PLHIV Input into the Revision of the WHO ART Guidelines

Final Report of GNP+ Consultations:

Technical consultation at IAS 2009, Cape Town
Technical consultation at ICAAP 2009, Bali
E-consultation

Global Network of People Living with HIV (GNP+)

August 2009

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Executive Summary

> ***"The WHO ART Guidelines have direct impact on the lives of people with HIV and on the care we will be receiving in our countries… The guidelines are critically important to us because our countries use it as a gold standard. They treat whatever WHO puts into the guidelines like it is engraved in stone."***
>
> *Vuyiseka Dubula, South Africa's Treatment Action Campaign (TAC)*

This report presents the key points and recommendations that emerged during two technical consultations with people living with HIV (PLHIV) at the IAS 2009 and ICAAP 2009 conferences and an e-consultation on the forthcoming revision of the WHO's *Recommendations for Antiretroviral Therapy (ART) for HIV Infection in Adults and Adolescents* (ART Guidelines).

The consultations represented the start of a unique consultative process between WHO and communities of PLHIV to understand what PLHIV want from their treatment programmes, and what will and will not be acceptable to include in the next ART guidelines revision.

Consultation participants agreed that many of their lives could be directly impacted by the revised ART Guidelines. However, they also noted that in many of their countries actual clinical practice was rarely up to the standards recommended by the ART Guidelines — including the treatment they themselves had received. They highlighted the role of PLHIV activism, with the ART guidelines as an advocacy tool, in ensuring that governments and funders see the long-term cost-effectiveness of starting treatment earlier and with better drugs.

Consultation participants recommend that the ART Guidelines should be based on the best, current scientific knowledge, focusing on a standard of care that all countries should strive to achieve. In addition, the ART Guidelines should recommend that treatment is initiated when CD4 cell counts fall below 350. However, individuals must be able to make their own decisions about when to start and change treatment based on accurate information about treatment options, side-effects, drug resistance and co-infections. Furthermore, the WHO guidelines should no longer recommend d4T and recommend tenofovir in its place. Finally, PLHIV should have access to regular CD4 counts and periodic viral load tests (at least to confirm treatment failure before switching to second line). The role for resistance testing needs to be assessed in resource constrained settings.

Methodology

GNP+ held two technical consultations and one e-consultation. The consultations sought to gather rich, meaningful input from PLHIV about what they want from their treatment programmes based on experience and expertise on ART. As such, the report presents qualitative information, highlighting in-depth evidence and perspectives of PLHIV.

Technical consultations

Face-to-Face

GNP+ partnered with the Treatment Action Campaign to hold a technical consultation on 20 July 2009 during the International AIDS Society Conference (IAS) in Cape Town. There were 30 participants (65% women, 35% men) representing 13 countries. The mean age of participants was 40 years.

GNP+ partnered with the Asia Pacific Network of People Living with HIV (APN+) to hold a technical consultation on 12 August 2009 during the International Congress on AIDS in Asia Pacific (ICAAP). There were 23 participants (26% women, 74% men) representing 8 countries. The mean age of participants was 39 years.

The questions employed at the technical consultations were developed and reviewed by GNP+ and its partners, including WHO. Partnering with regional organisations enabled GNP+ to ensure that questions were adapted to the regional context. The set of questions guiding the discussions are available in Appendix 3.

The technical consultations were facilitated by people living with HIV. The meeting reports were reviewed by partner organisations.

Full copies of the reports are available in Appendix 4 and 5.

E-consultation

GNP+ held an e-consultation over three weeks (27 July – 16 August 2009), which was hosted by NAM. A total of 317 advocates and activists living with HIV were invited to participate via email (300 were invited and 17 requested participation). 40% of invitees registered, of whom 52% posted comments. Participants were PLHIV who had attended previous GNP+ consultations: HIV+ Monaco, 2007; LIVING 2008, Mexico City; the International Technical Consultation on Positive Prevention, Tunis, 2009; IAS 2009, Cape Town; as well as partners from other GNP+ programmes. Participants came from 36 countries representing all six WHO regions: Americas (13 countries), Africa (9), Western Pacific (5), Europe (4), Eastern Mediterranean (3), and South-East Asia (2).

Following initial invitations, participants received weekly emails inviting them to share their experiences and opinions on specific topic areas. All six emails included the link to the e-consultation website (http://www.aidsmap.com/gnp+) as well as a personal password linked to the individual's email address.

The e-consultation was conducted in English and moderated by a GNP+ consultant living with HIV. Participants from Algeria, Bolivia, Morocco and Peru posted in their native tongue, namely French or Spanish: the moderator provided a rough English translation following their post. Several participants contributed via email: the moderator posted their comments on their behalf.

The moderator regularly monitored the discussions to ensure that the posts were applicable to the subject; to answer any specific questions; and to suggest further areas of discussion within each question.

The full report of the e-consultation is available in Appendix 6.

Limitations

The timing was a challenge as undertaking the consultations involved a series of activities: developing partnerships, designing context-specific questions, promoting the activities and conducting the consultations.

One limitation was the number of people reached through the technical consultations. As we chose qualitative data collection, this limited our numbers.

In order to ensure a continuous and in-depth dialogue amongst e-consultation participants, it was important that the e-consultation was moderated. This required a significant time investment.

Due to time restrictions, translation of the text and postings for the e-consultation was not feasible.

Key findings

Below are key findings, which emerged from the technical consultations and the e-consultation.

When to start and change treatment

Participants asserted that PLHIV globally should have the right to go onto treatment when CD4 cell counts are in the range of 350 cells/mm^3 — in light of recent data showing that treatment at this point improves survival and decreased progression to AIDS and TB. While treatment is still beneficial even when started later, waiting until CD4 cell counts fall below 200 represents an unacceptable risk.

> "Too late is of course a CD4 count of below 200 or after the first opportunistic infection occurred, and too early is when one is not prepared to start. It is not a clinical criterion. But there is a very strong link between the preparedness of an individual and his or her capacity to be 100 percent adherent." (Participant, IAS Cape Town)

In the absence of data showing that earlier treatment is better, there were very real concerns about the toxicity of ART, and whether initiating treatment too soon could limit future treatment options.

> "Many ask, how could I take drugs for the rest of my life. And when you are being prepared that these drugs has some side-effects i.e. vomiting, skin rashes, night mares and so forth, it creates fear. In addition, many of us come from countries without resources and are very poor — many are afraid to go onto treatment when they don't have enough to eat." (Participant from Uganda, IAS Cape Town)

At ICAAP Bali, participants raised concerns about side-effects from ART, which included putting on weight or not being able to put on weight, skin getting darker, anaemia, low blood pressure, osteoporosis, and bad dreams. They also raised concerns about developing drug resistance in settings where there are limited second-line options, including the recurrent problem of drug stockouts.

Ultimately, regardless of what CD4 threshold the ART Guidelines recommends, the decision to go onto treatment is a personal choice, which depends on an individual's decisions to start treatment or not based on relevant, comprehensive and accurate information. Unless PLHIV also have a life-threatening opportunistic infection, they should not be pressured to start ART before they are prepared for it.

"Before asking PLHIV to start their treatment, we should give them awareness and information on the effect of ARVs. Otherwise taking ARVs without willingness from ourselves will be nothing, because ART is long-term, and adherence will be the most important factor for successful ARV treatment." (Participant from Indonesia, E-consultation)

Recommended drugs for first- and second-line therapy

Participants recommended that d4T is discouraged on account of its toxicity profile.

> "In our context in South Africa, d4T is definitely *not* an option for women — it may not really be an option for anyone at all. Toxicity is present in increasing numbers of women - both lipodystrophy and lactic acidosis - amongst women who started on d4T." (IAS Cape Town)

Participants also recommended that tenofovir is made available as part of first-line ART — and the price must be reduced so that it becomes affordable for public health systems. Many felt that if tenofovir were made part of first line regimens, there would be increased pressure to increase generic production and lower its price.

> "Tenofovir is more expensive than d4T, we know. As we initially fought for d4T to be less expensive, we will fight for tenofovir to become less expensive. By not making demands, we could be perpetuating the situation, by making tenofovir first-line, it should or could lead to price reduction." (IAS Cape Town)

Participants acknowledged AZT as an alternative, but highlighted the risk of anaemia, which is a serious concern in many African countries where it is an endemic problem.

For the many difficult clinical situations where there is inadequate evidence about which treatment options are best, participants discussed how they approached such treatment decisions in general. For instance, many expressed concerns about the toxicity of treatment, treatment readiness, and stated a preference for a less medicalised and more holistic approach to treatment and care — until clinical data clearly demonstrates that more aggressive and/or complex care treatment approaches are truly in their best interest.

Monitoring to inform treatment decisions

Participants asserted CD4 counts and viral load monitoring should be made available and affordable when needed for important treatment decisions, especially to determine the need to switch treatment.

> "Viral load is very important to monitor the treatment together with the CD4 count. But unfortunately in our country we do not have enough equipments for these services. For someone who is on treatment I think doctors or health personnel can know well if the medication is working properly if there are regular tests on VL and CD4 counts. Now, because we are poor we just receive the medicine without proper check-ups; you end up with liver, kidney problems because of lack of equipment. So WHO has to look into this matter, especially in poor developing countries where access is a problem to health centres." (Participant from Malawi, E-consultation)

Participants at IAS 2009 Cape Town also discussed the appropriateness of (expensive) treatment options that are standard of care in industrialised countries, such as frequent laboratory monitoring. In some situations, the participants voiced a clear preference for the simplifying options being employed by the public health approach to HIV treatment. For instance, for people who are clinically stable, it was suggested that fewer clinic visits and less intensive laboratory monitoring would actually be more patient-centred. In addition to decreasing costs to the public sector, given the difficulty in accessing treatment centres (transportation, time and costs, etc), fewer visits places a lower burden on the patient as well as his/her family and carers.

Co-infections

Participants asserted that the ART Guidelines should stress the importance of integrating TB/HIV services, because of data demonstrating that people with TB who are coinfected with HIV do not get on ART while they are still on TB treatment, have a much higher risk of mortality.

There was a range of opinion as to whether all TB patients should qualify for ART however. Some participants said that, unless CD4 cell counts were very low, the practice in their country was to treat TB first and see whether CD4 cell counts increased. Others felt however, that CD4 cell testing takes time and represents an additional barrier to getting onto ART — and for many people with TB and HIV, there is little time to waste.

Participants at ICAAP Bali - from a region where a majority of PLHIV have an intravenous drug user background, with 70-80% of those being co-infected with Hepatitis C – highlighted the importance of information about and access to Hepatitis C treatment, monitoring of liver function, Hepatitis C viral load measurement and interferon.

Benefits and tradeoffs of starting earlier and using more expensive regimens

While a majority of participants acknowledged that their health systems are facing real financial, infrastructure, and human resource constraints, there was broad consensus that WHO should be cautious about including considerations of cost in the revised guidance, lest it inadvertently establishes a lower quality of care for poorer countries. PLHIV everywhere should have access to the best ART regimens and appropriate laboratory monitoring. These choices should be made on the basis of clinical evidence rather than cost.

An important principle emerged out of these discussions: that those who are on treatment should have access to treatment without fear of compromising the access of those not yet on treatment. Otherwise, the same argument could be used to deny people access to second-line ART because it is many times more expensive than first-line. Doing what is necessary to maintain the health of a PLHIV who has already made the effort to go onto treatment is important as well.

As to whether participants were afraid that recommending earlier treatment would lead to programmes facing stockouts and/or governments not able to supply sufficient ARVs for when more vulnerable people (with lower CD4 cell counts) present for treatment, it was noted that "even at the

200 level, a whole lot of people are not being treated." (IAS Cape Town) Therefore, the argument of CD4 level as a criterion for deciding on treatment based on ART availability is not valid.

PLHIV emphasized that the revised ART Guidelines "need to push the envelope like when they first came out." Issues of cost, access and equity will indeed need to be articulated, and the activist community, including civil society, will play an important role.

Treatment for prevention

Firstly, there was consensus that ART is first and foremost a way to improve the health and well being of PLHIV, although, in some situations, such as the prevention of vertical transmission to infants, it clearly can be used for prevention. Prevention could perhaps be seen as a consequence or added benefit of ART but should not be its primary goal.

While there was interest in the further clinical study of the potential of ART for prevention (beyond PMTCT), there were also concerns about whether going on treatment earlier (for the sake of prevention) would truly be in the best interest of PLHIV, or the best choice for their own health. Furthermore, some were concerned that if the approach were not as effective as its proponents are suggesting, that could result in more HIV transmission and possibly transmission of resistant virus, particularly in resource limited settings where there is not routine access to viral load. Thus the strategy, if it works, may only be safe with increased access to viral load testing and monitoring.

Secondly, there was broad consensus that within the context of potential mothers living with HIV and their children, it is important to treat both the mother with HIV and her child —not one or the other, but assess how the health outcomes of possible ART equates for the mother and the child.

However, there were a range of opinions about the best approach to treatment and prevention in this population. While everyone was in favour of access to a short course of ARVs to prevent the transmission of HIV to the infant, many in the group — some being mothers themselves — did not believe that combination ART was necessary for all potential mothers with HIV or to protect their infants.

> "Let's say I'm pregnant and my CD4 cell count is 1200. At that CD4 cell count, I don't need to yet be started on ART." (Participant, IAS Cape Town)

Some noted that PMTCT programmes have major problems with loss-to-follow-up after delivery, and attributed this to the fact that PMTCT programmes do not focus enough on the health of the mother.

> "The messages that are being preached at the clinics are: 'You must save your baby, you must save your baby!' There is little emphasis on the well being of the mother." (Participant from South Africa, IAS Cape Town)

However, others noted that during pregnancy, a mother is already vulnerable — and it may not be the best time for her to be making a lifelong commitment to taking ART. Some women may not really be ready to go onto ART right away — especially if they have only just learned that they are positive.

Another question is whether going onto ART versus PMTCT (as a short-term and limited duration treatment) will affect future treatment options? Although data suggest that ART remains effective in

women who have been in PMTCT programmes (if begun about a year after pregnancy), many women with HIV are having multiple pregnancies, and there is little data to show how multiple exposures to ARVs in PMTCT will impact on subsequent response to ART. At the same time, however, if women with higher CD4 cell counts begin taking ART before they are ready, adherence may suffer, and that could lead to treatment failure and fewer treatment options in the future.

Thirdly, many participants feel that ART for prevention could offer important additional benefit from treatment to PLHIV. They asserted that the WHO should clarify ART's role in reducing infectiousness on an individual as well as a population level in order to ensure universal sustainable access to timely ART; encourage undiagnosed individuals to know their status; reduce stigma; and to help individuals understand their personal risk.

> An advocate from Canada, where there are many criminal prosecutions for HIV exposure following non-disclosure of HIV status, suggested that WHO is both clear about the role of ART on infectiousness, and about the equal responsibility of both parties for the prevention of transmission. "WHO guidelines in terms of treatment and prevention should be well-balanced, clear and precise to ensure that there is no room for misinterpretation, especially with so many criminal charges being brought against people living with HIV/AIDS". (E-consultation)

WHO should also make it clear that treatment alone can only be part of an overall prevention strategy that must address those without, as well as those living with, HIV.

Participants felt the concept requires further study, particularly in resource limited settings. Many said that they might be willing to take in such a study if issues of ethics and informed consent are addressed.

Recommendations

The following recommendations can be drawn from the three consultations:

1. PLHIV must be educated and empowered about their options and treatment should begin:
   - When the individual is ready;
   - Based on the individual's overall health rather than focusing solely CD4 count criteria;
   - And that the individual, rather than the virus, should be the focus of treatment and care.
2. Recommended CD4 count criteria for starting treatment should be in line with current scientific knowledge of best outcomes, at 350 cells/mm^3.
3. d4T (stavudine) should be removed from the list of recommended drugs due to its toxicity profile, and tenofovir be recommended in its place.
4. PLHIV must have access to regular CD4 counts and periodic viral load tests. Monitoring frequency should be based on clinical issues, as well as individuals' preferences and context. WHO should consider the role for resistance testing over time as treatment becomes more widespread, and as more treatment options become available.

5. PLHIV must have access to more information on co-infections, such as TB, Hepatitis B and Hepatitis C, both before and during ARV therapy, as well as access to necessary treatment and monitoring.

6. The WHO should highlight and clarify the role of treatment for prevention, in particular the potentially beneficial effect of ART on infectiousness, on both a population and individual level.

Appendix 1

About the Global Network of People Living with HIV (GNP+)

GNP+ is a global network for and by people living with HIV. GNP+ advocates to improve the quality of life of people living with HIV. GNP+ programmes are organised under four platforms of action: Empowerment; HIV Prevention; Human Rights; and Sexual and Reproductive Health and Rights.

