

**2007 HIV/AIDS Implementers' Meeting
State of the Art
Male Circumcision
PEPFAR, The Global Fund to Fight AIDS, Tuberculosis
and Malaria, UNAIDS, UNICEF, The World Bank, WHO, GNP+
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DR. BEN CHIRWA: Good afternoon and welcome to this special session on male circumcision. My name is Dr. Ben Chirwa. I'm the Director General of the National AIDS STI/TB Council of Zambia.

Let me just give you a few opening remarks before I call on our expert panel. You'll recall yesterday during the official opening when the Global AIDS coordinator for PEPFAR, Dr. Michael Diebold, referred to the expanding knowledge base in our AIDS environment. One such area is circumcision. As you shall hear, there's compelling evidence of its protective effect of circumcision. And by the way, I'm referring to male circumcision. Female circumcision, I think, is a subject of discussion at another forum. You'll also recall that the U.S. Data Safety Board had to discontinue a number of studies because of their available evidence. Yesterday, one session was looking at options for testing and one subject that came up was mandatory testing. I was impressed when the session chairperson referred to male circumcision as also qualifying for mandatory. So again it's a subject that we'll be hearing about.

We have three experts to discuss this topic. And the topics range from giving an overview about evidence on male circumcision to cost effectiveness of male circumcision, and

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finally, to what countries can do in providing guidance on this subject. To start off the subjects, I have Mr. Timothy Hallett who'll give us impact and understanding of male circumcision currently. So, Mr. Timothy Hallett.

TIMOTHY HALLETT: Okay, well, thank you very much. I'm very grateful to the organizers for letting me contribute to this very important session. As you've heard a couple of times already over these few days, and we'll hear more in this session, the evidence showing that male circumcision can reduce the chance that men are infected is now compelling. And one might think that's all we need to know to understand how an intervention would work and predict its impact. But with infectious diseases, sometimes the interaction between the pathogen and the host can complicate matters and obscure those most important determinates for its success. So one way to get around this is to do the mathematical model, which is just a precise way of describing the interaction. That's what I'm going to be using today. Just make a few epidemiological observations about how male circumcision will work as an intervention. I'd like to say that this was done by several colleagues at Imperial College, led by Jennifer Smith and it's in her behalf that I'm talking today.

So randomized trials can quantify the individual level effect of circumcision, but the key impact of an intervention

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will be at the population level in terms of reducing instance across everybody and looking at future healthcare requirements and bringing down morphology. Male circumcision as intervention could have two benefits. It will have firstly a direct benefit which accrues to the men that receive the circumcision. There will also be an indirect benefit that could accrue to everyone in the population, women and men who aren't circumcised, to different degrees. So I want in this talk to understand the determinates of the overall impact of male circumcision encompassing both a direct and those indirect [inaudible].

So first look at direct effects. I have got a simple model here. I should say that the models we're going to present, I'm not going to discuss the methods behind them at all, but you can ask me in public or private if you want more details anyway. So let's first of all assume that the circumcised men are 60-percent less likely to acquire infection than uncircumcised men. We'll have a graph and on the vertical axis we've got the cumulative probability that a man is infected and across the horizontal axis we've got more and more sex acts with HIV infected women. And the purple line shows what happens for uncircumcised men, and the other line shows what happens to circumcised men. And what we see is that the difference between the pink and the other line is representing

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the protective effect of circumcision. But we see that it varies according to exposure. So for men who have a low level of exposure, a proportionate reduction in the transmission is 60-percent, whereas men which have a much greater exposure proportionate reduction in instance is lower. This could mean that the actual protective effect of circumcision cannot be quantified directly from trials. Just because we've seen a 60-percent reduction in incidents over a two year period during trial, doesn't mean that all circumcised men will be at 60% less risk forever and there will be 60-percent less infections among them. It also means immediately that impact of circumcision will be greater in circumstances where there is infrequent exposure to infection either among men that only occasionally are exposed to that risk or an epidemic which are growing or constrictors.

