Understanding the public health approach to HIV prevention, treatment and care.

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WHO Geneva

JOINT WHO/UNAIDS INFORMAL CONSULTATION WITH PHARMACEUTICAL COMPANIES
15 & 16 December 2008
Number of people receiving antiretroviral therapy in low- and middle-income countries, 2002–2007

- North Africa and the Middle East
- East, South and South-East Asia
- Europe and Central Asia
- Latin America and the Caribbean
- Sub-Saharan Africa

People receiving antiretroviral therapy (in millions)

- End 2002
- End 2003
- End 2004
- End 2005
- End 2006
- End 2007
PMTCT coverage

% pregnant women with HIV receiving ARVs for PMTCT in low- and middle-income countries

% Pregnant women with HIV who received ARVs to reduce MTCT increased from 2004-2007 - but almost half received single dose nevirapine

WHO - A Public Health Approach

Goal

*Maximize survival with improved quality of life*

Principles:

- **Population-based**
- **Evidence-based**
- **Simplified standardised integrated care pathways** *(regimens & monitoring)*
- **Decentralised and integrated service delivery**

..........making care more consistent and more efficient, irrespective of resources & capacity.
Translating global guidelines to national action

**GLOBAL**
- Regular periodic review of evidence
- Convene technical consultations
- Convene guideline groups
- Review and update guidelines
- Publish & disseminate

**NATIONAL**

Technical working groups:
- Adapt and adopt to simplify & standardise based on affordability & feasibility
- Develop/update tools for training, supervision and monitoring
- Stay updated
Core contents of the a Public Health Approach

- Comprehensive approach (prevention, care and ART)
- Provider-initiated testing and counselling (PITC)
- Prevention for those who test negative
- Positive prevention for those who test positive
- Pre-ART care for those who do not need ART immediately
- Treatment literacy & adherence
- Simplified clinical & laboratory monitoring

Health systems assumptions

- Continuum of care (time, person and place)
- Decentralised and integrated service delivery
Audience for WHO guidelines

- **Primarily national planners and policy makers engaged in establishing public sector HIV services**
  - Which ARVs to make available in public sector for *first and second-line regimens*
  - How to use: the four Ss of clinical management: *when to Start, Substitute, Switch and Stop*

- **Care implementers**
  - Knowledge on use ARVs according to national policy recommendations

- **Trainers, M&E experts**
  - To design/adapt appropriate tools and materials to support national policy recommendations
How is WHO guidance developed

- Review the evidence – focus on critical patient important outcomes (safety, efficacy – encourage less reliance on proxy markers)

- Assess risks and benefits of selected interventions

- Assess cost & feasibility of implementing the recommended intervention (in RLS or desired setting)

- Assess acceptability of intervention to:
  - Programmers/policy makers/PSM
  - Health care providers
  - Patients (adults & care givers for children)
# Understanding WHO recommendations

<table>
<thead>
<tr>
<th>Strong</th>
<th>Weak/Conditional</th>
<th>No recommendation</th>
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</table>
| **Implications:**  
panel confident desirable effects of adherence to the recommendation outweigh the undesirable effects  
i.e. must do or a must NOT do | **Implications:**  
panel concludes desirable effects of adherence to a recommendation probably outweigh the undesirable effects  
However:  
only applicable to a specific group, population or setting, or;  
new evidence may result in changing the balance of risk to benefit, or;  
the benefits may not warrant the cost or resource requirements.  
Consider doing | **Implications:**  
Further research is required before any recommendations can be made  
Don't do it yet- we need the research |


Key components of PHA & implications for commodities

Diagnosis

Pre ART care

ART care

Palliative care

HIV rapid & EIA tests
HIV viral tests
OI diagnostics
TB diagnostics
Condoms

OI diagnostics
Isonaizid
Cotrimoxazole
CD4

1st LR + 2nd LR + 3rd LR all as FDC (adult & children)
TB meds
POC CD4 & viral load (HIV DR)

OI management
Anti-emetics & analgesics
Psychotropics
Adults & children (1 year or over)

Clinical and/or immunological criteria to start ART

Standard first line regimen

NNRTI + 2NRTI

< 3 years

NVP + AZT + 3TC

> 3 years

EFV + AZT + 3TC

Standard second line regimen

PI + 2 new NRTI

Standard Third line regimen

???
Percentage of adults and children on 1st and 2nd line regimens (2007)
Median transaction prices for one year's treatment

Transaction prices for ARVs Summary Report form GPRM Oct 2008
Comparing individualized approaches to public health approaches

Failure / When to Switch

Virologic → Immunologic → Clinical

- Viral load & HIV DR
- CD4 count
- Clinical criteria

"Early Switch"
- Regimen selected on HIV DR profile
- Result = Multiple regimens

"Late Switch"
- Standard 2nd line based on 1st line used
- Standard 3rd line desired
Public health approach to patient monitoring

Outcomes from monitoring of patients on antiretroviral therapy in resource-limited settings with viral load, CD4 cell count, or clinical observation alone: a computer simulation model

Andrew M. Phillips, Jennifer Floyd, Ruth Munyai, Barrett Bennett, Charles C. Gilks, John Stell

Summary

Background In lower-income countries, WHO recommends a population-based approach to antiretroviral treatment with stratification by clinical stage and, where available, CD4 cell count, rather than viral load. Our aim was to study the potential consequences of such monitoring strategies, especially in terms of survival and resistance development.

