Use of antiretroviral agents in developing countries

Peter Mugyenyi
Joint Clinical Research Centre
Kampala Uganda
ICEID, Atlanta,
March 27, 2002
THE UGANDA EXPERIENCE

• 1982 - First AIDS cases in Uganda
• 1986 - National committee for HIV prevention (AIDS control Program)
• 1992 - Uganda AIDS Commission (multi-sectoral approach to AIDS control)

Cumulative numbers infected - 2 million out of pop. of 20m. of whom more than 50% are dead
Results of Uganda’s preventive program

By 1990, Uganda had the highest HIV prevalence in the world

• Early 1990s-HIV prevalence
  From 14% - to over 30% in some sentinel sites

• Strong preventive measures
  Brought down HIV rates to 6.2%.
  (March 2002)

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UGANDA’S SUCCESS

HIV positive (%)

Antenatal clinic sites

Nsambya  Tororo  Mbarara  Jinja  Rubaga  Mbale


UNAIDS, 1997
HIV Infection Rates among ANC Attendees at Selected Sites

Years

Rates (%)
What Lessons can be learnt from the Ugandan Success on AIDS Prevention?
Analysis of the Trends in the Ugandan HIV Epidemic
Phase 1 - The “Out of Control” epidemic
Countries in “Out of control Epidemic” Stage.

KENYA

HIV Trends and Projection in Kenya (PLWAs)

S.AFRICA

ETHIOPIA


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Phase 2 - Epidemic under "effective preventive measures"
Phase 3 - Prevention at the “Bottoming out” stage.
Example of a country in ‘bottoming out’ stage

HIV infections Trends among Pregnant Women: DAKAR

χ² for trend: HIV1: p=0.6  
χ² for trend: HIV2: p=0.6

Prevalence in 1998: 
HIV1 0.5 (95% CI [0 – 3.0])  
HIV2 0.2 (95% CI [0 – 0.7])
Ugandan Preventive program  Success in Perspective

6.2%  Prevalence remains unacceptably high and appalling
The need for New (Second Generation) Interventions in Uganda

For a further desirable fall in incidence there is urgent need for new, more appropriate, and effective interventions

THE MISSING LINK IS TREATMENT (ARVS)
Projected effect of adding Therapy (ARVs) to Prevention (Uganda model)

Schematic Projection of trends in HIV prevalence

Preventive measures alone ——— Treatment and Prevention
Projected effect of implementing both care and Prevention
Secondary epidemics of OIs caused by AIDS.

Data from JCRC admissions 1999-2001

Graph shows the distribution of OIs at JCRC Ward since 1999. The chart includes data on Cryptococcal Meningitis, Toxoplasmosis, PCP, Anaemia, Candidiasis, PTB, CMV, and GIE. The years 1999, 2000, and 2001 are represented with corresponding data for each disease.
The burden of HIV fueled epidemics; New Tuberculosis cases (Ethiopia)
The deteriorating social-economic situation

AIDS Orphans (Ethiopia)

Hospital Bed Utilization (Ethiopia)

Expected AIDS treatment costs as a share government health spending

Increase in mortality among men 15–60 between 1986 and 1997, selected African countries

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Justification for Treatment (ARVs)

• Huge numbers are already infected and are a source of continuing infection
• Majority of the infected do not know their sero-status and need powerful incentives (read ARVS) to go for VCT.
• Prevention is not matching with treatment, yet both are vital for successful AIDS control.
Justification for Treatment (ARVs)

- Equity and moral imperative;
  
  Continuing suffering and horror when effective therapy is available.
Orphan
Has multi-drug Resistance because Grandmother Could not afford drugs all the time
Stepmother and patient (15 years) (Perinatal acquired HIV)

Presented with CD4 <50
Survived to teens
Without therapy
History of ARV use in Uganda

- 1991 Low dose ZDV Study at JCRC
- 1993 ZDV +DDI introduced
- 1996 Triple Therapy (PI based)
- 1998 UNAIDS-Uganda project aimed at Accelerated ARV access.
- 1999 EFV based regimens
- 2000->10 centers qualify for safe use of ARVs
- 2000 NVP more widely available Generics side by side with brands
- 2001 Taking ARVs to the districts Currently 3 district AIDS Clinics are operational, at least 3 more are due to open this year
APOLOGIES FOR LACK OF ARVs IN AFRICA 1

(1) ARVs are too complicated

(ii) Lack of infrastructure for safe and effective treatment

(iii) Africans mainly illiterate, hence compliance will be problematic leading to widespread resistance
iv) Africa too poor to afford ARVs, use resources for prevention and OIs