So what do I mean now by the indirect effect? I've got a simple schematic of the rate transmission from the working population between circumcised men and females and between females and other men. What does circumcision do? Well, it reduces the chance of females infecting circumcised men. But if circumcised men are having less incidents gradually over time, prevalence of circumcised men will decrease. And that means that females contacting circumcised men will in turn be less likely to contract infections. And that's what I mean by

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the indirect effect and this I'm going to call the first time indirect effect and you'll see why. Because if females come to be infected less often, gradually over time prevalence among females will decline so that they become less likely to pass on infection to both circumcised men and other men. You see that circumcised men get both benefits. They get a direct benefit and a secondhand indirect benefit. Females get just the first time indirect benefit for circumcision, and even men who aren't circumcised get a secondhand indirect benefit. And this goes round and round and round so we can have circumcised men get less infected, problems go down among men and so they are less likely to affect females who get a further effect, and it goes on. So when we run the model and we look at the fraction of infections averted over say a 20 year period. We see that most of the infections averted will be among circumcised men. Not surprising that they're the winners in all of this, but we also see that first time indirect effect among women is not inconsequential. In this simulation we're getting 10-percent averted among women and also the infections averted among uncircumcised men is hovering at about five-percent.

The rest of the talk is going to be about behavioral and biological factors which determine this magnitude of the indirect effect. The 60-percent protection that circumcised men receive is stable over a wide range of assumptions and

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parameters, whereas the magnitude of the indirect effect occurring to women and uncircumcised men depends on many things. I'm going to talk about a few of them now.

First thing is the coverage of the program and the timing of which circumcised men are turning of age. So here I've got on the X horizontal axis increasing fraction of men circumcised in an intervention, and the vertical axis I've got a summary of benefit, in this case fractions of infections averted for 20 years. The yellow line shows when typically we're circumcising men when they've been sexually active for 10 years, whereas the red line shows what happens if they're circumcising men before sexually debut. So the first thing is that the lines aren't straight. The benefits of circumcision accrue not addedly but multiplicatively, meaning that if you increase by 10 the portion of men you are circumcising the benefits increase by more than 10. This is because a greater fraction of females contracts over circumcised men. It means that per operation the fraction of infections that will be averted will increase with bigger programs, which is an economy of scales effect. The difference between the red and yellow line shows the massive advantage in circumcising men as early as possible. The first years of sexual activity for a man are among his riskiest years. And if you can circumcise them before they get to that period, population advantage is great.

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This should be traded off against the delay before these pre-sexual debut men enter the population so you can be circumcising [inaudible] today but we won't see declining incidents for 20 years even though we would expect for the same number of operations that eventual decline of incidents would be much larger.

So we know that in HIV epidemiology those with the riskiest sexual behavior contribute disproportionately to new infections and we can use that when we're thinking about intervention because targeting can really improve efficiency. If, rather than circumcising men with equal validity according to whatever list they have, we instead give the same number of operations but give them disproportionately to the people with the highest risk. We see that the indirect benefit is occurring to women and to uncircumcised men more than doubles as one very obvious way to squeeze out extra efficiency from a program.

There's also some ambiguity about the biology of circumcision, about the effect it has on reducing male-to-female transmission. If there is circumcision that is associated with a 30-percent reduction in male-to-female transmission, again we see that the indirect effect more than doubles among females and uncircumcised men. And even though this isn't something we can change in the program, it's an

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important part of the uncertainty that we're faced when we're trying to project the impact of these interventions.

It's been talked about a lot in sessions already, I'm just going to talk a bit about it and that's behavioral disinhibition. This is the idea that after men are circumcised he might revert to riskier behaviors. So we have in this model a parameter which is behavioral disinhibition which determines the fraction of men whom after they're circumcised cease to use condoms. Everything else about sexual behavior stays the same, but after circumcision a fraction here, not 50-percent or 100-percent, never use a condom again. So looking at circumcised men, we see that even in 100-percent of them, all men who are circumcised, stop using condoms, they still get a net positive effect. There are still fewer infections among them because of the protective effect of circumcision is outweighing the protective effect of condoms had before. And I should say that the level of condom use is parameterized from a study in rural Zimbabwe.

For women the story is very different. Whether they get fewer infections or more infections is totally dependent on whether there is behavioral disinhibition or not. So this inhibition isn't an issue for the men, but for the women. And an important question is then whether these two benefits and disadvantages balance out a role? Do we get the nightmare

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scenario of more infections with the circumcision intervention than what level this intervention would generate to more infections overall? So this depends to two aspects of biology of circumcision. One, beginning at the vertical axis is a reduction in female-to-male transmission and our pilot data is 60 is a best guess for that number, would also running across the horizontal axis the reduction in male-to-female transmission. And observational studies have put this number somewhere between naught and 30-percent. And what the color in this grid represents is the fraction of men that need to be disinhibited after circumcision in order that there are net more infections overall. So the red squares show that there's a danger only if a small-percentage of men being disinhibited, 10-percent would lead to there being more infections overall in the whole population, whereas the blue areas show sort of a safety zone where you'd acquire a 100-percent or more of men disinhibited. So with the observed strength of the male circumcision effect, this disinhibition is unlikely to lead to more infections overall, especially if there's also reduction in male-to-female transmission.

