The KZN Program
A King George V Perspective
MDR-TB 2004-2008, by province
XDR-TB 2004-2008, by province
TB at King George V (KGV) and Fosa

- KGV is an exclusive provincial MDR TB facility (2000)
- Currently has 387 MDR beds in Ethekwini
  - KGV – 192 - (32 paeds)
  - Fosa - 195 (to ↓)
- In Jan 2007 – bed crises - waiting list for admission 150
  - Waiting period - 3 months

- 3 Interventions
  1. Decentralized MDR Units operational since March 2008
     • Thulasizwe, Greytown, Murchison, Manguzi (225)
     • Plans for future units – ? funding
  2. Outpatient Treatment in selected patients - referring back to
     • District hospitals / TB Centres (150)
       (Doris Goodwin, Catherine Booth, Madadeni, Hlabisa)
     • Clinic
  3. Province commenced a pilot outpatient project in Tugela Ferry
     • Short admission thereafter injections administered by mobile team
Bed State vs Waiting List

130 Beds: Decentralized Unit
Greytown, Murchison, Thulasizwe, Manguzi
600 Outpatients

160 Beds FOSA
600 treated as outpatients

200 Beds: Satellite Units
District Hospitals + Santa
600 Outpatients

Patients Waiting

Beds

Strike

Dr I. H. Master
## Current Waiting List – 20/09/2010

<table>
<thead>
<tr>
<th>Patients Waiting</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Males – awaiting beds</td>
<td>41</td>
</tr>
<tr>
<td>Females – awaiting beds</td>
<td>70</td>
</tr>
<tr>
<td>New Outpatients awaiting Rx</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>143</td>
</tr>
</tbody>
</table>

- Currently 143 patients waiting for treatment
- Waiting period - 6 weeks for inpatients + 3 weeks for outpatients
- 10 XDRs awaiting treatment
- The reality is there will never be enough beds
- An outpatient program is the only rational option.
DR TB Management – National guidelines (since March 2007)

- National Plan based on **WHO Guidelines** of 2008
- Intensive phase (with injectable) for a minimum of **6 months**
  - least 4 months after culture conversion.
- Most facilities admitted patients until culture conversion.
- Continuation phase - at least **18 months** after culture conversion.
- Treat for at least 24 months if extensive Disease
- After completion of treatment follow up – 6 monthly for at least 2 years
KZN/KGV – Management policy

- In KZN those admitted are kept for 6 months.
  - We allow early discharge for
    - Urgent social issues
    - Aggressive patients
    - Extreme shortage/pressure on beds
- Unfortunately with current bed pressures patients still having positive cultures at 6 months are sent home on treatment
- XDR and ill patients are prioritized
  - All XDRs are admitted to KGV
- Patients treated as outpatients
  - Are mainly admitted to district hospital
  - Treatment failures being given a 2\textsuperscript{nd} chance
  - Absolute refusal to be admitted
  - Commitment from the referring person/facility/clinic to facilitate supervision of treatment
- National is seriously considering outpatient programs for MDR TB
MDR TB Follow-up Clinic

- Discharged MDR patients attend monthly.
- Follow-up clinic operates twice weekly
  - Patients attend from throughout KZN (& Transkei).
- See up to 250 patients/clinic = 2000/month.
- New patients are seen on 3 x a week
  - Currently Initiating up to 40 new outpatients / week
- Up to 20 new inpatients admitted per week
- Transport issues
  - Difficulty in reaching King George V
  - Insufficient transport
  - Move to decentralize MDR treatment makes sense
Renovated multi-storey
For MDR TB

New star shaped ward
In South Africa, all newly diagnosed MDR-TB patients (with no previous exposure to second line drugs) receives a standardized regimen.

- 6Z-Km(Am)-Ofx(Lvx)-Eto-Trd / 18Z- Ofx(Lvx)- Eto-Trd
MDR Treatment

- **Intensive phase** – Minimum 6 months
  - 5 drugs – at least 6 x per week
    - Aminoglycoside (5 x weekly) (Kanamycin/Amikacin)
    - PZA
    - Ofloxacin (Levofloxacin)
    - Ethionamide
    - Terizidone/Cycloserine
    - Ethambutol can be added
    - Pyridoxine (B6) - 150mg daily with Terizidone/Cycloserine

- **Continuation Phase** – Minimum 18 months
  - Drugs at least 6 x per week
    - Ethionamide
    - Ofloxacin (Levofloxacin)
    - Terizidone/Cycloserine
    - PZA
### 1. Drug Dosages for MDR TB

