Wednesday Plenary
Kaiser Family Foundation
July 21, 2010

[START RECORDING]

MALE SPEAKER: Once a very historic event in that same place we were yesterday, with somebody called Hitler. And it's very paradoxic [misspelled?] if you want in my mind that yesterday we were calling for human rights in the same place, that such an outrage happened many years ago.

I'm here today to present with Jon Francois [misspelled?] the IAS/ANRS Young Investigator Awards, which is something that we do with great pleasure here at the conference.

The International AIDS Society and its partners are proud to sponsor a number of prestigious scientific prizes and awards at AIDS 2010. The prizes and awards are aimed at rewarding promising researchers doing outstanding research on HIV and AIDS. IAS/ANRS Young Investigators Awards consist of $2,000, jointly funded by the IAS and the [speaks in French], the ANRS, to support young researchers who demonstrate innovation, originality, rational and quality in the field of HIV and AIDS research.

To be eligible, the presenting author must have been accepted for presentation and be under 35 years of age. One prize is awarded in each one of the six conference tracks and I'm not going to read you all of the tracks, you know what they are. Let me pass it to Jon Francois to do the final formalities.

JON FRANCOIS: Thank you for you and good morning everybody, my name is Jon Francois [inaudible] professor of medicine in Paris and Director of the French National Agency for AIDS Research. And it's a great pleasure to be here this morning to present you terrific young investigators this year.

So the winners this year are Stephanie Planque from the University of Texas Health Science Center at Houston Medical School, United States [applause], on the abstract [inaudible] HIV vaccine for inducing antibodies as far as genetically divergent virus strains [applause].

The second winner is Gabriel Chamie from University of California, San Francisco, UCSF, U.S. [applause], for abstract on the TB microbiologic and clinical outcomes [inaudible] versus CD4 initiative on territorial viral therapy in HIV positive adults with high CD4 cell count.

The third one is Joseph Larmarange from the Institute of [Speaking in French] for his outstanding [inaudible] abstract [applause] making [inaudible] in Africa for better understanding of epidemics, example from [inaudible] using 2003 demographic and health survey data.

Michaela Leslie-Ruth from [inaudible] Health, U.S. and Tanzania for the abstract [applause] the language of love, Tanzanian women define intimacy, sexuality, and violence in the 21st century [applause].

Gesine Meyer-Rath from the Western University School of Public Health, U.S., for the abstract total cost and potential cost savings of the National IRV [misspelled?] program in South Africa 2010 to 2017 [applause].

And finally, Khalili Elouradighi from [speaks in French] for his outstanding [inaudible] abstract [inaudible] when [inaudible] clashes with research ethics [applause].

[Audio Silent 00:04:45 to 00:05:33]

PETER PIOT: Good morning, I'm Peter Piot. As we all know yesterday was a true milestone in the history and the future of HIV prevention with the publication of the results and the proof of concept that a microbicide containing tenofovir can protect women against HIV infection.

I hope that one of the next conferences we'll see the results of community randomized trials demonstrating that antiretroviral therapy prevents and reduces transmission of HIV in the community. Until that day, we'll have to set policy on the basis of circumstantial evidence modeling on imperfect data.

So it's my pleasure now to introduce Bernard Hirschel who will review anti-HIV drugs for prevention. Bernard is Professor of Medicine at the Geneva University Medical School where he's the head of the section of HIV/AIDS and Division of Infectious Diseases. He's also the Director of the Clinical Research Center at the Geneva University Hospital.

We all know Bernard for his work on antiretroviral therapy, particularly in novel treatment strategies, including planned interruption of antiretroviral therapy and the effectiveness of treatment and prevention, where he's been really the pioneer.

Bernard has authored or co-authored over 300 papers, book chapters and a textbook on HIV infection. He's a member of numerous scientific societies and editorial boards, including the New England Journal of Medicine from ‘98 to 2006. Bernard Hirschel. [Applause]

BERNARD HIRSCHEL: Thank you very much for this very nice introduction. It's a pleasure to be here. The reason we talk about using HIV drugs for prevention is that there are few new ideas about prevention that actually work. Almost 30 years into the epidemic we are still with the same old recipes; influencing sexual behavior, using condoms, circumcision may make a contribution, and then we have hopes, more or less distant, for microbicides and vaccines.

Now it's not that these tried and true methods are ineffective. The theory is just fine. If we take a serodiscordant couple, cohabiting for 10 years, and if we postulate that this ideal couple is using condoms perfectly, there's a very high chance of protection, even after a very long time. Unfortunately, real life is not like that. And at

typical rates of condom use unfortunately there is a high probability of infection.

The CAPRISA trial that was discussed yesterday is remarkable for many aspects, but to me one of the more striking findings was that in a context of intense condom promotion with monthly reinforcement visits, and 80-percent of sex acts protected by condoms, there was still a 9.1 rate of transmission of HIV in the women taking placebo gel.

So, condoms, particularly in an African context, lack efficacy. Against that background, ART appears potentially and let me underline the potentially, more efficacious to be used instead or in addition to other prevention methods.

You have probably all seen this graph from a very old study in the Raki region of Uganda where transmission risk was closely related to the level of HIV in serodiscordant couples. When the infected partner had very low viral loads, no transmissions were observed.

Regarding treatment, the prevention of mother to child transmission is one of the big success stories of HAART and this has almost disappeared in countries where ART is widely available.

Regarding the effect of HAART on heterosexual transmission, there is this recently published study from Madrid. About 500 heterosexual couples, where the index patient was HIV positive and consulted between 1989 and 2008.

What was peculiar about these couples was that, among the partners of these index patients, the only risk factor for HIV was exposure to the index patients. All partners were tested to establish prevalence of HIV.

Now, here's the situation at the start of the study when the index partner presented first to the clinic, when there was no HAART, when the index partner was not yet treated, 44 of the sexual partners were HIV positive. But there was no such HIV positivity in the 149 partners of index patients who were already on HAART. And during further follow-up, as you can see on this table, there were no infections in the partners when the index patient was on HAART.

We also have a few studies where condoms plus HAART was compared to condoms alone, from Africa. All these studies were done in serodiscordant heterosexual couples in the context of condom promotion. They differed, study A, there was no HAART, study B with HAART and study C just published appeared without HAART, followed by a period with HAART. And here are the results, Study A, no HAART, 12-percent of infections per year, Study B with HAART 0.5-percent and in Study C before HAART 2.23-percent per year and after HAART, 0.39-percent per year.

