

# HATiP

HIV & AIDS Treatment in Practice

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# Scaling up antiretroviral therapy (meeting report)

By Julian Meldrum

## Summary

There is still some debate on whether public funding should be devoted to providing HIV treatment - and especially ARVs - and the political will to do so cannot be taken for granted. However, the bigger debate now appears to be about how, not whether, to scale up provision of treatment.

WHO has made some important suggestions, embodied in guidelines on the use of antiretroviral treatment in limited-resource settings. These are being debated and questioned, but it is not always clear on what basis such questions are asked.

Using the agenda for a forthcoming meeting (to be reported by *aidsmap*) as a case study, this article raises additional questions about the evidence base for making recommendations as well as the risks of promoting as "good practice" strategies which have not been thoroughly evaluated in a range of different settings.

## Treatment in relation to HIV prevention

There is a wide consensus that a comprehensive response to HIV and AIDS must include provision of treatment and care, alongside continuing HIV education and prevention, including research on prevention technologies, and action to deal with the consequences of AIDS. Nonetheless, some international experts for example, Malcolm Potts and Julia Walsh, writing in the *British Medical Journal* on 21 June still argue that any public money spent on ARV treatment would be better spent on HIV prevention. (To read this article and early responses to it, visit the BMJ site - no subscription needed - [here](#)).

Preventing mother-to-child transmission of HIV, while allowing parents to die and add to the problems of child care for their relatives and communities, is an obvious example of why either/or thinking should end. The recent decision by the government of the Western Cape in South Africa to endorse an MTCT Plus programme to provide treatment for parents shows how this can be taken forwards - and this newsletter will be profiling MTCT Plus later this year.

It is also hard to reconcile the goal of destigmatising AIDS with a practice which means healthcare workers seeing their patients fall ill and die prematurely from an increasingly treatable condition. This was spelled out clearly by a group of South African doctors, as reported on *aidsmap*, [here](#).

As *aidsmap* will doubtless continue to report, the South African government is under pressure from a broad range of civil society agencies to establish a coherent national treatment plan for HIV and AIDS. Where South Africa eventually leads, many other countries will surely follow.

To go beyond ARV treatment as token programmes small-scale projects with no real prospect of widespread application requires at least two things. Political will to mobilise resources and secure affordable products is one of them. Another is strategic thinking, founded on practical experience, about how to provide treatment to make the most of the benefits in relation to the risks for individuals and the community as a whole.

Much of this strategic thinking has been embodied in the guidelines set out by WHO for the use of antiretroviral therapy in limited resource settings, which have been referred to in this newsletter and are a valuable resource, even if there are details on which they can be faulted.

As another round of international meetings and conferences loom, there will be much discussion of these and other ideas on which expanded access to treatment can be set out. Does this amount to mere non-evidence-based lobbying, as Potts and Watts describe it? Or is there real work to be done, to advance the response to HIV and AIDS?

## A workshop in Amsterdam

One effort to set out an agenda for scaling up access is a meeting in Amsterdam due to be held on 9 to 11 July, just before the International AIDS Society's meeting in Paris next month. It is co-sponsored by the Netherlands-based [AIDS Fonds](#) and the US AIDS Healthcare Foundation through its Amsterdam-based international arm, [AHF Global Immunity](#). The keynote speaker is Joep Lange, President of the International AIDS Society, who is also associated with a Dutch not-for-profit international HIV treatment programme called PharmAccess International. Other presenters are due to represent WHO, the Global Fund to fight AIDS, TB and Malaria, NGO- and drug-company-sponsored treatment programmes.

The programme for this meeting, which will be reported for *aidsmap*, raises a number of questions, in more than one way:

The programme itself asks many questions which meeting participants are invited to try and answer. Some of these may be excellent questions. Others might be unhelpful if a premature consensus is reached, in the same way that many have been disempowered by the emphasis in some guidelines on such things as the need for frequent viral load testing. Previous issues of this newsletter have identified the importance of undoing such damage. Can we learn from our collective mistakes?

