The NEW state antiretroviral guidelines: How good are they?

Prof Francois Venter
Reproductive Health and HIV Research Institute
University of the Witwatersrand
September 2010
“Not only do they give you a beautiful face and skin, but they also protect you from disease.”

— MANTO TSHABALALA-MSIMANG
South African health minister, who advocates garlic and lemon rind as AIDS treatments and warns against anti-retroviral drugs because of dangerous side effects
Get tested!

• "The country is burning." - Health Minister Aaron Motsoaledi, March 29 2010

• "we will be training young people for the grave, instead of the workplace" Higher Education Minister Blade Nzimande on prevention, March 29 2010
Implications

• HCT campaign 1\textsuperscript{st} April….
• 15 million tests, linked to TB, other chronic illness screening
Objectives

1. **Mobilize** people to know their status.

2. Support people with key prevention messaging in order to take proactive steps to a **healthy lifestyle** irrespective of HIV status; and

3. **Increase incidence** of health seeking behaviour; and

4. Increase the **access** to treatment, care and support
New guidelines
CLINICAL GUIDELINES FOR THE MANAGEMENT OF HIV & AIDS IN ADULTS AND ADOLESCENTS

National Department of Health
South Africa 2010
ART outcomes - good news

- National programmes reporting good outcomes
- 1 year survival estimated as 93-95%
- 2 year survival 91%
How long will people live for?

• ? 20 years or more on the treatment package!! – CROI 2005
• Danish study – 39 years!
• American – lose 12 years
• French – NORMAL after 6 years
• Geriatrics, fertility
In summary, what has changed:

- CD4 350, qualified, for adults
- Initiation of infants immediately
- New maternal health/ PMTCT
- New 1st line drugs for adults, kids
- Altered second line
- Expedited referral with timelines
- Decreased monitoring
- Nurse initiation focus
Major change #1: CD4<350

• NOT for all – pregnant women, TB
Therapy for Early HIV Infection

**Symptomatic (Stages 3 & 4)**

- CD4 Count (cell/mm\(^3\))
  - < 200

**Asymptomatic (Stages 1 & 2)**

- CD4 Count (cell/mm\(^3\))
  - 200
  - 350
  - 500
What happens if you get HIV?

Wellness – nutrition, exercise, stop smoking, safe sex, mental health, ↓ alcohol

Needs ARV’s

Gets HIV!

CD4

8 to 10 years
When to start according to CD4

<table>
<thead>
<tr>
<th>CD4 Count (Cells/μl)</th>
<th>Clinical Stage</th>
<th>Time after Starting ART (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1-3</td>
</tr>
<tr>
<td>&lt;25</td>
<td>Advanced</td>
<td>63.79 (44.67-91.10)</td>
</tr>
<tr>
<td></td>
<td>Less advanced</td>
<td>18.25 (9.15-36.41)</td>
</tr>
<tr>
<td>25-49</td>
<td>Advanced</td>
<td>38.32 (25.15-58.38)</td>
</tr>
<tr>
<td></td>
<td>Less advanced</td>
<td>10.96 (5.34-22.50)</td>
</tr>
<tr>
<td></td>
<td>Less advanced</td>
<td>6.25 (2.49-15.70)</td>
</tr>
<tr>
<td>100-199</td>
<td>Advanced</td>
<td>13.73 (7.20-26.19)</td>
</tr>
<tr>
<td></td>
<td>Less advanced</td>
<td>3.93 (1.57-9.84)</td>
</tr>
<tr>
<td>≥200</td>
<td>Advanced</td>
<td>10.20 (7.55-13.77)</td>
</tr>
<tr>
<td></td>
<td>Less advanced</td>
<td>2.92 (1.53-5.58)</td>
</tr>
<tr>
<td>Overall</td>
<td>Overall</td>
<td>21.20 (19.21-23.38)</td>
</tr>
</tbody>
</table>

“Death Zone”

Studies That may mean >350!