In conclusion, we have circumstantial evidence which indicates that HAART lowers mother to child transmission, lowers heterosexual transmission and appears more efficacious than condoms or has a marked additional effect when used in

combination with condoms in serodiscordant heterosexual couples in Africa.

Now what has been the effect of ART on the AIDS epidemic? Here I distinguish two phases; the phases of introduction of antiretroviral treatment, 1990 to 2000 and the phase of expansion of ART, first decade of 2000. Here are the numbers from Switzerland. In red the number of newly discovered HIV infections from 1987 to 2001 and you can see that during that time when the antiretroviral treatments were introduced that number decreased.

The reciprocal evolution of numbers for newly discovered HIV infection and expansion of ART is particularly well shown in this graph from Canada, where you can see in blue how the number of patients on ART increased with a concomitant decrease of newly discovered HIV infection, during the time when HAART was introduced.

I will skip this slide in the interest of time and conclude that the introduction of ARVs in the 1990s coincided with a decrease in new HIV infections. People have estimated that all the things being equal, but I will show that other things, are unfortunately never equal. Without HAART new infections might have been between 50 and 200-percent more frequent by 2000.

Now, what happened after 2000? Here is a graph again from Julio Montaner's group in Vancouver that I heard is just

being published in *The Lancet* this week. In blue again, the expansion of ARVs, the number of patients treated, and in red the number of newly discovered HIV infections in general and at the bottom in IV drug users only. You can see that in the latter half from 2005 to 2010 there was a decrease, particularly marked in IDUs.

Let's look at some numbers from Switzerland. Here is the statistics from the Swiss IV Cohort which includes about 60-percent of HIV positive patients in Switzerland. The number treated, as I will show, increased, but not only that, the efficacy of treatment increased. In green is the proportion of patients with stably suppressed viral loads. Shown in another way, here is the population of the Swiss HIV cohort divided in those patients who presumably are still infectious that have a viral load of more than 500 in pink and in green those who have a viral load of less than 500. You can see that the green part gets squeezed more and more when you go from 2003 to 2009.

Now, what does that mean? What can we predict about new infections in relation to this? Here you have the patients with viremia of more than 500 in the Swiss HIV cohort. Now if we think theoretically, if this decreases the number of new infections, what can we expect? Well, what we can expect here in red would be that the number of newly discovered infection after a lag phase would start to fall.

Why a lag phase? Because newly discovered infections represent both very recent and older infections. Now this is the theory. Now let's look at what the numbers really show. These are the actual statistics. Keep that in mind. I will come back to this graph in just a moment.

But to draw conclusions from the last decade, expansion of treatment and better efficacy in developed countries, diminish the pool of potential infectious persons and the number of newly discovered infections after years of stability or even increase may be declining again, in places like Switzerland, British Columbia, San Francisco and others which I may have forgotten to cite.

What would happen to the epidemic if even more infected persons were treated? We are leaving here the realm of statistics and go towards modeling. Now this topic was first brought to attention at the Toronto AIDS conference by Julio Montaner in 2006. This statistic compares a scenario where 30-percent of eligible patients were treated or all eligible patients with less than 350 CD4 cells were treated. And on the Y-axis, you have the calculated HIV infection rate, per 1,000 population. In this scenario, as you can see, if you wait long enough, HIV infections would disappear from the population, but long enough, note this is 2050.

Now, of course it would cost a lot to treat everybody. It's easy to calculate. If you treat 100-percent, cost about

three times more than treating 50-percent. But if you calculate this over the long-run a relatively small initial investment would be offset and then greatly exceeded by the savings realized by the lesser number of new HIV infections later on.

Now, modeling is a risky business. Models differ and these differences matter. Here is a drawing again with a number of new infections, according to the model established by Lima and Montaner. The scenarios are 50-percent of eligible patients with less than 350 CD4 cells treated, 75-percent, 90-percent, 100-percent. If you start treating 75-percent or more you can calculate that you'd have a fall, an initial steep fall in new HIV infections and then a continued slower fall, and if you wait long enough, you would have no new infections anymore.

Here is another such projection from the World Health Organization. Let's concentrate on the blue curve. This is the hypothesis where all people with less than 350 CD4 cells would be treated in South Africa and you can see that there are differences. Again, you have an initial rapid fall but later on new infections would not further discline [misspelled?], but stay stable at still quite high values. So HIV according to these authors could never be defeated by treating only those with CD4 counts below 350. One needs to test the whole population frequently and treat all those found to be infected in the green curve.

It has been said that all models are wrong, but some are useful and cost projections also are subject to some lively discussions. For instance, this prediction of great savings by a universal test and treat strategy in South Africa was vigorously contested by others who thought that the assumptions were wrong.

So let's declare a model armistice and instead get some data. And here we have to talk about the HPTN052 Study. It's a randomized study to evaluate HAART in preventing sexual transmission in serodiscordant couples. This study is fully recruited since May. It includes 1,750 couples where the infected partner has 350 to 550 CD4 cells. These couples claim to be endogamous, meaning they have no sexual partners outside their relationship. They are randomized.

In the intervention group, ART will start right away, meaning at CD4 counts between 350 and 550, whereas in the control group ART would only be given according to the local indication that used to be in the countries where this trial takes place, CD4 counts between 200 and 250, and will now rise to 350. The endpoints are transmission events and sustainability with a planned follow-up of at least five years, which means that results are only expected in 2015.

HPTN052 is a great pioneering studies but it has limits like all studies. It concentrates on stable serodiscordant heterosexual couples, that's only part of the HIV problem and

if you think about applying the main methods to the general population, this cannot be done. Individual randomization is not feasible because it would necessitate tracking and testing of all sex partners, which is not a practical proposition.

So what can we say about the general population? Well what has been done is what I'd call the before and after approach. Measure the incidents of HIV before and after introduction of ART or before and after expansion of ART. And I have shown you some examples from British Colombia and Switzerland.

This is the graph of which I told you to keep it in mind. The number of new infections, the fall in potential infectious patients caused by expansion of HAART and later on a fall in the new HIV infections.

Now, this looks pretty convincing, but if you start looking in more details at this data, you start to have some doubt. For instance, this is the same analysis restricted to men having sex with men. Here again, the number of potentially infectious persons and the number of newly observed infections, you see here a rise, but it's not obvious to put this in relation with the number of potential patients.

You see a fall, but can you really be sure that the fall in the pink curve later on called a fall in the red curve. Maybe there were other influences that explained the rise and the fall.