<table>
<thead>
<tr>
<th>Drug</th>
<th>&lt; 33KG</th>
<th>33 – 50kg</th>
<th>51 – 70kg</th>
<th>&gt;70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrazinamide</td>
<td>30-40 mg/kg</td>
<td>1g</td>
<td>1,5</td>
<td>2g(2.5g)</td>
</tr>
<tr>
<td>Kanamycin or Amikacin</td>
<td>15-20 mg/kg</td>
<td>500mg (10-15mg/kg)</td>
<td>750mg to 1g (10-15mg/kg)</td>
<td>1g</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>15-20 mg/kg</td>
<td>500mg</td>
<td>750mg</td>
<td>750mg (1g)</td>
</tr>
<tr>
<td>Ofloxacin (Laevofloxacin)</td>
<td>800mg (750mg)</td>
<td>800mg (750mg)</td>
<td>800mg (750mg)</td>
<td>800mg (750mg-1g)</td>
</tr>
<tr>
<td>Terizadone or Cycloserine</td>
<td>15-20 mg/kg</td>
<td>500mg</td>
<td>750mg</td>
<td>750mg (1g)</td>
</tr>
<tr>
<td>+/- Ethambutol</td>
<td>25 mg/kg</td>
<td>800mg</td>
<td>1.2g</td>
<td>1.6g (2g)</td>
</tr>
<tr>
<td>Drug</td>
<td>2008</td>
<td>2009</td>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td></td>
</tr>
<tr>
<td>PAS (4g BD)</td>
<td>R1600</td>
<td>R2360</td>
<td>R2358</td>
<td></td>
</tr>
<tr>
<td>Capreomycin (1g 5x)</td>
<td>R800</td>
<td>R1300</td>
<td>R2391</td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin (400mg OD)</td>
<td>R800</td>
<td></td>
<td>R911</td>
<td></td>
</tr>
<tr>
<td>Terizidone (250mg tds)</td>
<td>R650</td>
<td>R579</td>
<td>R566</td>
<td></td>
</tr>
<tr>
<td>Cycloserine (250mg tds)</td>
<td>R600</td>
<td>R522</td>
<td>R522</td>
<td></td>
</tr>
<tr>
<td>Klacid (500mg BD)</td>
<td></td>
<td>R228</td>
<td>R123</td>
<td></td>
</tr>
<tr>
<td>Amikacin (1g 5x)</td>
<td>R400</td>
<td>R216</td>
<td>R223</td>
<td></td>
</tr>
<tr>
<td>Kanamycin (1g 5x)</td>
<td>R250</td>
<td>R200</td>
<td>R239</td>
<td></td>
</tr>
<tr>
<td>Clofazamine (300mg) OD</td>
<td></td>
<td>R204</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethionamide (250mg tds)</td>
<td>R130</td>
<td>R177</td>
<td>R191</td>
<td></td>
</tr>
<tr>
<td>Ofloxacine (800mg OD)</td>
<td>R60</td>
<td>R54</td>
<td>R349</td>
<td></td>
</tr>
<tr>
<td>Augmentin (625mgs BD)</td>
<td></td>
<td>R112</td>
<td>R74</td>
<td></td>
</tr>
<tr>
<td>Rifafour (4 BD)</td>
<td>R80</td>
<td>R67</td>
<td>R67</td>
<td></td>
</tr>
<tr>
<td>PZA (1,5gm OD)</td>
<td>R50</td>
<td>R42</td>
<td>R33</td>
<td></td>
</tr>
<tr>
<td>Rifannah (300 – 2 BD)</td>
<td>R40</td>
<td></td>
<td>R42</td>
<td></td>
</tr>
<tr>
<td>EMB (1,2 OD)</td>
<td>R38</td>
<td></td>
<td>R43</td>
<td></td>
</tr>
<tr>
<td>Ciprobay (1,5gm) OD</td>
<td>R36</td>
<td>R32</td>
<td>R36</td>
<td></td>
</tr>
</tbody>
</table>
## Drug Costs

<table>
<thead>
<tr>
<th>Drug (&gt; 50KG)</th>
<th>Cost (per patient per month) 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STD TB</strong> (intensive phase)</td>
<td>R67</td>
</tr>
<tr>
<td><strong>STD TB</strong> (continuation phase)</td>
<td>R42</td>
</tr>
<tr>
<td><strong>MDR</strong> (intensive phase)</td>
<td>R1207</td>
</tr>
<tr>
<td><strong>MDR</strong> (continuation phase)</td>
<td>R968</td>
</tr>
<tr>
<td><strong>XDR</strong> (intensive phase)</td>
<td>R6654</td>
</tr>
<tr>
<td><strong>XDR</strong> (continuation phase)</td>
<td>R4263</td>
</tr>
</tbody>
</table>
Special Conditions in MDR TB