But what if that 60-percent represents an upper bound on the effect of circumcision? What if outside of a trial it's a little bit lower and actually the [inaudible] incidents on the estimates and the trials are quite wide? What if we're

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amiss in the zone actually really? And we see then that with a weaker biological effect than the headline number, the medium, the high levels of disinhibition could lead to more infections. So there is a danger that disinhibition could lead to the nightmare scenario of an intervention leads to more infections overall.

So in making projections of the impact of circumcision we're faced with three sources of uncertainty and I've talked about all of these, and I'll just be clapping up. The epidemiologic context determines the impact in terms of frequency of exposure to infection, the overall potential for epidemic spread are not for epidemiologist, and the pattern of partnership information and the pattern of heterosexual transmission in the population can all modulate the size of our indirect effect. Also, the biologic effect of MC, is there is uncertainty in it and it has, obviously, a strong determining power for male-to-female transmission, for female-to-male transmission and what about transmission during the wound healing phase. And there are also programmatic factors that we can control. Things like how far we can increase coverage to circumcision, how effectively this targets those at highest risk, how quickly it can be rolled out, and how effective the counseling measures are to minimize disinhibition.

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So here we have six different scenarios to show the range that for the same man you're doing intervention we get a range of different outcomes. So on the left hand side is one particular community where if we were to implement a medium-good intervention we avert only five-percent of infections, but if it can be effectively targeted and we can eliminate behavioral disinhibition, that impact could increase four fold, 20-percent. Meanwhile, in a different community with a different pattern of [inaudible] formation and a different potential for epidemic spread, that same medium-good program has a much, much bigger impact. Three times as great. And the benefit of targeting is much greater and behavioral inhibition is a less important determining factor. So what I want to show is that when your facing projections of the impact of circumcision, be aware that there's a lot of uncertainty hidden behind it, even though we know about direct effect, quantifying that indirect effect depends on a range of behavioral and biological assumptions that [inaudible] yet, but also that within that uncertainty that we can't control there are plenty of things the program can change to optimize its impact. I hope that's a good overview of the epidemiology of circumcision interventions. Thank you. [Applause]

DR. BEN CHIRWA: Thank you very much. We will now the next presentation for another 15 minutes and at the end of the

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three presentations, I'll then turn to the floor for observations and questions. The next presenter is Dr. Gayle Martin and her topic is Costing and also looking at the implication of cost effectiveness of male circumcision.

GAYLE MARTIN, PH.D.: Good afternoon everybody. I'm doing this presentation on behalf of the study team that I've listed here. I'm from the study team from the Futures Institute, the Ministries of Health in the various countries that we've studied here. Before proceeding with the presentation I also want to highlight the preliminary nature of these results is subject to a process of consultation as well as review with the countries involved.

The study has three components and I'm presenting the second component here. The first important thing looks at the social, cultural and policy context of circumcision in the countries in question. Second is the costing study that I'll present here, and the third is the modeling of the in potential impact of circumcision on the HIV epidemic.

Let me start by saying what this study will not tell you. First, it will not tell you how or whether circumcision should be implemented in any of the study countries mentioned here. The study is intended to provide some information alongside other considerations to inform the countries of process and planning. Some of the issues considered in the

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design of the study here. At first the study focuses on adult circumcision only. It is done from the perspective of the health facility. First stage was collected as to how circumcision was currently implemented in the countries, but consideration was also given to services that are not currently part of circumcision as it is currently implemented. Examples, are counseling with or without testing, training, communication, etcetera. Three countries were considered. The Lesotho, Swaziland and Zambia. This allows for standardization, comparison and validation of the findings. These countries have two characteristics. One, high HIV prevalence and moderate-to-low circumcision prevalence. And these factors were highlighted by Williams Ethow [misspelled?] as predictors of countries that could potentially benefit substantially from the implementation of circumcision.