For instance, in 2008, there was an intensive campaign aimed at MSMs in Switzerland to decrease risk behavior. It was called Mission Possible. Maybe that was one of the reasons why new infections fell in 2009, and so there are general problems with a before and after approach.

Not all evidence goes into the same direction, and if you have, in general, event B occurring after event A, it doesn't automatically follow that B happened because of A. So if HIV incidents falls after expansion of ART, it is not certain that the expansion caused the fall.

Now this sort of error has been know for more than 2,000 years, there's even a Latin saying related to it. But it is irresistible to many parts of the public, like mothers who listen to Mozart hoping that their children will be more intelligent. Or people who believe that their vaccines caused this or that event that happened afterwards.

Now it's easy to be dismissive but how to do better? We could compare two regions at the same time. In region one test and treat, in region two continue as before and measure in both regions the number of new HIV infections. That's better but not perfect. The two regions will differ in many respects—the number of type of sex partners, the use of condoms, the prevalence of circumcision, age, you name it.

But if one compared not two but 30 regions, 15 with expanded ART, 15 without and each time HIV incidents would fall

in the test and treat regions but remains the same in the control regions, that would be convincing. And that is the essential idea behind the methodology called Cluster Randomized Trial, where the unit of randomization is not the individual, but a community of individuals, for instance a village.

We have been involved for two years now, with a plan to do such a study, together with the French Agency [speaks in French]. We have identified this problem as a priority in AIDS research for the years to come, and have been looking and have found a partner in Africa to do such a study.

That partner is the Africa Center for Health and Population Studies in Labesa [misspelled?] north of Durbin, directed by Marie Louise Noelle [misspelled?]. And the group from the African, Africa Center has submitted a proposal with a very pretty Zulu title, which I won't attempt to pronounce. What is planned is a pilot phase from 2010 to 2013, with a trial phase from 2013 to 2015. It is a very large project, which will cost a lot of money, even for the pilot phase.

The current status is that ANRS is interested to fund this trial and is looking for additional partners to ease the financing. The basic plan is to screen everybody. And then have two arms. In the intervention clusters all who screen HIV positive would be treated and in the control clusters, HIV treatment would be given only with treatment indications according to local guidelines, but using the type of HAART

prescribed in the intervention clusters. Endpoints would be incidents, HIV infections, as measured by repetitive six monthly screening; there would be a lot of secondary endpoints. The most important are the acceptability and the results of widespread testing, behavioral modifications, cost and cost-effectiveness, and morbidity and mortality in the HIV positive population.

Such a trial resembles an obstacle course. And lets envisage some of the obstacles now; attrition, the question of harm versus benefit and the question of costs and sustainability. Attrition, the success of such a trial hinges on maintaining a difference between the intervention groups and the control groups. And the intervention groups "everybody should be treated," and in the control group, "nobody," but in the intervention group, not all will be tested. Of those who are tested, some will not receive their results. Of those who receive their results that are HIV positive, not all will be treated. Of those who are treated, not all will have effective treatment. Of those with effective treatment, some will stop.

Meanwhile, in the control group, some are already on ART. The proportion of those on ART is expected to increase because of hopefully expansion of access, because of the revision of indications for HIV treatment going from 200 to 350 as a result of the Haitian CIPRA Trial and of those who remain

off treatment, many will hopefully use other prevention methods, as condoms, microbicides, circumcision.

Attrition can be a terrible problem. Here's an example from an attempt to provide comprehensive prevention of mother-to-child transmission in Lusaka, Zambia. Originally, 40,000 pregnant women were to be captured in that trial but finally, only 17,000 and some were counseled. Only 12,000 were tested; 2,900 were positive. But of those, only 1,654 mothers and only 1,157 children received nevirapine prophylaxis. As to the intention to also test all the partners, it remained just that, an intention.

The second problem, harm versus benefit. Here we have to consider risks and benefits both to the individual and the community. Now there will be some health benefits. Persons in intervention clusters will probably have less HIV related diseases which will indeed be a secondary endpoint in the trial. The effect on TB could be particularly beneficial because it occurs at higher CD4 counts and there is a spillover into the HIV negative population.

But there are medical risks. Asymptomatic individuals with intact immune systems may derive little or no benefit and possible side effects from HAART. There are known medical risks that are probably even more important. Without widespread acceptance, test and treat cannot succeed. But test and treat programs must avoid undue pressure on individuals to

get tested and begin treatment. On the other hand, on the plus side, the perception that treated patients are no longer infectious may decrease stigma and discrimination.

Resources and sustainability; if treatment has a preventative effect, it will increase the pool of people potentially eligible for HAART; will increase the pressure for availability of ARV's, will increase cost in the short run. Long term sustainability and resistance is certainly an issue. So we can already foresee that operational research would have to provide years of follow-up and surveillance of infection without randomization.

So, here is the obstacle course. Here is what I hope will happen. But we have to admit this could be another outcome. Many people to which I'm indebted have provided input into this talk. They are listed here. Thank you very much. [Applause]

CARLOS PASSARELLI: Good morning ladies and gentlemen, my name is Carlos Passarelli, I'm the International Advisor of the STD/AIDS and Viral [inaudible] Department of the Minister of Health in Brazil and this morning in the session I'm speaking on behalf of Minister Jose Gomes Temporao, Minister of Health of my country.

Access to medicines is the ultimate goal of any form of [inaudible] public policy. Developing countries face growing difficulties and challenges in order to assure the access to

health as a human right, especially for new drugs. In these cases, intellectual property rights have a great impact on the high prices of medicines. The current [inaudible] system, seen as a model to enhance innovation is also the cause of high prices. Putting obstacles to access and hampering the financial sustainability of the health system.

In this regard, the management of intellectual property rights needs to be oriented toward a public health perspective. After having incorporated the elements of the [inaudible] agreement international legislations, we have not seen improvement on the innovative capacity of the pharmaceutical sector, especially in developing countries.

In Brazil, the compulsory license of [inaudible] in 2007 was a successful attempt to foster access to antiretroviral treatment considering that there is an evident relation among patents, prices and access. At international level, intellectual property, innovation and public health have become an important item within the WHO agenda.

One of the mechanisms explored by the Global Strategy on Public Health, Innovation and Intellectual Property approved in 2008 by the World Health Assembly is the patent pool [misspelled?]. Today we are going to have the opportunity to further discuss this new initiative in the field of public health. UNITAID has recently taken the first step towards this direction. As a member of its executive board, Brazil supports

the UNITAID Patent Pool and seeks to make this mechanism an opportunity to foster drug reduction in developing countries.