A question that leaps out, time and again, is precisely, what the evidence base for suggesting changes to treatment guidelines? Are there gaps in WHO guidelines that can already be filled, on the basis of sound evidence, and would help to deal with questions that arise in clinical practice? Of the many gaps in the evidence base, which are the most important to fill? WHO is already well aware of this problem and is making efforts to coordinate research. Is this better assisted by admitting areas of uncertainty, rather than trying to promote answers based on what people are currently doing in some clinical settings?

With funders for the Amsterdam seminar including the pharmaceutical companies Bristol-Myers Squibb and Pfizer, the question always arises, of how to ensure that public health interests come first and are not compromised by commercial interests. The enthusiasms of academic researchers and NGOs (including NAM!) may also need to be questioned, to make sure that the real priority improving the quality of people's lives and expanding their life chances is upheld.

Above all, how can the people most directly affected by such strategies best be included in their development? This may yet resolve itself as people with HIV throughout the world demand answers to their questions, about when and how wider treatment provision can be established. An effort has been made, to provide scholarships for a range of people from different settings to attend this meeting, but it clearly cannot be representative.

This article sets out the questions on the Amsterdam agenda, and raises some additional questions that might appear not to be on the agenda. It invites readers of this newsletter to comment and suggest areas that we can explore further, to open up this essential debate and make sure that it is properly rooted in real life experience. Only a few people will be able to take part in meetings this year in Amsterdam, Paris, Durban, Nairobi, Dakar and (SARS permitting) Kobe. But there is room for a great many more contributions on the way to achieving the ultimate goal of effective treatment for all who need it, effective prevention for all at risk, and support for everyone affected.

In the sections that follow, questions which begin with a bullet point are those asked in the meeting agenda; all other questions and comments are in response to them.

## Initiating treatment, drug regimens and laboratory testing

### Initiating Treatment

- Are WHO treatment guidelines sufficient?
  - Clinical vs. laboratory criteria vs. other criteria
  - Where should [the] point of entry be? VCT, STI, PMTCT+ sites? Primary care?
- Do we need to ask if WHO treatment guidelines can be simplified further, and how national experts and healthcare staff can be licensed to depart from guidelines when these become obstacles, not aids, to better treatment?

In relation to the 'point of entry', is there any point in trying to answer such a question internationally?

Is it not better to ask, how can people be assured of the same standard of treatment and care, regardless of how they approach health care services?

### Drug Regimens

- Ideal starting regimen in resource-poor settings with naïve population?
- Ideal second-line regimen for breakthrough or resistance
- Need for national/regional standard for naïve population to prevent resistance?
- How often to change standard regimen?
- Should surveillance sites with plasma banks be set up to monitor the emergence of resistance to ART?
- Implications for charging patients for ART?

When a phrase like 'ideal starting regimen' is used, isn't it important to be clear what it is supposed to be ideal for? If it is to be ideal for scaling up, then some additional criteria may apply, over and above the criteria that drive recommendations in other settings, even if the outcome may sometimes be the same.

Would it be better to identify some combinations that should never be given (such as d4T and AZT), drugs that should not be given to pregnant women (such as efavirenz) and combinations that should definitely not be used in first-line treatment (such as d4T and ddI)?

At what level of evidence should a recommendation to consider triple nucleoside therapy (abacavir plus AZT plus 3TC) be withdrawn, in the light of recent findings that this is inadequate in suppressing the virus? (In practice, of course, this has been too expensive anyway for widespread use in most settings.)

Another missing question is: what should be the priorities for fixed-dose combination treatment, if we could choose freely among

the products of different companies? And what more can be done to make such fixed-dose combinations available, to the same quality as products made individually?

Clearly, one of the dangers of charging is that patients are driven to take unsuitable combinations (such as ddI with d4T) merely because in a particular country they are the cheapest available. A specific policy to avoid this happening might be helpful and might be more achievable than free treatment for all.