VISION The GNP+ vision is to strengthen the worldwide movement of people living with HIV by providing leadership and a voice for people living with HIV. GNP+ is based on shared principles that include a commitment to ensuring that the network is driven by constituency's needs, the understanding that HIV is a human rights issue, an acknowledgement of the need to address gender inequalities and a commitment to solidarity, hope, compassion, inclusion and diversity.

ADDED VALUE GNP+ has developed and continues to develop tools that gather evidence from the community level to inform local, national, regional and global advocacy, policy and programming. As such, GNP+ added value is its ability to reach out to PLHIV at the individual level and translate their experiences into recommendations for action and change.

PARTNERSHIPS GNP+ always works in partnership. GNP+ has developed strong linkages with regional networks of PLHIV, other national and international networks of PLHIV such as the International Community of Women Living with HIV (ICW), and different international NGOs and agencies and other key stakeholders (IPPF, World AIDS Campaign, UNAIDS etc.). GNP+ partnerships make partners co-owners of a project. Partnerships with local and national PLHIV networks have led to implementation of programmes in over 60 countries. New partnerships with networks of young people living with HIV are expected. GNP+ collaboration with UN agencies such as UNFPA, UNAIDS, OHCHR and WHO provides GNP+ with the expertise needed to pursue technically challenging projects.

PLHIV DRIVEN EVIDENCE GATHERING GNP+ in recent years has led an attempt to modernise the movement of people living with HIV by refocusing from individual testimonies on people's life with HIV to systematic documentation and analysis of the experiences and expertise of people with HIV. GNP+ and its partners are implementing four evidence-gathering tools: *The PLHIV Stigma Index* (with ICW, IPPF and UNAIDS) to deconstruct perceived and experienced stigma by PLHIV; *The Criminalisation Scan* (with the Regional Networks of PLHIV) to gather information on laws, policies and cases of criminalisation of HIV transmission around the globe; *The Human Rights Count* (with the Regional PLHIV Networks) to document anecdotal evidence of human rights violations against PLHIV in a systematic manner; *The GIPA Report Card* (with ICW and UNAIDS) to measure the quality and level of application of the GIPA principle at national level. GNP+ is also implementing consultations with people living with HIV around specific issues that are not directly related to the implementation of programmes, including the *LIVING 2008* process and the consultations on the revision of the *ART Guidelines*.

Appendix 2

Project Implementation Team

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Global Network of People Living with HIV (GNP+)

Partner organisations

Asia Pacific Network of People Living with HIV (APN+)

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Appendix 3

Consultation questions

IAS 2009, Cape Town

Group 1: Quality and equity of HIV care

1. What are the strengths and weaknesses of tenofovir versus d4t versus AZT as part of the first line regimen?

2. What do people believe is the appropriate clinical and laboratory monitoring for people living with HIV in order to preserve treatment options and avoid poor outcomes?

3. Are people concerned that if it is recommended to start ART earlier and to use more expensive regimens, some of the sicker and more vulnerable people may not be able to access treatment so easily, or there may be less ART available overall?

Group 2: ART and Positive Health, Dignity and Prevention

1. Does taking ART have a role as a HIV prevention method, and if so, what is it?

2. Should all women living with HIV who are pregnant or trying to get pregnant start ART instead of just taking ARVs to prevent infection in their baby?

3. How willing would people be to take part in trials of taking ART perhaps earlier than now thought to be necessary for their own health, particularly in order to see if it prevents HIV being passed on to others?

Group 3: Clinical issues where the evidence base is hard to interpret

1. How early is too early and how late is too late to start ART?

2. If your CD4 cell count does not increase on treatment (or falls a little) should you be switched to second line therapy? What if you have an undetectable viral load?

3. People living with HIV who have active TB should start ART while they are on TB treatment. How do we do this in practice knowing that ARV medicines and rifampicin may interact?

ICAAP 2009, Bali

Group 1: Personal perspectives: how we feel about treatment and what we expect from ART

1. What are the main factors to consider in starting treatment?

2. What are the good things and what are the bad things about being on treatment?

3. What kind of support do we need from healthcare workers to answer our concerns about whether or not the drugs are working?

4. What kind of support do we need from healthcare workers to help us with side-effects, drug interactions and avoiding resistance?

Group 2: Advocate perspectives: balancing the tension between quality and equity of HIV care.

1. What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?

2. What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

3. What medical interventions do we want for people living with HIV who are co-infected with hepatitis C?

4. Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

Group 3: Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

1. How do ARVs play a role in HIV prevention? How do we use that information to advocate to governments?

2. Should all women living with HIV who are pregnant or trying to get pregnant start ART instead of just taking ARVs to prevent infection in their baby?

3. How willing would people be to take part in trials of taking ART perhaps earlier than now thought to be necessary for their own health?

4. How willing would people be to take part in trials of taking ART in order to see if it prevents HIV being passed on to others?

<u>E-consultation</u>

Week 1: Personal perspectives: how do we feel about treatment and what do we expect from ART?

1. When should we start and change treatment?

2. What drugs should be recommended for first- and second-line therapy?

3. What kind of monitoring is necessary to help inform our treatment decisions?

Week 2: Advocate perspectives: balancing the tension between quality and equity of HIV care.

1. What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?

2. What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

3. Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

Week 3: Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

1. How important is the link between treatment and prevention?

2. What should the WHO guidelines say about treatment and its role in prevention?

3. How relevant are human rights concerns in settings where there is no universal access to treatment?

Appendix 4

Consultation on WHO ART Guidelines

'Voting with your feet on antiretroviral treatment'

IAS 2009, Cape Town, South Africa

Global Network of People Living with HIV
Treatment Action Campaign

July 2009

Executive Summary

This report presents the key points and recommendations that emerged during the 'Voting with your feet on antiretroviral treatment' meeting, a technical consultation on the upcoming revision of the WHO's Recommendations for Antiretroviral Therapy (ART) for HIV Infection in Adults and Adolescents (ART Guidelines), held 20 July, 2009 during the International AIDS Society Meeting in Cape Town. The consultation was co-organised by the Global Network of People Living with HIV (GNP+) and the Treatment Action Campaign and aimed to:

- To gather the perspectives and values of people living with HIV (PLHIV) and their families related to the upcoming revision to the ART Guidelines, namely:
    - How should issues of cost of treatment be weighed against issues of access in the HIV treatment services available in resource-limited settings?
    - What should the guidelines say about when antiretroviral therapy should be initiated?
    - In clinical situations where there is not enough evidence to be certain what the best treatment decision is, what treatment options do PLHIV want, and how would they make their treatment choices?
    - How do PLHIV feel about the potential use of ART for HIV prevention?

The theme 'Voting with your feet on antiretroviral treatment' was chosen to encourage meeting participants to consider whether there was a difference between what they would recommend (on the basis of evidence and cost) for HIV care and treatment programmes public health systems, versus what they would choose for themselves or their family in a particular situation (what option would they walk or run to for themselves?).

This perspective is often missing from guidelines developed by technical experts, programme managers, clinicians and researchers. So WHO approached GNP+ and other organisations representing and advocating for PLHIV and offered them the unprecedented opportunity to provide input on the guidelines revision that will shape the kind care available for PLHIV for years to come.

The meeting was attended by about 30 PLHIV, about a third of whom were from South Africa, a third from the rest of Africa, and a third from Europe, the US and Asia. Participants had a quite a broad range of treatment experience — from those who were not yet on ART, to some who were on their first-line regimen and some who were much more heavily treatment experienced.

Consultation participants agreed that many of their lives could be directly impacted by the revised Guidelines. However, they also noted that in many of their countries actual clinical practice was rarely up to the standards recommended by the ART Guidelines — including the treatment they themselves had received.

This was one reason why participants stressed that WHO needs to take great care in the language included in the revised WHO guidelines. The minimum standard that WHO suggests is acceptable for HIV programmes will be the most that many governments will conclude that they need to provide. For instance, there was widespread agreement that the guidelines should recommend that treatment be initiated once CD4 cell counts fall below 350, and several people present said that the old standard, starting treatment only after CD4 cell counts fall below 200, should not even be

mentioned in the revised guidance.

Likewise, while many attending the meeting acknowledged that their health systems are facing real financial, infrastructure, and human resource constraints, there was broad consensus that WHO should be cautious about including considerations of cost in the revised guidance, lest it inadvertently establish a lower quality of care for poorer countries. PLHIV everywhere should have access to the best ART regimens and appropriate laboratory monitoring. These choices should be made on the basis of clinical evidence rather than cost.

For instance, tenofovir should be recommended as part of first line regimen (which could lead to it being made more affordable) — while the use of d4T should be discouraged on account of its toxicity. Likewise, viral load monitoring should be made available and affordable to confirm the need to switch to second line therapy.

That being said, there was general agreement that the other expensive treatment options, that are standard of care in industrialised countries (such as frequent laboratory monitoring), are not necessarily better or suitable for every setting. In fact, in some situations, the participants voiced a clear preference for the simpler options being employed by the public health approach to HIV treatment. For instance, for people who are clinically stable, it was suggested that fewer clinic visits and less intensive laboratory monitoring would actually be more patient-centred.

For the many difficult clinical situations where there is inadequate evidence about which treatment options are best, participants discussed how they approached such treatment decisions in general. For instance, many expressed concerns about the toxicity of treatment, treatment readiness, and stated a preference for a less medicalised and more holistic approach to treatment and care — until clinical data clearly demonstrates that more aggressive and/or complex care treatment approaches are truly in their best interest.

Finally, there was also general agreement that the purpose of ART first and foremost is for health and well-being of PLHIV, although, in some situations — such as the prevention of vertical transmission to infants — it clearly can be used for prevention. Of note, several people present said that they hate the term “mother to child transmission’ because it demonises the mother, and would prefer a shift to the term ‘vertical transmission.’

While there was interest in the further clinical study of the potential of ART for prevention, there were also concerns about whether going on treatment earlier (for the sake of prevention) would truly be in the best interest of PLHIV, or the best choice for their own health. Furthermore, some were concerned that if the approach were not as effective as its proponents are suggesting, that could result in more HIV transmission and possibly transmission of resistant virus, particularly in resource limited settings where there is not routine access to viral load.

"The WHO ART Guidelines have direct impact on the lives of people with HIV and on the care we will be receiving in our countries… The guidelines are critically important to us because our countries use it as a gold standard. They treat whatever WHO puts into the guidelines like it is engraved in stone."

Vuyiseka Dubula, South Africa's Treatment Action Campaign (TAC).

First published in 2004, the ART Guidelines are crucial reference tool for countries with limited resources that have been attempting to scale up HIV care and treatment programmes including the provision of ART. The guidelines adopted a 'public health approach' to ART management with an emphasis on improving survival at the population level in contrast to the highly individualised approach common in industrialised countries. This involved consolidating available treatment options into two sequential regimens (first- and second-line ART) with streamlined approaches to clinical and immunological monitoring. This simplified approach greatly facilitated the introduction of ART in many countries, and almost all the high burden countries soon used the ART Guidelines to frame their national policies.

Since first being drafted,

Much of the success of the ART Guidelines can be directly tied to the profound efficacy of the simple first-line regimens anchored by non-nucleoside reverse transcriptase inhibitors (NNRTIs: efavirenz or nevirapine) in combination with a nucleoside analogue 'backbone' such as AZT/3TC (Combivir) or d4T/3TC, or in some situations, a triple nucleoside analogue combination anchored by abacavir or tenofovir, such as in pregnant women on TB therapy (more on this below). But over time, the toxicity of some of the agents involved in the ART regimens, in particular, d4T, have become problematic, with people more likely to change their treatment regimens because of drug side effects than due to the loss of antiretroviral activity associated with the development of drug resistance.

Furthermore, because of the durable efficacy of first line ART, the approach to managing treatment failure and switching to second line therapy in the ART Guidelines has remained relatively untested in the field. But now that many PLHIV have spent several years on their first line regimen, this is no longer the case; and there are major differences of opinions among researchers and other key experts over how best to make the decision to switch to 2nd line treatment.

More evidence has also become available suggesting that starting ART earlier in the course of disease (when CD4 cell counts are higher) can achieve better health and survival. The current version of the ART guidelines recommend that ART should be 'considered' when CD4 cell counts fall below 350, but they also state 'the optimal time to initiate treatment between 200-350 cells/mm3 is unknown." (It should be noted however, that some countries still have only limited access to CD4 tests, so the guidelines also stress that ART can be initiated on the basis of clinical staging for PLHIV with signs or symptoms of advanced disease.)

Since that time, the SMART study reported that untreated patients with a CD4 cell count below 350 cells/mm3 had an increased risk of not only HIV-related illness, but some other serious conditions, including heart, kidney and liver disease, as well as some cancers. In response to this data, industrialised countries revised national recommendations to start ART when CD4 cell counts are in the region of 350. Since then, several large studies, including two very large cohort studies (with close to 40,000 participants) in mostly industrialised countries have both released consistent results: there is a significantly greater risk of AIDS or death when PLHIV wait to start ART after their CD4 count falls below 350. However, the

considerable more clinical data and programmatic experience on the use of ART in resource limited settings have become available. In 2006, the guidelines were revised to take into account the availability of more drugs, the use of ART in women (and pregnancy), and concurrent treatment of HIV and tuberculosis (TB) and hepatitis B and C.

But the field continues to evolve (see box).

In the current revision, it should be possible to refine the ART Guidelines to improve the standard of care being offered PLHIV — but the choices are not always clear-cut — particularly in resource limited settings.

"The next revision of the guidelines," Dr Marco Vitoria of WHO told participants at the GNP+/TAC meeting, "will still be evidence based —what science is saying — but we are now trying to consider other domains that can help us to make a recommendation that can be useful to maximize the benefit and minimize the risk for people living with HIV worldwide considering contexts that exist in different parts of the world."

Considerations of what should be included in the revised ART Guidelines, and the weight given to recommendations

- A review of the evidence, with a focus on what are the most critical outcomes for PLHIV
- An assessment of the risks and benefits of selected interventions (action, or drug recommended)
- Assessments of the cost and feasibility of implementing an intervention into different resource limited settings (the greater the cost-effectiveness, the stronger the recommendation)
- An assessment of the **acceptability** of the intervention to
    - programmers/policy makers
    - health care providers, and
    - ***PLHIV***

The meeting in Cape Town represented the start of a unique consultative process between WHO and communities of PLHIV, to understand what PLHIV want from their treatment programmes, and what will and will not be acceptable to include in the next ART guidelines revision. PLHIV were asked to consider how they would 'vote with their feet' regarding these treatment choices: For instance, would their recommendations for the guidelines (that will frame the options available within the public health system) be different from the choices they would make for themselves and their own health if they could afford different options outside the public health system?

"I think this is the most important meeting in this conference because I have the opportunity to see a different perspective that's been missing in the WHO guidelines and that we are now trying to incorporate in the new version we are starting to prepare," said Dr Vitoria.

Major issues that could affected in the 2009 revision

- When to start ART?
- What to start with? (Safety considerations may change if some antiretroviral agents are used earlier, for instance, it is not clear how safe nevirapine is in women with CD4 cell counts over 250)

- How should programmes monitor for treatment failure and when should people be switched to 2nd line regimens?
- What should be used for 2nd and 3rd line ART?
- How should ART be used in PLHIV who have other conditions at the same time (such as pregnancy, TB, and hepatitis B or C?)

Finally, there has been a surge of interest in the use of ART as a prevention tool — to prevent the onward spread of HIV to discordant partners and at the population level. At least one mathematical model suggests that widespread HIV testing and immediate treatment of PLHIV could actually stop the spread of the HIV epidemic. So another goal of these technical consultations is to assess how PLHIV feel about this new consideration in the "when to start treatment" debate.

The discussion groups and background on their questions

In light of these questions and the major considerations being in the revised guidelines, meeting participants were divided into 3 groups that addressed these issues though each through a somewhat different lens.

Group 1 was asked to address the following questions, considering how to balance quality of care (which is sometimes more expensive or complicated to deliver) with equitable access to care.

- What should be the CD4 threshold the guidelines recommend for when ART should begin, in light of the fact that earlier treatment will increase the demand for ART in programmes that are already facing severe constraints?

  Essentially, should the guidelines explicitly state that treatment should begin when CD4 cell counts fall around 350?

  If there are limits to how many people a programme can afford or has the capacity to put on treatment, then offering earlier treatment could lead to a situation where programmes reach the limit of their capacity and can no longer put new people on treatment, or mismanage drug supplies. If this happens, there are concerns that when some sicker and more vulnerable people present for care, they may not be able to access ART, or programmes may have stock outs — and lead to treatment interruptions for people with more advanced disease.

