

WHO CONSULTATION

**THE STRATEGIC USE OF ANTIRETROVIRALS
FOR TREATMENT AND PREVENTION OF HIV INFECTION:
2ND EXPERT PANEL MEETING**

Executive Summary

2-4 MAY 2012 GENEVA



**World Health
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INTRODUCTION

The global commitment to meet ambitious HIV targets, including the 2011 UNGASS report and the UNAIDS 3 Zeros strategy to ensure universal access to treatment, halve the number of new infections, and substantially reduce stigma and discrimination by 2015, requires renewed strategic and programmatic approaches. A number of important challenges need to be faced which include; accelerating access to HIV testing and immediate linkage to care and treatment, and initiation of antiretroviral therapy (ART) earlier in the course of HIV disease, to a larger number of persons living with HIV (PLWH); improving long-term adherence to treatment and retention in care among those receiving treatment; and capitalizing on the potential broader preventive benefits of ART, both in terms of reduced incidence of HIV and potential decrease in tuberculosis incidence.

In May 2012, the World Health Organization (WHO) held a second expert consultation on the Strategic Use of Antiretrovirals for Treatment and Prevention of HIV/AIDS. This consultation, following an initial consultation held in November 2011,* was attended by national program managers, modellers, epidemiologists, economists, ethics and human rights experts, community representatives, and representatives from bilateral and multilateral funding organizations. This multidisciplinary group was brought together to reflect and consult, collectively and within working groups, on the challenges for planning, priority setting and decision making to realise the ambitious vision for the HIV response.

The overall aim of the consultation was three-fold: First, to solicit guidance on how to best support the translation of clinical/technical recommendations into policy and practice at the national and local level; Second, to review parameters for priority setting and decision making when considering implementation of new recommendations; Third, to determine the best method of incorporating and integrating strategic and programmatic guidance into the 2013 WHO Guidelines.

* Meeting report at http://www.who.int/hiv/pub/meetingreports/consultation_20111116/en/index.html

CURRENT PROCESS FOR MAKING STRATEGIC AND PROGRAMMATIC DECISIONS

Perspectives on how strategic and programmatic decisions are made currently were provided by three panels composed of representatives from governments, non-governmental organizations, programme implementers, funders, and organizations of PLWH. Participants indicated that a range of factors are taken into account when deciding whether to adopt a certain recommendation. While evidence of clinical efficacy is often necessary to support uptake of interventions, it may not be sufficient as issues such as cost and cost effectiveness, the legal and regulatory environment, programme feasibility and convenience all play an important role. For this reason it is important to involve a multiplicity of stakeholders, including the community, in articulating the rationale for the adoption of a recommendation/intervention. Decision making is often iterative and multi-layered, involving consultation with numerous technical groups and levels of government. Consequently, the consultative processes required in translating new WHO guidance or clinical evidence into policy change at country-level may take up to 1-2 years. Given the urgent need to leverage the clinical and preventative benefits of ART, participants noted the importance of finding ways to accelerate the process from WHO guidance development, to national adaptation, to actual implementation.

The availability of domestic and international funding for HIV treatment and prevention interventions are critical determinants of the adoption of new recommendations. The need for making an investment case was highlighted. For example, providing information that earlier initiation of ART could be cost saving in the long term is important. Similarly, while long-term projections are critical, it is also important that investment cases support decision-making within political timeframes, which are shorter (e.g. 5 years). Panellists suggested that WHO guidance should encourage research and the evaluation of innovations that may help inform design or implementation of recommendations (e.g. Malawi's decision to implement PMTCT Option B+).

Conclusions:

- Parameters needed to prepare and make decisions should be better defined
- WHO can assist by providing methods and tools to support the process of decision making regarding adoption of recommendations/interventions
- WHO guidance should include recommendations for research/innovations to inform implementation and advance knowledge

MODELLING OF EPIDEMIOLOGICAL IMPACT, CLINICAL IMPACT, AND COST-EFFECTIVENESS

The potential long-term impact of the latest WHO recommendations to initiate ART at CD4 \leq 350 cells/mm³ has been assessed by a number of different models, all of which predicted a reduction of HIV-incidence, some by as much as 50% by 2020. However, some of these models included optimistic assumptions such as high rates of testing, retesting, linkage to care, initiation of ART and excellent rates of adherence that do not reflect current programme realities.

