities in these countries who can perform the services and I mean, what, I mean do we know which populations, how much it would cost to have it done?

Dr. Anthony Fauci: Well let me take this. This is Dr. Fauci. Let me just take a very quick shot at this and then I will refer it to others to comment. As you probably can imagine, it varies from country to country. In Sub-Saharan Africa, the availability and capability of these types of services, what we are providing today is the scientific basis for the ability of this procedure to be able to be accomplished in a safe and effective way with the results that I just mentioned.

How this is implemented in individual countries will depend very greatly on coordinating and collaborating and running this through the Ministries of Health and the proper authorities in the individual countries.

Having said that, I would like to just now have maybe Kevin De Cock from WHO make a comment in that regard and also we have with us Dr. Jeckoniah Ndinya-Achola of the University of Nairobi who I would like to ask to make a comment after Dr. De Cock makes his comments because he will be representing what will be going on with the Ministry in Nairobi. Kevin?

Dr. Kevin De Cock: Yes, thank you Tony. Let me make some general comments. First the demonstration of a prevention intervention with the potential of reducing new infections by about 50 percent in heterosexual men in Sub-Saharan Africa is obviously very important.

But the point that Dr. Fauci emphasized that this is an additional strategy rather than a replacement is absolutely essential. This must not reduce our emphasis on other preventive interventions, behavioral interventions, regular and consistent use of condoms.

So it is not a magic bullet but it is potentially important intervention. WHO and partners, that is WHO, other UN agencies in the UNAIDS secretariat intend to convene a meeting in the sometime early in the new year to including the investigators and some of their funders and other concerned parties view these findings more broadly and discuss their implications.

Because clearly, these very important research findings now need to be translated into policy and potentially implementation for those countries who wish to take that up. The specific question about availability and the cost, obviously it's the countries most effective in Sub Sahara and Africa are in southern Africa and in eastern Africa and male circumcision happens very considerably across those countries and even within them.

And we do have some (date on) the distribution of circumcision. As far as cost is concerned, it varies tremendously. It could be as low as about $25 but as high as $500 or so.

And again, the very careful words emphasized by Dr. Fauci concerning safety of the procedure, the conditions in which it's performed, the training of practitioners and so on, all of these are important. They're not the only, but they're the very important logistic constraints and there are very important cultural and social issues that also will need to be addressed.

So I think in summary, we're at the very important point of beginning translation of these findings into policy and then potentially into practice. But that's all a process in itself. And a final comment is that I mean, our congratulations from the UN side to the investigators and their funders to emphasize, this is the culmination, not just of some trials, but of work, research work that actually dates back many years because these trials were preceded by observational studies and analytic studies.

And I think this is a very good demonstration of science, very logically conducted, very well conducted in a very careful manner, but in a very logical manner. So I think this is very important, we're now at an important translational point.

Dr. Anthony Fauci: Thank you very much, Kevin. And let me just ask Jeckoniah Ndinya-Achola of the Nairobi and Kenya to make a comment regarding Kenya and Nairobi.

Dr. Jeckoniah Ndinya-Achola: Thank you very much. The issue about the availability of the services is very critical. Indeed, the Kenyan government the Ministry of Health of the Kenyan government is already holding this guidance on how these can be made available.

If we lead a certain amount of improvement of the health facilities that are existing in terms of making those facilities available at the site, but also making sure that we have the personnel who are capable of conducting circumcision on a professional manner.

Dr. Anthony Fauci: Thank you Jack. Next question please.

Operator: We'll take our next question from Lauren Neergaard.

Lauran Neergaard: Hi. Can you tell us a little bit about the adverse events that you alluded to and then discuss a little bit of the biologic rationale why would this have such a great effect?

Dr. Anthony Fauci: OK. The adverse events, as we said, were few and some severe and all manageable by subsequent medical follow up. They, as you know, there were two studies, one was the Ugandan study in which there were five adverse events and in the study that was smaller in the sense of less people in Kenya, there were not any.

So I am going to ask Ron Grey to comment on the adverse event in Kenya and then ask Bob Bailey to make a comment about the – excuse me, Uganda, Ron will talk about Uganda and Bob will mention the Kenya study.

Dr. Ron Gray: Thank you. Dr. Fauci was alluding to five let's call serious adverse events that required treatment. The rate was .2 percent in this population of almost 5,000 – well, there's actually 2,500 men who received the surgery.

These were largely infections some unrelated to the surgeries per se but they were flare-up, for example, of severe herpes or they were damage to the wound caused by external force.

Dr. Bob Bailey: Yes, with regard to Kenya, we said we had 24 total adverse events in 23 different clients over some 1,340 circumcisions. So, the rate was just about 1.5 percent.

And most of them were mild infections and some wound disruptions. Young men who are in our trial are extremely active. They all are – or most of them were casual laborers and they undergo – they do very vigorous activities.

So the number of wound disruptions were really related to their high activities. But the adverse events rates were very low even compared to neonatal circumcisions or they were comparable to neonatal circumcision rates in the United States.

Male: Bob, you just said that we – avoid confusion. When I mentioned the five and the zero, those were what are considered severe adverse events, the events that Bob Bailey from the Kenya study were talking about were adverse events in general.