This initiative may allow the development of [inaudible] to improve the quality of life of people living with HIV and AIDS in the developing world. Since it's being implemented on non-inclusive and non-discriminatory basis, by stimulating technologic transfer and linking it to the objectives of the global strategy [misspelled?]. In other words, Brazil does not wish a patent pool at any price. We want a patent pool that's should assure a better balance between brand name and generic drug production. We want a patent pool that really could break the monopoly of just a few companies over innovative products. We want a patent pool that instead of such fine commercial interests show effective address to therapeutic needs of AIDS patients in the developing worlds.

Having said so, I have the pleasure and the honor to introduce Mrs. Ellen 't Hoen. She's Senior Advisor for Intellectual Property and Medicines Patent Pool with UNITAID. Ellen is a lawyer and an expert in medicines policies intellectual property law. From 1999 to 2009 she was a Director of Policy and Advocacy at the [inaudible] campaign for access to essential medicines. She is the author of the book *The Global Politics of Pharmaceutical Monopoly Power - Drug Patents, Access, Innovation and the Application of the WHO*

Declaration on TRIPS and Public Health published in January of 2009. Mrs.'t Hoen, you have the floor. [Applause]

ELLEN 'T HOEN: And now I'm bigger. Good morning. Thank you very much for this introduction. It is very exciting to be here. Ten years ago when the world prepared to gather in Durbin, South Africa for the first international AIDS conference to be held on the continent devastated by this disease, the statistics were very grim. I seem to be falling off the stage already. Let me fix this. Better? [Applause]

However, no laughing matter at the time, only one in 1,000 African people who could get good access to AIDS treatment. The drugs were not available; they were only available from originator companies and they came with a paralyzing price tag of around $10,000 to $15,000 per patient per year.

It is through an immense mobilization of people living with AIDS, their organizations, courageous medical leaders, dedicated ministries of health, donor governments and industries that we have achieved today what most delegates in Durbin thought was impossible.

Access to ARV treatment to 4 million people in the developing world. This achievement has had a number of key ingredients. First of all, the AIDS treatment movement put AIDS crisis on the political agenda alongside medical professionals who were willing to take risks. Increased funding

became available for AIDS treatment because of that and the availability of low cost medicines and its wide availability has been absolutely key.

Why these achievements are enormously important? There are huge challenges ahead of us. The last 10 years have shown how through AIDS treatment/HIV treatment we can have a tremendous impact on reducing illness and death in developing countries. But in the current climate of wavering support for achieving universal access to treatment, a promise that is only five years old, we must look ahead and see how we can have even greater impact. To make sure that people who receive treatment today can continue to receive so and to treat the millions of people that are still waiting.

The latest WHO treatment guidelines recommend that people should start treatment earlier before they become ill and weak. This is a critical step towards bringing treatment for people in developing countries in line with treatment standards practiced in wealthy nations and is expected, as we have heard, to help potentially with the prevention of the transmission of the virus. This also means that of course many more people are currently in need of receiving treatment.

Today I have been asked by the International AIDS Society, and I would like to thank them for having done so, to address the particular issue of intellectual property, how patents and access to medicines are related. I will look today

at what we have learned over the last 10 years and what we should do to make sure that change continues for the future.

I don't think it's an exaggeration to say that the AIDS crisis and all its actors have caused a radical change in the approach to intellectual property in the field of medicines. This is reflected in changes in law, but also reflected in changes in policies including policies of some pharmaceutical companies. This history starts in 1996 when a small group of NGOs met in Bielefeld, Germany which is a small sleepy town which was made famous by John le Carre's book *The Constant Gardener*. They discussed access to medicines and the WTO GATT agreement. In those days that was a very rare event.

The World Trade Organization's TRIPS Agreement are only just coming to force. The TRIPS Agreement, a 500 word annex to the World Trade Organization's rule book, which overall is designed to encourage trade amongst its members, sets out minimum standards for intellectual property protection for all the members of the WTO. When the negotiations leading to this agreement took place, those were primarily driven by trade concerns and commercial concerns by powerful nations.

Public health was not their focus, and civil society organizations and certainly public health organizations did not take part in the process. These new World Trade Organization rules globalized intellectual property standards that were very much the norm in some wealthy industrialized countries. They

were made enforceable, obligatory and enforceable through this system.

Before the TRIPS Agreement came into force, the patent practices of countries was very diverse; it was very different. Some countries took the view that patenting medicines or food for that matter was really not in the public interest and they did not do so. That was the case also amongst a number of European countries, but the ambient countries, for example, explicitly excluded essential medicines from patentability.

Now the World Trade Organization's rules put a stop to that because it harmonized their requirements and introduced, in the field of medicines for example, the requirement to provide patents with a term for at least 20 years. So the policy states that countries used to have was rapidly shrinking.

The potential of this, in the late '90s was really not known and it was very little understood what those consequences would be for public health, or could be for access to medicines and certainly an understanding within the public health community was very, very rare. A couple of things changed that. In 1998, 39 drug companies and their representative organizations took the South African government to court over the amendments to its medicine [inaudible]. Those amendments were designed to help increase access to medicines and accelerate the availability of low cost medicines.

This legal action was taken against the backdrop of the growing AIDS treatment crisis in the developing world and in particular in South Africa where you all know the situation was very, very severe. This was also done against a backdrop of increasing HAART becoming available in western countries and increasingly knowledge was spreading about the positive effects of these treatments.

Big pharma versus Nelson Mandela, as this case became known, provided a shock therapy to the public health community and it was a call to action that pulled many different actors onto the stage. In 1999, at the United Nations in Geneva, a group of non-governmental organizations and AIDS activists met to discuss compulsory licensing of AIDS drugs. Now someone who read this speech a few days ago said to me, why would you mention that? What's the news in that? This happens all the time. Well, I assure you, in ’99, this was quite something. People concerned about public health, AIDS, people living with AIDS and their medical treaters met to discuss compulsory licensing. That caused quite a bit of concern in particular amongst those that actually held the patents of this drug.

The Thailand and Brazil, which were the first developing countries with AIDS treatment programs had embraced the notion of universal access, heavily relied, at the time, on the ability to produce low cost medicines, often in government

facilities and through that they illustrated the enormous cost reductions that could be achieved.

But, both countries experienced pressures from wealthier nations that were concerned had the strategies to expand alternative sources of low cost medicines could be detrimental to their industries. Now, this growing discontent culminated at the World Trade Organization's Ministerial Conference in Seattle in ’99 with a call to humanize the trade agreements which was at the time the rallying call of the NGOs that went to Seattle to discuss these matters. In Seattle, a strong coalition of NGOs in developing countries was forming.