- What do people believe is the appropriate clinical and laboratory monitoring for people living with HIV in order to preserve treatment options and avoid poor outcomes?

  A variety of laboratory tests are routinely used in industrialised settings to assess the safety for starting treatment, the time to start treatment, the effectiveness of treatment, and to monitor for treatment failure.

  The ART Guidelines are quite clear that settings without access to laboratory tests can still initiate people on treatment on the basis of clinical staging (signs and symptoms of advanced HIV disease). However, WHO also supports wider access to CD4 cell tests in order to determine when to start treatment (when CD4 cells fall below a certain threshold, such as 200 or 350 CD4 cells).

  However, numerous studies are demonstrating that neither clinical monitoring or CD4 cell count tests are very good indicators of whether an ART regimen is still exerting an effect on the levels of HIV in a person's body. Only viral load tests, widely available in industrialised countries, can do that. However, the infrastructure to perform viral load tests has yet to be scaled up in many countries, and is quite expensive. There are also questions about what level of viral load suggests the need to switch treatment (detectable virus, or viral loads above a certain threshold, such as 10,000 copies/mL)?

  Routine viral load testing would be extremely expensive, and there are questions about whether it is really necessary. Other researchers are looking at the use of targeted viral load in order to confirm immunological or clinical indications of treatment failure — and have

shown that it may be more costly to switch to expensive second line prematurely on the basis of immunological or clinical failure.

One criticism of this approach, however, is that for the money it will take to scale-up viral load, many other people could be initiated on first-line treatment.

- What are the strengths and weaknesses of tenofovir versus d4T versus AZT as part of the nucleoside analog backbone in the first-line regimen?

d4T was included in WHO recommended first line regimens on account of being initially better tolerated than AZT, because it could be given without requiring haematological screening (which was felt to be necessary for AZT) and because it was available in the cheapest fixed dose ART combinations. However, after several months, there have been extremely high rates of regimen limiting treatment toxicity including life-threatening lactic acidosis, peripheral neuropathy, lipoatrophy and fat redistribution (including breast enlargement in men).

AZT has been widely used and is preferred in pregnant women. However, it is harder for people to tolerate at the start of treatment (initially causing nausea and vomiting), and it can cause serious anaemia. However, long-term metabolic toxicity is somewhat less common than on d4T.

Tenofovir is the newest agent, which has quickly become the preferred choice in industrialised countries. However, at present, it is considerably more expensive than d4T or AZT. Initial side effects are mild. Some would say is less well characterized than the two older drugs, and there are questions whether it could have longer-term toxicities (to the bone and kidney). So far, these have been reported to be rare. There have also been concerns about the safety of using it in the absence of kidney function tests — though the findings of the DART study released at IAS2009, suggest that such tests may not be necessary to administer tenofovir safely in Africa. Finally, there has been less data on the safety of tenofovir in pregnancy or young children (there is some concern about it having an effect on bone development in the foetus). Thus far, however, birth registries suggest no increase in congenital abnormalities in infants born to mothers taking tenofovir.

Group 2 was asked to discuss the following questions pertaining to the use of ART for HIV prevention, through the lens of Positive Health, Dignity and Prevention — considering prevention together with the needs of PLHIV for treatment, care, support and human rights.

- Does taking ART have a role as a HIV prevention method, and if so, what is it?
- Should all women living with HIV who are pregnant or trying to get pregnant start ART instead of just taking short courses of ARVs for the prevention of vertical transmission?

In industrialised countries, the standard practice for most HIV positive women who become pregnant is to go onto ART, regardless of their CD4 cell count, in order to provide more complete protection against vertical transmission to their infants.

In resource-limited settings, different countries have somewhat different CD4 cell count thresholds for when pregnant women should begin ART. Above this threshold, women are given a short course antiretroviral drugs (the exact regimen varies, but it is usually AZT in the third trimester, and a single dose of nevirapine (sd-NVP) during labour, along with sd-NVP for the infant).

However, some experts are now recommending that pregnant women in countries with limited resources should be given ART at a higher CD4 cell threshold than for other PLHIV.

- How willing would people be to take part in trials of taking ART perhaps earlier than now thought to be necessary for their own health, particularly in order to see if it prevents HIV being passed on to others?

  Early ART may well have other benefits besides the potential use for prevention, however, the primary endpoint of some of these studies could be prevention.

Group 3 was asked to consider clinical issues where the evidence base is hard to interpret. What would their preferences be in these situations, and upon what evidence or principles would they be basing their choices?

- How early is too early and how late is too late to start ART?
  The clinical data suggest that waiting till CD4 cells fall below 350 may be too late to start treatment, however they are unclear about when is best to start. When do PLHIV in resource limited settings want to start treatment and why?

- If your CD4 cell count does not increase on treatment (or falls a little) should you be switched to second-line therapy? What if you have an undetectable viral load?

  What would PLHIV who aren't doing very well on treatment want to do, knowing that there may not be any remaining treatment options for them after switching to second-line ART? Would they want a viral load measurement first? How would they feel about that if their last CD4 cell count went from 650 to 600? How would they feel if their last CD4 cell count went from 210 to 180?

- ART should be started in people living with HIV who have active TB while they are on TB treatment. How do we do this in practice knowing that ARV medicines and rifampicin may interact?

  There is now mounting clinical evidence demonstrating that PLHIV with active TB disease who begin ART while they are still on TB treatment are much more likely to survive. However, the precise time to start ART (simultaneously, after one or two months on TB treatment) is still unclear.

  The decision is also complicated by drug interactions between rifampicin and many of the ARVs. For instance, rifampicin lowers levels of nevirapine and the protease inhibitors. Efavirenz is the preferred option, but may not be safe in pregnant women with TB. A triple

nucleoside analogue combination may be an alternative, but there are questions about its potency relative to NNRTI-based regimens and how it might affect subsequent ART options?

Reports back, discussion and feedback

Given the rather short time that the groups had to report back to the meeting, the following has been augmented with comments recorded during the group discussions. Also, some participants made comments pertaining to another group's questions — these are included where relevant.

However, it should be noted that the matter of cost of care came up in all the discussions. While recognising that public health systems are operating under real infrastructure and human resource constraints, many PLHIV at the meeting expressed strong reservations about whether the financial cost of an intervention should really be factored into the ART Guidelines:

"We keep on talking about poorer countries and cost implications but I would really say 'Universal Access' means universal standards. You must have the same standards everywhere. Otherwise it's not acceptable," said one woman from Nigeria

"I'm not comfortable with the price coming into the guidelines at all. We don't need to talk about the guidelines and affordability. It's not our job to talk about. Aren't guidelines supposed to be based on clinical evidence?" said a participant from India

"You will always find, sitting in a room of PLHIV activists, that when somebody says it's too expensive, you say "WHY? We don't believe you" and number two, "take things to scale!" When countries take things to scale, it reduces the price," said another activist.

Group 1

Question 1: Should the guidelines recommend earlier treatment (when CD4 are around 350)?

"The WHO ART Guidelines should specify that ART should be available at 350 CD4," the group's rapporteur said, "though the guidelines should also recognize the range of error in CD4 testing and state that a slightly higher CD4 cell count shouldn't be grounds for refusing treatment."

Participants were quite passionate about these points.

"We need to be really explicit about this because people are looking for any excuse not to let this change in the WHO guidelines," said one participant.

"We don't want to see anywhere in the WHO guidelines, anything that says to 'start at 200.' Because if we still put 200, some governments are still going to be using 200 as a criteria," said another.

Participants suggested that governments interpret the ART Guidelines quite rigidly in order to provide as little care as possible.

"If for example, the guidelines continue to say start treating when CD4 cell counts fall below 200, governments will use it as an excuse to continue to turn away people seeking treatment whose CD4 cell counts is 210 — and they often don't make it back before they have developed a serious AIDS-

related illness," she said.

Such a case was mentioned in the group discussion. Because monitoring is performed at regular intervals, sometimes a person will come in with symptoms before they are due for another CD4 cell test, but when their last CD4 cell count was above 200, their symptoms may be disregarded.

"Sometimes this even happens when a person is showing symptoms. Sometimes, even if they have an AIDS defining illness, they are not given treatment," said one group member. "There is a girl who passed away about 3 weeks ago —she had CMV. But nobody was 'able' to check her out. She was given a referral letter from the clinic to the hospital. At the hospital, they did not check her eyes, they just said: 'no, just go and eat more carrots and then go and see an optometrist!' Then she went back to the hospital, because she could not see. Two days later she was admitted into a hospice and a week later she died."

According to current WHO guidelines, of course, those symptoms should have been investigated and would have been cause for starting ART — even without another CD4 cell count. But where CD4 cell counts are available, programmes look at the numbers — which need to be higher to prevent events like that from ever occurring.

As to whether participants were afraid that recommending earlier treatment would lead to programmes running out of ARVs or not having enough drug for when more vulnerable people (with lower CD4 cell counts) present for treatment, it was noted that "even at the 200 level, a whole lot of people are not being treated."

"The most vulnerable people are still not on treatment - even with the guidelines at 200! So we are not changing anything, really, by asking for better drugs and for earlier clinical treatment. We'll do the same thing we've always done - fight for better drug prices and fight for better services," said one group member.

"I don't want to be reasonable and say that 200 is okay. No, I think we have to fight for 350 despite the fact that it will increase the burden of services. But we will have to deal with that thereafter and we will have to deal also with human resources issue," said a participant during a different group discussion.

Question 2: What is the appropriate level of laboratory and clinical monitoring?

Most of the discussion focused on the need to have some access to viral load.

"Viral load should become an important part of monitoring for PLHIV on treatment, especially when considering changing meds," the group's rapporteur said.

Group members felt that a strong statement was needed stressing the importance of viral load testing to, at the very least, confirm treatment failure.

"In this version of the book it starts off, 'Although viral load testing is not yet widely available...' Now we know that is true but it sort of lets people off the hook from not trying to make viral load monitoring available," said one group member.

There were a range of views about how routine viral load monitoring would need to be, however.

"There's a difference between having a viral load every three months or every six months, or using a strategic viral load just to confirm whether the change or lack of change in CD4 cell count has anything to do with whether somebody has become resistant to therapy," said one meeting participant. "We need to at least be able to put in enough capacity in programmes to confirm failures before switching treatment."

As for concerns that the money used to scale up access to do routine viral load might be better used putting more people (perhaps thousands) on first-line treatment?

"What we were saying is there needs to be a level of viral load monitoring. We are not saying that with each and every appointment when you come, we'll do a viral load. At some point after going on ART, maybe one viral load per year when you are stable- at least I won't feel ashamed that I have denied 20 000 people treatment — I might have denied 10 people. But this is important for me too," said one group member.

[At the end? An important principle seems to be emerging out of these discussions: that the rights of those who are not yet on treatment do not supersede the rights of those who are… Otherwise, the same argument could be used to deny people access to second-line ART because it is many times more expensive than first-line. Doing what is necessary to maintain the health of a PLHIV who has already made the effort to go onto treatment is important as well.]

"I have a feeling that even from an economical point of view, it will cost less to investigate further — even with viral load, and even, if it's available, with resistance testing — than switching too soon to second-line therapy," said a participant in another group.

There was also a brief discussion on the appropriate amount of clinical and laboratory monitoring in general — in the work-up before going on ART, and when people are relatively stable.

"I take treatment at a public sector clinic, and we have established things called 'A stable patients' adherence club,'" said one group member. "We only come to the clinic six times a year, we only see a doctor once a year because there are very few doctors. In the meantime, we are only seen by a nurse when it's needed. Most of the time we see each other, help each other, we get meds from the pharmacy and it reduces the burden that I have to take time away from work. I'm only needed there when I need to do blood monitoring twice a year. I don't have to come in the other times, I can send somebody else to go and fetch my medication. Because the clinics are saturated seeing people who are already on treatment — we are taking up space for those who need to be initiated on treatment. We are doing a review of the clubs right now but already we are starting to see signs of people with the numbers of new initiations are increasing"

Several others said that although they want monitoring to be available when needed for important treatment decisions (again, especially to determine the need to switch treatment), they would otherwise welcome less frequent monitoring when they are stable on treatment.

"Requiring too many clinic visits can really just be a way of putting people off from actually accessing what they have as a right for health!" said another meeting participant.

Question 3: d4T vs AZT vs tenofovir:

"All of these drugs have their disadvantages and advantages," said one member. However, there

was broad consensus upon a number of matters.

1) Tenofovir *must* be made available as part of first-line ART — and the price must be reduced so that it becomes affordable for public health systems. Many felt that if tenofovir were made part of first line regimens, there would be increased pressure to increase generic production and lower its price.

"Tenofovir is more expensive than d4T, we know," said one group member. "As we initially fought for d4T to be less expensive, we will fight for tenofovir to become less expensive. By not making demands, we could be perpetuating the situation, by making tenofovir first-line, it should or could lead to price reduction."

Group members did say they wanted to see more long-term safety data on tenofovir's use in sizable African cohorts. Incidentally, such data were presented the very next morning at IAS from the DART study, conducted in Uganda and Zimbabwe. Most of the participants in the study were on a tenofovir-based triple nucleoside analogue regimen, and after nearly 5 years of efficacy and safety data, survival was quite good, at around 90% (and 87% among those managed clinically, without any laboratory monitoring).

2) Continuing to recommend d4T as part of the preferred first-line regimens *is not* acceptable:

"In our context in South Africa, d4T is definitely *not* an option for women — it may not really be an option for anyone at all," said one group member during the discussion. "Toxicity is present in increasing numbers of women - both lipodystrophy and lactic acidosis - amongst women who started on d4T."

"Definitely d4T is out - for us it has been totally thrown out of the guidelines. Even those who are on d4T are being switched, except for those who say "I want to remain on it!" said one woman from Nigeria.

One woman in South Africa even 'voted with her feet' against d4T, going to great lengths when she started treatment to be prescribed the only available alternative in her country at the time, AZT. She remains on AZT even though she has anaemia that is so bad that she "feels cold all the time. In winter in Cape Town, I have to wear three suits because I can't feel my feet, they are freezing cold, and my hands."

Even so, she is much more against d4T.

"My sister had to start treatment and I said: 'I refuse, you are NOT going to be taking d4T! I would rather you change all clinics in South Africa and go all over from one clinic to the next!' so we ran around to all the clinics, until one agreed not to use d4T."

AZT is clearly an alternative, although the risk of anaemia is a serious concern in many African countries where it is an endemic problem.

One remaining concern about tenofovir was its safety during pregnancy.

"In my case I was on tenofovir when I became pregnant and I had to change because my doctor was not sure about the safety of tenofovir in pregnancy," said one participant. Group members were

uncertain whether these concerns have been adequately addressed yet.

In general, there was a lot of discussion about how any of these drugs affect pregnant women and the need for a better review of the evidence that should be reflected in the guidelines, since there are many pregnant women on ARVs in resource poor settings (further comments about pregnancy and ART have been incorporated into Group 2, question 2).

Finally, participants said that the idea that only one or two regimens would be available in resource-limited settings *is not acceptable* and the ART Guidelines need to reflect this. "WHO needs to make universal guidelines for first, second, third *and fourth-line treatment* so that people have an idea of what they should be able to expect," said the group rapporteur. Since the drugs used in ART could affect subsequent treatment options, class-wide drug resistance issues need to be considered in the selection of these regimens.

Group 2

Question 1: Does taking ART have a role as an HIV prevention method? And if so, what is it?

There was consensus that ART is first and foremost a way to improve the health and well being of PLHIV, although, in some situations, such as the prevention of vertical transmission to infants, it clearly can be used for prevention.

Prevention could perhaps be seen as a consequence or added benefit of ART but should not be its primary goal. In fact, many in the group were uncomfortable with ART being seen as an alternative prevention method (although it may confer additive protection).

There was discussion about the Swiss Statement that concluded after an extensive review of the literature that a treatment adherent PLHIV who has had an undetectable viral load for more than six months and with no co-factors such as the presence of sexually transmitted infections (STI) would have a very low or no risk of onward transmission.

Some participants in the group felt more evidence was needed in resource limited contexts. One woman noted that, at present, she would not be confident of her partner being protected, even though she has been on treatment for 9 years.

"I'm HIV-positive and my husband is negative. I wouldn't risk putting him into a position of getting HIV by just saying that I'm on ART or he might be infected" she said.

Clearly reducing viral load would lower the risk of transmission, and ART on a mass scale may reduce the burden of HIV at the population level in the absence of complete behavioural change. However, there is a danger that this approach might lead to the treatment of PLHIV against their will or before they are ready.