So just so that there's no confusion when you're talking about severe events in the total of both studies there were five. And those were manageable by subsequent follow up.

And I think that really raises the issue that I try to get to in my opening statements that we have to make sure that when we think in terms of this being a modality that it's done under the conditions of optimum medical capability where that is available. And if not then the relevant countries need to address the issue before any programs get involved in making this a policy.

Dr. Anthony Fauci: I'm sorry. Lauran, you asked about the biological? Yes. There are several issues with regard to the biology of why circumcision would be effective in preventing infection in the circumcised person.

And I'll try to be as simple as possible. First of all the mucosal surface of the foreskin of the penis is rich in a group of cells that are particularly susceptible to being targeted by HIV. And those are dendritic Langerhan-type cells which bind very readily the virus itself and then bring it to the appropriate vulnerable targets.

Also, since it's more of a mucosal surface than the, what we call, keratinized skin, and by keratinized we mean that the rougher layer of the dermis of the skin, the epidermis of the skin, is a protector, a physical barrier for anything including HIV.

When you have mucosal surface, which is what the inner component of the prep use of the penis that's removed in circumcision. When you get rid of that A, you remove some of the targets and you get rid of a surface that is much more likely to have micro tears in the area as well as the fact that when you have the foreskin over the gland penis that provides a moist area that might actually be able to trap physically the virus close to what would be a mucosal surface.

And in addition there are some secondary issues that the uncircumcised penis is more likely to get inflamed for example with (genitory), alter the diseases, what we call balanitis which is an inflammation of that area. They are more common in circumcised individuals.

So in summary it's both an area where cells are more susceptible but also it's a more fragile mucosal service as to both to a more protective skin like service.

Female: Thank you.

Operator: And we'll take our next question from Christy Feig with CNN.

Christy Feig: Two questions. Number one, has anyone calculated how many infections might be prevented if most men got circumcised? And my second question deals with the education hurdles that we've been talking about. You know we're talking about this needs to be done in a sterile environment, we're talking male circumcision here and not female circumcision and you know just because you get circumcised doesn't mean you won't get infected. It is not virtual – kind of things that really need an education program to go with it.

And I'm wondering who's in charge of getting those messages out there and is there an education plan already under way? I guess my concern is if you toss this information out there without a strong education plan you might do more harm then good.

Dr. Anthony Fauci: Those are very good questions. Let's see. Well let me talk first about the how many.

Certainly there will be mathematical modeling that has been going on and that will go on. When you have data that you can put into the assumptive components of the mathematical model you can come out with numbers.

In the study from South Africa that they actually modeled some of that and we're talking about over a period of perhaps a decade that – and again I hesitate to even give these numbers because then it gets translated in that this is exactly the number of infections but it could be actually measured in a considerable number of infections.

You know if you look at for example the South Africa population the model that was used so that you could possible avert, you know, up to two million infections. But again having said that, I'd like to please caution the press on this call that we've got to be very careful when you talk about mathematical models. OK.

Plus mathematical models will be helpful and they will occur based on the data that we're collecting; so from this study and in the orange form study in South Africa and any other information that we have.

With regard to education I think this is extremely important because as I mentioned in the opening statement that is very clear that this is not a substitute for but in addition to. So we

anticipate certainly that the prevention messages that come from us, that come from the CBC, that come from USAID, that come from WHO – and I'll ask Kevin in a moment to make a comment about that. We'll have to have the big caveat that A, we've got to make sure that the message of the effectiveness of this goes right in parallel with the message that this does not mean that you have an absolute protection.

So let me just stop there for a bit and then maybe Kevin would you please comment from your standpoint about that?

Dr. Kevin De Cock: Yes. Thank you, Tony. As far as the mathematical modeling is concerned WHO and UNA have done some collaborative work on this. So I'll turn that over to Cate Hankins first of all.

Dr. Cate Hankins: Yes, hi. I would just say that, as Tony has said, it's what you put into a model that makes the difference. And these new results are going to be very useful to us. We can then introduce them into models and look at what would be a reasonable scale-up in coverage if that's the recommendation.

Again, models are going to be very sensitive to what actually happens with people's behavior and if there are reductions in current HIV prevention behaviors, we will have difficulty. Some people have called this risk compensation where people believe they may be more protected and therefore drop the use of condoms or stop negotiating condom use. And this is something we're going to put a lot of emphasis on.

Dr. Kevin De Cock: So, let me ask Kim Dickson to comment specifically on the prevention implications and the – some of the discussions we've had about this subject.

Dr. Kim Dickson: OK, I just wanted to comment on what WHO is planning to do in terms of communication. Once we've had a meeting to look at the policy and program guidance in providing technical support to countries we all provide specific support to countries around communications. We will be looking at global communication strategy, we'll be looking at what kind of communication we can provide at regional levels, but specifically to countries helping them to shape messages at national and at community level and specifically emphasizing that this particular intervention is not 100 percent effective and therefore all the other prevention strategies that have been mentioned by my colleagues no this call need to be promoted and encouraged with – along with male circumcision.