Some soothing statements were made at the time, which was a good sign because it meant that political leaders were starting to look at these issues and starting to take these issues seriously but it was still quite far from any fundamental change. At the time, the editor of *Pharmaceutical Executive Journal* read by the industry commented, “Unlikely as it seems, the pharmaceutical industry may have reason to thank the demonstrators who brought Seattle and the ministerial meeting of the WTO to a standstill. Had the demonstrators not disrupted the gathering, the forecast for global pharma might be much cloudier.”

But, those that thought that the collapse of the WTO talks in Seattle would mute the demands for more fundamental change were wrong. The periods between the Seattle ministerial

and this ministerial conference in Doha saw a number of developments that have been absolutely crucial for the change in the IP environment.

Both Brazil and Thailand began to experience consequences of pharmaceutical patents on AIDS drugs, which both countries had already introduced and they significantly limited their ability to continue to produce at much lower cost.

In May 2000, five pharmaceutical companies announced their accelerating access initiative together with a number of other organizations aimed at improving access to more affordable HIV medicines and diagnostics for developing countries. However, the voluntary price discounts offered through this initiative, paled in comparison to the prices that were becoming available from low cost generic producers that could produce these medicines in countries not yet hampered by patents.

This, for example, brought us the drug triomune, the first fixed-dose combination very widely used in the developing world and which helped to scale up access to those treatments tremendously. Now, the generic production in India has been absolutely key for the scale up to treatment in this epidemic. This production is possible in India because of the Indian patent tax of 1970 which did not recognize the granting of

pharmaceutical product patents. India did not do that until it had to in 2005.

In 2001, when one Indian producer offered a triple AIDS treatment for $350 per patient per year to non-governmental organizations, it really showed to the world what actually could be done. It also hammered the message home that the prices that were charged by those who had a monopoly position were really, really much too high. But it also showed that something could be done about it. India quickly became the AIDS pharmacy of the developing world.

The same year, a controversy broke out over the cost of the drug Stavudine D14. That came to a head at the Yale University campus. This product was actually developed by researchers at the Yale University and students and researchers demanded that the license that Yale had with the company would be changed so that developing countries could access generic versions of this medicine. At the time, the brand product produced under license from Yale was 35 times the price of the generic product. This action actually sparked a very vibrant movement in the United States for more humanitarian licensing practices which is very much alive today.

In 2000, the GA paid unprecedented attention to health and the need to take action in the area of increased access to medicines. It outlined an agenda for the prevention and the treatment of AIDS to enhance research and development for

international public goods and it included a recommendation to new approaches to managing intellectual property; perhaps most importantly Okinawa Summit was the birthplace of the Global Fund.

When in April 2001 after a global and domestic public outcry under the very, very fierce leadership of the South African Treatment action campaign, the 39 drug companies dropped their case against the South African Government. The landscape had dramatically changed. Access to medicines and the need to revisit the patent rules and practices that governed them had become part of a much larger political agenda and was no longer the exclusive domain of trade negotiators. So when in November 2001, governments at the World Trade Organization Ministerial conference met in Doha, they had an entirely different agenda. They adopted the Doha declaration on TRIPS and public health. This declaration has been absolutely important. One of the key paragraphs of that declaration states that the TRIPS Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and in particular to promote access to medicines for all. Not access to medicines for a few; access to medicines for all.

This represented the first significant pushback to the relentless march to strengthen private IP rights without regard to the societal consequences of that in the developing world.

Subsequently in 2003 the WTO adopted the so-called August 30 decision which was an attempt to find a remedy for legal barriers to exporting sufficient amounts of medicines to produce under a compulsory license and to ensure that countries that rely on the import for their medicine supply and those are most countries in the developing world, could benefit from compulsory licenses and from the production of medicines under a compulsory license elsewhere.

While this solution that was adopted is deeply flawed and in my view needs revision, it was the first amendment to not only the TRIPS agreement, but the first amendment ever to any of the WTO text. What is exciting about it is that it was public health considerations and especially the AIDS crisis that moved this.

On the first of December 2003, WHO together with UNAIDS declared the lack of HIV/AIDS treatment to be a global public health emergency and announced the very ambitious Three-by-Five campaign. The Doha declaration on TRIPS and public health has been essential in making low-cost medicines available on a large scale. While the compulsory licenses in certain countries such as Thailand and Brazil, later Ecuador have been widely publicized, it is actually little known that low and middle income countries have enabled procurement of low-cost medicines on a large scale.

In using the flexibilities contained in the Doha declaration, 16 low and middle income developing countries have used compulsory licenses or government use licenses on a routine basis in their procurement practices and 28 out of the 32 least developed World Trade Organization members authorized importation of generic ARV's with a reference to the Doha declaration on TRIPS and Public health, which granted them the right to delay the granting or enforcing of product patents until 2016.

When India became compliant with TRIPS in 2005, it incorporated a number of important public health safeguards in its patent sect [misspelled?] including strict patentability criteria and the possibility for anyone to oppose the granting of those patents. People living with AIDS, together with the Indian Lawyers Collective have very effectively made use of those provisions and opposed patents on AIDS medicines that did not fulfill the patentability criteria India had adopted.

We have also seen companies responding to the challenges to their patents. We've also seen them responding through the granting of voluntary licenses through their patents often as a response to legal pressure or public pressure by organizations of people living with AIDS and we've, for example, learned about the case in South Africa where people living with AIDS successfully filed complaints with the Competition Commission.

The AIDS crisis has been an engine for change, not only for the thinking about IP and health, also in the way healthcare is delivered, for example, through task shifting. Treatment literacy, which empowered people living with AIDS and made them central to their own treatments versus systems-driven treatment; increased political attention for health well beyond AIDS; the roll of civil society and decision making and global health, the establishment of access strategies by pharmaceutical industries; the establishment of the World Health Organization's prequalification program which has helped create the market for low-cost medicines and it brought about new financing mechanisms such as the Global Fund, PEPFAR, UNITAID—the organization that I work for—whose beneficiaries go beyond AIDS. It's also currently fueling the campaign for the Robin Hood Tax.

Market competition for the early generation ARV's resulted in price per patients per year dropping by 99-percent over the past decade. The medicines that paralyzed us 10 years ago by the cost of $10,000 per patient per year, today cost $67.