1. Pregnancy

2. Diabetes mellitus
   - overlapping toxicities

3. Renal Insufficiency
   - reduce frequency (+/- ? dosage)
   - watch out for tenofavir & aminoglycosides adverse event

4. Acute or Chronic Liver disease
   - stepwise reintroduction

5. Thyroid disease - hypothyroidism
Paediatric MDR

- Children generally have primary disease
- Children often have paucibacillary disease, (seldom culture-positive)
- In culture-negative children with active TB and a close contact with MDR/XDR TB use the contacts DST results as a guide
- Limited experience in the use of the 2nd line Drugs
- Adjust dosages as the child gains weight.
- Ethambutol to be used with caution in small children (optic neuritis)
Paediatric Patients treated 1998 - 2009

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>3</td>
</tr>
<tr>
<td>1999</td>
<td>3</td>
</tr>
<tr>
<td>2000</td>
<td>5</td>
</tr>
<tr>
<td>2001</td>
<td>4</td>
</tr>
<tr>
<td>2002</td>
<td>8</td>
</tr>
<tr>
<td>2003</td>
<td>13</td>
</tr>
<tr>
<td>2004</td>
<td>19</td>
</tr>
<tr>
<td>2005</td>
<td>24</td>
</tr>
<tr>
<td>2006</td>
<td>26</td>
</tr>
<tr>
<td>2007</td>
<td>41</td>
</tr>
<tr>
<td>2008</td>
<td>50</td>
</tr>
<tr>
<td>2009</td>
<td>59</td>
</tr>
</tbody>
</table>
Age Distribution of MDR TB in Paeds

- <1: 4%
- 1-4: 29%
- 5-12: 67%
Adverse Drug Reactions in MDR

- Aminoglycosides
  - Ototoxicity + Nephrotoxicity
- Terizidone/Cycloserine
  - Severe CNS side effects
- PAS
  - GIT side effects / cold chain
- Capreomycin
  - Renal problems/ Hypokalaemia
- Beware overlapping toxicities
  - TB/HIV as well TB Rx and ARVs
MDR and XDR at KGV

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP

XDR

Total patients

MDR

OP
Male vs female for All TB KGV
Distribution of MDR by district

Dr I. H. M. Master
Distribution of MDR by district

- Durban: 50%
- DC21: 6%
- DC22: 10%
- DC23: 2%
- DC24 (COSH): 3%
- DC25: 3%
- DC26: 3%
- DC27: 12%
- DC28: 7%
- DC29: 3%
- DC43: 2%

Slice 12
XDR TB

- COSH had a high incidence of XDR.
- 80% of COSH XDRs died (initially)
- Little community spread of XDR TB.
- Suspicion of nosocomial spread.
- Infection control has been improved.
- XDR numbers are decreasing
“Individualized Treatment”

- Reserved for XDRs and MDR patients previously exposed to other 2\textsuperscript{nd} line drugs.
- Based on
  - History of anti-TB drugs previously received
  - DST results available
- Important in MDR - Failures / Defaulters / Retreatment
- Drugs used previously in a failing patient should be considered as probably resistant.
Basic principles of XDR treatment

- Use at least four drugs expected to be effective
- Must receive an injectable.
- Can use drugs used before but don’t rely on them
- Add drugs based on susceptibility, drug history, efficacy, side-effect profile.
- Regard group 5 drugs as ½ drugs
  - Clofazamine is preferred group 5 drug
Standardised (core) regimen for XDR-TB

- 6 Cm-Mfx-Eto-Trd(Cs) - Z-PAS-Clofazimine
- 18 Mfx-Eto-Trd(Cs) - Z –PAS-Clofazimine

- Treatment should be modified based on DST results & previous 2\textsuperscript{nd} line drug exposure
- Ethambutol can be added as an additional drug
### WHO – Grouping of MDR-TB Drugs