Dr. Kevin De Cock: Let me – this is Kevin De Cock. Let me just add two final comments on that. Firstly, obviously this intervention, if decisions are made to scale this up by different countries, it does have the potential to prevent many tens, many hundreds of – many tens of thousands, many hundreds of thousands and perhaps even millions of infections over coming years with the caveats we've already said. The impacts of that in terms of disease – reductions in disease and death will obviously take a long time because of the natural history of HIV infection.

Secondly, these concerns about having to emphasize and maintain other prevention behaviors are, of course, not specific to this discussion of circumcision. They will also apply if, for example, we were to develop – to get an effective microbicide or a partially effective microbicide and also a vaccine, because no intervention is likely at least initially to be 100 percent efficacious. So, we will see these discussions about having to maintain other preventive behaviors with any emerging technology for prevention.

Dr. Anthony Fauci: Thank you, Kevin. I just very, very briefly – this is Tony Fauci again. To just emphasize that we take very seriously the possibility of the – of deleterious behavioral changes on the basis of this, within the study framework itself over a two-year period, there did not appear to be any change in the sexual behavior that would put them at extra risk. However, now that the

announcement is out, we are clearly cognizant of the fact that there is a possibility that there could be, so we're watching this very closely.

And as part of the follow-up in these studies we will be looking very carefully at the possibility of there being any behavioral changes. And in the prevention components, obviously from the CDC in the United States, from USAID, and from the Global AIDS Coordinator's Office, they are very cognizant of this and will be integrating these kinds of education campaigns into their prevention methods.

Christy Feig: Thank you.

Operator: We'll take our next question from Helen Branswell with the Canadian Press.

Helen Branswell: Thanks very much for taking my questions. If I could ask two, please. We've seen sort of global numbers in terms of reduction in the – in the number of people who are in the study. Can anybody tell us how many circumcised men actually became HIV infected in the course of the study? That's my first question.

My second question relates to cultural barriers to circumcision. Dr. Fauci, at the beginning, I think you said that patterns – or maybe it was Dr. De Cock, but patterns of circumcision vary quite widely including even within countries, and I'm just wondering the only barrier to circumcision isn't going to be the availability of circumcision. It may also be cultural barriers – resistance on the part of men. And I'd like some answers about that, please.

Dr. Anthony Fauci: Thank you, Helen. Let me just very quickly give you the numbers, and then we'll have the individual principal investigators mentioned in the other question.

You know, in the Uganda study, as I mentioned in the – in the opening statement, there were 400 – 4,996 individuals, and there was a total of 65 infections. Twenty-two were in the circumcised group and 43 were in the uncircumcised group.

In the Kenyan study, there was an enrollment of 2,784 individuals. There were 69 total HIV infections, 22 among the circumcised group and 47 among the uncircumcised group.

With regard to the cultural barriers and others that were brought up, we're going to ask first from the Uganda study I'll ask Ron, and then Bob Bailey from the Kenyan study to comment on that or any other issue that you'd like to bring up – Ron.

Dr. Ron Gray: Thank you. We did a lot of preliminary acceptability studies, and because the trial in Kenya was meant for the population, we know that 55 percent – sorry, in Uganda – my apologies. Uganda trial was (nestled within) the population, we know that 55 percent of eligible men in that population enrolled in the trial and 80 percent of the control are men who became eligible for circumcision after two years of follow-up agreed to have the procedure.

So, it does seem to be highly accessible. And our social science studies do not suggest that there are major cultural impediments in this ((inaudible)). Thanks you.

Dr. Bob Bailey: Bill, this is Bob Bailey. With regard to the Kenya trials, the trial took place in western Kenya where the predominate ethnic group, the Luo, do not practice traditionally circumcision. And so in the town of Kisumu where the trial took place, approximately ten percent of people are circumcised.

So it is not part of their tradition, but they are surrounded by Kenyans who all do circumcise. So 80 percent of people in Kenya do circumcise. The cultural barriers were really with respect to Luo

themselves don't see circumcision. It is not part of their tradition and yet they don't see it as a part, an important part of their identify.

So they are open to circumcision. They are not opposed to it. And generally across East and Southern Africa, there have been 13 studies of acceptability of circumcision in nine different countries. And they have shown that between 30 percent and 80 percent of men who are living in non-traditionally circumcised communities have a very high level of acceptability, and that they are actually, they want the services available to them.

So – and the biggest barriers aside from tradition are really cost is the biggest barrier. When we talk to men, they won't do the procedure unless it is really at minimal or no cost.

Female: Thank you.

Dr. Bob Bailey: I would like Dr. Ndinya-Achola perhaps to make a comment as well.

Dr. Ndinya-Achola: Yes, I quite agree with the comments that Bob has made. And indeed as a member of the Luo community myself, I have no problems with the circumcision issue. The only problem there is that we actually are not traditionally circumcised. We are surrounded by most of the other ethnic groups who traditionally circumcise. But I don't see that as a barrier.

Dr. Kevin De Cock: This is Kevin De Cock. Could I add two comments? I certainly support everything the colleagues on the call have said. One is that I think we do have to be cautious about not extrapolating from one country to another or from one cultural group or region to another.

So there is from that perspective, there is a need for, there will be a need for ongoing work on this. simply from the point of view of insuring adequate gathering of opinion and so on, in addition to the extensive work that has already been done, the good work that has been mentioned.