• SMART trial\(^1\)
  – Reduced risk of both opportunistic disease and serious non-AIDS events observed in patients who initiated and remained on antiretroviral therapy at CD4+ cell counts > 350 cells/mm\(^3\)

• ART-CC\(^2\)
  – Smaller absolute risk of AIDS or death seen for patients starting ART at CD4+ cell counts > 350 cells/mm\(^3\) vs ≤ 350 cells/mm\(^3\)

• NA-ACCORD\(^3\)
  – Survival benefit with earlier vs deferred ART
    • Risk of death 69% higher for patients deferring ART until CD4+ cell count ≤ 350 cells/mm\(^3\) vs 351-500 cells/mm\(^3\)
    • Risk of death 94% higher for patients deferring ART until CD4+ cell count ≤ 500 cells/mm\(^3\) vs > 500 cells/mm\(^3\)

New Studies Supporting Earlier Antiretroviral Therapy

• Low CD4+ nadir associated with
  – Increased rates of HIV-associated neurocognitive disorders[1]
  – Arterial stiffness contributing to CV risk[2]
  – Increased risk of fracture[3]

• Patients with acute opportunistic infections (OI)
  – 2-fold higher risk of clinical progression in patients who deferred HAART vs those started immediately[4]
  – Improved immunologic outcomes in patients starting early vs deferred HAART during acute OI[5]

When to Start: 2009 DHHS Guidelines

<table>
<thead>
<tr>
<th>CD4+ Cell Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CD4+ cell count &lt; 350 cells/mm³</td>
<td>• Start ART</td>
</tr>
<tr>
<td>• CD4+ cell count 350-500 cells/mm³</td>
<td>• Start ART*</td>
</tr>
<tr>
<td>• CD4+ cell count &gt; 500 cells/mm³</td>
<td>• Panel divided†</td>
</tr>
</tbody>
</table>

**Clinical Conditions Favoring Initiation of Therapy Regardless of CD4+ Cell Count**

- History of AIDS-defining illness
- Certain acute opportunistic infections
- Pregnancy
- HIVAN
- HBV coinfection when HBV treatment is indicated
- CD4+ count decline > 100 cells/mm³ per yr
- HIV-1 RNA > 100,000 copies/mL

*Panel divided: 55% strongly recommend and 45% moderately recommend. †50% favor initiating therapy at this stage. 50% view initiating therapy at this stage as optional.

When Is Antiretroviral Therapy Started?

- Review of data from 2003-2005 from 176 sites in 42 countries (N = 33,008)

When to start – CD4 (adults)

- Any CD4 – WHO 4 and MDR TB
- < 200 or
- CD4 count ≤350cells/mm³
  - in patients with TB/HIV
  - Pregnant women
Children

- All children less than 1 year of age
- Children 1 – 5 years with clinical stage 3 or 4 or CD4 ≤ 25% or absolute CD4 count < 750 cells/µl
- Children ≥ 5 years to 15yrs with clinical stage 3 or 4 or CD4 ≤ 350 cells/µl.
Children

• All children less than 1 year of age
  • Children 1 – 5 years with clinical stage 3 or 4 or CD4 ≤ 25 % or absolute CD4 count < 750 cells/µl
  • Children ≥ 6 years to 15yrs with clinical stage 3 or 4 or CD4 < 350 cells/µl.

Huge implications for PCR screening!
Why TB?


• SAPIT study – deferred ART in low CD4 stopped early (55% lower mortality in integrated vs sequential treatment arms (5.1 vs 11.6 deaths per 100 patient-years; P = .0049); Abdool Karim SS, NEJM, 2010)

• Less mortality at cost of possibly more IRIS

• ?how fast to ART – but mortality is high if deferred

• MDR – ANY CD4

• Debate – why not ALL TB
Why CD4 Threshold of <350 for Treatment?
Includes Most Maternal Deaths and Postnatal Infections
ZEBS Study – L. Kuhn personal communication 2009

CD4 < 200: 55% of maternal deaths, 47% of postnatal infections
Treatment as prevention

• Prevention programmes results very disappointing
• Can reducing the viral load earlier have a public health impact?
• Convenient convergence!
HIV Transmission Risk in Heterosexual Serodiscordant Couples Initiating ARV

- 92% lower risk of HIV transmission in African serodiscordant couples when HIV-infected partner receiving ARV therapy
  - 102 of 103 cases of confirmed HIV transmission occurred in couples with HIV-infected partner not receiving ARV therapy
    - Unadjusted relative risk: 0.17 (95% CI: 0.004-0.94; \( P = .037 \))
    - Adjusted relative risk: 0.08 (95% CI: 0.002-0.57; \( P = .004 \))
      - Adjusted for visit and CD4+ cell count at initiation

Final word:

- DoH: wants <350 for all
- Reason for qualification was cost and perceived burden on services
Major change #2

- Why was tenofovir chosen for adults?
- Why abacavir for kids?
1st line adults

• All new patients needing treatment, including pregnant women
  - TDF + 3TC/FTC +EFV/NVP
• Contraindication to TDF: renal disease
  AZT+ 3TC +EFV/NVP
• For those on existing d4T, remain, but vigilance urged
Toxic! Failure – VL > 5000

- d4T
- 3TC
- Efavirenz/nevirapine

- AZT
- ddI
- Kaletra

Protease
New ARVs for man with boobs

Alfred Moselakgomo
A Mpumalanga hospital has changed the type of antiretroviral drugs which allegedly made a man develop breasts.