So, what is the problem? Well, first of all, the cost of treatment is increasing. It is increasing again because AIDS medicines are likely to be patented in developing countries where they previously would not have been, including in India. Without production sources, the countries that rely

on the importation will find it hard to find sources of low cost medicines. New fixed-dose combinations will not automatically, without a deliberate intervention be developed because of patents on the individual compounds.

Second, increasing numbers of people will need access to new generation treatments. These treatments in general are more widely patented and they are more expensive. We will also need to expand access to first line medicines to people that do not benefit from those treatments today. We have heard this week about the access crisis in a number of countries where people are waiting, including countries in Eastern Europe.

The current licensing practices of companies, while laudable, are still too scattered and sometimes come with limitations that hamper the full effect of generic competition and the ability to develop, for example, the fixed-dose combinations with the key components.

Also, it is important that we can respond to the new knowledge and the emerging evidence. New treatment recommendations and strategies to discuss here this week require large scale availability of low-cost treatments. For example, the need to replace all the treatments that have significant side effects with newer, better tolerated treatments. But, the cost of doing so might be a barrier to making full use of this new knowledge.

We're faced with a serious financial crisis that risks setting back treatment achievements of the last 10 years. The UK All Party Parliamentary group on AIDS called this situation the treatment time bomb and it called for political activism. We need to go further than where we are today. We need to expand the use of existing flexibilities. We need to fix them where they don't work, but we also need to develop and put in place new models. And when I use the word model, I obviously hope this is a model that will work.

Without generic competition, prices for newer drugs will not come down to the same level as they did before. UNITAID is committed to making that happen. UNITAID is a new financing mechanism which is based on a small solidarity levy on the sales of airlines tickets, implemented by its participating countries.

Today, 29 countries, the Bill and Melinda Gates Foundation, NGOs, and community organizations take part in UNITAID. And our mission is to increase access to treatments for AIDS, TB, and malaria. UNITAID is innovative in the way it raises its money, but it is also innovative in the way it spends its money, because our objective is to, through our spending, influence the market dynamics in such a way that it leads to sustainable benefits in the area of access to treatments for all.

Together, with our implementing partner for example, the Clinton Access Initiative, we have helped to create the market for pediatric AIDS medicines. We have stimulated the development of new second-line antiretroviral formulations. We also support the World Health Organization's pre-qualification program, which has helped create the market for those medicines.

UNITAIDS's overarching principle is to help markets work for health and that is also the explanation why UNITAID could be the birthplace to the medicines patent pool that will go live in the weeks to come. Now the idea of the AIDS medicines patent pool was actually born at one of the AIDS conferences at the 2002, Barcelona Conference, where Jamie Love from Knowledge Ecology International, who has studied U.S. airplane pattern pools, which were established in 1917 by the U.S. government to overcome patent barriers, suggested why don’t we do something similar for AIDS drug patents.

Now, a number of people have taken that idea, all in developed further plans, have taken that plan to UNITAID, which took it on in 2007. Now how will this work? The idea is that we persuade the pharmaceutical companies and other patent owners because those are not always pharmaceutical companies, to make through the patent pool licenses to their ARV patents available.

Those licenses will be made available to others. For example, generic manufacturers or non-for profit drug development initiatives, to bring lower cost or better adapted medicines to the market. In exchange for the use of that intellectual property, those companies will pay royalties over the sales of those products.

So there is something in it for everyone and if this works, if we manage to get this off the ground, we will be able to solve many, many problems. A key feature of this proposal is that it is a voluntary patent pool and that it will require the will of key players to make this happen.

That also means that it will require the support for many, certainly all of you here in the room, to make this come about. We have some good news. We have had a number of interactions with key companies that have shown a keen interest, that see the potential of this proposal. We have also met with some that have let us know that they think that they already do enough.

I do not share that view, but I think that is not a secret. One warning, sorting out intellectual property difficulties cannot be a proxy for financing. They have to go hand in hand. Without an assured market for even the lowest cost medicines, we cannot expect that anyone will step up to the plate and develop and produce and bring these medicines to market.

So efficient funding for AIDS is absolutely crucial to protect and to make the desperate progress that we need to make, to fight for access to medicines has been and will be a continuous fight, sometimes an uphill battle and not always easy to win, but I believe that the lessons of the past 10 years have shown what we can achieve if we mobilize together.

We are at a crucial point in time and we cannot slip back. I have a very, very vivid memory of a session at the Barcelona conference where I was sitting next to friends from Malawi. Fred was a village farmer, who for the first time in his life had left his village to come to the AIDS conference in Barcelona. Fred was and is, I'm happy to say, living with AIDS. We were listening to a presentation by an economist on the cost effectiveness of ARV treatment. It had lots of graphs, it was very complicated, I could barely follow it.

At some point, Fred leaned over to me and he said, “Are these people saying it costs too much to keep me alive?” And I'll never forget that moment because that is exactly what was being said. And I would like to be able to say luckily, those days are over, never to return.

Cost considerations simply cannot be a grounds [applause] for withholding life-saving treatments for people. Access to treatment is a fundamental human right. This puts the obligation on all of us to do all we can to make sure that it happens right here, right now. Thank you. [Applause]

BETTY KING: Good morning. I am Betty King. I am the United States Ambassador to the United Nations Organizations in Geneva. And given that I spend most of my time on intellectual property issues, I am sorely tempted to follow-up on the previous presentation, but I'll stick to my narrowly defined task, which is to introduce the third speaker in this morning's panel, James Hakim.

James Hakim is a Professor of Medicine at the University of Zimbabwe College of Health Sciences where he is Director of the University of Zimbabwe Clinical Research Center. Dr. Hakim graduated from Makerere University Medical School in Uganda and then specialized in internal medicine at the University of Nairobi, Kenya, and the Royal Colleges of Physicians in the United Kingdom.

He later received training as a clinical epidemiologist with the University of New Castle in Australia. And of particular relevance to this presentation, Dr. Hakim was a member of the panel that worked on the 2010 WHO Adult and Adolescent ART Guidelines. It is my pleasure to introduce Dr. Hakim to you. Thank you. [Applause]

JAMES HAKIM: Thank you, Ambassador King, for that very kind introduction and it’s my pleasure in the next 20 minutes or so, I'll share some thoughts on antiretroviral therapy advances into the next decade.

I have organized my talk around three points. Initially, I'll give you some idea of some historical perspectives and I'll proceed to do current stages ART and we'll go on to talk about ART in the next decade.