### Laboratory Testing

- Are WHO guidelines sufficient? What is basic minimum?
- Lower cost CD4 analyses, viral load testing for infants born to infected mothers?
- How many CD4 test sites are necessary per patient population?
- Overview of the best rapid tests: Capillus and Determine being used now, but how about OraQuick?
- Which set of 2 rapid tests would be the best and how many centres per patient population need to provide ELISA/WB?
- Emerging low cost technologies?
- Implications for scale-up?

Again, the question might be better asked: are WHO guidelines open to misunderstandings that may restrict access to treatment unnecessarily, and when should healthcare workers be encouraged to disregard or limit them?

Should any targets for laboratory provision be framed in terms of numbers per head of population, or in terms of travel times and costs to reach testing sites, and time taken to get results?

## PMTCT and paediatric treatment issues

### Prevention of Mother-to-Child Transmission

- Should PMTCT be done in a setting where HAART is available?
- Short-course, triple-therapy vs. nevirapine mono-prophylaxis and treating more children?
- Resistance issues on nevirapine?
- Short-course, mono-prophylaxis and breastfeeding vs. triple therapy and breastfeeding vs. short-course mono-prophylaxis and formula (pasteurizing of mothers own breast milk, using a breast pump, acceptability of a wet-nurse) and making artificial feeding safe in resource-poor environments.

The first question is difficult, as well as unclear, as different models of treatment provision may work better in different settings.

Are these questions which should really be left to specialists? Is it better not to pronounce on some issues, such as the risks of drug resistance to nevirapine from giving a single dose to women during labour, until there is solid clinical research evidence on which to base conclusions? Also, it is easy to anticipate that in research studies where there is additional support to mothers, e.g. to train them how to pasteurise breast-milk and monitor how well they do it, the results might be very different to those that would be seen in a community setting with less support.

### Paediatric Treatment Issues

- How to assure trained staff for treatment, appropriate protocols, medications?
- Should there be modifications to childhood immunization schedules for HIV-infected children, especially addressing live oral polio vaccine, BCG and Measles?

When to start and what to start with, dearth of paediatricians, orphan issues.

Where there is a lack of specialists, should their role shift towards supporting HIV specialists treating adults to provide appropriate care for children too?

Given that the risks of disease, compared to those of immunisation, vary enormously between countries and over time, is it right for any international group to pronounce on such matters? Should this not be left to national authorities to judge? And how can the evidence be collected, so this is driven by a real assessment of the risks rather than theoretical concerns?

Should there be an international effort to collect data on the effects of vaccination in settings where disease risk are high, to inform decision making where the risks of particular diseases (e.g. polio, measles) are much lower? If so, who pays?

## Opportunistic infections management and minimum package

### Opportunistic Infections Management

- When do you start Bactrim, if you do not have a CD4 count?
- Should a total lymphocyte count be used to approximate CD4 (i.e. TLC of 1,200 approximates a CD4 of 200)?
- How do you use INH? For all HIV positive persons? For how long?
- What role does PPD play? Should all HIV+ persons have a chest X-ray, or does the clinician need to wait for evidence of full-blown AIDS symptoms?

Is it sensible to ask these questions, in the absence of a careful assessment of the immediate risks to the lives of people with HIV in a particular country or community?

The question about the usage of isoniazid (INH) was explored in a previous issue of HATIP. One factor that needs to be considered is the quality of TB DOTS provision and screening for active TB. Another is the level of community exposure to mycobacteria. This implies that it is not possible to give a simple, universal answer to this question.

Similarly, PPD [skin testing for exposure to TB] is often impractical. Should the question be: when and how can INH be used when PPD is not considered practical?

A missing question: how far healthcare providers should go, to organise facilities and schedule clinics so that people with HIV are not exposed to other patients who are coughing?

#### Minimum Package

- What other minimum HIV primary care services/meds should be offered?
- What else should this include (food, safe water, shelter, social support, financial assistance, transportation, funeral costs)? Case management approach?
- How to integrate prevention?
- Integration of HIV and TB diagnostic and preventive strategies?
- How much is the minimum package going to add per person (over and above ART) to the cost of providing competent HIV care?
- Recent survival analysis data in Brazil suggests that ART alone improves survival, should there be recommendations to get drugs out first, phase in nutritional support, etc, later?