Sowetan reported last week that Sabelo Maepa (not his real name), 42, of Sakhile township in Standerton developed breasts after he took antiretroviral drugs which he said did not suit him.

The biological terms for the man's condition is gynecomastia (development of breasts in men).

A doctor at Standerton Hospital where Maepa was admitted initially said Maepa, who is also on TB medication, was taking a drug called Stavudine when he developed breasts.

Stavudine was approved by the US Food and Drug Administration for adult use in June 1994. It was also approved for pediatric use in 1996, and again as an extended-release version for once-a-day dosing in 2001.

It is the fourth antiretroviral drug on the market, and its patent will expire in the US on June 25 next year, according to Aids InfoNet.

Another Standerton hospital doctor, who did not want to be named, said: "Stavudine had an adverse impact on Maepa and he will now be given another drug called Zidovudine."

Zidovudine was the first drug approved for the treatment of HIV. It is a nucleoside analog reverse transcriptase inhibitor, or nuke, according to The Body, a comprehensive website featuring in-depth information on topics ranging from HIV prevention to state-of-the-art treatment issues.

The Body states that these drugs block the reverse transcriptase enzyme. This enzyme changes HIV's genetic material into a form of DNA.

This has to occur before HIV's genetic code gets inserted into an infected cell's own genetic codes.

A source said Standerton Hospital last week referred Maepa back to the wellness clinic in Standerton for examination.

The results of his examination were not immediately available.

"Maepa has been booked for surgery on November 21 at a Johannesburg hospital," said the source.

"No cost implication has been attached as he is a public patient."

"The cost will be carried by government," he said.

Mpho Gabele, a health department, said he was not aware of any development in Maepa's case.

EFFECT: A different ARV may help this man.

Case sends shockwaves

Zinhle Mapumulo
The disturbing story published by Sowetan on Wednesday last week of a man who grew breasts due to the side-effects of antiretroviral treatment, has sent shockwaves through the medical industry.

Sowetan has been inundated with calls from ordinary people and HIV lobby groups concerned about this sad and unusual condition.

Venter is a specialist doctor in private practice treating HIV patients. See adjacent report.

What people on ARV treatment should know:
- The names of pills
- Your weight
- CD4 count
- Viral load

What they should be cautious about:
- Lossing weight
- Painful feet
- Stomach pain or vomiting for over...
Preferred First-line Regimens: 2009 DHHS Guidelines

Preferred regimens: those with optimal and durable efficacy, favorable tolerability and toxicity profile, and ease of use

<table>
<thead>
<tr>
<th>Regimen Type</th>
<th>Preferred Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI based</td>
<td>EFV + TDF/FTC</td>
</tr>
<tr>
<td>Boosted PI based</td>
<td>ATV/RTV + TDF/FTC</td>
</tr>
<tr>
<td></td>
<td>DRV/RTV + TDF/FTC</td>
</tr>
<tr>
<td>INSTI based</td>
<td>RAL + TDF/FTC</td>
</tr>
</tbody>
</table>

SUMMARY
Several groundbreaking trials and over 1 million years of patient experience have established tenofovir as an important component of HIV treatment. Tenofovir has demonstrated potent antiviral efficacy, with a low risk of developing resistance when used as part of an effective combination regimen. It is generally well tolerated, with a low risk of lipoatrophy and a favourable effect on lipid profile compared with older nucleoside analogue agents such as stavudine or zidovudine. Clinical data suggest that switching from thymidine analogues to a tenofovir-containing regimen can benefit patients with lipid abnormalities or lipoatrophy. This article reviews the development of tenofovir, including pivotal studies that have influenced HIV clinical practice.

Review Criteria
A search of the Medline database was performed in December 2007 using the search terms outlined in 'keywords'. In addition, the reference lists from retrieved articles were searched for additional citations, and abstracts from recent scientific meetings were reviewed.