There are some very important historical milestones which we cannot escape from. The Vancouver conference stands in my mind because I attended it as well, as an exceedingly important milestone in antiretroviral therapy. This is when antiretroviral therapy was baptized as the most important intervention in addressing AIDS.

Dorbin again stands as a very important milestone and you heard from the previous speakers how Dorbin stands as a very important point when antiretroviral therapy became a right and it was something that was considered possible for the resource limited setting.

Barcelona similarly was important because this is when WHO announced three by five. Even though three by five was not achieved by 2005, it took on up to 2007, but that was an important rally call for treating more people with antiretroviral drugs.

The question of financing, the question of policies, the question of setting the correct stage cannot be escaped. And all these players were really important in bringing about the current status of antiretroviral therapy. So apart from these big players, let's not forget that national governments,

NGOs, and a variety of other groups have played a critical role in bringing about the possibility of treating large numbers of people.

When or shall I say what is the next milestone? Universal access—is it in 2010 or will it be later? That's an important point and that really brings to mind the theme of this conference. The status of antiretroviral therapy by the end of 2009, we know that more than five million people living with HIV are on antiretroviral therapy. And most of these are in that brown part of the graph in middle and lower-income countries, and especially in Sub-Saharan Africa that we know that infection still outstrips treatment by five to two.

And there are five million more people according to the old WHO guidelines and country guidelines who still require to be on treatment. However, with the 2010 guidelines, even more people require treatment and that is alright.

Achievements of antiretroviral therapy—this is quite familiar to all of you—improvement in survival, decrease in opportunistic infections, and improvement in the quality of life, but if we take this picture which was published in the *New England Journal of Medicine* in 2006 from Haiti, it really brings home what antiretroviral therapy can do, the before and after picture of an individual who was destined for the grave, but with antiretroviral therapy was healthy and was able to hold a baby once again.

I'll run through some data just to show you the differences in the outcomes of the use of antiretroviral therapy between resource rich and resource poor countries. This is an old publication, but it captures what I would like to share with you. Mortality in patients who were on antiretroviral therapy from resource limited countries is extremely high. And you can see from the bottom of the slide here that in the first six months, mortality compared to that in patients on antiretroviral therapy in the developing world is up to more than four times higher.

And in the next six months, still one and one half times. Now, another important observation of course is that, in the resource rich countries, meanwhile, patients on antiretroviral therapy still die of AIDS events. An important consideration now is non-AIDS events and I'll touch on this a little more later in my presentation.

Whilst mortality in the resource limited sectors is brought to you clearly by these publications from the very prolific African groups researching in antiretroviral therapy and other issues related to AIDS, and we can see that the mortality initially observed after starting antiretroviral therapy is dependent upon a number of factors including factors pre-ART, during ART itself, and the endemic conditions that exist and I've just tabulated the most important TB, acute sepsis, crypto malignancy like [inaudible] sarcoma, PCP, and

many others. And in the other study Sylvia Huang [misspelled?] has very clearly shown that time spent with a low CD4 count below 200 has a very important impact on mortality.

What are other achievements of antiretroviral therapy? Decrease in the prevalence of tuberculosis and there's a potential in improvement in maternal and child mortality, as if one reads the publication by Hogan and colleagues. And there is improvement in school attendance and work force. Work done in Kenya by [inaudible] and as you heard from Herschel's presentation, that there are ecological and other evidences that HIV transmission could be impacted. Tuberculosis, the study in South Africa by a [inaudible] and others which was presented in Cape Town and later on published in the *American Journal of Respiratory and Critical Care* this year, shows that at a survey done in 2005, the prevalence of HIV in all groups, including HIV negative individuals was 3.2-percent.

But another survey done in the same area in 2008 showed that this has dropped to 1.6-percent. And the impact was greatest in those who were HIV positive with 9.2-percent in 2005 and 3.6-percent in 2008.

Why else? If you look on the right side, the study, the CIPRA study published in the *New England Journal of Medicine* by Patrice, Sylvia, and others showed clearly that starting antiretroviral therapy early resulted in only 18 cases

of tuberculosis, while those who are delayed resulted in 36. Clearly there was a significant difference in the two.

The WHO has led the fight or indeed the expansion of antiretroviral therapy in the developing world through a number of ways, but much more importantly, through the development of guidelines.

We're all familiar with the development of these guidelines from 2002 right until 2006 and now of course, we have the 2010 WHO guidelines, which importantly now bring in line treatment in the developing world with treatment in the developed world in certain critical areas.

There are other areas, of course, which we need to address. And probably the most prominent aspect of the guidelines is really the CD4 threshold for starting antiretroviral therapy. And this has again been shown by Patrice Severe and group in their study that in those who started antiretroviral therapy early, deaths were six and in those who delayed treatment, there were 23 deaths and this was clearly statistically significant.

And there are many other publications, cohort analysis that clearly demonstrate that there is an advantage to starting antiretroviral therapy early. And I've just shown the [inaudible] study which has also impacted the U.S. guidelines.

And this is just a quick summary of the threshold of different guidelines and as you can see at the bottom, the WHO

2006 guidelines stood out alone as recommending a threshold of 200, but clearly now with the 2010 guidelines, we have moved to 350.

So to start earlier is the right thing to do. Harmonize treatment guidelines, and that's what the WHO 2010 guidelines are really there to do. And importantly, the WHO guidelines stress that one should seek and treat patients earlier, not just wait for them passively.

The public health approach is a critical delivery system of antiretroviral therapy in the developing world. The DART [misspelled?] study which looked at routine, aggressive clinical driven monitoring is an important study in that regard. The CIPRA South Africa study which compared nurse versus doctor management of antiretroviral therapy and the gender [misspelled?] Uganda study which looked at antiretroviral therapy delivered either in a health facility or in the home. Those are important delivery systems that can be used in resource limited settings.

And this very dramatic picture from the DART studies shows you if you look at the lower part here, this is just a historical cohort in [inaudible] in individuals who were observed over five years before antiretroviral therapy. And you can see after five years survival is only 8-percent.

In the DART study, which compared clinically monitored versus laboratory monitored individuals, those who are in the

laboratory monitored arm, there was 90-percent survival at the end of five years and without intense laboratory monitoring, you still got 87-percent survival at the end of five years.

I talked about lay workers assisting in the monitoring of antiretroviral therapy and this study in gender [misspelled?] showed that really home-based care is as effective as facility-based care. And the South African CIPRA study, which was published in *The Lancet* a few weeks ago, nurse-monitored versus doctor-monitored therapy and they showed that nurse versus doctor-monitored therapy is not inferior.