There were also concerns that if ART were seen as a prevention method it might discourage people from having safer sex. Others said that this is an assumption that will need to be studied further to see if it is true — people may continue to use condons because there are other sexually transmitted

diseases that people do not want to get. At the same time, however, the desire to have unprotected intercourse (and enjoy full sexual and reproductive rights) is quite strong. For instance, many serodiscordant couples take this risk in order to have children.

If this were to occur in a context without routine access to viral load (to confirm that someone has an undetectable viral load in the first place), people who believe that ART is a prevention strategy may continue to have unprotected sex long after their treatment has failed. This might not only spread HIV, it might spread drug resistant strains. Thus the strategy, if it works, may only be safe with increased access to viral load.

A participant in another group discussion suggested that, in contexts where the 'ART as prevention' approach is being considered, access to viral load may become a new human right — that PLHIV will have a right to know whether they are infectious or not. However, it was also pointed out that checking one's viral load isn't like checking blood sugar levels. There are, as of yet, no cheap point of care viral load tests that can tell a person their viral load at the moment. Furthermore, people often do not know whether they have contracted an STI and even common conditions such as urethritis or bacterial vaginosis may increase genital viral load.

During feedback discussion, it was noted that the complete burden for prevention should not be placed upon the HIV-positive partner. Another approach to keep a serodiscordant partner HIV negative would be for them to take antiretrovirals as pre-exposure prophylaxis (PREP). There was consensus that further study of this approach is warranted, and that, if it works, it could help grant PLHIV full sexual and reproductive health rights while providing a tool to protect his or her partner.

Finally, the group also noted that ART does 'prevent' opportunistic infections from developing. While the core question was about HIV prevention, this observation could have important consequences when it comes to other communicable infection, such as TB. At IAS, new studies from the Western Cape of South Africa reported that there has been a stabilisation in the rates of TB across the population in periurban communities where most PLHIV with advanced disease have now been put on ART. This raises a sticky issue if PLHIV who are not on ART start being blamed for TB in the community, or if there is pressure for PLHIV to go onto treatment because it is 'good for the health of the community.'

Question 2: Should all women living with HIV who are pregnant, or trying to get pregnant, go onto ART or just take short course ARVs to prevent infection of their baby?

There was broad consensus that it is important to treat both the mother with HIV and her child — not one or the other, but both.

However, there were a range of opinions about the best approach to treatment and prevention in this population. While everyone was in favour of access to a short course of ARVs to prevent the transmission of HIV to the infant, many in the group — some being mothers themselves — did not believe that full ART was necessary for all potential mothers with HIV or to protect their infants.

"Let's say I'm pregnant and my CD4 cell count is 1200. At that CD4 cell count, I don't need to yet be

started on ART," said one woman.

Indeed, data suggest that women with high CD4 cell counts and low viral loads are much less likely to transmit HIV. In such cases, short courses of ARVs offered by programmes to prevent mother to child transmission (PMTCT) prevent most cases of HIV transmission to the infant.

On the other hand, most women with HIV who wish to become pregnant don't have such high CD4 cell counts. Rather, they may have CD4 cell counts that are just above the threshold for starting treatment in their local programme. Some meeting participants said women must have the right to go onto ART for themselves and their child — especially if the local threshold is at 200 CD4 cells. Clinical data now suggest that maternal and infant survival is better and HIV transmission is lower if women with HIV go onto ART, even with CD4 cells between 200 and 500.

A woman in another discussion group reported that she had gone onto ART simply because she was planning to become pregnant — and she wanted the best possible chance of protecting her health, her infant, and her partner.

"Right now we are in an era where ART is the best possible way to prevent the mother from dying but also the child from getting infected, and also, from preventing the father from getting infected if he is not infected," she said.

Some noted that PMTCT programmes have major problems with loss-to-follow-up after delivery, and attributed this to the fact that PMTCT programmes do not focus enough on the health of the mother.

"The messages that are being preached at the clinics are: 'You must save your baby, you must save your baby!' There is little emphasis on the well being of the mother," said one woman from South Africa.

However, others noted that during pregnancy, a mother is already vulnerable — and it may not be the best time for her to be making a lifelong commitment to taking ART. Some women may not really be ready to go onto ART right away — especially if they have only just learned that they are positive.

Another question is whether going onto ART versus PMTCT will affect future treatment options? Although data suggest that ART remains effective in women who have been in PMTCT programmes (if begun about a year after pregnancy), many women with HIV are having multiple pregnancies, and there is little data to show how multiple exposures to ARVs in PMTCT will impact on subsequent response to ART. At the same time, however, if women with higher CD4 cell counts begin taking ART before they are ready, adherence may suffer, and that could lead to treatment failure and fewer treatment options in the future.

Clearly, this is a choice each woman should make for herself without feeling pressured.

Part of the problem may in fact be the very term 'prevention of mother to child transmission' demonises women. Another important consensus that emerged was that people want the term dropped from the revised ART Guidelines.

"Mother-to-child-transmission suggests that the mother is the bad person," said one.

"Personally I hate the name 'Mother to Child', I hate that name because it means you as the mother have the burden of disease. It means, if for any reason, treatment fails and that child is born HIV-positive, then it is your fault. So that name totally turns me off," said another woman

"Let's re-brand it as vertical transmission," said many others.

Question 3: Would people be willing to take part in trials taking ART for prevention?

As indicated in question 1, many participants feel that ART for prevention could offer important additional benefit from treatment to PLHIV — but the concept requires further study, particularly in resource limited settings.

Many said that they might be willing to take in such a study.

"I've been on trials in the past and I went on trials simply because I knew that there's possibly a benefit for me but I also thought it was a way of making a contribution," one woman said.

"Many times there are white people from America or from Geneva that come to do trials," said one woman from Kenya. "But to me it's okay, anyway, if at the end of it all if that drug that they are doing the trial may work."

However, there was also consensus about considerations around ethics and informed consent for such a study:

- One would be whether the study is solely to determine the prevention activity of ART or to assess the benefits of earlier treatment? It would be important to look at the potential health benefits of early ART.

- The potential downsides of going into the study should also be explained to potential participants, including the possibility of experiencing side effects from treatment before HIV causes noticeable symptoms, the possibility of running out of treatment options before they are needed for one's own health.

- There needs to be support and services for people who experience side effects or illness in the study.

- How might participation in the study affect pregnancy?

- Participants need to be told about the outcomes of the study. Some noted that this often doesn't happen.

- Also, participation *must* be totally voluntary and up to the individual. Cluster-based studies, where village elders or community leaders give consent for their entire community to be randomised to one treatment approach or another, may not be appropriate for this type of study. Every PLHIV in the study setting needs to be given the choice for whether they participate in this sort of a study or not.

Group 3

It became apparent during Group 3's discussion on treatment decisions in situations where the clinical evidence is unclear, that PLHIV need more data to make informed decisions. So the group primarily focused on what was important to PLHIV, their fears and desires in relation to what they want from health services and the ART Guidelines.

Question 1: 'How early is too early and how late is too late?'

Group 3 acknowledged that PLHIV everywhere should have the right to go onto treatment when CD4 cell counts are in the range of 350 cells — in light of recent data showing that treatment at this point improves survival and decreased progression to AIDS and TB. While treatment is still beneficial even when started later, waiting until CD4 cell counts fall below 200 represents an unacceptable risk.

"Too late is of course a CD4 count of below 200 or after the first opportunistic infection occurred, and too early is when one is not prepared to start. It is not a clinical criterion. But there is a very strong link between the preparedness of an individual and his or her capacity to be 100 percent adherent," said one participant.

Some felt that treatment at higher CD4 cell counts, long before people with HIV experience symptoms, might be too early, because it would be before the person being treated could observe clinical benefits from treatment. Consequently, they may be less likely to be adherent to treatment if they experience drug side effects.

In the absence of data of showing that earlier treatment is better, there were very real concerns about the toxicity of ART, and whether initiating treatment too soon could limit future treatment options.

Indeed, it is a mistake to think that all PLHIV want to go onto treatment whatever the ART Guidelines recommend. Even people with CD4 cell counts below 200 and symptoms may be afraid to go onto treatment.

"Many ask, how could I take drugs for the rest of my life?" said one PLHIV from Uganda. "And when you are being prepared that these drugs has some side-effects i.e. vomiting, skin rashes, night mares and so forth, it creates fear. In addition, many of us come from countries without resources and are very poor — many are afraid to go onto treatment when they don't have enough to eat."

"People do not want to start treatment because of the side effects that they have heard of, or because they know other people who have died from side effects," said one activist from South Africa. She said that simple, straight-forward information, based on sound clinical evidence was needed to address these fears. Therefore, clearer evidence of the benefits of earlier treatment from resource limited settings would be needed to convince people at higher CD4 cell counts to go onto treatment.

Ultimately, regardless of what CD4 threshold the ART Guidelines recommends, the decision to go onto treatment is a personal choice, depending upon whether one feels ready for treatment or not.

Unless PLHIV also have a life-threatening opportunistic infection, they should not be pressured to start ART before they are psychologically prepared for it.

Question 2: Should people who fail treatment immunologically (with a poor CD4 response) be switched to second-line therapy?

The ART Guidelines need to recommend further investigations to determine why someone's CD4 is failing, said Group 3's rapporteur who noted that he himself had been in this situation.

Investigations should include an adherence assessment — to make certain that an individual is taking their regimen correctly and consistently (and hasn't, for instance, taken a drug holiday). In general, participants felt it important to have adherence projects in place and regularly assessing people on ART long before treatment failure sets in.

But if the person has been adherent and treatment failure is suspected, participants felt that it was absolutely crucial to be able to check viral load, to determine whether treatment is still working or not.

"There is no need to switch, if after further investigation, your viral load is very very low or undetectable," said one group member.

Without access to viral load, there is a danger of switching unnecessarily to a more expensive and complicated second line regimen — and potentially using up all of one's treatment options too soon.

Many people do have suppressed viral loads and are still failing immunologically, so discussion centred on what could be done in these cases.

One meeting participant stressed that this was linked to beginning treatment late: "The later you start, the less the chance that you – or your immune system – recovers," she said.

However, it is also possible that the toxicity of some of the ARVs in the regimen are having a dampening effect on the CD4 response, and that a switch of regimens might be of benefit — even in people with suppressed viral loads. This option would be less risky if more treatment options were available in resource limited settings, complained one activist from South Africa.

But South Africa only has two regimens available. Why has South Africa got only two regimens? Why have some other countries got four, five regimens?" she said.

In the absence of other solutions, participants recommended 'positive living.'

"After going on ART, the paradigm shifts. You have already taken your drugs and you are okay and you go back to drinking, smoking and having unprotected sex — and that can account for reduction in CD4 cell count," said the group's rapporteur.

Finally, immunological failure could indicate another infection as well, so further investigations should include screening for TB and other infections that could lower CD4 cell counts.

Question 3: How to start ART at the same time in people on TB treatment?

The ART Guidelines should stress the importance of integrating TB/HIV services, because of data demonstrating that people with TB who are coinfected with HIV don't get on ART while they are still on TB treatment, have a much higher risk of mortality.

There was a range of opinion as to whether all TB patients should qualify for ART however. Some participants said that, unless CD4 cell counts were very low, the practice in their country was to treat TB first and see whether CD4 cell counts increased. Others felt however, that CD4 cell testing takes time and represents an additional barrier to getting onto ART — and for many people with TB and HIV, there is little time to waste.

One participant from India said that her personal preference would be to complete TB treatment first, given the potential for toxicity and the drug interactions between rifampicin and many ARVs.

The group recommended that people on TB treatment who start ART do not use a nevirapine regimen but rather an efavirenz-based or triple nucleoside based regimen. Unfortunately, time was too short to go into what the optimum ART regimen would be to use in pregnant women on TB treatment, or how to manage people who are on second-line protease inhibitor based regimen.

There was also some brief discussion on the management of active Hepatitis B virus (HBV) in people with HIV. The drugs used in the treatment of HBV (3TC, FTC and tenofovir) are also ARVs. ART treatment may thus need to be given earlier in people with both active HBV and HIV since giving these drugs as mono or dual therapy may lead to HIV drug resistance.

Conclusion

This meeting represented the first of several opportunities for PLHIV, and participants in the meeting were urged to go back to their communities to gather further input.

"We are giving this input or perspective from the PLWAs perspective, or people living with HIV/AIDS themselves, rather than waiting for the researchers and the managers and the bureaucrats to decide what the guidelines should look like," said Dubela.

PLHIV emphasized that the revised ART Guidelines "need to push the envelope," one said, "like when they first came out." Issues of cost and access will indeed need to be worked out — but that is a role for the activist community.

At the same time, PLHIV want care and treatment programmes of the highest quality, but they also prefer them to be as simple and unobtrusive as possible. They don't want programmes to require people who are stable on treatment to come into the clinic too often unless it is absolutely necessary. They don't want unnecessary and overly complicated treatment. Finally, they would prefer that programmes to place more emphasis on the individual's holistic needs rather than treating them just as a patient or even worse, someone who must be kept from spreading HIV.

Appendix 5

Consultation on WHO ART Guidelines

Defining Standards of Treatment and Care
ICAAP9, Bali, Indonesia

Global Network of People Living with HIV
Asia Pacific Network of People Living with HIV

August 2009

Introduction

This report presents the key discussions and recommendations that emerged during a meeting held during the International Congress on AIDS in Asia Pacific in Bali (ICAAP 2009) on August 12 2009. The meeting was held as a satellite meeting of ICAAP9 and was open to People Living with HIV (PLHIV) who attended ICAAP 2009. The meeting was co-hosted by GNP+ and APN+ (Asia Pacific Network of People Living with HIV). There were 23 participants from 6 countries of the region, with ages from 27 to 67 years.

At the last minute a demonstration at the plenary of the ICAAP9 conference was called on access to treatment for Hepatitis C at the same time as this meeting. Several of the pre-registered PLHIV for this meeting were mobilised for that demonstration. Because Hepatitis C is such a serious issue for many PLHIV in the region, their involvement in the demonstration was understandable, but it did reduce the number of participants in the discussions on WHO guidelines on ART.

The purpose of the meeting was to provide an opportunity for PLHIV from Asia and the Pacific to have input into the upcoming revision of the WHO's Recommendations for Antiretroviral Therapy (ART) for HIV infection in adults and Adolescents.

Overall the discussion aimed to gather the views and issues to be considered relating to the upcoming WHO ART Guidelines review and specifically to look at:

- how people feel about treatment
- the sort of support that people on treatment need
- when to start treatment
- balancing quality and equity of care in treatment
- how people see treatment as prevention

After an introduction to the session by Dr Susan Paxton, an Advisor from APN+ who facilitated the meeting, Dr Marco Vitoria from WHO, set the scene with a short presentation entitled “Considerations on WHO ART Guidelines”.

The participants then self selected one of three groups for the discussions. The questions each group considered were asked to discuss were as follows:

Group 1: Personal perspectives: how we feel about treatment and what we expect from ART

1. What are the main factors to consider in starting treatment?
2. What are the good things and what are the bad things about being on treatment?

3. What kind of support do we need from healthcare workers to answer our concerns about whether or not the drugs are working?

4. What kind of support do we need from healthcare workers to help us with side-effects, drug interactions and avoiding resistance?

Group 2: Advocate perspectives: balancing the tension between quality and equity of HIV care.

1. What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?

2. What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

3. What medical interventions do we want for people living with HIV who are co-infected with hepatitis C?

4. Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

Group 3: Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

1. How do ARVs play a role in HIV prevention? How do we use that information to advocate to governments?

2. Should all women living with HIV who are pregnant or trying to get pregnant start ART instead of just taking ARVs to prevent infection in their baby?

3. How willing would people be to take part in trials of taking ART perhaps earlier than now thought to be necessary for their own health?

4. How willing would people be to take part in trials of taking ART in order to see if it prevents HIV being passed on to others?

Feedback was taken from each group. Because of the time pressure on room availability at ICAAP9, the meeting was very limited in time and one of the constraints of the discussions was that the other two groups were not able to comment on the findings of each group.

Feedback

Group 1

Question 1 What are the main factors to consider in starting treatment?

Most people started treatment on the strong recommendation of their doctor in the face of falling CD4s and feelings of tiredness, and symptoms of fever or weight loss. Clinic nurses were also seen as being quite influential in persuading people they needed to start treatment. As one participant mentioned, “The nurse said that I had no option but to start”. There was apprehension about side effects and concern about resistance developing. But generally people felt that if they wanted to live longer and not get sicker, they had to start treatment. They were encouraged by seeing colleagues who had started treatment and were doing well on it.

Question 2 What are the good things and what are the bad things about being on treatment?

The good things were around their health and how they felt, and having more hope for the future. People talked about feeling fresher, more active and having a normal appetite. They did not get sick as often and looked healthier. People reported starting to look to the future and in some instances, being ready to have a baby.