Message for the Clinic
Tenofovir in combination with emtricitabine should be considered as a first-choice component of an HIV treatment regimen for antiretroviral-naive patients. Switching from thymidine analogues to tenofovir may also benefit patients with lipid abnormalities or lipoatrophy.
Why not AZT?

• AZT/3TC/EFV
• Good question!
• Anaemia, lipoatrophy, used in second line
Why not abacavir for adults?

- ABC/3TC/efavirenz?
- For kids – good choice (lots of data)!
**ACTG 5202: Virologic Failure With ABC/3TC vs TDF/FTC**

**In pts with screening VL < 100,000 c/mL**
- Similar time to virologic failure with ABC/3TC vs TDF/FTC regardless of ATV/RTV or EFV
  - With ATV/RTV, HR: 1.26 (0.76-2.05)
  - With EFV, HR: 1.23; (0.77-1.96)

**In pts with screening VL ≥ 100,000 c/mL**
- Shorter time to VF with ABC/3TC vs. TDF/FTC with either EFV or ATV/RTV
  - With EFV, HR: 2.22 (1.19-4.14)
  - With ATV/RTV, HR: 2.46 (1.20-5.05)

**Virologic Failure Free at 96 Wks for Pts with Screening VL < 100,000 copies/mL**

<table>
<thead>
<tr>
<th></th>
<th>ATV/RTV</th>
<th>EFV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/3TC</td>
<td>88.3</td>
<td>87.4</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>90.3</td>
<td>89.2</td>
</tr>
</tbody>
</table>

Why not abacavir for adults?

- **Cost**
- ?? Fixed dose combination n/a
- ??? Rash
- ??? Less potent
Why not TDF for kids?

- toxicity
Why not raltegravir?

- TDF/3TC/raltegravir
Protocol 004: 192-Wk Virologic Response to RAL vs EFV in Naive Patients (NC = F)

Using observed failure approach: RAL 91% and EFV 88% at Wk 192

*After Wk 48, patients in all RAL groups continued at 400 mg BID. All patients received TDF+3TC.

Why not raltegravir?

- Cost ($90/R750 /month)
- Experience limited
- EFV is good!
1\textsuperscript{st} line kids

- All infants and children under 3 years ABC + 3TC + LPV/r
- Children 3 years or over ABC + 3TC + EFV
Who is still taking d4T?

Side effects potentiated by TB Rx

• Those on d4T currently will remain on it, as long as no side effects
Any problems seen with TDF?

• Supply

• Renal dysfunction — creatinine clearance somewhat predicts BUT we will get renal failure cases
Major Change # 3: 2\textsuperscript{nd} line
2\textsuperscript{nd} line adults

- Failing on a d4T or AZT based 1st line regimen - TDF + 3TC/FTC + LPV/r
- Failing on a TDF based 1st line regimen - AZT+3TC+ LPV/r
- Beyond 2\textsuperscript{nd}: “refer”
2\textsuperscript{nd} line children

- Children above 3 years - Failed ABC +3TC + EFV get: AZT + ddi +LPV/r
- Failed on AZT or d4T based regimen: ABC + 3TC + LPV/r
- Failed LPV/r OR less than 3 OR failed second line – “refer”
Results are very good with boosted PIs as second line

High Rates of Survival, Immune Reconstitution, and Virologic Suppression on Second-Line Antiretroviral Therapy in South Africa

Matthew P. Fox, DSc, MPH,*† Prudence Ivey, MBBCH,‡ Lawrence Long, MCom,†
Mhairi Maskew, MBBCH, MSc,‡§ and Ian Sanne, MBBCH‡§

Abstract: To determine rates of survival, viral suppression, and immunologic change after 1 year on second-line antiretroviral therapy, we conducted a cohort study among 328 patients initiated on zidovudine, didanosine, and lopinavir/ritonavir. All patients who switched to standard second-line therapy at a large urban public-sector clinic in Johannesburg, South Africa, were included. Among

Key Words: human immunodeficiency virus, antiretroviral therapy, second-line therapy, South Africa, viral load, CD4 count, sub-Saharan Africa

(J Acquir Immune Defic Syndr 2010;53:500–506)
Monitoring

- Lipids at 3 months if lop/rit (adults), annually if children
Major change #4: Expedited care
High death rate while waiting for ART