(v) Donors view ARVS for Africa as ‘a bottomless pit’ and hard to sustain

(vi) Political commitment
Real Issues in ART practice in developing countries

- ARV drugs affordability
- Cost of Monitoring tests (PCR and CD4)
- Inadequate capacity (trained care givers and infrastructure)
- Logistics for drugs purchase, storage and distribution
- Compliance and proper (supervised) use of ARVs
Issues in ART practice in Uganda-2

• Extending access to the districts
• Setting up a system of referrals of both patients and laboratory specimens.
• IEC to sensitize the public about ARVs.
• Integration of ARVs into Ministry of Health Public care system
• Funding and sustainability of the program
Main constraint to ARVs use in resource poor settings

Unaffordable cost of ARV

Access to ARV correlates with the cost of the drugs
Trend of ARV drugs prices in Africa

Annual cost per person for triple therapy in Africa (US$)

- $14,000
- $12,000
- $10,000
- $8,000
- $4,000
- $3,000


February-April 2001 offers

Outcry for equity, market Pressures.
activism, generic competition
Cost of ARVs in Uganda

Before (October 2000)
2NRTIs +NVP/EFZ, (Brand) $515p/m
PI base regimens cost $600-$800

Current (March, 2002)
Brand cost of NRTI +NNRTI $80/m
Generics $38/m
EFFECT OF COST REDUCTION ON NUMBER OF PATIENTS ON ARVs IN UGANDA

Introduction of Generics
Capacity building and training

1998: Only 3 centers were qualified to competently handle ARVs
2001: Over 10 centers including private practices qualified in Kampala
2001-2002: ARVs extended to the districts. 3 centers now fully operational

*Infrastructure constraints in Africa can be overcome and are not a constraint to ARV use*
Stepwise National Coverage
Extending care and treatment to the districts

Target
- Central Referral center (s)
- Main regions of country
- Extend to districts
- Health centers
- Rural communities

Methodology
- Set criteria/minimum standards at each level and logistics of coordination.
## Countrywide Network of Referral System

<table>
<thead>
<tr>
<th>Location</th>
<th>Infrastructure</th>
<th>Personnel</th>
<th>Services</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capital city; Main Coordination</strong></td>
<td>State of the art Laboratories (university Hosp.)</td>
<td>Experts, Researchers, Trainers &amp; data.</td>
<td>- ARVS, - Resistance Testing, - Severe Complications + All below</td>
</tr>
<tr>
<td><strong>Regional</strong></td>
<td>Referral lab. For the region</td>
<td>Specialist Doctor/s, Counselors, Lab Technologists</td>
<td>- ARVS and CD4 Monitoring tests, LFTs, Kidney FTS, X-Ray, ELISA + All Below</td>
</tr>
<tr>
<td><strong>Districts</strong></td>
<td>Laboratory</td>
<td>Doctors, Lab Technologists, Counselors</td>
<td>- CD4 or Referral Facilities. - ARVs -optional - ELISA/ Chemistry/m.biology - MTCT</td>
</tr>
<tr>
<td><strong>County; (Health centers)</strong></td>
<td>Basic Lab Microscope</td>
<td>Junior Doctor, Medical Assistant, Nurse Practitioner, counselor.</td>
<td>- Care for Opportunistic Infections Referral system</td>
</tr>
<tr>
<td><strong>Rural Health Facility</strong></td>
<td></td>
<td>Medical assistant Health Visitor</td>
<td>Home visits, Clinical Diagnosis of complications, DOTS, follow up on complications, Referral and Prevention</td>
</tr>
</tbody>
</table>
Joint Clinical Research/referral lab. well equipped to support a nationwide program for the more sophisticated tests.
Current ARV use status in Uganda (Joint Clinical Research Centre)

Laboratory Facilities include:

CD4, PCR, Genotyping, diagnostics for Ois, microbiology (+biotech for TB) chemistries and other specialized tests.
Main Uganda Teaching and referral Hospital, Kampala.
Health Center in Rakai District, Southern Uganda
Health facility in a poor area
Increasing access to ARVs in Uganda. Study supported by World AIDS Foundation.

To study issues associated with ARV drugs access in Uganda including;

• Affordability
• Compliance
• Drugs distribution logistics
• Clinical and laboratory monitoring
• Impact etc.
Can Africa District/Rural AIDS treatment centers succeed?