<table>
<thead>
<tr>
<th>GROUP</th>
<th>DRUGS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong> First-line oral drugs</td>
<td>Ethambutol (E)</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide (Z)</td>
</tr>
<tr>
<td><strong>Group 2</strong> Injectable Anti-TB agents</td>
<td>Streptomycin (S)</td>
</tr>
<tr>
<td></td>
<td>Kanamycin (Km)</td>
</tr>
<tr>
<td></td>
<td>Amikacin (Am)</td>
</tr>
<tr>
<td></td>
<td>Capreomycin (Cm)</td>
</tr>
<tr>
<td></td>
<td>Viomycin (Vm)</td>
</tr>
<tr>
<td><strong>Group 3</strong> Fluoroquinolones</td>
<td>Ciprofloxacin (Cfx)</td>
</tr>
<tr>
<td></td>
<td>Ofloxacin (Ofx)</td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin (Mfx)</td>
</tr>
<tr>
<td></td>
<td>Gatifloxacin (Gfx)</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin (Lvxx)</td>
</tr>
<tr>
<td><strong>Group 4</strong> Oral bacteriostatic 2nd line anti-TB agents</td>
<td>Ethionamide (Eto)</td>
</tr>
<tr>
<td></td>
<td>Prothionamide (Po)</td>
</tr>
<tr>
<td></td>
<td>Cyloserine (Cs)</td>
</tr>
<tr>
<td></td>
<td>Terizadone (Trd)</td>
</tr>
<tr>
<td></td>
<td>Para-aminosalicylic acid (PAS )</td>
</tr>
<tr>
<td><strong>Group 5</strong> Agents with unclear efficacy – not recommended routinely</td>
<td>Clofazamine (Cfz)</td>
</tr>
<tr>
<td></td>
<td>High Dose INH</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin/Clavulanate (Amx/Clv)</td>
</tr>
<tr>
<td></td>
<td>Azithromycin (Azr)</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin (Clr)</td>
</tr>
<tr>
<td></td>
<td>Imipenem</td>
</tr>
<tr>
<td></td>
<td>Linazolid (Lzd)</td>
</tr>
<tr>
<td></td>
<td>Thiacetazone (Th)</td>
</tr>
</tbody>
</table>
## 1. Drug Dosages for XDR TB

<table>
<thead>
<tr>
<th>Drug</th>
<th>&lt; 33KG</th>
<th>33 – 50kg</th>
<th>51 – 70kg</th>
<th>&gt;70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrazinamide</td>
<td>30-40 mg/kg</td>
<td>1g</td>
<td>1.5g</td>
<td>2g</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>25 mg/kg</td>
<td>800mg</td>
<td>1.2g</td>
<td>1.6g (2g)</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>15-20 mg/kg</td>
<td>500mg</td>
<td>750mg</td>
<td>750mg (1g)</td>
</tr>
<tr>
<td>Terizadone or Cycloserine</td>
<td>15-20 mg/kg</td>
<td>500mg</td>
<td>750mg</td>
<td>750mg (1g)</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>15-20 mg/kg</td>
<td>500 to 750mg</td>
<td>750mg to 1g</td>
<td>1g</td>
</tr>
<tr>
<td>Para-amino salicylic acid</td>
<td>4g bd</td>
<td>4g bd</td>
<td>4g bd</td>
<td>4g bd</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td></td>
<td>400mg</td>
<td>400mg</td>
<td>400mg</td>
</tr>
<tr>
<td>Clofazamine</td>
<td>200mg OD</td>
<td>300mg OD</td>
<td>300mg OD</td>
<td></td>
</tr>
<tr>
<td>Augmentin</td>
<td>1 g bd</td>
<td>1 g bd</td>
<td>1 g bd</td>
<td></td>
</tr>
<tr>
<td>High Dose INH</td>
<td>10-12 mg/kg</td>
<td>10-12 mg/kg</td>
<td>600mg</td>
<td>600mg ( ?more)</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500mg bd</td>
<td>500mg bd</td>
<td>500mg bd</td>
<td></td>
</tr>
</tbody>
</table>
Distribution of XDR by District

Dr. I.H. Master
Distribution of XDR by district over years

- DC21: 6%
- DC22: 8%
- DC23: 2%
- DC24 (COSH): 30%
- DC25: 4%
- DC26: 4%
- DC27: 4%
- DC28: 5%
- DC29: 3%
- Durban: 35%
- DC43: 1%
- DC28: 3%
Progress of XDR Cohort (60) since 2006

XDR OUTCOMES

- DIED: 51%
- UNKNOWN: 3%
- DEFAULTED: 10%
- CURED: 18%
- FAILED: 18%

Data courtesy of Max O Donnel
Who to refer to KGV

- Proven MDR/XDR patients.
- INH mono-resistance or poly-resistance not responding to standard TB treatment.
- Rifampacin only resistance (these patients invariably need to be treated as MDRs)
- Extrapulmonary TB or sensitive TB not responding to full course of TB treatment.