Expeditied care decreased mortality by 60%
Expedited adults

• Require fast track (i.e. ART initiation within 2 weeks of being eligible)
• Pregnant women needing lifelong ART
• Patients with very low CD4 (<100)
• Stage 4, CD4 count not yet available
• MDR/XDR TB
Fast track children

- Child less than 1 year
- Stage 4 and CD4 count not yet available
- MDR or XDR TB
Major issue #5: Monitoring
Monitoring adults and kids

- Clinical stage
- CD4 at month 6 and then every 12 months
- VL at month 6 into ART, then every 12 months
- ALT if on NVP and develops rash or symptoms of hepatitis
- FBC at month 1, 2, 3 and 6 if on AZT
- Creatinine at month 3 and 6 then every 12 months if on TDF
- Fasting cholesterol and triglycerides at month 3 if on LPV/r (adults); baseline and annually in kids
- No hep B
Why fewer VLs?

- Development of resistance is slow
- PI’s work as second line even in presence of resistance
Major issue #6: PMTCT
Measurement of Generally Accepted Indicators Reveals that the South African Healthcare System is Functioning Poorly by International Standards


<table>
<thead>
<tr>
<th>Country</th>
<th>2000</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>1,900</td>
<td>1,800</td>
</tr>
<tr>
<td>India</td>
<td>540</td>
<td>450</td>
</tr>
<tr>
<td>South Africa</td>
<td>230</td>
<td>400</td>
</tr>
<tr>
<td>Iraq</td>
<td>250</td>
<td>300</td>
</tr>
<tr>
<td>China</td>
<td>230</td>
<td></td>
</tr>
<tr>
<td>Namibia</td>
<td>300</td>
<td>210</td>
</tr>
<tr>
<td>Brazil</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Chile</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Netherlands</td>
<td>16</td>
<td>6</td>
</tr>
</tbody>
</table>

Note: MMR = Number of Maternal deaths per 100,000 *Public Sector deliveries estimated. Live births is used as a proxy for the number of pregnancies annually. MMR is an indicator of the quality of a health care system.

Maternal health

- Eligible for ART (i.e. ≤ 350 cell or clinical stage 4) - TDF + 3TC/FTC + NVP and start ART as soon possible
- Not eligible for ART i.e. CD4 > 350 - AZT from 14 weeks, sdNVP at delivery TDF + FTC single dose after delivery
- Unbooked and presents in labour - sdNVPTDF + 3TC/FTC one week
- ** repeat HIV testing
Infant regimens

• Mother on lifelong ART - NVP at birth and then daily for 6 weeks irrespective of infant feeding choice
• Mother on AZT for MTCT prophylaxis - NVP at birth and then daily for 6 weeks continued as long as any breastfeeding
• Mother did not get any ARV before or during delivery - NVP as soon as possible and daily for at least 6 weeks continued as long as any breastfeeding
What are the targets for this?

- 1\textsuperscript{st} April
- NSP: 420 000/ year next year (10% children)
What can stop us?

• Human resources
• Budget and treasury
• Beaurocracy and legislation
Major issue #7

• Nurse initiation of therapy
Human resources

Actually we thought he might be dead... then he realised where we were taking him.

A GAUTENG PROVINCIAL HOSPITAL

Patients: bring your own
- Food
- Medicines
- Bed sheets
- Bedpans
- Beds
- Any kitchen or garden implements which could double as medical equipment
### Table 2: Cross-country comparison of physician and nurse density per 100 000 population

<table>
<thead>
<tr>
<th>Country</th>
<th>Medical practitioner density per 100 000</th>
<th>Nurse density per 100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mozambique</td>
<td>3*</td>
<td>21#</td>
</tr>
<tr>
<td>Lesotho</td>
<td>5*</td>
<td>62#</td>
</tr>
<tr>
<td>Zambia</td>
<td>12*</td>
<td>174</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>16*</td>
<td>72#</td>
</tr>
<tr>
<td>Namibia</td>
<td>30</td>
<td>306</td>
</tr>
<tr>
<td>Botswana</td>
<td>40</td>
<td>265</td>
</tr>
<tr>
<td>South Africa</td>
<td>77</td>
<td>408</td>
</tr>
<tr>
<td>United States of America</td>
<td>256</td>
<td>937</td>
</tr>
<tr>
<td>France</td>
<td>337</td>
<td>724</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>230</td>
<td>1212</td>
</tr>
</tbody>
</table>

*Countries falling below the WHO minimum level for medical practitioners per 100 000 population (20:100 000). #Countries falling below the WHO minimum level for nurses per 100 000 population (120:100 000) (Hall & Erasmus (2003)).


