Use of antiretroviral agents in developing countries

Peter Mugyenyi
Joint Clinical Research Centre
Kampala Uganda
ICEID, Atlanta,
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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

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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)
UGANDA’S SUCCESS

HIV positive (%)

Antenatal clinic sites

1990
1991
1992
1993
1994
1995
1996

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

Years

Nsambya  Rubaga  Mbarara  Jinja  Tororo  Mbale

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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

![Graph showing rates over time]
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
The burden of HIV fueled epidemics; New Tuberculosis cases (Ethiopia)

Thousands

- Not Due to HIV
- Due to HIV


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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.

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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
APOLOGIES FOR LACK OF ARVS 2

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$)


Outcry for equity, market Pressures.
activism, generic competition

February-April 2001 offers
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>Capital city; Main</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>Coordination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional</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>Districts</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>County;(Health centers)</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>Rural Health Facility</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

No of Patients

Visits

1 2 3
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>8</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

Number of Patients

Age Groups

20-29 30-39 40-49 50+

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Marital status of JCRC Mbale patients by sex

Number of patients

Marital status of patients
JCRC-2002

<table>
<thead>
<tr>
<th>Marital Status</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widow</td>
<td></td>
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</tr>
</tbody>
</table>
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
CD4 COUNTS FOR PATIENTS COMING AT MBALE JCRC CLINIC

![CD4 Counts Scatter Plot]

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Graph Showing Drug Combinations taken by Patients on ARVs at JCRC Mbale Clinic
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)

| 1. Zidovudine (Combivir) 3TC/DDI Nevirapine | Nevirapine Efavirenz |
| 2. Stavudine 3TC/DDI Nevirapine | Nevirapine Efavirenz |
| 3. ZDV/d4t 3TC/DDI | RTV+CXV RTV+FTV NFV/CXV Kaletra |

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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 resources
- 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