And secondly there are strong feelings about this subject in different quarters. And from our perspective what is probably most important is to get the opinion and the involvement of the communities that are being discussed and there needs to be country ownership.

But we do need to be aware there is quite strong opinions in different parts of the world, actually, some outside of Africa about this. And I mean these will need to be listened to. But I can't overemphasize the importance of country ownership.

Dr. Anthony Fauci: Right and this is Anthony Fauci again. And again to reemphasize a point I made before, these studies are providing the scientific basis for countries and regions and whatever to make their policy. We are providing the science. The policy needs to be country sensitive and appropriate and acceptable to the countries involved.

Operator: And we will take our next question from Tina Rosenberg with the New York Times.

Tina Rosenberg: Thank you for taking my question. Dr. Fauci alluded to this but I wanted to ask the investigators if they could talk a little bit more if any ((inaudible)) you found among participants in the study.

Do we know anything about whether they took riskier behaviors than they otherwise would? And also do we know anything about whether they, in fact, complied with the suggestion that they not have sex for the appropriate number of weeks after the circumcision?

Male: Thank you. ((inaudible)), very first from Uganda and then Bob Bailey from Kenya.

Male: The data we have preliminary, but there is no evidence that we see that men who receive circumcision increase their risk behaviors. When we look at these risk behavior over time, in fact, many of them tend to be more common in the control group who didn't receive circumcision.

We did ask men to abstain from intercourse until we certified that the wound had been completely healed and approximately 90 percent of men said that they had abstained for that length of time. So we are getting highly responsible behavior.

Dr. Maria Wawer: Excuse me. This is Maria Wawer. Of the approximately ten percent of men who indicated that they had started to have sexual intercourse before they were certified as having had wound healing, the vast majority did so within a mere number of days before certification.

So in all likelihood their surgical scars were also healed. We didn't have men who started shortly after surgery or a long time before certification. So overall, men really did comply well.

Male: And the other point is that they substantially used condoms during this period.

Dr. Bob Bailey: Yes, I am reticent to really talk about our results at this point. You know we have really only done a preliminary analysis and I think it is safer to say that the results will be becoming available after we have a chance to really analyze the data further. I would say that we did certainly counsel men vigorously not to have sex in the first 30 months after surgery – 30 days sorry. I don't think they would have accepted 30 months.

And most men, the great majority did comply with that. But we don't have the data right now. You know, I don't want to quote you data. But, essentially we put a big emphasis on this and it was a very important part of our whole counseling procedure.

Male: And again to reiterate the point that I made before, there will be considerable follow-up to track and monitor the points that Bob and Ron made.

Tina Rosenberg: Could I ask a follow-up please?

Male: Sure.

Tina Rosenberg: Of the – in the Uganda study, it is interesting that there might have been more risky behavior in the control groups. Was there any difference in how they were counseled, obviously, except for wound care and things related to the circumcision? But was there any difference in the way they were counseled about condom use and partner reduction?

Male: No. Men in both groups received identical health education which was reinforced at each follow-up visit. So, there's no way that they would have been differentially educated about risk.

I don't know ((inaudible)). Maybe our colleague Dr. Serwadda wants to respond to this.

Dr. Maria Wawer: Well, we're getting David – again this is Maria Wawer, when Ron referred to some differential behavior, he was really talking about extremely small, a percentage point here or there, he was not talking about any major differential behavior between the two groups. Overall, specifically there were not ((inaudible)).

Dr. Kevin De Cock: Well actually, that is correct, things little. As Dr. Fauci said earlier, there were no substantial differentials in behavior that are likely to effect HIV risk. Because of large numbers, there were some behavioral differences that were significant, but they are, as Maria Wawer was saying, trivial in terms of HIV risk.

Male: Is David Serwadda on the phone? David…

Dr. David Serwadda: I am on the line. I am on the line.

Male: Will you comment on the question that was just asked please?

Dr. David Serwadda: Yes. Tony I don't think I have anything more to add on what my colleagues have. The data we have doesn't show any substantial differences in behavior as we have alluded to.

But as you did point out, we need to follow this a little bit more closely over time so that we could further understand whether this might come later on in the course of follow-up. So that is something we have got to look at very carefully in time.

Male: Thank you David. And for those – that was David Serwadda, of the Institute of Public Health in Makerere University in (Kampala) who just made that comment, go ahead.

Male: Right.

Operator: We'll take our next question from Craig Timberg with the Washington Post.

Craig Timberg: Hi. Thanks for taking my question. In the high risk – higher risk incidents countries in southern and eastern Africa. There's not a lot of medical circumcision that goes on, it's mostly ritual circumcision.

So now we have three studies that show that medical circumcision makes a tremendous difference in the rate of infection. So is it incumbent now on the international community to put major resources, financial and technical into helping these countries improve and expand their offerings of circumcision. Is that something that's now kind of a moral necessity?

Dr. Anthony Fauci: I will in a second. This is Tony Fauci. I will in a second ask Kevin and his colleagues to address that. But from the United States standpoint, certainly the office of global AIDS coordinator is seriously right now looking at these data.

And as you know, there's an important component of the entire PEPFAR effort that is prevention. And the issue of circumcision being one of many of potential modalities of prevention will certainly be seriously looked at in to being integrated into their program.