Ref: HUMAN RESOURCES FOR HEALTH: A NEEDS AND GAPS ANALYSIS OF HRH IN SOUTH AFRICA, November 2009, HEARD
Haemorrhage from SA and out of practice…

Table 5: Ratio of medical practitioners per 100 000 population across provinces, 2001 and 2004

<table>
<thead>
<tr>
<th>Province</th>
<th>2001</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Cape</td>
<td>34</td>
<td>27</td>
</tr>
<tr>
<td>Free State</td>
<td>69</td>
<td>54</td>
</tr>
<tr>
<td>Gauteng</td>
<td>173</td>
<td>126</td>
</tr>
<tr>
<td>KwaZulu-Natal</td>
<td>70</td>
<td>52</td>
</tr>
<tr>
<td>Limpopo</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>Mpumalanga</td>
<td>42</td>
<td>30</td>
</tr>
<tr>
<td>North West</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>Northern Cape</td>
<td>54</td>
<td>42</td>
</tr>
<tr>
<td>Western Cape</td>
<td>182</td>
<td>147</td>
</tr>
</tbody>
</table>

Source: Hall and Erasmus (2003); HPCSA (2004)
Some of the pressure for NHI...
Context of care
What health services are available?

• Primary health care: predominantly nurse driven with doctor support, overloaded
• Last 10 years slight dip in absolute numbers of people attending PHC sites

Is it easier to develop vertical programmes than integrated programmes eg ARV, PMTCT?
Legal issues

- Nurses
- Pharmacy dispensing
Budgeted!
What we can learn…

Professor Gesine Meyer-Rath, HeRO
What we can learn…

*CD4 350 for all, children at diagnosis

• Tenofovir, abacavir

• Cost it!
The cost of the national antiretroviral treatment programme

How big can we go, and how much can we save?

Gesine Meyer-Rath

Health Economics and Epidemiology Research Office (HE²RO)
Wits Health Consortium, Johannesburg, South Africa/
Center for Global Health and Development, Boston University, Boston, USA

Southern African HIV Clinicians Society Johannesburg Branch meeting, 26/08/2010
Background: Situation in 2008/09

- South Africa has the largest ART programme worldwide
  - 919,923 patients in November 2009
- Initiation rates of >300,000 patients/year put pressure on funding and capacity
- Discussion about changes to guidelines
  - Increased eligibility
  - Better drugs
  - Changes to drug procurement
  - Changes to staffing levels and tasks
Objectives of analysis

- Department of Health convened Costing Task Team in April 2009

- Objectives for National ART Cost Model:
  - Calculate the relative costs of changes to the South African ART guidelines
  - Based on these, calculate the resources required for national ART provision between 2009/10 and 2015/16 by both government and donors
### Scenarios

#### Old South African Guidelines

| Eligibility | Adults: CD4 \(<200\) cells/mm\(^3\) or WHO stage 4  
             | Children: CD4 15% to 20% or WHO stage 3 or 4 |
|-------------|------------------------------------------------|
| Regimens    | Adults: d4T + 3TC + EFV/NVP; AZT + ddl + LPV/r  
             | Children <3 yrs: d4T + 3TC + LPV/r; AZT + ddl + NVP |

#### New South African Guidelines

| Eligibility | Adults: CD4 \(<350\) cells/mm\(^3\) **for TB/HIV co-infected or pregnant pts**, <200 cells/mm\(^3\) or WHO stage 4 for all others  
             | Children: **Early Paediatric Treatment** |
|-------------|--------------------------------------------------------------------------------|
| Regimens    | Adults: TDF + 3TC + EFV/NVP for all new initiates; TDF + 3TC + LPV/r if failing d4T- or AZT-containing regimens/ AZT + 3TC + LPV/r if failing TDF-containing regimens  
             | Children <3 yrs: ABC + 3TC + LPV/r; AZT + ddl + NVP |

#### Full WHO Guidelines

| Eligibility | Adults: CD4 \(<350\) cells/mm\(^3\) or WHO stage 4 **for all**  
             | Children: **Early Paediatric Treatment** |
|-------------|--------------------------------------------------------------------------------|
| Regimens    | As in “New South African Guidelines” |
Additional conditions