For the facilities in question direct costs as well as indirect costs per persons circumcised were collected from the various provider types. Variation in clinical practices were taken into account in the cost analysis. Several provider types were also considered. A combination of hospitals, referral, and district hospitals, as well as clinics. An ingredients approach to costing was followed and this allows for flexibility and greater potential use of the analysis to inform country specific planning and policy making.

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As I mentioned, direct as well as indirect costs were collected. The direct costs example starting includes drugs, other medical supplies. And then the indirect costs include a combination of fixed as well as recurrent costs. Examples are facility, equipment, utilities, and facility supervision costs, etcetera. And these indirect costs were apportioned to the unit costs of male circumcision based on the share of the total health facility operation that circumcision accounted for. We also costed the cost of the most common complications that occurred and the cost of these complications were taken into account by weighting them according to the probability of those complications occurring. And these unit costs were then used to project the total cost to each country scaling-up circumcision. The costs were discounted and inflation adjusted as well.

In each country four sites were selected. This included a combination of rural and urban facilities, hospitals, as I mentioned, referral and district facilities were included, as well as clinics. It should be mentioned, though, that hospitals accounted for the largest number of the facilities visited and only two of the eleven facilities included in the study were clinics.

On average we noticed that there were generally about four health facility visits associated with the implementation

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of circumcision. The first was the initial visit for the booking of the surgical procedure, examination and some information about the surgical procedure was provided at that time. The second visit was the actual surgical procedure. The third visit, postsurgical visit at two to three days after the circumcision, and then another followup visit at seven days after the circumcision.

This slide just shows you some of the staffing time inputs and the staff inputs that were collected in the study. You will notice at facility one, a combination of doctor and nurse time was included, but it is also worth noting that consult was not routinely provided at the facilities studied. Generally, the procedures were performed under local anesthesia. This was not the case for the private sector facilities that we visited in the study. And then antibiotics were not routinely prescribed in all the facilities. Analgesics were provided in all facilities. And then the other source of variation that I would like to highlight was at the first postoperative visit. Dressings were not routinely reapplied after that visit.

The slide shows the variation in the direct cost of circumcision. There's generally some convergence in the direct costs with little variation. This is not the case for the indirect costs of circumcision in the facilities visited, and

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I'll discuss that later. As I mentioned in the methodology we also included the costs that are not routinely included as part of circumcision. So in addition to the surgical procedure, we included the cost of counseling, testing, and it is assumed that not all individuals coming for circumcision will necessarily will be required or volunteer for testing, and in the cost of communications. And this study, these results showed the preliminary costs estimates for the various countries. The estimate ranges from about 54 U.S. dollars to about 47 U.S. dollars and this is in 2007 dollars.

There is a general convergence in the surgical practice among the non-private providers. I also have to highlight that some of the variation in practice that I've shown in the earlier slide did not suggest suboptimal clinical care. They just suggest different clinical practices.

There's small variation whether or not antibiotics were originally prescribed as well as whether or not dressings were reapplied at the postsurgical visit. Commodity costs variation was not an important contributor to facility differences in the unit costs and an important driver of the unit costs differences was the indirect costs. And this varied by the level of facility and particularly the referral the hospitals had expectedly higher indirect costs and the complexity of the

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services available at the facility was another important determinant.

What are the implications for cost effectiveness analysis? This slide shows some of the results from the impact part of the study. It shows one particular scenario for each of the countries. The scenario considered is that if circumcision were to be scaled-up to 50-percent coverage to Lesotho and Swaziland and 57-percent coverage in Zambia. This coverage targets reform by the current level of circumcision. Based on the epidemiology modeling it is estimated that the number of circumcisions's current costs per infection averted for Lesotho is 7.6, Swaziland 8.4, and higher for Zambia. In order to avert one infection, one needs to have about seven or eight circumcisions and slightly higher in Zambia.

The implied cost per infection averted for Lesotho and Swaziland are just in excess of \$400 and higher for Zambia at 600 U.S. dollars. Scaling-up to the level that we've just described have substantial health service implications. For example, the number of circumcisions required per week in Swaziland is about 550, Lesotho 870, and substantially higher in Zambia. The facilities that we visited on average performed about 30 circumcisions per month. As I mentioned, the unit costs estimates were used to estimate the total cost of scale-up. And I'm showing you the average annual cost of achieving

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the coverage targets that I showed in the first slide. For Lesotho and Swaziland average range is between one to two million per year, and Zambia, because of the largest number of circumcisions and population size, 12 million per anum. The cumulative costs over the period of 2008 to 2015 is also shown here.