They obviously, I can't speak for any final decisions with them, but they are very interested in these data and the possibility of integrating that into the program. Kevin)?

Dr. Kevin De Cock: Yes. Thank you. Obviously the demonstration now in a total of three trials with all that other data previously available from observational and analytic research that we have a halving or we can potentially have an approximate halving of risk for HIV infection in men in Africa raises very important questions.

And as I said earlier, we're at the point of translating this into policy and then practice. I – the first thing that needs to be done – I mean, this is how global health decisions get made, the first thing that needs to be done is there needs to be a gathering as soon as possible. And I hope this will happen, you know, earliest in the new year.

There needs to be a gathering of, you know, concerned parties which should include the investigators, some of their funders, groups, countries that are potentially relevant to this, the international agencies, the development community, et cetera, et cetera.

PEPFAR and representatives from the Global Fund to review all of this and discuss it, you know, in greater detail we can do on this call and with great availability of data than is available right now. This is not to, you know, suspect the data that we have at all. It is not to do that.

It is just to look, try and discuss it more broadly and discuss potential advantages and disadvantages.

I mean, I think, I don't want to preempt the discussions but once only intervention that confers 50 percent efficacy is obviously a very important development. And I am sure that this is likely – countries are likely to say, well we need to invest in this.

The question then arises, what are the benefits and what are the risks? And those are already alluded to by Dr. Fauci and others. You need a certain kind of health system. You need human resources. It has to be done safely and in hygienic conditions. It has to be accompanied by other prevention messages.

There are cultural issues, et cetera, et cetera, much of which has been already discussed. Just to emphasize, this is not just a sort of pull the switch and let's go. It is more complicated than that. But is it, I mean are we likely to see circumcisions scale up? I think that is almost inevitable to varying degrees in different countries, owned and directed by those countries.

Will this require external assistance? Absolutely. What is the role of – what is the role of WHO and UNAIDS and their partner organization in all this and how do they link to groups such as PEPFAR, the office of the global AIDS coordinator? I think this is exactly the kind of role that WHO as the, you know, as the leading health agency, the agency that should lead health policy in the world.

This is exactly where we need these sorts of partnerships because for the United States technical assistance and aid to channel resources into this will be much more effective if there is global consensus, if this is the right thing to be doing.

So, this is, you know, I think this is exactly the way that scientific and public health policy should be developed in partnerships leading to program implementation.

We all have to do this together and we all play a different role. But this is an important, you know, this is an important culmination of a long process and, you know, we are at the process – at the time now of translating and moving forward.

Male: I couldn't agree more with Kevin and very clearly it is obvious that we in the United States federal government are very enthusiastic about working with WHO in executing what Kevin said about having country, specific countries sensitive and involved and getting buy in from outside groups that could help in this process.

Operator: We will take our next question from Sabin Russell with the San Francisco Chronicle.

Sabin Russell: Ah, yes. Thank you for taking my question. I was wondering if we could talk a little bit about, you know, putting this 50 percent achievement in perspective. It is lower than the Orange Study and lower than some of the 76 percent effective rates that some subgroups in that study seem to have had.

So I wonder if it's at some level this isn't a little disappointing from what people might have been looking for. And also that this study was stopped – how long was it to have gone on? And if it had gone on, wouldn't it be reasonable to assume that those numbers would go down? And was there some sort of threshold of failure or success below 50 percent at which point people wouldn't be quite so happy?

Dr. Anthony Fauci: Sabin, this is Tony Fauci. Let me just respectfully disagree with you about significant difference between these two studies and the South African Orange Palm study.

There really is no statistical difference between about a 50 percent and about a 60 percent decrease. So there really – I can tell you there was no looks or feeling or body language of disappointment when the data and safety monitoring board called the study.

The reason for calling the study is as you know, the data and safety monitoring boards of virtually any study monitor fundamentally the safety of a study and to determine not only is it too unsafe to go on, but are the results so good that it would be unethical to continue it as a study without making available to the other components on the other arm, mainly the people who are not getting circumcised, and that's where the data and safety monitoring board came down.

So this was pretty much of an unequivocal type of a decision based on the data ((inaudible)). So this is not iffy data, this is serious data.

Sabin Russell: And, if I could just have a follow-up. There were 15-year-olds in the study who received circumcision and condom counseling. Condom counseling is obviously important. Is there any data to indicate how much actual condom use went on among the participants so that we're not confusing the effectiveness of condoms with circumcision?

And would that policy square with U.S. policy regarding condom promotion among younger people?

Male: I'll have Ron, who was the PI in the Ugandan study. But I can tell you right off the bat that of – there are no policy decisions that have been made about that, nor will there be any statements about that now because we need to get policy makers to first analyze the data and see how it appropriately fits in.

But with regard to your specific question about 15-year-olds and that was in the Uganda study, I'll ask Ron to answer that.

Dr. Ron Gray: Firstly, all minors had parental consent and then the young men themselves provides ascent for participation. I don't have the data on condom use by age during the follow up because that was not available to the investigators, we were blinded to it.

All I can say is that at the beginning of the study at enrollment, condom use was modest in that age group.