• **New drug purchasing system (RL):**
  – ARV drugs at prices set in reference list modelled on prices negotiated/ maintained by
    • Clinton Foundation
    • Global Price Reporting Mechanism (WHO)
    • Supply Chain Management System (Pepfar)
    • South African government tender

• **Task shifting (TS):**
  – ARV initiation and management by nurses under physician supervision
  – ARV dispensing by pharmacy assistants under pharmacist supervision
Cost data collection

• Bottom-up cost analysis of ART provision from provider perspective
• Fixed and variable cost
  – Drugs (ARVs and others)
  – Diagnostics
  – Staff
  – Overheads (building, utilities, equipment, communication)
• Excludes inpatient cost
• Includes cost of VCT and pre-ART care for eligible patients
• ARV cost for **children** adjusted by age and weight
• All costs updated to 2009
  – ARV cost: Tender prices from Feb. 2010
  – Staff cost includes OSD from August 2009
• **New regimens** costed using ingredients approach and 2010 tender prices
## Cost per patient year (2009 ZAR)

<table>
<thead>
<tr>
<th>Cost per patient year (*half-year)</th>
<th>Old guidelines</th>
<th>New guidelines + Full WHO guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>d4T regimens</td>
<td>TDF regimens</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line &lt; 6 mts*</td>
<td>3,520</td>
<td>4,320</td>
</tr>
<tr>
<td>First line &gt; 6 mts</td>
<td>5,151</td>
<td>6,126</td>
</tr>
<tr>
<td>First line failure</td>
<td>5,281</td>
<td>6,149</td>
</tr>
<tr>
<td>Second line</td>
<td>11,747</td>
<td>8,740</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age [years]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line &lt; 6 mts*</td>
<td>3,269</td>
<td></td>
</tr>
<tr>
<td>First line &gt; 6 mts</td>
<td>4,135</td>
<td></td>
</tr>
<tr>
<td>First line failure</td>
<td>4,407</td>
<td></td>
</tr>
<tr>
<td>Second line</td>
<td>6,252</td>
<td></td>
</tr>
</tbody>
</table>
Total number of patients

Number of patients over time

- + 10%
- + 14%
- + 233%


Guideline Categories:
- Old Guidelines
- New Guidelines
- Full WHO Guidelines
Results:
Total cost [million 2009 ZAR]

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Full cost (Staffing and drug cost as current)</th>
<th>Reduced cost (With task-shifting and reference list for drug prices)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2010/11</td>
<td>2016/17</td>
</tr>
<tr>
<td>Old Guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7,729</td>
<td>19,053</td>
</tr>
<tr>
<td>New Guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8,317</td>
<td>22,869</td>
</tr>
<tr>
<td>Change on Old GL (Full cost)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8%</td>
<td>20%</td>
</tr>
<tr>
<td>Full WHO Guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9,731</td>
<td>25,209</td>
</tr>
<tr>
<td>Change on Old GL (Full cost)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>27%</td>
<td>33%</td>
</tr>
</tbody>
</table>

→ The total cost of the programme increases by 17% and 32%, resp., for the New Guidelines and WHO Guidelines scenarios, as a result of both higher numbers of patients and higher drug cost for TDF-containing regimens.
If the new drug purchasing mechanism and task-shifting are implemented, the New Guidelines and the Full WHO Guidelines will cost less than the Old Guidelines.
## Budget impact

[Budget Review 2010, National Treasury]

### Comparison with public health service budget

<table>
<thead>
<tr>
<th></th>
<th>2010/11</th>
<th>2011/12</th>
<th>2012/13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of budget at full cost</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old Guidelines</td>
<td>8%</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>New Guidelines</td>
<td>8%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Full WHO Guidelines</td>
<td>10%</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>Percentage of budget at reduced cost (TS and RL/FDC)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old Guidelines</td>
<td>5%</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>New Guidelines</td>
<td>5%</td>
<td>7%</td>
<td>8%</td>
</tr>
<tr>
<td>Full WHO Guidelines</td>
<td>7%</td>
<td>8%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Training and implementation

• National and provincial processes
• Chaotic
Reflections…

• Strange consultation process
• Tension between clinicians, public health, DoH and Treasury – lack of transparency
• Hep B, nurses, PMTCT big tension points
• Tender delayed
• FDCs still an issue
The End

hello the future