Now we may ask, well what are we getting in return for this level of expenditure, which is not trivial? This slide shows how much future savings in terms of ARV treatment can be avoided for a given level of circumcision investment in circumcision in countries studied here. So these first bars show the cumulative expenditure on circumcision implied at the level of coverage that I've showed previously. And the other bars show, in the first set of bars the future ART costs that would be avoided if this level of investment were to be made in male circumcision over the period of 2008 to 2015. This scenario here assumes people will remain on ART for five years, and in the second scenario assumes people will remain on ART, for on average, for about eight years. So as you can see, there is the potential for substantial costs saving for the circumcision investment that have been projected here.

One of the issues that we considered is what if we were to keep the level of coverage for circumcision in 2015 constant, but do the analysis for a longer period, extending

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the analysis period to 2020? And this addresses some of the multiplicative effect that the first presenter mentioned. And essentially showing that the number of circumcisions required to avert one infection will reduce in each of the country examples. The result also is that the cost of infection averted would also be lower over that projection period.

The results presented here assumes a linear scale-up between the start period and the end period of the projection and shown in red here. And what we look at is what would be the indication if scale-up were to happen slightly slower than the linear scale-up that is in the purple, or if it were to happen slightly faster than the linear projection shown in the blue. And the results are shown here relative to a linear scale-up scenario. The total number of circumcisions on a slower scale-up would obviously be less by six-percent for the scenario we considered here, but the number of infections averted would also be substantially less, by about a fifth. The costs of infection averted would be higher by 15-percent. Then if we consider the picture of a faster scale-up, the results show here that the number of circumcisions would increase by about nine-percent, but that the number of infections averted would be by about a third, and the cost of infection averted would be reduced by about 16-percent.

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So in conclusion, from the cost analysis we found that there's some variation in the level of service where circumcision is implemented. Secondly, the pace of scale-up matters and the results of the slower versus the faster pace of scale-up reinforced this point. And the conclusion is that relative to other prevention interventions, circumcision can potentially be a cost effective intervention. Obviously subject to the sources of variation that the first or third described, and hopefully some of the investment in behavior change communication as well as counseling would address some of the behavioral uncertainty.

But scaling-up the circumcision is not without challenges. And I'd like to highlight a few things. Firstly, the indirect costs should not be underestimated. Many of the costs results that have been reported previously did not only include some of the direct costs of implementing circumcision and this study again highlights that would lead to a substantial underestimate of the true costs of circumcision. Secondly, that the health service and human resource report the implications of circumcision are substantial but not insurmountable if one considers some other innovative ways of involving a variety of service providers in the implementation of circumcision. Thank you. [Applause]

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DR. BEN CHIRWA: Thank you very much Dr. Martin. Last but certainly appropriate because representing the U.N. Committee, UNAIDS, and the WHO. Having reviewed the compelling evidence we've come up with policy guidelines especially for implementers. Dr. Tim Martin [Farley] will just take us through the processes of countries begin design policies and then programs to implement circumcision.

TIM FARLEY, PH.D.: Thank you Mr. Chairman, ladies and gentlemen, good evening. I'm sorry it's getting late. I have the privilege to present to you some of the evidence about male circumcision and also the work that we in the World Health Organization, UNAIDS, UNICEF, UNFBA, and the World Bank have been doing over the last few years and will continue to do over the next quite several years as this intervention becomes more widespread.

This is not a new observation; this is taking you back almost 20 years. John Bongards [misspelled?] noticed that the HIV prevalence was much higher in countries where there is a low circumcision prevalence. This plots data as were available at that time for countries in the African region. In 1999, almost 10 years ago, Halpin [misspelled?] and Bailey did a similar analysis of plotting HIV prevalence this here with countries within the African region and noting the countries with the low male circumcision prevalence at the top of this

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graph and the countries with the high circumcision prevalence and you see that the HIV prevalence is considerably low. Interestingly this observation also applies in the Asian region. Notice the horizontal scale here is an order of magnitude different. Here we're going from 0 to 3-percent, while in the African region we were going from 0 to 30-percent on the scale, but the same pattern is seen. Very interesting and suggestive evidence.