Dr. Kevin De Cock: This is Kevin De Cock, can I just make a technical comment. I'm – I think one thing that's impressive about this whole field of work is how consistent all the results actually are because the, you know, the approximate level of efficacy from these clinical trials is actually very similar to what are the estimates of efficacy from the observational and analytic data of which there have been, you know, dozens of studies. So it's actually all rather consistent.

Normally, when we have a clinical trial result, we sort of say well in the real world it is never quite as god as that observational data from the real world and actually gave that level of efficacy. So it will be interesting in the future if programs do scale up, it will be very interesting and important to see how that efficacy actually does hold up.

Operator: We will take our next question from Stephen Smith with the Boston Globe.

Stephen Smith: Good afternoon and thanks for taking my question – actually couple of questions. First, are there any countries in the Sub Saharan Africa at the moment where the health ministries have adopted circumcision as a preventive strategy o do you know of countries where this sort of consideration is being seriously weighed?

And secondly, and this is something that Dr. Fauci alluded to, what are potentially the implication of these findings for the epidemic in either South Asia or in the developed world?

Male: Well first of all, with regard to countries that are making a policy in their public health for circumcision, I believe Botswana does but it is not necessarily for HIV prevention. I will have to ask first (Jeckoniah Ndinya-Achola) whether he has any information about the broad African policy and then Kevin, perhaps, you have an answer to that. And then I will get back to your other question Steve in a second.

Dr. Jeckoniah Ndinya-Achola: Thank you. So far there is no African country that can say have adopted this as a policy. But there are five African countries who are already considering putting this in place as a policy. There was a consultative meeting which took place in Nairobi not long time ago, convened by UNAIDS ((inaudible)).

And these countries include Kenya, ((inaudible)), Botswana, Swaziland and Zambia. But, this is part of the process of making sure that we can have policies on medical conditions. But I think it is a process in the right direction.

Stephen Smith: I am sorry, could you please recount, the line was breaking up, the five countries.

Dr. Kevin De Cock: ...this is Kevin. Can I just jump in? Kevin De Cock from WHO. I think no country has adopted a firm policy and please take Botswana off the list because that is what we said earlier about Botswana is not correct. Kim Dickson will tell us about five countries where there have been consultations and discussions and very helpful discussions but not firm policy setting. Those five, (Kim), over to you.

Dr. Kim Dickson: ... health country consultations in Kenya, Lesotho, Zambia, Swaziland and Tanzania. Now these consultations included a wide range of stakeholders. It included government. It included civil society. They included traditional. And of course in the different countries, we had these groups involved to different extents. But all the countries had these key players.

And the countries discussed what it would mean to them if this intervention was proven to be effective.

There is interest in these countries if male circumcision is proven to be effective, there's interest in looking at how it would be scaled up.

There was also regional consultations that included additional countries such as Malawi…

Female: Mozambique.

Dr. Kim Dickson: Mozambique.

Female: Zimbabwe and South Africa.

Dr. Kim Dickson: Zimbabwe and South Africa. And so there are discussions and a way around this issue.

What all these countries are saying is that if we need to scale up, we will require technical support to do this. And in these consultations, we outlined what some of the technical support needs were.

Some of the technical support needs were for example, conducting situational analysis to look at the current practices, to look at the service availability.

They also require technical support for training and also for certification and follow up. So these are issues that we will be considering later.

Dr. Cate Hankins: This is Cate Hankins from UNAIDS. Two countries you might want to follow up with that are taking this forward are countries like Swaziland that's holding circumcision Sundays in which they are advertising the service and seeing what kind of demand is created using hospital facilities that already exist and trained practitioners. And Zambia where UNA, WHO and (JPIVO) have been working with the Zambians on development of a surgical manual for male circumcision under local anesthesia.

I just wanted to say that we've also developed guidance for the regulator, the human rights ethical legal considerations that countries will have to address in either introducing this service or expanding it ranging from issues to do with consent to what level of healthcare provider would be able to provide the service.

Dr. Kevin De Cock: Can we please get it right? Please, there is no country that has a definitive policy and WHO, UNAIDS and partner agencies have not issued any policy. And we were waiting for the results of these trials to initiate these necessary meetings.

In the meantime, of course, because of all the interest in the subject, it hasn't been a complete vacuum and these sort of proprietary holding type discussions led by countries themselves have been held.

Dr. Anthony Fauci: Thank you for clarifying that Kevin, make sure we get the people to know that there are not policies that have been established.

Kevin could you answer the second part of Steve Smith's question regarding what implications this might have in China and Asia. Is there any information on that that you would be willing to share or that you know of?

Dr. Kevin De Cock: No, not really, no. I mean, I do emphasize in your opening comments, Tony, the – this work has been conducted in Sub Saharan Africa and it applies to heterosexually acquired HIV infection amongst men.

Now, this work may have relevance in some areas outside of Sub Saharan Africa, but in the rest of the world, as I think everybody knows, generalized epidemics – that is epidemics that are self sustaining in heterosexual general populations, are very rare and very limited in scope.

But the potential relevance of this to concentrated epidemics, for example in the clients of sex workers in some other countries elsewhere, for example India, I think those discussions need to be had and a starting point actually would be, you know a sober discussion as the kind of research information and data one would need from those sorts of settings. I also would emphasize that the, you know, the relevance of this issue amongst men who have sex with men also is a completely separate discussion, but probably one that will need to be considered.