The bad aspects reported were mainly around side effects. Some were concerned about putting on weight and others about not being able to put on weight. There were reports about problems with eyes and ears, and their skin getting darker and wounds taking longer to heal. Anaemia, low blood pressure, osteoporosis, were mentioned. Bad dreams and feeling more emotional were also raised. From a practical point of view people had problems making sure they took their medication on time.

Question 3 What kind of support do we need from healthcare workers to answer our concerns about whether or not the drugs are working?

Concerns centred around the need for more information and the stigma and discrimination people felt in the healthcare setting. A common experience was being told they needed to start treatment but not receiving sufficient explanation about why and about what to expect. They wanted to know about what side effects to expect, and drug interactions especially with supplements. Additional information on nutrition was lacking as most reported hearsay about certain foods (coconut, soya and broccoli) that were supposed to be beneficial for PLHIV.

Most of the recommendations were from well-meaning people who were trying to be of help. Moreover in Asia, there is a tendency to consider treatment of HIV and/or its side effects by using traditional medicines. These were sometimes positioned as “miracle cures” or direct-selling (Multi-level marketing) companies, and left PLHIV vulnerable to scams. Traditional therapy is also seen as an alternative rather than a complementary treatment. They felt they should be told about problems such as taking grapefruit (with Efavirenz) and some detox regimes (that could reduce the efficacy of the antiretrovirals). There was a lack of any emotional support which they felt they needed. Many of the healthcare providers are not well qualified, and the positive people felt they are discriminated against. Often they had to wait for two hours to spend just five minutes with the doctor. Doctors were too rushed.

Question 4 What kind of support do we need from healthcare workers to help us with side-effects, drug interactions and avoiding resistance?

Concerns about reactions to medication were often not taken seriously. When people experienced side effects such as dry lips or skin problems they were just told, “That is normal” without any suggestions on what to do about it. Healthcare providers are more concerned with opportunistic infections than side effects. It was suggested that a booklet could be made available which described the various drugs, their side effects and what actions could be taken to deal with them.

Group 2

Question 1 What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?

The group was clear that starting treatment earlier at a CD4 count of 350 offered significant benefits. The advantages in starting earlier include preventing opportunistic infections and bringing down viral load and increasing CD4s. Starting treatment earlier also potentially prolongs lives.

However, the group identified some serious concerns in starting earlier. These centred around two main issues. One was side effects and the other was the risk of resistance in a situation where there are limited second-line options. There are stockouts from time to time in many countries of the region, and the group expressed fear that by starting treatment earlier, the chances of a stockout would be greater and that could then cause resistance to develop. As one participant said, “distribution problems of ARVs is still a big issue here”. As people develop resistance and with more people on ARV this would put more pressure on second-line regimens which are more expensive. Would there be money to pay for those expensive second-line drugs? On an individual level people feared being in a position where they started treatment earlier, became resistant earlier and then found themselves without treatment options available to them at all.

The resistance issue could also be compounded if people started medication, felt better, stayed healthy and then decided that they did not really need to take the medication and may not adhere to their regimen.

It was clear that people did not like the thought of being on treatment unless it was essential, and starting earlier meant that "people would be on medication for a longer time". By starting treatment earlier people would have to suffer toxicities and side effects for a longer period of time.

Question 2 What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

There was a difference in what people felt between what they saw as the practical situation and what the ideal should be. As one participant said, "This is a 'Catch 22' situation and a tough choice". The question implied a situation where a choice had to be made between two options whereas they felt that they wanted to not have to make that choice.

This group agreed unanimously that given the current situation, they would prefer to postpone treatment, and start treatment at CD4s of 200 if necessary, in order to have a better range of drug choice and better monitoring later.

However, ideally they would like to have the option of starting treatment earlier if there was a guaranteed greater range of drugs available and if drug distribution problems were resolved.

In this context they wanted to see patent rights on new drugs abolished so that there would be a greater affordable choice of drugs. They also suggested that the quality and the monitoring of quality of drug production within countries should be improved. This is because in some countries in the region it has been claimed that there is a variation in the active ingredient in some local drug production. This can lead to resistance where levels are too low and variable, and that then limits the options for the future.

Question 3 What medical interventions do we want for people living with HIV who are co-infected with hepatitis C?

There was energetic comment on this subject especially because both hepatitis C and TB are common co-infections in the region with many PLHIV having an intravenous drug user background, and with 70 – 80% of those people being co-infected with hepatitis C. The group was quite clear in that hepatitis C treatment must be available at affordable prices. This includes access to monitoring of liver function and other monitoring, hepatitis C viral load measurement, and interferon. While interferon might be available in some countries, it is far too expensive for most people to consider. The group felt that if ARVs can be accessible, then so should hepatitis C treatment be.

Although TB was not part of the question, the group discussed its treatment too. They would like to see TB and ARV drugs combined into one tablet. They would also like to see more

monitoring to address side effects of TB drugs and want more research on how drug interactions between TB drugs and ARVs could be reduced.

Question 4 Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

The group was again unanimous and unequivocal in its response to this question. WHO should state the best treatment and monitoring options in the guidelines. The guidelines should not take into account resource constraints. Then governments should take on board the responsibility for the implementation of those guidelines.

Group 3

Question 1 How do ARVs play a role in HIV prevention? How do we use that information to advocate to governments?

The group felt that it is clear that taking ARVs lowers transmissibility of HIV and leads to better health, but the extent to which this is considered as a factor in treatment programs depends on the country. Treatment as a role in prevention is not a common notion in countries where there are low rates of access to ART. In some countries there is a fear of side effects that might delay uptake of ARVs and so the prevention effect is not as great.

The group felt that there were two views of treatment as prevention, the individual view and the population view. In the individual view, for example in the case of sero-discordant couples, the issue is one of the sexual health of both partners and issues such as family planning. It is doctors, PLHIV and their groups that are more interested in the individual view.

The population view looks at it in a way that says if you treat 'x' percent of positive people you have a 'y' percent decrease in infections and a consequent 'z' percent reduction in costs to the state. Governments are clearly more interested in population than individual issues and the previous equation may be a good argument to use in advocacy to governments.

It was also felt that ART contributes indirectly too, by changing social attitudes to HIV and hence leads to less stigma and more testing, in turn leading to less transmission. It can even act to mobilise treatment for other diseases which might be lagging behind in treatment access.

Question 2 Should all women living with HIV who are pregnant or trying to get pregnant start ART instead of just taking ARVs to prevent infection in their baby?

The participants started off by making the observation that it depends on when the woman finds out that she has HIV. The reality for many pregnant women is that it is in fact as a result of testing because of the pregnancy that their diagnosis is made. It can also be

because they feel unwell, or their partner is diagnosed. For this reason it is very important to continue to promote earlier testing for most-at-risk populations.

It also depends on what ARVs are available in that area.

The decision should be a personal choice for the woman, and that decision should be made on the basis of correct and balanced information. The information should take into account that there are two lives involved, each with rights, and should be delivered in an appropriate way. This implies the need for more resources, such as counselling, to assist the woman in the process of making a decision. Even group counselling in low resource settings is better than no counselling.

If the pregnant woman decides she wants to start ART she should be allowed to do so.

Question 3 How willing would people be to take part in trials of taking ART perhaps earlier than now thought to be necessary for their own health?

It was thought that fear and concerns may prevent people from taking part in such a trial. Part of that fear is about side effects and having to suffer them before necessary and potentially for longer. And part of the consideration is that in starting earlier it might cause resistance to occur earlier and before the availability of second-line treatments. By starting later, people would feel that it might delay the need to go onto second-line regimens. As long as their CD4s can be maintained at what was described as 'an acceptable' level, people would tend to delay treatment.

Another factor mentioned was the fear of stockouts that are currently common enough to be of very serious concern in many countries. People are likely to want to delay starting treatment (even if it is a trial) until stockouts are no longer an issue. (It is interesting to note that these are exactly the same concerns raised by Group 1 independently when they discussed starting treatment earlier.)

A necessary condition of people going onto such a trial would be that stockouts are addressed, and second-line regimens are available.

Question 4 How willing would people be to take part in trials of taking ART in order to see if it prevents HIV being passed on to others?

It was pointed out that studies to date have been conducted retrospectively so that couples were not 'taking risks' for the study. Such a study as the one suggested, requires if it is to be useful, that the negative partners are potentially putting themselves at risk. This was felt by the group to be ethically 'tricky".

The question about participating in the trial must also be addressed to the negative people who would be involved in the trial. Because of the possible risk involved, all partners involved must have clear and full information before making a decision.

The difficulty in conducting a trial was also discussed. It may be that behaviours will change during the trial just by being part of it, and that might affect the results.

It was felt that provided there is a sound ethical consideration, sound methodology, and both HIV+ and HIV- partners are informed then some PLHIV will probably be willing to participate in such a trial, but not all.

Group 3 also made some general comments about the subject covering all questions. ART guidelines are only one of many components and sources of information that PLHIV and their partners need in order to address wellness and a healthy life. People should have full information to inform their decision about starting treatment, trials and so on. Before embarking on trials or implementing new guidelines there needs to be guaranteed access, no stockouts, and trained healthcare providers.

In an overall sense they believed that WHO guidelines focus on the public, whereas clinical guidelines focus on the individual. As well as input into WHO guidelines, PLHIV should have input into clinical guidelines. There may be a tension between the two.

Summary

PLHIV see huge benefits in treatment and know that eventually they will need to take ARVs. But in the Asia Pacific region there is some reluctance to start treatment earlier based purely on some practical issues. In starting they want to be assured there will be nothing that will threaten their long term treatment effectiveness related mainly to resistance and the need to rely on second-line regimens which are either not available or not affordable right now. People are also very aware of side effects and their fear of them causes a reluctance to take treatment until it is 'really necessary'.

They do not believe that guidelines should be compromised by lack of financial and other resources and that the new guidelines should be based on 'best practice'. If this seems at odds with the first statement, it is because they aspire to optimum treatment but live with the day-to-day practicalities of what is possible, even if it is not optimal.

Note: The participants in this discussion were attendees of a regional conference. By definition they do not represent the huge majority of PLHIV living in the region who could never aspire to be at such an event. However, the participants were well-informed and sincere people whose views most likely reflect those of many PLHIV of the region.

Appendix 6

Consultation on WHO ART Guidelines

Defining Standards of Treatment and Care E-consultation

Global Network of People Living with HIV

27 July 2009 – 16 August 2009

Executive Summary

This report presents the key points and recommendations that emerged during the e-consultation on the forthcoming revision of the WHO's Recommendations for Antiretroviral Therapy (ART) for HIV Infection in Adults and Adolescents (ART Guidelines), held between July 27th and August 16th, 2009. The e-consultation was organised by the Global Network of People Living with HIV (GNP+) and hosted by NAM. It aimed to gather the perspectives and values of people living with HIV (PLHIV) related to the upcoming revision to the ART Guidelines.

Each week the e-consultation focused on a different topic area with three broad questions that covered different aspects of the guidelines:

- **Week 1 (July 27th - August 2nd)** Personal perspectives: how do we feel about treatment and what do we expect from ART?
- **Week 2 (August 3rd - 9th)** Advocate perspectives: balancing the tension between quality and equity of HIV care.
- **Week 3 (August 10th - 16th)** Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

A total of 317 advocates and activists living with HIV were invited to participate via email (300 were invited and 17 requested participation), of whom 128 registered, and 66 posted comments: a 21% response rate. Participants came from 36 countries representing all six WHO regions: Americas (13 countries), Africa (9), Western Pacific (5), Europe (4), Eastern Mediterranean (3), and South-East Asia (2). Participants were extremely well informed about treatment issues and most had personal experience of ART.

One of most important points to emerge from this e-consultation was the broad consensus that PLHIV must be educated and empowered about their options – whatever they may be – in order to make a joint decision with their clinician, and that treatment should begin:

- When the individual is ready;
- Based on the individual's overall health rather than focusing solely CD4 count criteria;
- And that the individual, rather than the virus, should be the focus of treatment and care.

CD4 count criteria for starting treatment should be in line with current scientific knowledge of best outcomes, at 350 cells/mm^3. A minority of PLHIV advocated for starting treatment at 500 cells/mm^3 and/or immediately following an HIV diagnosis in areas of high TB prevalence.

There was also broad consensus that d4T (stavudine) be removed from the list of recommended drugs due to its toxicity profile, and that tenofovir be recommended in its place. It was agreed that PLHIV require a broader choice of first- and second-line therapies with a focus on drugs that are easier to tolerate than currently recommended regimens. In addition participants highlighted the following concerns:

- The potential for NNRTI-associated toxicity;
- The difficulties of trading side-effects for potency;
- The realities of unnecessary drug switches due to stock-outs;

- Drug resistance issues, requiring third-line and salvage therapies;
- And improved patient education about the availability of second-line therapies – where they are available.

PLHIV feel very strongly that CD4 counts and viral load tests must be considered standard monitoring tools regardless of setting. Many also argued that resistance testing prior to starting treatment and following treatment failure was both necessary and cost-effective, and that if the WHO ART guidelines recommend them, this will help advocates fight for their funding on a local level.

Understandably, advocates are both optimistic and pragmatic regarding the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens. However, PLHIV feel that it is important to save lives now and worry about paying for it tomorrow. Although participants from sub-Saharan Africa, especially, were concerned about current and future levels of funding on drug access issues, many advocates argued that the guidelines could be used as a tool for PLHIV activism, and it that it was up to PLHIV and civil society to ensure that governments and funders see the long-term cost-effectiveness of starting treatment earlier with better drugs.

Consequently, PLHIV are not prepared to give up anything in return for guidelines that recommend earlier treatment with a greater choice of better-tolerated drugs. Nevertheless, participants appreciated that, in reality, the question of what PLHIV are prepared to give up was moot since "this is not a choice that is ours to make."

Those participants who had seen the results of the DART study recently presented to IAS 2009 were ready to consider a compromise on monitoring frequency if that meant earlier treatment with better drugs could be made affordable. Concerns were raised, however, regarding the interpretation of the DART study with some advocates noting that this could result in problems if task-shifted healthcare workers are not properly trained.

Regardless of the situation in their own country, participants were unanimous that the guidelines should reflect the best, current scientific knowledge and standards. Participants were of one voice that "the WHO guidelines should be a standard of care that all countries should strive to achieve, regardless of resources." Anything else "permits a differential set of standards which cannot be acceptable."

PLHIV understand that the link between treatment and prevention is extremely important and believe that the two "should be seen as a continuum and not a dichotomy." They noted treatment's effect on:

- Infectiousness, on both a population and individual level;
- Incentives to test, since untested people play an important role in new infections;
- And improved safer sex skills and safer behaviours of PLHIV accessing treatment and care.

Participants also highlighted that personal knowledge regarding the effect of treatment on transmission:

- Can be an incentive for better adherence for people on treatment and therefore better health;

- And makes it easier for PLHIV to start and maintain relationships.

Participants strongly advocated for WHO to highlight and clarify the role of treatment on prevention based on these reasons and, in particular, to:

- Ensure universal sustainable access to timely ART in order to prevent illness and promote wellness;
- Encourage undiagnosed individuals to know their status;
- And to reduce infectiousness on an individual, as well as a population, level.

However, they also agreed that 'treatment as prevention' should not take away the focus from a broader approach to prevention, and whilst calling for WHO to acknowledge and to clarify ART's role in reducing infectiousness, participants also agreed that WHO should state that treatment alone can only be part of an overall prevention strategy that must address those without, as well as those living with, HIV.

Finally, participants unanimously agreed that, "a human rights-based approach to health-related issues is of the upmost importance" and the "universal foundation of the response to the epidemic."

Recommendations

1. WHO guidelines should be based on the best, current scientific knowledge, focusing on a standard of care that all countries should strive to achieve, regardless of resources.

2. WHO should be aware that if their treatment guidelines are not harmonised with those in well-resourced countries, they run the danger of being seen to promote global inequalities.

3. The WHO ART guidelines should state that individuals begin treatment when CD4 counts reach 350 cells/mm^3. However, although CD4 count is an important indicator of when to start treatment, just as important is making sure that the approach to treatment is holistic, and that the individual is educated about treatment and ready to commit to lifelong therapy.

4. The WHO ART guidelines should no longer recommend d4T (stavudine) and recommend tenofovir in its place. More choice of first- and second-line therapies is required, with a focus on drugs that are easier to tolerate than currently recommended regimens with enough alternatives to allow for choice based on toxicity profile. Guidance on third-line therapies and beyond is required.