In 2000 this is the results of a meta analysis conducted by Ellen Weiss and her colleagues. All various observational studies. And on this graph here, the vertical line on the right, would show an alter ratio of one which would be there was no protective effect. Points to the left would show a protective effect of circumcision, and points to the right would show an adverse effect of circumcision. So these are observational studies, not ecological correlations as you've just seen. And a summary of those data showed, as I said this is in 2000, that the crude odds ratio was about 50-percent. There was a two-fold reduction in HIV incidents and prevalence amongst men who were circumcised. The adjusted odds ratio notice is slightly less than the crude odds ratio. This is adjusting for behavioral factors and is very interesting that as you adjust more for behavior factors the odds ratio moved away from one showing a greater protective effect.

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Notice also that in the high risk groups a greater protective effect than in the general population.

Two other bits of important information published around 2000. That in a study of discordant couples in Rakai, Tom Quinn and colleagues looked at the HIV incidents in circumcised men, in men who were not circumcised, and incidents of 17 per 100 person years, and there were zero infections in the 50 circumcised men in these discordant couples. Very strongly suggestive. Also, similarly information on the risk of transmission from a HIV infected circumcised man to his uninfected partner and we see on the two left poles that at low viral loads there were no transmissions from circumcised men to partners. Now this is the context in 2000. We convened at the AIDS Conference in 2000 a review of these observational evidence. Remarkably consistent pattern, greater reductions in HIV prevalence and incidents in highly exposed individuals and this adjustment for behavioral factors leads to an enhancement of the observed protective effect.

But, and it was a big but, have all potential confounding factors been adequately measured and adequately adjusted for? How can we be sure that there isn't something that is associated with behavior which is also associated with risk for HIV? And have we been able to eliminate those factors completely? And then another question, even if one has been

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able to adjust completely to confounding factors, the key question is does promoting circumcision in men who would not otherwise be circumcised actually result in a lower HIV incidence? And also if there really is a direct [inaudible] in the face of this emerging evidence when the plan was put together and we defined priority actions pending the availability of this new evidence.

And the first thing was to support countries assess the potential impact of this new evidence. So a number of countries' stakeholders' consultations were conducted. Some issues preparations on the human rights dimension, and this is a big issue, situation analysis tool kit to assess facilities and potential demand was started and also technical guidance on male circumcision techniques service package and training modules was started. Now this work was funded by the three groups who were involved in supporting the three randomized control trials, the NRS, the National Institutes of Health, and the Bill and Melinda Gates Foundation and UNAIDS and this work was funded in November of '05.

During 2006 these country stakeholder consultations were convened and here are some of the highlights from the five countries where these consultations took place. Kenya, Tanzania, and Zambia. In selected areas each of these countries has high circumcision prevalence but it's not

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uniform. The key questions there are how to extend to non-circumcising groups not only in terms of service provision, but in terms of cultural identity or tribal identity and in terms of stigma. And also the big question is how to expand safely to meet an anticipated growing demand. And these were some of the key questions that we did in those countries.

In Swaziland there was already a high demand in the private and the NGO sectors the biological sectors for male circumcision, and they were acting already on the information from the observational data, but also from the Orange Farm studies, and male circumcision was already being reintroduced into the country through some very good advocacy work that was happening.

Lesotho, a very interesting country, very interesting pattern of circumcision. There's widespread traditional male circumcision in the mountainous regions, but in fact there is a very limited amount of cutting that is done. There is just a small nick that is made in the foreskin and they whole foreskin is not actually removed. So there is a very interesting setting here. There are huge cultural sensitivities in Lesotho about circumcision and there are big tensions between the traditional and the modern health systems in the country. And these were perceived as issues that will have to be addressed

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if the country wished to move ahead with expanding circumcision services.

In November of 2006 we convened a regional consultation. The first set of countries were the ones who participated in those stakeholder consultations, and then other countries that have not had yet stakeholder consultations also participated. And here are just some of the challenges that were highlighted at that discussion. Some of the legal issues, the policy issues, the ethical issues, the human rights framework, so we can come onto that if we have time in a minute.

The key question of how to ensure safe circumcision practices, the training needs, the types of provider, the types of post circumcision care, management and reporting of adverse events, getting a handle or measure of risk compensation, these were some of the key questions that were being posed there. And whether to prioritize, how to prioritize which age groups, which population groups if at all? Should it be offered generally?