Dr. Anthony Fauci: Steve Moses is in India right now taking this call. Steve, are you on the line?

Dr. Stephen Moses: Yes, yes I am.

Dr. Anthony Fauci: You have anything to add to that?

Dr. Stephen Moses: Yes, I didn't catch the last portion. The line was breaking up.

Dr. Anthony Fauci: I am sorry. It was probably not worth it. It was just a question about China and Asia. And Kevin made the relevant point that this was a study conducted in Sub Saharan Africa that applied to Sub Saharan Africa to the degree to which you apply to other countries would need to be examined on a country to country basis.

Dr. Stephen Moses: Yes. I think it is really important to understand what the tradition dynamics are in those settings and whether male circumcision is really necessary to bring epidemics under control in countries like China and India. These epidemics are also very heterogeneous and vary tremendously from area to area within those countries. So it would be difficult to develop a policy at country level.

Dr. Anthony Fauci: Sure, right. Thank you, appreciate it.

Operator: And our next question comes from Mark Schoofs with the Wall Street Journal.

Mark Schoofs: Yes, thank you for taking my question. I guess I am a little bit surprised that no country has adopted a policy on this and that there is not even policy guidelines that have been issued, because this is not new data. I mean it has been more than a year ago since a randomized controlled study, as you mentioned the Orange Farm study came out with this data. And before that there was a really quite large amount of data from observational retrospective studies that showed that circumcision was likely to work.

And given the number of new infections that are going on every single year, it is really quite startling that there are no guidelines. Would you please justify that?

Dr. Anthony Fauci: Kevin, you want to take that because you had answered that original question?

Dr. Kevin De Cock: Yes, sure. I think the question really goes to, you know, the discussion about evidence. What evidence do you need to make a particular decision and to roll that out into public health practice?

Now, I think it very, a very clear and important discussions were held about this. And it was decided that firstly, you know, we have 15 years or more of observational analytic data that were persuasive.

But the decision was made that these results could not exclude the possibility of confounding bias and therefore a clinical trial was necessary. Do you set global policy on the results of one clinical trial? That is generally not – many people are uncomfortable to do that. And there was discussions about this.

But since there were two other trials ongoing, it was felt well actually we should wait. And I think that decisions was defensible because if I think back to the discussions about the role of sexually transmitted infection control in HIV prevention a decade ago or slightly more, ten to 15 years ago, you know, we probably got into trouble globally making major policy recommendations and funding decisions, which today we probably, you know, don't do in the same way any more. So, I think it was the right thing to do.

Mark Schoofs: Would you also weight if there was a vaccine study that showed a 50 percent reduction – would you wait for two other vaccine studies before you started implementing a vaccine?

Dr. Kevin De Cock: I – you know, let me finish the answer. I also think that, you know, getting global guidance on something that says, you know, we're having this discussion about male circumcision, but we, you know, it sounds easy, but, you know, this is not as quite a straight – this is not just like sort of, you know, taking a pill. I mean it's more difficult than that then the reality of African health systems.

This also has huge cultural implications, which perhaps we haven't made enough emphasis on in some countries. So for this to be – for this to go forward, there has to be much more involvement of countries themselves, they have to own it if this is going to happen with outside support.

It's not just a question of, oh, you know, the office of the global AIDS coordinator can just say well we can do this, it's not as simple as that.

Mark Schoofs: Fair enough. Well then actually, why don't we move them to the couple of ((inaudible)) I think David Serwadda, Dr. Achola, what is the outlook for your countries particular David, during Uganda – and Dr. Achola I believe you're in Kenya.

What is the outlook for your governments to actually push for this to be done on a large scale?

Dr. Anthony Fauci: Why don't you take that first. And then we'll ask Jack to answer for Kenya.

Dr. David Serwadda: OK Tony. Mark, I think Uganda has been looking very keenly to the outcome of this research. And I think the ((inaudible)) is going to be as strong demand I think given what we have seen from our trial when we are conducing this trial in an area that does not traditionally circumcise.

We are encouraging the acceptance of circumcision by the general population at least in this part of the area, which we are watching is going to be very, very high and therefore there is going to be a big demand for circumcision, at least in our country.

And I think the minister of health will have to come up with a challenge of providing safe circumcision facilities to be able to cope up with this demand otherwise if you really don't do this, then tendencies are for opportunistic health practitioners to come in and be able to provide unsafe for circumcision that you could not guarantee about it safety.

So the government really will have to come up with some form of plan on how to be able to scale up this very successfully. And I think the minister of health is very – ((inaudible)) of this fact and that they will have the efforts to get the resources and the plan to be able to come out.

But as Kevin did point out, this is not a very easy – it's not like giving an injection. This is a surgical procedure and it will require some very careful planning as to who, where and when and, you know, is circumcised.

So I think the process of getting up has to be looked at very carefully, but I think this is something that is yet going to be provided as one form of services for HIV prevention for our country. I just don't see any way out.

Male: Thank you and Dr. Achola?

Dr. Jeckoniah Ndinya-Achola: Thank you. Like Uganda, the Kenya government was also waiting for these results to come out. They are out now. And as we were waiting the Ministry of Health had already initiated discussions on what would be done in case we needed to roll out ((inaudible)).