(Decision to treat will be done on a case by case basis after discussion with KGV doctors)
Management of co-infected patients & MDR

- Treatment - the same as HIV-negative patients.
- HIV patients can be smear neg. making diagnosis difficult
- Adverse events are commoner
- Patients on ARVs – just add MDR treatment
- Recent studies suggest earlier treatment has better outcomes (within 2 weeks)

Complicating Treatment
- Drug-drug interactions;
- Overlapping toxicities;
- Adherence to multiple medicines
ART Policy

Previous policy
- All HIV pos. patients with CD4s < 200/ Stage 4 offer ARVs
- On ARVs →MDR/XDR Rx added
- D4T/3TC/EFV commonly used

New policy - April 2010
- All MDR/XDR TB patients who are HIV pos to get ARVs irrespective of CD4 count (within 2 weeks)
- All HIV positive children under 1 year – for ARVs
- All Patients with TB with CD4 under 350 for ARVs
- All Other patients with CD4 under 200 to get ARVs
- New 1st line regimen (TDF,3TC,NVP/EFV)
- Patients stable on previous regimens to continue.
- Bactrim prophylaxis recommended
- INH prophylaxis is also part of the program
HIV at KGV: 1997-2010

<table>
<thead>
<tr>
<th>Year</th>
<th>POS</th>
<th>NEG</th>
<th>UNK</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>11</td>
<td>16</td>
<td>73</td>
</tr>
<tr>
<td>1998</td>
<td>23</td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td>1999</td>
<td>31</td>
<td>27</td>
<td>42</td>
</tr>
<tr>
<td>2000</td>
<td>28</td>
<td>34</td>
<td>38</td>
</tr>
<tr>
<td>2001</td>
<td>28</td>
<td>32</td>
<td>39</td>
</tr>
<tr>
<td>2002</td>
<td>27</td>
<td>26</td>
<td>47</td>
</tr>
<tr>
<td>2003</td>
<td>28</td>
<td>26</td>
<td>46</td>
</tr>
<tr>
<td>2004</td>
<td>29</td>
<td>21</td>
<td>50</td>
</tr>
<tr>
<td>2005</td>
<td>38</td>
<td>22</td>
<td>40</td>
</tr>
<tr>
<td>2006</td>
<td>46</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>2007</td>
<td>51</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>2008</td>
<td>64</td>
<td>22</td>
<td>14</td>
</tr>
<tr>
<td>2009</td>
<td>66</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>2010</td>
<td>68</td>
<td>23</td>
<td>9</td>
</tr>
</tbody>
</table>
% HIV POS MDR on ARVs

- 2003: 3%
- 2004: 11%
- 2005: 27%
- 2006: 50%
- 2007: 60%
- 2008: 56%
- 2009: 58%
- 2010: 65%
Outcomes MDRs 2004 - 2006
HIV Neg / On ARVs / Not on ARVs

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HIV Neg</th>
<th>On ARV</th>
<th>No ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure</td>
<td>54</td>
<td>51</td>
<td>39</td>
</tr>
<tr>
<td>Default</td>
<td>9</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Died</td>
<td>11</td>
<td>22</td>
<td>29</td>
</tr>
<tr>
<td>Fail</td>
<td>3</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>
STAFF, TB & Infection Control
Our responsibility to infection control

- Reduce exposure of staff, patients and visitors to TB
- Ensure
  - Have proper infection control guidelines in place
  - Implement these guidelines
  - Educate everyone
  - Do formal risk assessments
  - Implement triaging of patients
  - Implement air exchange assessment
  - Have personal protection available
  - Implement fit testing (N95 resp.)
  - Have regular staff wellness monitoring
Screening of Staff

- Routine monitoring of weight – (monthly)
- Serial X-rays – (annually)
- Sputa testing for AFB and CXR if coughing for more than 2-3 weeks
- Offer anonymous VCT for all HCW
- Provide confidential ARVs
- Relocation of staff at risk
Most of the patients were referred by General Hospitals
They were not from TB hospitals or from KGV
Most of the staff were immunocompromised
The risk of MDR TB may well be higher in a general hospital
HCW Outcomes 2000-2005