Key policy questions for which no answers were available then, and only limited answers are now beginning to emerge. Costs and sustainability of services you've just heard previous presentation where we are beginning now to get a handle on costs and cost effectiveness. Additional technical

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consultations, strategies and approaches to circumcision programming, targeting, how mobile to scale-up? Do you have the sort emergency flying in doctors and surgical teams, or do you gradually strengthen the health services to be able to provide this in a sustainable manner? What is the minimum package of services and counseling that must go around circumcision?

One very important thing is that this is an opportunity if circumcision to be expanded to reach young men. We have great difficulties in reaching young men other than in bars and in football matches, other than that there are no times that they're very receptive to health education messages. So this is a great opportunity to get young men who are not good participants in health services and to talk to them and talk to them about HIV prevention, responsible sexual relations, and so forth.

The social science issues. The social science issues on circumcision were discussed in a meeting in January 2000 and several, the cultural and the ethnographic dimension of promoting male circumcision, saw the potential for risk compensation, how to integrate between traditional and clinical circumcision. The role of women, their role in this, their perspectives, their attitudes towards circumcision. The issues of communication in an effective and responsible way. Stigma,

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again, came up. Another consultation in March about adolescence and how one integrates sexual health counseling and services with circumcision if one is going to offer it.

Now new evidence from the two ongoing trials emerged at the end of 2006, and on the 12th of December of 2006 the Kenya and the Uganda trials were stopped by the Data and Safety Monitoring Board. One Data and Safety Monitoring Board for both trials, so it was easy for them to coordinate.

Immediately WHO and UNAIDS announced plans for a global consultation to review the evidence. On the 24th of February the results from these two trials were published and then set together with a number of opinion papers and commentaries just over two months from the date the trials were closed, which is impressive.

But what I would like to point out to you what is even more impressive that just over one week later, 24 February was a Friday, 6 March was the following by a week, an international technical consultation on male circumcision and HIV prevention was convened in Monture and Switzerland by WHO, UNAIDS and partners. This here shows the summary of the evidence. In the top three bars here, notice firstly the vertical bar which corresponds to the no effect at risk ratio of one. The observational data are in the middle here above the line, and the protective effect in the three randomized trials, South

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Africa, Kenya and Uganda, about 40-percent to 50-percent lower risk. So from two fold to two-and-a-half fold reduction in risk. Remarkably consistent between the trials, remarkably consistent with the observational data.

The conclusions and recommendations were finalized, discussed with the consultation and released on the 28th of March, so just one month after the data were published and three months after the trial was stopped. There were 11 key conclusions to this. The first one is the research evidence is compelling, it may not seem strong to you, but it's remarkably strong work for WHO to use here. Promoting male circumcision should be recognized as an additional important strategy for the prevention for heterosexually acquired HIV infection in men, but also male circumcision should never replace other known methods for HIV prevention and should always be considered as part of a comprehensive HIV prevention package. Recommendations, conclusions, 11 key conclusions. This is just highlights of three of them. If you want to know all the recommendations, my time is up, I will take this opportunity to point you towards the next session that's going on in the Serena [misspelled?] Auditorium where there will be a greater discussion of the content of those recommendations.

I will not, since I've run out of time, discuss the future work that we will do. I will just turn to thank the

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interagency task team on male circumcision that I've already mentioned, but also the key partners, the Bill and Melinda Gates Foundation, the U.S. National Institutes of Health, the French National Agency for AIDS Research, the USAID, The office of the Global AIDS coordinator, the CDC, The Clinton Foundation, Family Health International, Populations Service International Gerpigo [misspelled?] and others if you are involved I do apologize I've left you off. Thank you very much indeed. [Applause]

DR. BEN CHIRWA: Thank you very much. We have heard from the experts. You'll recall the first one referred to the modeling of the direct and indirect benefits. The second one looked at the costing and the benefits which were also demonstrated. And last for countries to look at policy and programs for implementation of male circumcision. As is indicated, basically we have run out of time, but I'll three questions and after that we can continue the questions in the next session at Serena, where we will be meeting experts on the same topic. So I'll take three quick questions and then we'll break it up. One, two, and three at the back. Let's start with the two in front and then we go on my left at the back.

MALE SPEAKER 1: Has study also looked into advantage of male circumcision to anal sex? And second is my comment on the cost benefit. I think the benefit is markedly savings on

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ARTs, but probably much more than that, like treatment of opportunistic infections. There are things that cannot be measured. There are immense psychological benefits to the individual. Thank you.