## VCT, staffing model, adherence and chronic care

### VCT (Voluntary Counselling and Testing)

- How can this be done efficiently and sensitively?

- How many VCT counsellors are needed per 100,000 patient population?
- What level of staff/training is needed?
- Opt-in vs. opt-out in pregnant women?
- Integration of STI and TB screening with VCT?

### Staffing Model, Adherence and Chronic Care

- Most efficient use of staff in treatment provision?
- Appropriate ratio of staff (doctors, nurses, community health workers, counselors, adherence monitors/accompagnateurs, administrative staff) to treatment population?
- Human Resources development, training, staffing and unmet need?
- Adherence? DOT model vs. counselling or "buddy" system?
- When to follow up, how often?

Is it reasonable to suggest that these questions can be answered in one way across different societies, with widely different starting levels of knowledge about HIV and about modern medicine? Even when research studies are carried out (as they should be) is it safe to assume they will give the same results in different settings?

## Scaling up infrastructure

### Cost & Scaling Up Infrastructure (Human Resources & Physical)

- How should we measure cost? Cost vs. cost-effectiveness
- How to account for the cost of infrastructure in scaling-up?
- Implications for charging for ART and labs in resource-poor settings?
- What is the role of the health system? Minimum infrastructure for scale-up? Role of NGOs?

One of the underlying questions here is: to what extent do services which operate on a larger scale become more efficient?

In developed countries, a key role of voluntary organisations is to act as watchdogs, to identify when systems are not working as they are supposed to. Will this become increasingly important elsewhere?

## Operating management and logistics/monitoring and evaluation

### Operating Management and Logistics

- How to ensure and manage drug and reagent supply chain? Forecasting?
- How to procure drugs and reagents at best price for a country or clinic (regional cooperatives)?
- How to ensure effective basic management, administrative models? Unmet need?
- What is the minimum physical infrastructure needed for ART provision?

### Monitoring and Evaluation

- What are the basic needs for effective implementation and ongoing monitoring and evaluation? Role of informatics?
- Role of research and quality assurance in resource-poor settings

A question in some healthcare systems, which may need to be anticipated here, is who owns the data? It has been known for pharmaceutical companies, for example, to supply equipment and

software to manage drug supplies, in return for access to the information generated. Is this acceptable?

In many countries, there are effective drug distribution systems. In many more, systems periodically run out of drugs, in a way which can be disastrous for people who need reliable, continuous supplies of products such as ARVs. Is it desirable to have parallel/alternative distribution systems, and if so, how many?

How important is it, to have paper-based systems which can be kept going easily in the absence of computers?

(Examples of simple stock control and ordering systems are provided in a section on sourcing drugs in the International HIV/AIDS Alliance Treatment Handbook, available on this site [here](#).)

### Law, policy and human rights issues relating to treatment in resource-poor settings

- Implications of treatment scale-up approaches?
- How to ensure equity in treatment for women, children, AIDS orphans, the poorest and socially disenfranchised groups?
- How to minimise stigma in treatment and prevention?

- What are the appropriate ethics of informed consent in resource-poor environments?

Denial of treatment is one of the most stigmatising experiences that people can undergo. Recovery from serious illness often motivates people to tell people about their experience and so to counter the stigma that comes from the association of HIV, AIDS and early death. The challenge is to provide treatment in a way which protects patients' confidentiality while supporting them to tell those who matter to them and people who could benefit from knowing a person's HIV status.

The last of these questions is odd: the ethics of informed consent are the same everywhere. All that may vary, in settings where few are literate and some medical and scientific concepts are unfamiliar, are the methods used to explain what a procedure or trial is about, and the method used to record that consent.

## about HATiP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

For further information please visit the HATIP section of [aidsmap.com](http://aidsmap.com)