5. The WHO ART guidelines should recommend that all PLHIV have regular CD4 counts and periodic viral load tests. Most PLHIV are not prepared to give up anything in return for better, earlier treatment. A minority, however, concede that reduced lab monitoring frequency may be a compromise that is acceptable. If monitoring frequency is to be reduced whilst on treatment to save costs, then the guidelines must recommend that adequately trained healthcare workers are made available in order to assess toxicity and treatment failure. WHO should also consider recommending resistance testing prior to starting treatment and following treatment failure.

6. WHO should be aware that PLHIV will rise to the challenges faced in their own countries should guidelines recommend earlier treatment with more choice of better-tolerated drugs. WHO should argue strongly that such recommendations would be cost-effective, and take the lead in persuading governments to find the funding for drugs, personnel and healthcare infrastructures to deliver such treatment and care.

7. WHO should be aware that PLHIV in every setting appreciate and understand the link between treatment and prevention, and in particular the potential effect of ART on infectiousness, on both a population and individual level. WHO should highlight that access to treatment will result in population-wide prevention benefits, through reduced individual and population infectiousness; increased incentives to test; and improved safer sex skills and safer behaviours of those PLHIV accessing treatment and care.

8. WHO should clarify ART's role in reducing infectiousness on an individual as well as a population level in order to ensure universal sustainable access to timely ART; encourage undiagnosed individuals to know their status; reduce stigma; and to help individuals understand their personal risk.

9. WHO should also make it clear that treatment alone can only be part of an overall prevention strategy that must address those without, as well as those living with, HIV. Biomedical approaches, and prevention focused solely on diagnosed individuals, must be seen as part of a broader prevention

strategy that highlights structural power imbalances in society, such as gender inequities, gender violence and poverty.

10. WHO should ensure that a human rights framework forms the foundation of their approach to 'treatment as prevention' as a way of attempting to achieve universal access, and that a study on the feasibility, acceptability and sustainability of such an approach is necessary.

Methodology

The e-consultation took place over three weeks, from Monday July 27th to Monday August 17th 2009 inclusive. It was hosted by NAM, a community-based HIV information provider. A total of 300 advocates and activists living with HIV were invited to participate via email. Invitees included PLHIV who had attended previous GNP+ consultations: HIV+ Monaco, 2007; LIVING 2008, Mexico City; the International Technical Consultation on Positive Prevention, Tunis, 2009; IAS 2009, Cape Town; as well as partners from other GNP+ programmes.

Participants were informed that their perspectives and values would directly influence discussions for the revised WHO ART guidelines, and that this e-consultation was closed and limited to people living with HIV. In the first week, participants were encouraged to suggest other people living with HIV who might like to take part: a further seventeen individuals joined the e-consultation this way.

Each week of the e-consultation, on Mondays and Thursdays, participants received emails inviting them to share their experiences and opinions on specific topic areas. Each topic area included three broad questions that covered different aspects of the guidelines:

- **Week 1 (July 27th - August 2nd)** Personal perspectives: how do we feel about treatment and what do we expect from ART?
- **Week 2 (August 3rd - 9th)** Advocate perspectives: balancing the tension between quality and equity of HIV care.
- **Week 3 (August 10th - 16th)** Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

All six emails included the link to the e-consultation website (http://www.aidsmap.com/gnp+) as well as a personal password linked to the individual's email address. Participants were invited to fill in a short user profile and were given the option to choose a user name and to upload a photo. Name, sex, organisation and country data were provided for GNP+ internal use only.

The e-consultation was conducted in English and moderated by a GNP+ consultant living with HIV (who also authored this report – Edwin Bernard). The moderator regularly monitored the discussions to ensure that the posts were applicable to the subject; to answer any specific questions; and to suggest further areas of discussion within each question.

Participants from Algeria, Bolivia, Morocco and Peru posted in their native tongue, namely French or Spanish: the moderator provided a rough English translation following their post. Several participants contributed via email: the moderator posted their comments on their behalf.

Each discussion lasted a week, and comments were closed at 12.00 GMT each Monday. Due to several participants contacting GNP+ with technical issues during the first week of the e-consultation, the first discussion was left open until the following Thursday at 12.00 GMT. Once

the discussion was closed, participants were no longer able to post new comments but were able to read previous discussions.

Links were provided to the WHO website for further information on the revision process and access to current guidelines; to news reports by NAM from the 2009 International AIDS Society (IAS) Conference held in Cape Town; and to in-depth articles about a range of relevant issues from NAM's email newsletter, HIV and Treatment in Practice (HATIP).

Participants

Of the 317 individuals emailed, a total of 128 registered, and 66 posted comments: a 21% response rate.

Twenty-four participants were female. Three individuals posted anonymously without identifying their country. In all, 36 countries from all six WHO regions were represented:

Americas (18 individuals from 13 countries): Argentina; Bahamas; Bolivia; Brazil; Canada (3 individuals); Colombia; Jamaica (2); Mexico; Panama; Peru; Trinidad & Tobago; US (3); and Venezuela.

Africa (18 individuals from 9 countries): Algeria, Kenya (5); Ivory Coast; Malawi; Namibia; South Africa (3); Swaziland; Uganda (3); and Zambia (2).

Europe (13 individuals from 4 countries): France; Netherlands (4); Russian Federation; and the UK (7).

Western Pacific (7 individuals from 5 countries): Australia (3); Cambodia; China; Malaysia; and Papua New Guinea.

Eastern Mediterranean (5 individuals from 3 countries): Iran; Lebanon (3); and Morocco.

South-East Asia (2 individuals from 2 countries): Indonesia and Thailand.

Participants were extremely well informed about treatment issues and most had personal experience of antiretroviral therapy (ART). The 19 individuals from well-resourced countries had previous, personal experience of treatment issues in a low- or middle-income country and/or were working for international organisation that assisted and/or advocated for PLHIV in low- and middle-countries.

Week 1: Personal perspectives: how do we feel about treatment and what do we expect from ART?

Current WHO guidelines *suggest* starting treatment once CD4 counts have reached 350 cells/mm^3, but *recommend* starting treatment before CD4 counts reach 200 cells/mm^3. In practice, people tend to have much lower CD4s when they start ART, and most people only start once they are very sick. In addition, many people do not take treatment even when they are eligible, and some drop out of treatment once they've begun.

It is likely that the revised guidelines will recommend starting treatment earlier, at 350 cells/mm^3, which is already the recommendation of guidelines from experts in the North America, Europe and Australia as well as those of the South African HIV Clinicians' Society.

The guidelines will also discuss the benefits and tradeoffs of:

- Using AZT (zidovudine) versus d4T (stavudine) versus TDF (tenofovir) as a preferred first line therapy drug;
- Non-nucleoside- versus protease inhibitor-based first line regimens; and
- The role of triple nucleoside regimens.

Participants were asked to discuss three broad treatment-related areas but were encouraged to discuss specific issues within each discussion area:

1. When should we start and change treatment? (32 posts by 29 individuals)
2. What drugs should be recommended for first- and second-line therapy? (22 posts by 20 individuals)
3. What kind of monitoring is necessary to help inform our treatment decisions? (20 posts by 18 individuals).

A total of 41 individuals participated in Week 1 discussions around antiretroviral therapy (ART) from a personal perspective. Although the aim was to discuss personal experiences and share opinions on what PLHIV would like the WHO guidelines to say to make sure their treatment and care needs are met, broader issues of access inevitably came into play.

1. When should we start and change treatment?

Most participants focused on the issue of starting rather than changing treatment, which was discussed more thoroughly during the question 3. The most important points to emerge from this discussion was the broad consensus that PLHIV must be educated and empowered about their options (whatever they may be) in order to make a joint decision with their clinician, and that treatment should begin:

- When the individual is ready;
- Based on the individual's overall health rather than focusing solely CD4 count criteria;
- And that the individual, rather than the virus, should be the focus of treatment and care.

If CD4 count criteria are used, they should be in line with current scientific knowledge of best outcomes: at 350 cells/mm^3, with a minority advocating for 500 cells/mm^3 and/or immediately following an HIV diagnosis in areas of high TB prevalence.

Patient literacy

Participants were unanimous that PLHIV must be partners in their treatment and care in order to achieve the best health outcomes. This, noted an advocate from the Netherlands, is about "putting the 'patient' in charge of their treatment and treatment options so that they (alongside peer educators from a community) are coming to an informed choice that is good for them."

"More often than not we don't have the luxury to even ask this question [i.e 'when should we start and change treatment?'] of health care providers whose opinion and advice in many instances remains unquestionable," wrote an advocate from Thailand. "We are just supposed to do as we are told: basically it's take it or leave it and doctor knows best. I think this is really the way that treatment roll-out is made available in developing countries in Asia and the Pacific. This top down approach to dealing with clients making us just recipients of services with no voice is why treatment education and literacy is so vital among PLHIV and communities, and the need to ensure we are sufficiently empowered to question when we are given the wrong kind of treatment."

An advocate from Bolivia who has been on treatment for over four years says he only managed to access treatment because he was an activist who knew his rights and was not afraid to ask for treatment, but that many people still die untreated in his home country. *"Estoy con tratamiento por mas de 4 años, y empece cuando teniía 120 CD4, ahora solo he suvido 175 CD4, los riesgos que se vive son complejo, mi persona porque es un activista ha podido exigir y hacer cumplir mis derechos y no tengo miedo de dar la cara, es que ahora estoy vivo, pero en mi ciudad la mortalidad por cuestiones clínicas de SIDA es la mas alta de mi país (Bolivia)."*

"I think education is the most important part of taking your treatment," concurred an advocate from the Bahamas. "Persons who do not understand how the medication works and what are the side-effects need to sit down with their physician and discuss what the medications are for; what the side-effects are; what can be done to reduce side-effects; and what can be done if the meds are not working."

"Before asking PLHIV to start their treatment," added an advocate from Indonesia, "we should give them awareness and information on the effect of ARVs. Otherwise taking ARVs without willingness from ourselves will be nothing, because ART is long-term, and adherence will be the most important factor for successful ARV treatment."

When the individual is ready

Continuing the theme of patient literacy, participants also argued strongly that, "a positive patient has to be ready to start drugs. If a person is not ready," wrote an advocate from the US, "no doctor can make them start."

"I started my treatment from a CD4 of 42, because of not knowing when and what to take," wrote an advocate from South Africa. "I strongly feel that information is still needed for people to make informed decisions about the benefits of taking treatment earlier as well as the benefits

of delaying it. ...personal readiness and psychological support is needed; we need to address fears of drug toxicity while considering access to treatment."

Individual health

Participants also agreed that although the WHO ART guidelines are "needed to guide practice and to help forecast appropriately financial, human resources and medical goods needs," they "do not allow for a personalised approach." (French advocate).

It was argued strongly that a public health approach to ART should not preclude treating individuals living with HIV rather than simply the virus itself. "Many physicians only see the virus and not the person who is carrying it," noted an advocate from Canada.

An advocate from Russia wrote: "My CD4 was between 350 and 500 during 13 years and I never felt sick - only few times. I finished hep C treatment one month ago with good results and my CD4 is 200 now. Taking into account strong health condition during 13 years, I think that each person's health condition has to be the criteria for starting ARVs. It is not appropriate to say that a person has to start treatment immediately if CD4 is 350 because of the WHO guidelines. Some people need treatment on 500 CD4 and some need on 350 or 200."

"Personally, I would have preferred to be on treatment before the required stage and the same can be said about the many friends and relatives that I have lost, while they were waiting for treatment," wrote an advocate from an unnamed African country. "I have recently lost my best friend that died due to incompetence and inefficiency. He was completely exposed and the waiting worsened his situation. While on the other hand, my CD4 count was below 50, and I managed to qualify for the treatment at a very dangerous stage, I nevertheless, managed to overcome the worse. I therefore believe that an individual approach should be adopted, taking into the individual's circumstances."

CD4 count criteria

Most participants agreed that the criteria for initiating therapy based on CD4 count should be when it reaches 350 cells/$mm^{3.}$ "In many developed countries, national guidelines recommend to start when CD4 count drops to 350," wrote an advocate from France. "There is no scientific, medical reason not to have the same recommendation for people living with HIV in developing countries."

"As many have commented I think it is high time treatment should start a bit earlier, say when CD4 count is between 300 and 400," wrote an advocate from Malawi, "because it is when the treatment can work well. I live in a sub-Saharan developing country where a lot of people start treatment when the CD4 count is low which is very dangerous: many people die and they think the medicine is killing people. So there should be a standard set to say that even when someone is not feeling sick they should start treatment [based on CD4 criteria]."

Advocates from Argentina and Lebanon advocated starting treatment earlier, at 500 cells/mm^3. "I read many articles on the best practice of beginning therapy," wrote the Lebanese advocate, "and I think PLHIV have the right to start taking their medicines when their CD4 count is lower than 500...but on the other hand, they have the right to know exactly what kind of medicines

they need, what are their side-effects, why they should start, if they are able to wait and until when."

An advocate from Uganda argued that in settings with a high prevalence of TB, pegging initiation to CD4 counts "is becoming irrelevant" and that people should start treatment as soon as they are ready, soon after a positive HIV test result. "I think that as long as one tests positive and physically and clinically feels s/he needs the treatment, the person should be allowed to start rather than waiting for the person to be bed-ridden and become an issue for their dependants (children)."

Finally, an advocate from the US notes that his "view on this issue has changed in the past year. Before, I would have said to wait until CD4 count is low or there is symptomatic disease. I thought that once we start, we would have to take pills for our lifetime, so why not delay until necessary. Recent discussions on Positive Prevention have caused me to realign my thinking since it appears that people on medications with an undetectable viral load are far less infectious (or possibly not infectious at all). So, by starting effective treatment at diagnosis, people with HIV/AIDS will be contributing to AIDS prevention. Additional studies have shown that the earlier that people with HIV/AIDS start therapy, the better their health outcomes. So, this appears to be a win-win situation."

Treat holistically

"I think it would be good for WHO to be taking a holistic approach to treatment," writes an advocate from the UK, "which reflects not only the importance of drugs themselves but the much wider context of care, respect, solidarity and support which we all know to be so important to our well-being, our adherence and our capacity to cope with the virus and its consequences in our bodies. The WHO definition of health is a very holistic definition, but sadly this holistic definition often gets forgotten about in its day-to-day work, and the word 'treatment' often gets very narrowly defined - and interpreted - as just something just referring to ARVs."

Recommendation

The WHO ART guidelines should state that individuals begin treatment when CD4 counts reach 350 cells/mm^3. However, although CD4 count is an important indicator of when to start treatment, just as important is making sure that the approach to treatment is holistic, and that the individual is educated about treatment and ready to commit to lifelong therapy.

2. What drugs should be recommended for first- and second-line therapy?

There was broad consensus that d4T (stavudine) be removed from the list of recommended drugs due to its toxicity profile, and that tenofovir be recommended in its place. It was also agreed that a broader choice of first- and second-line therapies should be made available with a focus on drugs that are easier to tolerate than currently recommended regimens.

In addition participants highlighted the following concerns:

- The potential for NNRTI-associated toxicity;
- The difficulties of trading side-effects for potency;
- The realities of unnecessary drug switches due to stock-outs;
- Drug resistance issues, requiring third-line and salvage therapies;
- And improved patient education about the availability of second-line therapies – where they are available.

Remove d4T from list of recommended drugs

This issue dominated the discussion, with many advocates having had personal or professional experience of the impact of d4T's toxicities. "I for one experienced a lot of side-effects with stavudine during first-line therapy," wrote an advocate from Malawi. "I had prolonged neuropathy which lasted almost a year and a half. My legs were completely dead with no feelings at all. Thankfully I am responding well to second-line therapy."

An advocate from Zambia compared his experience of treatment in the UK with that in his home country. "Where it all seems to have fallen apart is the prescription of stavudine (D4T) as the medicine of first choice by clinicians. As a treatment support counsellor, it was always a depressing time as one after another patient told of harrowing tales of having to cope with difficult, unbearable side-effects; in most cases resulting in a terribly diminished quality of life. I admire the African Spirit. I can't imagine what the outcome might have been like if similar treatment were meted out at, say, Kings College, London where I was a patient for at least two of my four year ARV treatment in the UK."

A French advocate with extensive support experience in Africa amplifies these points: "Regarding access to first-line regimens, there is an absolute emergency: ban d4T!"

Nevertheless, an advocate from Iran wrote: "As for myself, D4T worked very well for 10 years although for many it is not an easy drug to use."

NNRTI toxicity

Several participants highlighted issues around the potential toxicities of efavirenz (notably central nervous system side-effects) and nevirapine (notably rash and liver toxicity). "It is imperative that clinicians fully disclose the side-effects of *Stocrin* (*Sustiva*) and not downplay them (as is now customary)," wrote an advocate from the US.