DR. BEN CHIRWA: Let's take the next question.

JOHN MORGAN: Thank you. I am John Morgan from the Aback Project in [inaudible] India. I congratulate the three of you for making wonderful presentations. I actually want to ask of you two clarifications. One of them is when you spoke about a cost benefit analysis. You spoke about infections averted. What kind of materials have you followed for calculating the infections averted, that's number one? And number two is basically WHO has among one of its technical recommendations, it need not be promoted as a stand-alone kind of an intervention, but as a larger part of a basket of interventions. But don't you think that still the risk remains, while it reduces the risk, it definitely does not negate risk and how do you sort of visualize responding to a situation where people will start indulging in high risk behavior merely because they have been circumcised? Thank you.

DR. BEN CHIRWA: Thank you. And the last one on my left. Yes, please.

MALE SPEAKER 2: My name is [inaudible], Zimbabwe. My question is for your presenter of Imperial College. On one of

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your slides you showed 10-percent likely not safe, 90-percent and likely safe. After reading everything and making in simple world, I came to the conclusion that it is [inaudible] and safe. Can you give more explanation?

DR. BEN CHIRWA: Thank you very much. I notice that somebody is desperate to ask a question. Yes, please.

MALE SPEAKER 3: Thank you Mr. Presenter. Thank you for the presenters for the excellent presentation. My question is for Tim. I would like to know if there is additional analysis on the impact of ARVs on the effect of circumcision in preventing transmission?

DR. BEN CHIRWA: Thank you very much. I think what we'll do is we'll take the questions. I'll ask each of the experts just to take the questions that is attached to them briefly, and then pass on to the next. Thank you.

GAYLE MARTIN, PH.D.: Hi, in response to the question that costing future ART cost averted as the sole benefit of investment in circumcision, I fully agree. It is just something that is simply quantifiable and would certainly would be a very true underestimate of the total benefit. So I fully acknowledge that. It would just take too much time to go through some of the other benefits.

The other question to me was about how the calculation of the infections averted. We can talk about that after the

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session. I think it will take too much time of this session, but essentially the model divides the population into various risk groups and takes into account the risk behavior, benefit sexual and as well as IV transmission of HIV, and those project and including some of the Sentinel Surveillance data to validate the projection pattern, but I know I'm giving a very short version of it, but it's obviously much more complex. Let's talk about it after the session. Thanks.

TIM FARLEY, PH.D.: If I can address the questions. There were two questions; well there were two that I understood. There were three questions, one I didn't understand. The first question was about anal sex. Firstly, we would not expect male circumcision to have any protective effect for a man or a woman who's receptive anal sex. There's no biological reason why there should be any protection there.

For the insertive partner there may or may not be a protective effect and I don't know whether we will ever get any data that will answer that question. It's possible that if we think of the mechanisms by which men are protected from insertive vaginal intercourse, one might consider some similar protection, but equally the risk of HIV infection for the insertive partner from anal sex is very, very much higher than for the risk for HIV infection for the insertive partner during vaginal sex. So if there is a two-fold risk reduction, men who

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have unprotected anal sex with an HIV positive partner are at very, very high risk of HIV infection whether they are circumcised or not.

The second issue was about the fact that circumcision reduces but does not eliminate HIV infection, how are we going to cope with this? I mean frankly, I don't know. It's obviously a major concern and it's a major concern to us that we must promote circumcision within the context of an overall HIV prevention package. We are no more going to cut our way out of this epidemic as we are going to test or to treat our way out of this epidemic. It's a whole package that we have to be concerned with.

The question about IRBs, I'm sorry I didn't understand it. Maybe we can have a discussion later. Thanks.

TIMOTHY HALLETT: And the question came to me about safe or unsafe levels of disinhibition. I hope I understand the question correctly, if I don't, let's talk afterwards. I mean maybe the use of the word safe or not safe was inopportune. What I meant to say was that we can reinforce existing safe sex messages and that will have some effect and maybe if we can stop 90-percent of the people being disinhibited, then that's likely. But maybe there'll always be an original 10-percent that will be disinhibited no matter what we do. So that gives us an idea of the margin of error we have

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when implementing this kind of intervention. But we can discuss that more, obviously in the next session. Thank you.

DR. BEN CHIRWA: Thank you very much. Let's give them a round of applause. [Applause]

[END RECORDING]