So, these are delivery mechanisms which we can use for antiretroviral therapy. I've just put this here to capture the six classes of antiretroviral drugs. You may find that I have missed your favorite antiretroviral drug. But it's important to appreciate that not all those drugs are available for deployment in resource limited settings.

And indeed the guidelines attempt to organize this into a standardized and simplified form so that we can use the delivery mechanisms which I've described in a way that we can yield the kind of positive results that you have heard me describe. And the first line of antiretroviral therapy does need to be available to the majority of patients. And indeed in the 2010 guidelines, there's been an attempt to harmonize this to ensure these drugs are available to pregnant women, are

available to those with TB, available to those with hepatitis, and so on and so forth.

And again, sequencing the drugs in such a way that it becomes easy for people down the health delivery line to be able to follow. So there's an NNRTI regimen, as an initial regimen and when failure occurs, people move into a boosted PI, this becomes easy to train people in and to be able to implement in a programatic setting.

The difficulty here of course is how do you diagnose failure? As [inaudible] and many others, many other publications which I have not put here, have shown that using only clinical or clinical plus epidemiological [misspelled?] monitoring, there is poor specificity and sensitivity of diagnosing failure. Now, in a public health approach, how would one go around this? There is indeed a need for studies that would provide a way of being able to approach deployment of second line therapy in this kind of scenario.

And there is a study, the ERNA [misspelled?] study sponsored by ADCTP, which is currently enrolling in Zimbabwe, Malawi, and Uganda, which attempts to use either a new class of drugs or drugs that the patient has certainly not been exposed to without having to go the route of doing resistance testing or indeed having to do expensive tests to prove failure repeatedly.

There is similarly as NCTG study and there is another study led by Derek Cooper and others which is also looking into this. What about the place of purchasing inhibitor [misspelled?] therapy? A lot has been talked about this and this is certainly on the table and needs to be considered.

And the question of third line antiretroviral therapy. In the 2006 guidelines, this was mentioned, but it was mentioned in a very cursory sense. In the 2010 guidelines, this has been mentioned in a much more definitive way, although there is still a statement to the effect that each country needs to develop a way of ensuring that this is available to its citizens. If we're going to give second-line antiretroviral therapy, there is no doubt if it will fail and they will need to go into salvage regime, and so the third-line therapy is an important consideration that must now come into our minds as more and more people go to antiretroviral therapy and will begin to fail first-line therapy.

The question of resistance is obviously essential to this. Monitoring is a big issue in antiretroviral therapy, especially monitoring for efficacy. We've shown, as I described earlier on in the DART study, that you can't give antiretroviral therapy with simply clinical monitoring and doing tests as when required. But as I've also described, clearly you cannot be certain about the viability of your second-line option if you do not have a way of confirming

whether the patient is simply non-adherent or the patient has truly failed.

So, biological monitoring becomes an issue and its important and we know the reasons why biological monitoring is not being done in the developing world, the issues of cost and other logistics is very well known to this audience.

Monitoring for toxicity, this is a routine type of monitoring in the developed world, but in DART we clearly showed this was not cost effective. One has to deploy this in a directed manner and not repeatedly just do CBC and other tests.

But having said that, it is important to appreciate that there are certain drugs which do have specific toxicities and you do need to be on the lookout and you do need to be able to test for those kinds of toxicities. So it becomes important. So laboratories are indeed very important and there are other tests. If you want to use the full range of drugs that I've mentioned earlier on, obviously a question of being able to do troponin tests or doing HLA-B5701 for a [inaudible] and other tests may come on the scene to guide deployment of a variety of antiretroviral drugs.

Into the next decade, the pipeline for new drugs, as you know, many years ago there have been many drugs that have been put into the pipeline. The pace appears to have diminished and we think that this pace needs to be accelerated.

Current drugs are efficacious, yes, and have a good safety and tolerance. But there is still need for drugs that are more efficacious, better tolerated so that there is better adherence, more safe so that there's less monitoring, more forgiving so that there is less resistance, compatible with TB, pregnancy, hepatitis, malaria, and all the other endemic conditions that exist in places that are highly impacted by the HIV epidemic. In other words, Treatment 2.0.

Again, into the next decade, we know that these organs and more are more affected by either HIV or indeed, antiretroviral drugs. And I've just quoted a few seminal studies, the SMART study and the DAD analysis, but there are many other studies that will bring this to the fold. So, non-AIDS outcomes whether due to unmitigated HIV replication or due to antiretroviral therapy is important, but we know that there’s very limited data from resource limited setting and more research into this area is required.

I've talked about laboratory monitoring, how do we make this available? How do we make this useful to the majority of patients in the developing world who are on antiretroviral therapy? We need to definitely accelerate the roll-out of point of care technology and make this available for those tests where there is still no available instrumentation at the moment.

HIV eradication, we all heard the very eloquent presentation by Tony Fauci. And HIV eradication is definitely something that will never leave the table. A vaccine is an important immediate step, but the eradication and cure of HIV remains the only victory that we can celebrate. The science and strategy required to achieve this is of the highest priority and I've simply quoted some studies that have looked at ways of HIV eradication and HIV cure in different ways.

In conclusion, Madame Chair, ladies and gentlemen, the last decade has seen a momentous expansion of antiretroviral therapy in low and middle-income countries. We continue to see the benefits of antiretroviral therapy and improved survival, reduction in disease progression, and improved quality of life. Antiretroviral therapy impacts non-AIDS conditions in both negative and positive ways. This must continue to be a focus of research.

Into the next decade, a quest for efficacious, tolerated, safer, and more forgiving antiviral drugs must continue, better delivery modes of ART are needed to improve access to all. Preventive value of antiretroviral therapy has come of age, we know from PMTCP that prevention works and we have other evidences that prevention is certainly something to pursue. We really need to push this much further.

An HIV cure remains the ultimate prize in the response to AIDS. There are many I would like to thank who have helped

me in preparing this discussion and on top really Dan Havener [misspelled?] who has been very instrumental in guiding a lot of the points that I have shared with you. Michaela Clayton from Russia has also been very helpful. Mike [inaudible] and the rest of my team from the University of Zimbabwe have contributed in various ways in educating me about HIV and enabling me to share this with you. [Speaking in a foreign language] Tom Campbell from the University of Denver, Mark Vittorio [misspelled?] from the WHO, and there are many from whom I have borrowed slides but have asked for comments and they have not been found wanting. Finally, to you all I thank you for your attention. [Applause]

[END RECORDING]