"I think nevirapine is over-prescribed," wrote an advocate from Zambia. "The high levels of hypersensitivity observed at my treatment centre demands treatment advocacy to mobilise resources to lower prices of new non-nucleoside reverse transcriptase inhibitor(s), along with expanding second-line regimens."

Trading side-effects for potency

An advocate from Trinidad & Tobago illustrated the conundrum of wanting better-tolerated drugs when resources (and options) are limited when he stated: "I would say we need drugs

with less side-effects, especially lipodystrophy. Although I suffer with that side-effect, I maintain my present meds, since they work very well for me."

"Suffice to say, regardless of how the patient feels," noted an advocate from Zambia, "if CD4 counts tell a good story, one is forced to endure these side-effects. People are known to have lost use of once-healthy limbs prior to ARV treatment due to the uncompromising practitioner stances regularly taken."

Stock-outs

Participants from Cambodia and Jamaica highlighted experiences of having to switch successful drug combinations due to stock-outs. "In my country," wrotes the Cambodian advocate, "sometimes physicians change people to D4T from AZT and from D4T 30mg to D4T 40mg" due to stock-outs. "The WHO guidelines should not allow a change from AZT to D4T when there is no AZT in stock." In the case of the Jamaican advocate, however, his enforced switch from *Combivir* to *Truvada* occurred with no problems.

Drug resistance issues

An advocate from Swaziland highlighted issues of drug resistance due to a variety of issues, many of which – such as stock-outs – are outside of the control of the individual. "People are initiated on treatment at a very compromised immune system of 200 but they are defaulting due to economic status, some due to fatigue, other due to treatment failure and many other reasons. The guidelines need to be concerned about drug resistance because over the years as you are taking the treatment even if you are complying and adhering in the long run you will end up with drug resistance and you will need to be changed to the second-line expensive regimen. So my question is: are the guidelines going to come up with third-, forth-, fifth-line and so on regimens since we will be in need of new drugs to tackle the resistance challenges that will come up?"

Patient education

Finally, an advocate from the UK working in Africa also highlighted the need for patient information on the availability of second-line therapy. "Ministries of Health in Southern African countries are dumping second-line therapies because the uptake is so bad," she wrote. "I cannot believe that the need is not there - it is just people do not know about second-, third- and fourth-line therapies."

Recommendation

The WHO ART guidelines should no longer recommend d4T (stavudine) and recommend tenofovir in its place. More choice of first- and second-line therapies is required, with a focus on drugs that are easier to tolerate than currently recommended regimens with enough alternatives to allow for choice based on toxicity profile. Guidance on third-line therapies and beyond is required.

3. What kind of monitoring is necessary to help inform our treatment decisions?

Participants argued strongly that CD4 counts and viral load tests must be considered standard monitoring tools regardless of setting.

Many also argued that resistance testing prior to starting treatment and following treatment failure was both necessary and cost-effective, and that if the WHO ART guidelines recommend them, this will help advocates fight for their funding on a local level.

Concerns were also raised regarding the interpretation of the recent DART study and frequency of monitoring.

CD4 and viral load

Participants highlighted the difficult situation they currently find themselves in: knowing that CD4 counts and viral load tests are necessary, but being unable to access them. "A combination of CD4 and VL count is necessary for treatment decisions like starting and changing treatment," wrote a Kenyan advocate. "We demand CD4 count machines and we demand access to quality laboratories with VL count machines. This is currently lacking in Kenya." A South African advocate concurred: "CD4 count is important with the staging of HIV and treatment of OIs. Viral load also should be used, but it is often used too late, putting most of our lives in danger."

Expectations were high amongst some participants that the WHO ART guidelines could 'fix' this problem. "Viral load is very important to monitor the treatment together with the CD4 count," wrote an advocate from Malawi. "But unfortunately in our country we do not have enough equipments for these services. For someone who is on treatment I think doctors or health personnel can know well if the medication is working properly if there are regular tests on VL and CD4 counts. Now, because we are poor we just receive the medicine without proper check-ups; you end up with liver, kidney problems because of lack of equipment. So WHO has to look into this matter, especially in poor developing countries where access is a problem to health centres."

Some advocates argued that information regarding the personal risks of infectiousness based on knowledge of viral load was an extremely important part of deciding if and when to start treatment. "If you are in a sero-discordant relationship," wrote an advocate from Australia, "and for whatever reason you do not want to use condoms, then you might want to go onto meds whatever the counts are as a prevention measure, weighing up whether you fit the criteria they define in the 'Swiss Statement'."

Resistance testing

An Iranian participant reiterated the power of the WHO guidelines when advocating for resistance testing in his country. "In a country like mine," he wrote, "these guidelines have an important role in the mind of health decision-makers and they presume if WHO does not require it therefore it is not that important. Drug resistance testing before starting ARVs is of upmost importance, but unfortunately is not included in WHO recommended guidelines. Please note that ARVs are costly, and if not prescribed properly does more harm than benefit, therefore I believe a 200-300 dollar drug resistance test can be cost-effective."

Participants also highlighted the utility of resistance testing when deciding when to switch to second- and third-line therapy. However, one advocate pointed out that this is moot where access to drugs beyond the second-line is non-existent. "Phenotype resistance testing is not available at all except for those who have money to pay for private health care," noted a South African advocate. "For people like me who depend on the public health care system in South Africa it's not done purely because if I become resistant to my second-line drugs (AZT/DDI/*Kaletra*) there is no other option as we don't have third-line regimens."

Monitoring frequency

An advocate from Argentina highlighted that annual CD4 monitoring, which is common in Latin America, is not frequent enough. "You know the situation in countries in Latin American, access to health systems is so difficult, especially for poor people. Healthcare visits are few, often a year apart, and this is too late to catch people before they get sick."

Advocates who had seen the results of the DART study recently presented to the IAS Conference were torn between welcoming the possibility of reduced monitoring frequency freeing up funds for more drugs with the concern that this could result in problems if task-shifted healthcare workers are not properly trained. "The DART study that was conducted in Uganda and Zimbabwe showed that if healthcare workers are trained to clinically assess PLHIV compared to those who rely on lab monitoring there really wasn't a big difference in outcome," noted a South African advocate. "But we met with the investigators because I was concerned about their conclusion, that it may be misunderstood as saying lab monitoring is not needed at all. They said, 'No, their recommendation is that the frequency of lab monitoring pushes the clinic budget high and this can be reduced by maybe doing viral load at three months rather than at baseline and then maybe yearly or six months after that.' I think this can be explored and it seems cost-effective, but PLHIV cannot accept no lab monitoring at all because in areas where healthcare workers are task shifting, they need to be confident when they are making decisions about treatment changes and side-effect issues."

Concerns over frequency of monitoring were placed in sharp focus when advocates highlighted co-infection issues. "Currently I think there is a lot of uncertainty in developing countries as to how, why and when people are put on treatment and what are the minimum standards for effective monitoring," wrote an advocate from Thailand. "How long between CD4 and VL tests and when to start treatment. For those who are IDU and co- infected with HCV this is another complexity to the issue that is hardly raised by healthcare workers."

The importance of regular monitoring for pregnant and nursing mothers was also highlighted. "On a recent visit to Zimbabwe," wrote a UK advocate, "a colleague told me about a positive woman not on medication who was breastfeeding her three-month-old baby. We heard today that that baby died. Why oh why is this happening? None of the women in her support group were regularly accessing a medical practitioner or had an in-depth knowledge of their HIV. I can't imagine where I would be now if I was solely relying on the medical visit I had when I was diagnosed. So much about treatment is education and being on top of our own conditions and being empowered to make those decisions ourselves and not have them imposed by clinicians. So what kind of monitoring? Every kind. From the personal holistic monitoring to the global monitoring, and most importantly dialogue between health care providers and support services and positive people's organisations."

Recommendation

The WHO ART guidelines should recommend that all PLHIV have regular CD4 counts and periodic viral load tests. If monitoring frequency is to be reduced whilst on treatment to save costs, then the guidelines must recommend that adequately trained healthcare workers are made available in order to assess toxicity and treatment failure. WHO should also consider recommending resistance testing prior to starting treatment and following treatment failure.

Week 2: Advocate perspectives: balancing the tension between quality and equity of HIV care.

The aim of Week 2's discussions was for advocates to appreciate the difficult task faced by the WHO ART guidelines writing committee and to weigh up the desire for the best possible quality of care against making sure as many people as possible get access to ART.

Governments, healthcare managers and advocates in low- and middle-income countries with large unmet treatment needs face an unenviable dilemma: attempt to treat more people by continuing to use cheaper drugs and increase (or maintain) CD4 count, viral load and resistance tests and toxicity monitoring or use more expensive, better-tolerated drugs but reduce (or eliminate) some monitoring.

As Keith Alcorn of NAM writes in his coverage of the DART study at the recent IAS conference: "The results of the DART study are likely to stoke the growing controversy over the best way to monitor HIV treatment in resource-limited settings. In the past year, there have been growing calls to incorporate viral load monitoring into treatment programmes, both in order to detect failure of first-line treatment early and in order to determine whether patients apparently failing treatment on the basis of recent declines in CD4 count are genuine cases of treatment failure. However, trial investigator Professor James Hakim of the University of Zimbabwe told delegates that it would be possible to treat up to one-third more patients with antiretroviral drugs if laboratory monitoring were limited to the use of CD4 counts after the second year of treatment."

Drug costs aside, there are also concerns about the availability of certain drugs and drug monitoring equipment as well as concerns about the additional personnel required to deliver treatment and care as the numbers of people eligible for ART increase, with an increased focus on task shifting.

Again, participants were asked three broad questions and encouraged to debate the issues:

1. What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?
2. What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

3. Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

Although there were fewer participants during the second week of discussion – possibly due to the extremely difficult questions being asked – out of the 20 participants who took part, ten were new to the discussion.

1. What are the benefits and tradeoffs if WHO recommends starting ART earlier and recommends using more expensive regimens?

Responses to this question ranged between optimism and pragmatism. Participants from sub-Saharan Africa were particularly concerned about funding and drug access issues. "The point is that although it is great to get people on treatment earlier, we are having drug stock-outs even for those with CD4 counts of below 200," wrote an advocate from Uganda. "I'm worried that a person having a CD4 count of 100 will not get drugs while we have put on treatment a person with a CD4 count of 300. The inconsistent supply of antiretroviral drugs in our Government's health system is causing us to not do what is right for our people. Three of our major US-funded sites are no receiving more funding and no new patients will be recruited. Our country can't afford those expensive regimes."

"The benefits of earlier initiation have been scientifically proven to help prevent the onset of opportunistic infections," wrote an advocate from Swaziland. "However, in my country only 32,000 of the 68,000 who require treatment based on current WHO ART guidelines are on treatment – a clear indication that as a country we are failing when it comes to delivering ART services to people. This early initiation would now increase the number of people who are suppose to be on ART and will overwhelm our ARV programme. Already we are told that the Global Fund will reduce funding of our ARV programme by 10%, so how will we manage to put people on treatment early when we are expected to cut by 10%?"

"We in Africa have not even managed to put half of all the people infected with HIV on ART, which clearly improves the lives of PLHIV, with the available 'cheap' regimens, so we cannot start asking for more expensive ones," argued an advocate from Uganda. "It is like asking someone who has failed to get a share of the main course of a meal what they want to have for a desert!"

"Using expensive regimens can't work", added a Malawi advocate. "The expensive regimens are a non-starter."

And yet, many advocates argued that PLHIV activism following the revision of the WHO ART guidelines could make a difference, as it has in the past. "Is it really reasonable to now change our goals?" asked an advocate from France. "Certainly not, and that's why we should do it [i.e. have earlier treatment with more choice of drugs]. From the very beginning of the history of our common fight, we have accomplished mainly unreasonable things." Although, noted an advocate from Thailand, "the pressure on systems in terms of cost and how it could effectively be managed and rolled-out - is kind of a scary thought, yet we see that to address H1N1, for example, money does flow when necessary."

Some argued strongly that it was important to save lives now and worry about paying for it tomorrow.

"Definitely earlier treatment is the right approach as it keeps the person healthy," wrote an advocate from Lebanon. "The challenge is to have more generic versions of the new meds at a reasonable price."

"This will cost at the beginning," wrote an advocate from South Africa, "because it will force funding to be found for earlier treatment for more people, but in the long term it will reduce the cost of hospitalisation, reduce TB – especially in sub-Saharan Africa, and reduce maternal and child mortality related to HIV."

"Starting ART earlier is the right choice," wrote an advocate from China. "It keep people living with HIV healthy and ensures our quality and length of life. But this needs support and commitment from the local government and healthcare sectors."

"Starting at 350 can increase attention of governments to HIV in countries with limited resources," noted an advocate from Russia. An advocate from Papua New Guinea concurred: "We need to start people earlier on drugs in order for them to contribute to the countries growth."

Some argued that governments and funders would see the long-term cost-effectiveness of starting treatment earlier with better drugs. "People will live longer and healthier lives, and due to decreased viral load, more infections will be prevented," argued an advocate from the US. "In the long run, this will actually save money. Using this line of reasoning we may motivate countries and more private funders to invest in treatment today, in order to save funding tomorrow."

Recommendation

WHO should be aware that PLHIV will rise to the challenges faced in their own countries should guidelines recommend earlier treatment with more choice of better-tolerated drugs. WHO should argue strongly that such recommendations would be cost-effective, and take the lead in persuading governments to find the funding for drugs, personnel and healthcare infrastructures to deliver such treatment and care.

2. What, if anything, are we prepared to give up in return for earlier treatment, more drug choice and/or better monitoring?

Participants appreciated that, in reality, the question was moot since "this is not a choice that is ours to make." Consequently, many responses were uncompromising. "I am not prepared to give up anything," wrote a Canadian advocate. "Treatment and monitoring to me are one and the same when it comes to improving the health of an individual."

"In a world of limited funding, this is a very hard question," wrote an advocate from the US. "I always think it is best to ask for the moon and be grateful for all that comes our way. If we ask for less, we will receive less."

"Basically, being asked to give something up in favour of something else is asking us to be complicit in 'bigger' political processes that promote global differentials, economic and

otherwise. As a global community we should be demanding the moon and demanding it for everyone," added a UK advocate.

It wasn't just advocates from well-resourced countries who felt this way, however. "Not ready to give up anything in return for earlier treatment," wrote an advocate from Malawi. "The drugs, along with better drug choice and monitoring, should be available to all so that our friends that need to start the treatment can have their lives prolonged."

An advocate from China pointed out that PLHIV should not suffer due to the inefficiencies of their governments. " Too much money has been abused. In some countries we need to demand for better relocation of HIV/AIDS grants to support free ART and earlier treatment with better monitoring and more drug choice."

However, those participants who had seen the results of the DART study recently presented to IAS 2009 were ready to consider a compromise on monitoring frequency, if that meant earlier treatment with better drugs could be made affordable. As an advocate from Lebanon noted this often happens anyway: "The patient is often responsible for paying for CD4 and viral load tests anyway, and since it's expensive, most people do it once a year instead of every six months.

"Lab monitoring prices are very high," concurred an advocate from South Africa, "and this results in too few people accessing ART, but it's not the only reason why we will not meet universal access to treatment. This discussion [about monitoring frequency] will help countries to reduce cost to treat more people but maintain quality standard of care."

Recommendation

WHO should be aware that if their treatment guidelines are not harmonised with those in well-resourced countries, they run the danger of being seen to promote global inequalities. Most PLHIV are not prepared to give up anything in return for better, earlier treatment. A minority, however, concede that reduced lab monitoring frequency may be a compromise that is acceptable.

3. Should the WHO guidelines reflect only what is thought possible given the many resource issues, or state the acceptable minimum based on the best and current scientific knowledge and standards?

Participants were of one voice that "the WHO guidelines should be a standard of care that all countries should strive to achieve, regardless of resources." Anything else "permits a differential set of standards which cannot be acceptable."

Regardless of the situation in their own country, participants were unanimous that the guidelines should reflect the best, current scientific knowledge and standards. "Coming from a resource-poor community," wrote an advocate from Kenya, "I feel that issues of care and treatment should not be negotiable. Equal standards should be set for all governments. Aiming at this goal would be a good assignment for such governments." An advocate from Lebanon added: "WHO guidelines should reflect the best rather than simply reflecting what is thought possible, provided it also helps our governments change their perceptions."

"Clinical need of what is best for the 'patient' should always take precedence over a notional economic scarcity argument," stated an advocate from the Netherlands. "I say notional because I seriously do think that if there is the political will then the money can always be found. To accept sub-optimal treatment regimes does not make good economic sense and does not serve the public health: if we give too little, too late, then people will continue to opt out of testing, thinking that they don't need treatment, and continue to think (with some justification perhaps) that it is the ARV's that are causing people to get sick."