Methods A validated computer simulation model of HIV infection and the effect of antiretroviral therapy was used to compare several, one of second-line regimens, and development of resistance that results from different strategies—based on viral load, CD4 cell count, or clinical observation alone—for determining when to switch people receiving antiretroviral treatment with the WHO-recommended first-line regimen of stavudine, lamivudine, and nevirapine to second-line antiretroviral treatment.

Findings Over 5 years, the combined proportion of potential life-years (PLYs) was 83% with viral load monitoring (PLYs when viral load <500 copies per ml), 88% with CD4 cell monitoring, and 85% with clinical monitoring (PLYs when new WHO stage 3 occurs or a WHO stage 4 event occurs). Corresponding values over 20 years were 67%, 77%, and 71%. Findings were robust: variations in model specifications to simulate unobservable and unobservable mortality, and survival were consistent with the decisions of WHO and WHO-CHOICE team.

Interpretation For patients on the first-line regimen of stavudine, lamivudine, and nevirapine, the benefits of viral load or CD4 cell count monitoring over clinical monitoring alone are modest. Development of resistance and increased mortality of these cases are important, but widespread access to antiretrovirals is likely with or without laboratory monitoring, if currently the highest priority.

Funding None

Introduction

For antiretroviral treatment to be introduced as widely and rapidly as possible in low-income settings, clinical treatment models must be available that do not require monitoring of viral load or CD4 cell counts, and resistance monitoring is likely to be limited to confirm the occurrence of resistance and to guide drug choices. Thus, such models can be useful in assessing the benefits of viral load or CD4 cell count monitoring over clinical monitoring alone for assessing the development of resistance and to guide drug choices.

Methods

The model of HIV infection and the effect of antiretroviral therapy (HIVCalc) that we used was originally developed to model the transmission and dynamics of HIV infections. The model simulates the transmission of HIV infection and the progression of HIV infection in a community.

Figure: Summary of differences in outcome of key monitoring strategies over 20 years

Figure: Summary of differences in outcome of key monitoring strategies over 20 years

- Viral load <500 copies per ml
- CD4 drop from peak
- New WHO 2/4
- Multiple WHO 3/new WHO 4
- New WHO 4

Proportion of full potential 20 life-years lived

Proportion of life-years spent on second line

Proportion of life-years with resistance to nevirapine and viral load >1000 copies per ml

www.bmj.com | Vol 328, April 26, 2004

1123
The WHO HIVResNet is a global group of experts, laboratories, and organizations constituted to support HIVDR prevention, surveillance, and monitoring as antiretroviral treatment (ART) is rolled out worldwide.

WHO HIVResNet
• Laboratory Network
• Surveillance and Monitoring Network

Steering Committee

WHO Secretariat
WHO-recommended national HIV drug resistance strategy

A. Development of a national HIVDR Strategy Working Group, five year plan & budget

B. Regular assessment of HIVDR "early warning" indicators from all antiretroviral treatment (ART) sites (or representative sites)

C. Surveys to monitor HIV Drug resistance prevention & associated factors in sentinel ART sites

D. HIVDR transmission threshold surveys in geographic areas where ART has been widespread for ≥ 3 years

E. HIVDR database development

F. Designation of an in-country or regional WHO-accredited HIVDR genotyping laboratory

G. Review of & support for HIVDR prevention activities

H. Preparation of annual HIVDR report & recommendations; use of data for ART and prevention planning
Transmitted HIV drug resistance

Articles reporting results from HIVDR transmission surveys in 7 countries all showed <5% HIV DR in incident cases
Public health approach – prevention agenda

**PRIMARY PREVENTION**

- Prep and PEP
- Condoms

**POSITIVE PREVENTION**

- Pre ART care – condoms safer sex
- Disclosure & partner testing
- MTCT prevention
- OI (TB) & STI prevention

**ART CARE**

- Reduce Viral load
- Likely reduction of transmission

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In our study’s utopian, unrealistic, improbable model — not a recommendation — we argue that if one day we chose to treat everyone with HIV at once, you could see a situation where HIV could eradicate itself over 30-50 years. ..............why the hell aren't we doing it?

J. Montaner  Sept 2006 Toronto AIDS
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<thead>
<tr>
<th>Year</th>
<th>Incidence/year</th>
<th>Prevalence</th>
<th>Mortality/year</th>
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<tbody>
<tr>
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<td>ART</td>
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<tr>
<td>Universal ART</td>
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Acknowledgments:

Paediatric and Adult Guideline groups
HIV DR team
HIV - dept staff
Paediatric ARV dosing working group
Charlie Gilks, Marco Vitoria, Lynne Mofenson, Ying-ru Lo, Rueben Granich
HIV - AMD & GPRM
HIV- SIR (Soutyrandy)

Thank you