YES
Celebrations at the opening Ceremony of JCRC District AIDS Clinic Eastern Uganda
Operational Research - scaling up to the districts
Make Operational Research/data collection an integral part of increased access to ARVS

Emerging data from new district AIDS Clinic.
Patients started on ARVs

<table>
<thead>
<tr>
<th>Visits</th>
<th>No of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>
Distribution of JCRC Mbale patients by estimated distance to the clinic

<table>
<thead>
<tr>
<th>Distance (Km)</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>19</td>
</tr>
<tr>
<td>6-25</td>
<td>9</td>
</tr>
<tr>
<td>26-45</td>
<td>4</td>
</tr>
<tr>
<td>45+</td>
<td>2</td>
</tr>
</tbody>
</table>
Age Sex distribution of JCRC Mbale Patients

Age Groups

Number of Patients

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>30-39</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>40-49</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>50+</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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Marital status of JCRC Mbale patients by sex

Marital status of JCRC-2002 patients by sex

Number of patients

- Single: Males 5, Females 5
- Married: Males 5, Females 9
- Separated: Males 1, Females 2
- Widowed: Males 0, Females 1
Employment Status of patients attending JCRC Mbale clinic

- FullTime: 69%
- Parttime: 6%
- Unemployed: 25%
Bar graph showing patients' reasons for attendance per Week in JCRC Mbale Clinic

Clinic Dates

- Week 1
- Week 2
- Week 3
- Week 4
- Week 5

Number of patients

- Laboratory tests
- Inquiries/Counseling
- Totals

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CD4 COUNTS FOR PATIENTS COMING AT MBALE JCRC CLINIC
Graph Showing Drug Combinations taken by Patients on ARVs at JCRC Mbale Clinic

- D4T+3TC+NVP
- D4T+3TC+EFV
- CBV+EFV
- CBV+NVP
- DDI+D4T+CXV
- D4T+3TC+NVP
AIDS treatment in other African countries

- **SENEGAL** - Operational research project involving free ARVs, and evaluation of low cost monitoring tests
- **COTE D IVOIRE** - Evaluation of ARVs use in the districts
- **BOTSWANA** - Working with Harvard to implement a countrywide free AIDS treatment program
- **MTCT PROGRAMS** - Planned in many countries
- **Special access programs** - Rwanda, Zambia etc
Special ARV access initiatives

- **Employers treatment Sponsorships**
  South African miners, Banks, Industries, NGOs, Embassies, etc.

- **Insurances** - planned in Uganda for employees

- **Special NGO programs** -
  - Academic Alliance for training and increased ARVs access,
  - African Dialogue on AIDS (ADAC) African expertise to advise on the possible way forward for the continent, etc.
### Commonly used ARV Regimen

(Dictated by cost of drugs)

<table>
<thead>
<tr>
<th>1. Zidovudine</th>
<th>3TC/DDI</th>
<th>Nevirapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Combivir</td>
<td>Nevirapine)</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>2. Stavudine</td>
<td>3TC/DDI</td>
<td>Nevirapine</td>
</tr>
<tr>
<td></td>
<td>Nevirapine</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>3. ZDV/d4t</td>
<td>3TC/DDI</td>
<td>RTV+CXV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RTV+FTV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NFV/CXV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kaletra</td>
</tr>
</tbody>
</table>

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The Ugandan strategy to therapy

ACT WITH URGENCY

- Set up planning sub-committees of experts
- In building capacity aim at quality by setting up qualification criteria for ARVs use in new centers. (Clinical and laboratory)
- Private - public sectors collaboration
- Plan for AIDS care and necessary logistics in the districts
- Mobilize and maximize recourses
- Planning, implementation, and evaluation to proceed contemporaneously.
Key to Expansion of quality care.

• Network of a nationwide referral system
• Training and facilitation to achieve necessary skills
• User friendly, reliable, affordable and sustainable treatment and monitoring tests
Expected Outcome

(1) Increased access to ARVs/care:
(2) Increased willingness for VCT and adoption of preventive behavior
(3) Saving of lives and improved quality of life
(4) Further fall in incidence of HIV
Reduce or Stop Suffering without ARVS
The Way forward
Increasing ARV access in resource poor settings

PARTNERSIPS

Public Sector
Ministry of Health

Private Sector
NGO’s, Employers
Insurance etc.

International Donors
GF, World Bank, etc.
2 ultimate requirements for a successful AIDS care and treatment program

- ARVS must be on the essential drugs list
- Care and treatment must be accessible to all.

Uganda has demonstrated that these are achievable. The main constraint remains the high cost of drugs and lab. tests.
END