Other scenarios that have been assessed in various models include starting ART irrespective of CD4+ cell count, and/or initiation of ART at higher CD4+ thresholds for certain subpopulations including PLWH with active TB disease, pregnant women, HIV-positive partners in serodiscordant couples, and sex workers - each with varying effect in terms of effect on HIV incidence. Substantial HIV incidence reductions were demonstrated to be achievable by optimizing the cascade of care and strengthening implementation of the current guidelines. It was concluded that the optimal strategy for expanded ART use depends on the relative importance of therapeutic and prevention benefits, the assessment of which requires the use of realistic assumptions, ideally grounded in local epidemiological data. In addition, other criteria such as cost-effectiveness, feasibility and acceptability would be important to consider.

The role of modelling in helping to inform strategic decisions at country levels was highlighted by the example of Cambodia, where they are currently modelling the impact of a number of different ART scenarios to help inform strategic decisions to eliminate new HIV infections in Cambodia as part of the health sector response towards “Three Zeros” by 2020. These scenarios include combinations of: ART initiation at CD4 threshold of <500 cells/mm³; immediate ART for high risk groups; and PMTCT option B+ as part of combination prevention.

A number of models have assessed the cost-effectiveness of various expanded ART initiation scenarios. In contrast to epidemiological modelling, costing models have tended to assume more realistic rates of HIV testing, ART acceptance and retention in care. Overall, the consensus of recent modelling analyses point to earlier initiation of ART now being cost-effective in the short-term due to factors such as averted inpatient costs, averted infections, and averted morbidity and mortality. Additionally, earlier initiation is very likely to be cost-saving in the longer-term when the dynamic population-level benefits are incorporated. Importantly, these models also highlight the need for increased investment in treatment in the short term in order to achieve long-term epidemic benefits.

Broadly, the marshalling of additional resources to enable expansion of treatment could be achieved in three ways: increase the resource envelope, through external resources (e.g., PEPFAR, GFATM) and internal resources (e.g., increased allocation towards health, tax revenues, insurance schemes); delivering programs more efficiently by identifying delivery models with improved technical efficiency; and allocating resources to those interventions that maximize health impact.

Conclusions:

- Modelling can help guide strategic decisions but models are sensitive to assumptions and there is a need for transparency about what assumptions are made and the use of realistic assumptions

- To be credible, models need to include data that are up-to-date, relevant to local settings, and available and understandable to decision-makers. Working together, modellers, implementers and programmers can ensure realistic inputs are utilized and appropriate data are collected to inform the models
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- There is a need for simple, generic, pragmatic tools for countries to input data and extract useful information to guide priority setting and undertake risk analyses (for example to assess the risk of drug resistance associated with earlier ART initiation at different adherence thresholds)
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- WHO could assist by developing a simple decision tree or algorithmic approach for programme managers to help make decisions based on different parameters

ETHICS, EQUITY AND HUMAN RIGHTS

In the absence of sufficient resources, fair procedures are needed to adjudicate between the ranges of available HIV interventions. Principles of ethics, equity and human rights are important components of the rationale and framework for interventions and can be used to aid the decision making process when deciding upon the allocation of scarce resources. At a country level, there are minimum '*core obligations*' that should be met to ensure judicious practice. This obligation under The International Covenant on Economic, Social and Cultural Rights (ICESCR) entails the provision of both treatment and prevention interventions to those in urgent need thereof, in a reasonable, fair and incrementally sustainable manner. One important component of human rights law is the notion of progressive realization, which recognizes resource-limitations yet nevertheless obliges countries to implement a given intervention in an incremental and sustainable way in order to realize targets in a stepwise manner.

Policy makers are faced with many challenges in order to respect these obligations and thus prioritize those in '*urgent need*' when adopting new guidelines for HIV treatment and prevention. However, defining those in '*urgent need*' is a difficult task which demands the involvement and active dialogue between HIV/AIDS stakeholders as well as policymakers. Concerns were raised highlighting the sensitive issue of prioritising key populations. In certain countries, key populations such as sex workers, men who have sex with men (MSM) or injecting drug users (IDUs) are criminalised and therefore the methods by which to deal with the HIV epidemic within these populations is a complex matter that requires clear guidance from WHO.

The history of the HIV epidemic is unique in that, in contrast to other health areas, many people refused to accept resource limitations as a reason for inaction. Priority setting can create conflict between equity and efficiency, which can be overcome or alleviated by a strong case for more resources. The current shortfall of resources should be countered by a strong case demonstrating the opportunities for making major progress in reducing mortality, morbidity, transmission, and costs, through the application of the latest evidence. Human rights, equity and ethical considerations can be used to support investment claims and thus leverage for increased resources.