These discussions are still at fairly early stage but already the Minister of Health has formed a task force looking into what it is going to take to roll out male circumcision. And as I say it in my earlier remarks, we are going to require a lot of – the government will require a lot of support in terms of strengthening the health facilities to be able to conduct male circumcision safely and that also goes with explaining ((inaudible)).

Mark Schooff: Thank you very much. I appreciate the answer.

Make: OK.

Operator: And we will take our next question from Geoffrey Carr with The Economist.

Geoffrey Carr: That's all right. My question has been answered thank you.

Operator: We will go next to Maureen Taylor with CBC.

Maureen Taylor: Thank you very much. I realize that this is difficult but I wonder if somebody is willing to put aside the research hat for a moment and just be sort of a family friend who is a doctor and what would your advice be to somebody expecting a baby boy about circumcision in light of this? And I am referring here to developed countries like Canada and the U.S.

Dr. Cate Hankins: This is Cate Hankins. I can comment based on the work that we have done in the legal, ethical human right's review. And I think as is currently the case in Canada, parents are basically provided with the facts and make a decision one way or the other.

In the context of Africa, we are basically advising countries to consider situations where parents are provided with the facts and weight the advantages and disadvantages. The point of view of HIV prevention since this is something that will not go into effect for the boy child until he becomes sexually active, they may decide to wait until he can assent to the procedure or they may decide to proceed and in the best interests of the male child to have him circumcised. But it remains the parent's decision.

Maureen Taylor: Thank you.

Operator: And we have a follow up question from Brenda Wilson with NPR.

Brenda Wilson: Thank you. I am just curious because in Southern Africa there have been recent reports and every year there are reports on deaths from ritualistic circumcisions. And if there is a

danger or a risk that these practices, it will be hard to control them in light of these sort of reports and have the studies in Southern Africa have effect on that. I mean there were reports as early as this year on a number of deaths there among young men who were given ritualistic circumcision.

Dr. Anthony Fauci: Brenda, that is an excellent question. And in some respects that really abuts a bit on the question that Mark Schoofs from the Wall Street Journal asked about, you know, the difference between vaccination and circumcision. And that yes, indeed, there is a risk of surgical infectious disease type of a complication or even just a pure surgical complication. It is actually for that reason that these two trials were done in groups of varying risk.

So, it is clear that under the conditions of this study this is a safe and effective procedure. But it is very important, as we heard multiple times on this call, for the individual countries when they make a decision as to what their policy would be to make sure that is accompanied by either the capability within themselves or from the outside to make sure that the appropriate medical expertise and surgical capabilities are available before you undertake this. Because the risk of this was clearly one of the reasons why we wanted to do the study and show how when you provide the appropriate medical and surgical capabilities, that in fact it is a safe and effective procedure.

Brenda Wilson: And one follow up question. Another one, I'm sorry. And that is there has been very little discussion about the benefits to women in countries where, you know, in some instances they outnumber the number of men who are at risk of HIV. And how soon will you know – will we know what benefits there are to women whose partners are circumcised.

Dr. Anthony Fauci: That's obviously a very good question. One would anticipate – and that's why I said and hopefully this will have a broader impact that if you decrease the burden of HIV infected men that you would have a secondary effect on woman.

But the precise question, directly that you're talking about is actually a study that is ongoing now in Uganda that is funded by the Gates Foundation that is specifically looking at this question when you have a circumcised male, what is the direct effect on the infectability to the female sexual partner.

So that study is ongoing and it will likely be analyzed in over a year, 2008 in the fall of 2008, I think the data may become available.

Brenda Wilson: Thank you.

Dr. Anthony Fauci: You're welcome.

Operator: And we have a follow up question from Helen Branswell with the Canadian Press.

Helen Branswell: Thanks very much. I understand that when a study reaches a certain threshold when you get a certain level of results you have to end for ethical reasons, but sometimes that leaves important questions unanswered and I'm wondering if that might be the case here.

Are there any questions that the researchers will not be able to address because the studies were ended early?

Dr. Anthony Fauci: I will, Helen, just give Bob and Ron the opportunity to answer it also. But I think it's important to point out that the data, the scientific data that shows that something is medically slash surgically safe and be effective the DSMB made the decision that in fact the data clearly indicated that it would be unethical to continue.

The question that you're asking goes beyond that like what about the long term effect. Does the realization now of the effectiveness of this, is it going to have a behavioral change that might negate the positive results.

And if for that reason why there will be considerable follow up of this cohort built in to the study. So although the actual procedures now have come to the point where it will be offered to the uncircumcised group, nonetheless, the follow up will be very carefully looking at any anticipated or unanticipated negative effects of this.

Operator: And that's all the time we have for today for questions at this point. I'd like to turn the call back over to Ms. Laurie Doepel.

Laurie Doepel: Thank you very much for calling in to today's tele-briefing. We do appreciate your interest. If we did not get to your question today, please contact the news and publication branch at the National Institute of Allergy and Infectious Diseases at 301-402-1663 or via email at niaidnews@niaid.nih.gov.

Again, thank you for your interest.

Operator: This does conclude today's conference call. We appreciate your participation, you may disconnect at this time.

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