Recommendation

WHO guidelines should be based on the best, current scientific knowledge, focusing on a standard of care that all countries should strive to achieve, regardless of resources.

Week 3: Positive Health, Dignity and Prevention: how important is a human rights-based approach to treatment when used as a prevention tool?

The aim of Week 3's discussions was to discuss what PLHIV thought about the use of treatment as prevention. Participants were informed that WHO is currently examining the impact of antiretroviral treatment (ART) on prevention, since it is known that ART significantly reduces (but does not completely eliminate) the amount of virus in our bodies, and so reduces the possibility that we are infectious to others.

They were aware of the concept that reducing the viral load of a country's population could help with prevention, and so making sure that everyone who needs ART gets it might go a long way towards preventing new infections. However, they were also aware that WHO does not currently support providing this information to people living with HIV to prevent transmission on an individual level primarily because knowledge about individual risks is still incomplete.

One of the stated relevant outcomes of the WHO treatment guidelines is the reduction of HIV transmission although 'treatment as prevention' is not currently WHO policy. Nevertheless, more radical ideas about how ART might be used for prevention, such as universal testing and starting ART immediately at diagnosis, are currently being explored by the research community and by WHO.

At the recent GNP+/UNAIDS technical consultation on Positive Health, Dignity and Prevention HIV advocates discussed how this more radical approach could have a major impact on people living with HIV. On the one hand, a policy of 'treatment as prevention' might allow many millions more to obtain earlier access to treatment and care, and even get close to eliminating new infections. However, undertaking such an approach could be problematic from a human rights standpoint: could universal testing and treatment threaten our right to choose if, and when, we want to start treatment? Is it also a human right to know your HIV status and to be able to access treatment?

Given these issues, participants were asked to consider whether a policy of 'treatment as prevention' is in our best interests, and specifically the following three questions:

1. How important is the link between treatment and prevention?
2. What should the WHO guidelines say about treatment and its role in prevention?
3. How relevant are human rights concerns in settings where there is no universal access to treatment?

Week 3's theme proved to be popular, with 31 participants taking part in the discussions, of whom 15 had not previously posted in Weeks 1 or 2.

1. How important is the link between treatment and prevention?

Participants strongly agreed that the link between treatment and prevention is extremely important and that the two "should be seen as a continuum and not a dichotomy."

They noted treatment's effect on:

- Infectiousness, on both a population and individual level;
- Incentives to test, since untested people play an important role in new infections;

- And improved safer sex skills and safer behaviours of PLHIV accessing treatment and care.

Participants also highlighted that personal knowledge regarding the effect of treatment on transmission:

- Can be an incentive for better adherence for people on treatment and therefore better health;
- And makes it easier for PLHIV to start and maintain relationships.

However, they also agreed that 'treatment as prevention' should not take away the focus from a broader approach to prevention. "Since prevention is not just a scientific or technological intervention, prevention must also address structural power imbalances in society, such as gender inequities, gender violence and poverty." (UK advocate)

Continuum, not dichotomy

"Treatment is an important element that makes our prevention efforts works. If there is no treatment, prevention is not realistic," wrote an advocate from China.

Treatment and prevention "are as linked as the two sides of a coin," noted an advocate from UK. "They must never be disassociated," concurred an advocate from Brazil. "Treatment cannot be thought about without prevention and vice-versa."

"Separating prevention from treatment leads to a fictitious polarisation between those who have HIV and those who don't: the villains and the victims," wrote an advocate from the Netherlands. "Integrating prevention and treatment will better reach the great majority of people living with HIV: those who do not know they have it! Indeed by integrating budgets on prevention and treatment both programmes in one will be more effective."

"I believe that there should not be one without the other," wrote an advocate from Jamaica, "and I strongly believe that one should not be treated less than the other. In my country the National AIDS Programme concentrated so much on prevention for people who were not yet infected that people who were already infected were left out and pushed to the back burner. A multi-disciplinary approach is required when working out treatment and prevention for both infected and uninfected persons."

Effect of treatment on infectiousness

"I see a great link between prevention and treatment," wrote an advocate from Algeria. "If one is undetectable there is a chance the treated person does not infect others, and women could not have a children without prevention and treatment, so they are the same thing for me." *Moi, je vois qu'il ya un grand lien entre la prévention et le traitmaint ci en as dépisté plus tout en la chance de se traité et ne pas contaminé les autres et pour la femme encante pour qelle peura avoir un enfant san la prévention et le traitmant si parce que la méme choue pour moi.*

Participants cited studies and statements from global experts regarding the effect of treatment on infectiousness and transmission. "Professor Montaner, the President of the International AIDS Society, stated that there is enough scientific evidence to tell policymakers that 100% ART will decrease infection rates, and this has been shown in countries like Taiwan, for example, where infection rates fell by more than 50% after ART was introduced," noted an advocate from the US.

The recent paper published by WHO members of staff in *The Lancet* exploring the potential impact of universal voluntary HIV testing followed by immediate ART irrespective of clinical stage of CD4 count was endorsed by some participants, including an advocate from Kenya. "Universal treatment is paramount if prevention strategies are to be successful. PLHIV should be in the forefront demanding for universal access to treatment." "In my mind treatment has to be seen as a tool in prevention," added a South African advocate. "Given that we are unlikely to ever get 100% behaviour change then this is an invaluable asset in the prevention toolbox."

Not everyone was convinced about ART's role on infectiousness, however. "I don't personally associate being on treatment as being linked to prevention," wrote an advocate from Canada. "As long as you are HIV-positive, you are still infectious!" And an advocate from Panama added, "I am really concerned about the spread and poorly understood fact that a low [viral load] means automatically there is no possibility of infection. I think there are alternatives to consider before you determine without doubt that this is so."

Others argued that one cannot rely on treatment alone as prevention and that if would be better to treat based on clinical need than for public health reasons. "We can't rely on treatment alone to stop this epidemic, but need both treatment and population-wide prevention," wrote an advocate from the UK. "People who have been recently exposed and are at their most infectious will in most cases not be aware of their infection and so universal treatment will have no impact on this transmission dynamic - which becomes more important as more people who know they have HIV get tested and treated. We also must take into account that up to 75% of those with HIV don't know, or have no means of knowing, their status, let alone getting access to reliable treatment with a second-line back up. So, we need to continue with prevention activities, and offer *treatment as treatment* on the basis of need. There will be an effect on transmissibility, and that's terrific, but the primary reason for rolling out treatment should be the health promotion needs of PLHIV. If we had the choice of just enough money to pay for first-line regimens for all (irrespective of CD4 count); or first-line plus second-line back up for all those with a CD4 count below 350, which is the ethical choice? In my view, it's the latter, backed up with good, effective, community-led prevention and anti-stigma activities."

Treatment as an incentive to test

"Treatment is key in prevention because in communities where PLHIV are on treatment and their quality of life has improved, many other people will seek to be tested knowing there something that can be done for them if they are found to be HIV-positive," writes an advocate from Uganda.

Ensuring good access to treatment is a key element to prevention, noted an advocate from Lebanon. "Treatment and prevention are dependable on each other. You can't have good prevention unless the treatment is good. In countries where shortage of medicines is a chronic problem and treatment is barely available then prevention measures will fail."

Treatment as prevention of illness

Advocates also argued strongly that 'prevention' is far more than simply prevention of HIV transmission. "Treatment is not to just about avoiding infection but, to avoid two developing HIV sickness and death," wrote an advocate from the Ivory Coast. "So we live normally, have sexual partners, have children – have a normal life."

An advocate from the Netherlands continued this theme. "The link between treatment and prevention is an obvious element of the dynamics of prevention for and by people living with HIV. Irrespective of the term used, the building blocks of a 'positive prevention' approach (promotion of human rights, involvement of people living with HIV, embracing shared ownership and responsibility, and recognition of diversity) aim to proactively address the sexual and health needs of people living with HIV."

Recommendation

WHO should be aware that PLHIV in every setting appreciate and understand the link between treatment and prevention, and in particular the potential effect of ART on infectiousness, on both a population and individual level. WHO should highlight that access to treatment will result in population-wide prevention benefits, through reduced individual and population infectiousness; increased incentives to test; and improved safer sex skills and safer behaviours of those PLHIV accessing treatment and care. Biomedical approaches, and prevention focused solely on diagnosed individuals, must be seen as part of a broader prevention strategy that highlights structural power imbalances in society, such as gender inequities, gender violence and poverty.

2. What should the WHO guidelines say about treatment and its role in prevention?

Participants strongly advocated for WHO to highlight and clarify the role of treatment on prevention based on many of the reasons discussed above, and, in particular, to:

- Ensure universal sustainable access to timely ART in order to prevent illness and promote wellness;
- Encourage undiagnosed individuals to know their status;
- And to reduce infectiousness on an individual, as well as a population, level.

"The recent indications that antiretroviral treatment might be used as prevention should encourage WHO guidelines authors to expand access to ART because the more you treat now, less virus will be circulating, fewer people will be infectious and then you would reduce the need for treatment later," stated a French advocate. "Monitored, successful treatment prevents HIV," noted a Kenyan advocate.

However, whilst calling for WHO to acknowledge and to clarify ART's role in reducing infectiousness, participants also agreed that WHO should state that treatment alone can only be part of an overall prevention strategy that must address those without, as well as those living with, HIV.

"WHO should make clear that prevention must be viewed at all its levels – primary, secondary and tertiary. This will help policymakers at various national co-ordinating committees to create candid and solid prevention guidelines that address prevention issues and challenges at each level," wrote an advocate from Kenya.

Treatment to prevent illness

An advocate from Peru wrote that the guidelines should use the principle of 'treatment as prevention' to achieve the best possible outcome - to allow more countries to gain access to ARVs. He added that the guidelines should also talk about ensuring access to lower priced drugs through restricting patents or trademarks to allow for generics, and push for policies that provide incentives for research into new drugs or vaccines and clinical studies that help define appropriate care regimes in order to improve patient quality of life, such as reduced side-effects. "*Referente a las directrices que tenga a bien emitir sobre Tratamiento como prevención, creo que lograr que mas paises logren el acceso a los ARV será nuestro mejor logro, y es sobre este tema creo yo el princiipal. Otras directrices podrian ser acerca de lograr que se accedan a precios menores los medicamentos de marcas o con patentes que tengan restricciones para obtener copias (medicamentos Genericos). Que se impartan politicas para incntivar la investigación de nuevos medicamentos o vacunas y su vez tambien estudios clinicos para un adecuado regimen de atención de aplicacion en los pacientes sobre medicamentos ARV (efectos secundarios).*"

"The guidelines should stress the need for universal access to treatment as a key driver for prevention and the need to ensure universal access for all in all communities," wrote an advocate from Kenya. "WHO should give treatment first priority because it's the base for everything," concurred an advocate from Lebanon. "You can't build a building without a good foundation or base. Universal treatment is crucial."

"Sustainability of treatment when someone has begun ART must be ensured because one of the commonest causes of poor adherence to drugs is stock-outs of all or some of the drugs," argued an advocate from Uganda. "In many of our communities where treatment literacy is low PLHIV may be forced to take half doses or miss some doses in order to 'stretch' the drugs over a longer period. This will certainly lead to resistance and drug failure and should such people pass on the virus to others though whatever means, ARVs will not work on them. At the moment, PEPFAR and Global Fund moneys that are running most of the ART programmes in poor countries have levelled off. With no increase in funding, sustainability for those already on ART is hanging in the balance and yet at the same time no new PLHIV can be put on ARVs! The new treatment guidelines should address this and help or make all governments to have sustainability plans."

Treatment to promote wellness

"If there is a more holistic approach to treatment, there will be more general recognition that HIV is not just a bio-medical problem, but has to be addressed across many different sectors and levels of societies," wrote an advocate from the UK. "If treatment is approached holistically – rather than simply being about providing ART – then this will be promoting prevention. Studies have found that increased care and support increase both ART adherence and condom use, and therefore our bodies become less able to transfer the virus to others. If our mental health is adequately supported, more of us will be able to stand up in public and talk about what has happened to us and more people who are currently negative will be able to learn from meeting us and feel more ready to try to remain negative And if treatment and care also provided good access to sexual and reproductive health (SRH) information, care support and supplies, then there would be fewer positive women finding themselves pregnant without wanting to be, and being able to access more choice over when they want to have a child, and feeling confident and happy that they can have their children in safety and with full support of all around them - better for them and for their - HIV-negative - children."

ART as prevention

"WHO needs to reinforce the fact that ART is effective and that it can help reduce the risk of transmission," stated an advocate from South Africa.

An advocate from Australia argued that WHO should recommend viral load testing in order to ensure that individuals know when they have undetectable viral loads. "If 'treatment as prevention' initiatives go ahead, then it seems to me even more important that access to VL testing becomes standard, otherwise there will be significant gaps in knowledge of personal risk," he wrote.

An advocate from the UK argued that WHO should trumpet ART's effect on transmission. "If there was wider knowledge by the general public that PLHIV on treatment are much less infectious that can play an important role in challenging stigma," he wrote. "Less stigma would increase capacity for prevention by allowing PLHIV to be more open about their status within sexual relationships and negotiate safer sex."

An advocate from Canada, where there are many criminal prosecutions for HIV exposure following non-disclosure of HIV status, suggested that WHO is both clear about the role of ART on infectiousness, and about the equal responsibility of both parties for the prevention of transmission. "WHO guidelines in terms of treatment and prevention should be well-balanced, clear and precise to ensure that there is no room for misinterpretation, especially with so many criminal charges being brought against people living with HIV/AIDS," he wrote.

Treatment as part of a wider prevention strategy

"WHO must acknowledge and make a strong statement that treatment alone is not a prevention tool but only one piece of the overall strategy that one must undertake in preventing the spread of HIV," wrote an advocate from Canada. "I believe that WHO can make the statement that treatment and prevention go hand in hand provided that all other elements are in place to support it."

"There is evidence to suggest that early and widespread treatment coverage will have a very cost effective and direct correlation in reduction of infection rates," wrote an advocate from the US. "But guidelines should also note caution that while treatment may reduce infection rates, it isn't 100%, there are still questions and debates going on about this, and that any policies and statements should be framed in a way so that people aren't given the impression they don't need to continue with other prevention practices (e,g, condoms)".

Recommendation

WHO should clarify ART's role in reducing infectiousness on an individual as well as a population level in order to ensure universal sustainable access to timely ART; encourage undiagnosed individuals to know their status; reduce stigma; and to help individuals understand their personal risk. WHO should also make it clear that treatment alone can only be part of an overall prevention strategy that must address those without, as well as those living with, HIV.

3. How relevant are human rights concerns in settings where there is no universal access to treatment?

Participants unanimously agreed that, "a human rights-based approach to health-related issues is of the upmost importance" and the "universal foundation of the response to the epidemic."

"The importance of human rights in the response to the epidemic is not just a 'moral' issue," wrote an advocate from the UK. "There are numerous evidence-based studies which show that programmes rooted in a human rights approach give better results. Human rights are particularly crucial when supporting marginalised populations, such as people who use drugs, people in prison, people who sell sex and men who have sex with men. Those groups experience several barriers to access treatment and prevention because they are discriminated on several grounds. A human rights approach can also ensure that those of us who belong to such groups have access to appropriate treatment and prevention programmes."

Another advocate from the UK highlighted that "the only potential problem is that some commentators in low- and middle-income countries have rejected the notion of human rights on the alleged grounds that human rights are a Western conceptualisation (and hence to be resisted)." He noted, however "that human rights do not necessarily look the same everywhere, but take on a local inflexion."

Regardless of setting, participants from Algeria, Brazil, China, Kenya, Ivory Coast, Iran, Lebanon, Malawi, Panama, Uganda and Venezuela agreed with a South African advocate who wrote that, "'treatment as prevention' has the potential to restore the human dignity and health of people living with HIV because it will give us an opportunity to be treated as early as possible – as long as all countries respect the International Human Rights Declaration as a framework to change the conditional or environmental barriers that prevent people accessing health services due to coercion, or being forced to test, or their being criminalised."

"Testing and treatment should always been done with the consent of the person involved and a human rights approach can ensure this," concurred an advocate from the UK.

Finally, participants agreed with the suggestion from a South African advocate that WHO should plan "a feasibility and acceptability study" into the concept of 'treatment as prevention' as a way of scaling-up universal access to treatment "to check how this tool could be sustainable given the current human rights abuses of PLHIV."

Recommendation

WHO should ensure that a human rights framework forms the foundation of their approach to 'treatment as prevention' as a way of attempting to achieve universal access, and that a study on the feasibility, acceptability and sustainability of such an approach is necessary.