Conclusions:

Future WHO guidance should include ethical, human rights considerations in four ways:

- To help inform decision analysis so that programme managers can decide among competing options
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- As part of the justification for the investments proposed

- To define non-ethical options and highlight interventions that are not effective or potentially harmful
- By providing operational guidance on how best to reach key populations and retain these populations in treatment and care

HEALTH SYSTEMS REQUIREMENTS

The feasibility of scaling up ART for treatment and prevention is critically dependent on the ability of the health system, not least the enduring shortage of human resources, to deliver more services. The following critical areas need to be taken into account as recommendations/interventions are considered for prioritization and inclusion in policy and programs.

- Existing programme capacity, burden of disease and status of implementation of prevailing guidelines need to be reviewed ("a situational analysis") to assess key issues such as human resource distribution, number of sites delivering ART, laboratory capacity, procurement, supervision, and costing and financing
- The vision and goals need to be set, together with a strategy, input and output indicators, and an implementation plan that is specific, objective, and costed
- The pace of transition needs to be established (will interventions be introduced all at once, or phased in, and if so how?)
- Necessary health systems adaptations, and resources to carry out activities, should be identified to break through bottlenecks in the system (for instance, investigating innovative opportunities to leverage resources through actively engaging and partnering with the private sector; proactive policy to support and retain health care staff)
- Local guidelines, monitoring and evaluation tools, and training materials need to be developed, together with a national plan of training, and regular supervision to ensure that the vision and goals are met

These critical areas will require that overall leadership for the implementation process is clearly established at the appropriate level of government.

Allowing space for innovation and operational research was identified as an important factor in helping to define the next set of key programme modifications that are needed to accommodate further scale up. While systematic reviews are important to help inform certain key future guideline recommendations, WHO will also need to review the 'grey literature' to identify best practice models to support future operational guidance. Best practice case studies could provide valuable illustrations of how countries have addressed various components of ART delivery. Finally, the need to provide guidance on how to tackle the legal and regulatory environment was reiterated, as this can be a major barrier to taking innovative approaches to scale up.

Conclusions:

- In depth situation analyses are needed on the current country context with regards to health systems response and ability to deliver on prevailing guidelines

- Future programmatic guidance should include guidance on operational research and programme monitoring and evaluation
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- WHO should also consider providing guidance on legal and regulatory requirements
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- Monographs of best practice should be presented, across a range of epidemic settings

POLICY FORMULATION AND DECISION MAKING

Four approaches to decision-making were summarized: (1) Informal, in which decisions were made by those with power or the loudest voice; (2) Technocratic, which relies on cost-effectiveness criteria alone; (3) Pragmatic, which addresses the real policy space available to programme managers; (4) and Comprehensive, which integrates all relevant criteria (burden, cost-effectiveness, affordability, feasibility, ethics, equity) in a rational and transparent fashion. A number of approaches to rational priority setting were outlined. The WHO CHOICE model offers general guidance to select interventions by cost/benefit analyses. Another approach, multi-criteria decision analysis, combines equity analysis and cost-effectiveness analysis to rank different options in an explicit and transparent way. Such approaches depend critically upon the availability of reliable data to inform choices. There was a recognition that WHO's guidance to strategic and programmatic decision making should in no way be construed as accepting that resource constraints should dictate technical and normative standards.

Decision-making should not only involve programme and technical staff, but engage stakeholders from a broad range of fields. The role of civil society was recognized as essential to challenging inefficiencies within the health system and bringing in energy and passion for change, and the urgency of overcoming resource constraints faced by implementing governments and donors. Traditional leaders and healers were also identified as critical to pushing through certain policies (e.g. couples testing in Zambia, or male medical circumcision in South Africa).

Conclusions:

- WHO should provide guidance to assist decision making for ART programmes

Next steps

- WHO will establish a programme guideline working group in the next few weeks, to complement the clinical and operational working groups that have already been established to develop the 2013 Consolidated Guidelines on the Use of ARVs
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- WHO will aim to have a draft set of consolidated guidelines by the end of 2012, at which time the core recommendations will be communicated to countries
 - The format of the guidelines remains to be determined, but attention will be paid to the need for simplicity and accessibility
 - Major recommendations will be provided in a concise format (possibly in modular format), with supporting evidence reviews made available separately
 - A distribution plan will be made, involving capacity building events at regional level



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