- Cured: 57%
- Died: 20%
- Default: 6%
- Not Rx.: 3%
- Unknown: 3%
- Failed: 10%

HCW Outcomes 2000-2005
DECENTRALIZED MANAGEMENT OF MDR-TB

A POLICY FRAMEWORK FOR SOUTH AFRICA

DR. NORBERT NDJEKA
MD, DHSM (Wits), MMed (Fam Med) (MED), Dip HIV Man (SA)
DIRECTOR DRUG-RESISTANT TB, TB & HIV
NATIONAL DEPARTMENT OF HEALTH
Issues

- ~25% diagnosed cases are not started on treatment
- 1-2 months of waiting for admission, sometimes more
- Long distance of transportation for admission and follow up
- Negative impact on social and economic status of the individual and family due to a long stay in hospital
- Risk of transmission in hospital due to inadequate implementation of infection control measures
- Non-uniformity in current, sporadic efforts of decentralized management
- Issues of refusal to admission and aggressive demand for early discharge
- Poor outcome of DR-TB cases
<table>
<thead>
<tr>
<th>Solutions</th>
<th>Advantages</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase no. of hospitals/ beds</td>
<td>• Convenient to the health system</td>
<td>• Cost to the government/patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Socio-economic problems</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of transmission if inadequate IC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sustainability</td>
</tr>
<tr>
<td>Decentralized management of</td>
<td>• Early initiation of treatment</td>
<td>• Establishment of new infrastructure</td>
</tr>
<tr>
<td>DR-TB cases including community</td>
<td>❖ Reduce morbidity/mortality</td>
<td>• Increase training need</td>
</tr>
<tr>
<td>DOT</td>
<td>❖ Reduce transmission</td>
<td>• Other sector s/Community involvement</td>
</tr>
<tr>
<td></td>
<td>• Convenient for the patients</td>
<td>• Increase demand for supervision</td>
</tr>
<tr>
<td></td>
<td>• Cost effective</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Improve adherence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• More sustainable</td>
<td></td>
</tr>
</tbody>
</table>
Provincial level

- Each province should have a network comprising a specialized MDR/XDR Unit at its apex
- Decentralized – independent MDR unit
- Satellite units – hold & treat patients started at above units
- Injection/mobile teams – administer at home/clinic
Units for decentralized management of MDR-TB

- Provincial MDR/XDR-TB Unit
- Decentralised MDR-TB Unit
  - Satellite MDR-TB Unit
    - Satellite MDR-TB Unit
      - PHC CLINIC
        - Mobile MDR-TB Unit
          - Mobile MDR-TB Unit
            - Dot/Treatment Supporter
            - Dot/Treatment Supporter
            - Dot/Treatment Supporter
            - Dot/Treatment Supporter
<table>
<thead>
<tr>
<th>Functions</th>
<th>Provincial/Centralized MDR-TB unit</th>
<th>Decentralized MDR-TB unit</th>
<th>Satellite MDR-TB unit</th>
<th>Mobile MDR-TB clinic/Injection team</th>
<th>Community Supporters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation of treatment of all DR-TB cases</td>
<td>√</td>
<td>√</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Admission of all MDR-TB cases till two successive smear negative</td>
<td>√</td>
<td>√</td>
<td></td>
<td>No, unless no bed at Prov. Or dec. unit</td>
<td>NO</td>
</tr>
<tr>
<td>Admission of all XDR-TB cases till two successive culture negative</td>
<td>√</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Monthly follow up of all DR-TB cases attending at clinic</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>NO</td>
</tr>
<tr>
<td>DOT to all DR-TB patients attending daily</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Recording and reporting (R &amp; R) to the provincial department of health</td>
<td>√</td>
<td>√</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Monitoring and supervising DR-TB clinical management in the province</td>
<td>√</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>
PHC / Injection Team / CHW

- Link between decentralised units and MDR-TB patients in community
- Daily injectables at home or in a facility
- Monitor side effects and refer complications appropriately & adherence
- Patient / family education
- CHW/Supporters to do DOT /Assess home infection control & Risk
Infection control at home and in the community

- Ventilation/Open windows
- Isolation of patient (own bed room where possible)
- Cough hygiene
- Refrain from close contact with children
- Maximise time in open-air environment (e.g. receive visitors outside)
- Minimise contact with known HIV positive patients
Conclusion

- All smear \textit{microscopy negative} MDR-TB patients who are in \textit{good condition} and may access treatment near their homes may be started on outpatient treatment.
- All smear positive patients are to be admitted until they get 2 negative TB smear microscopy.
- Very sick MDR-TB, extensive disease, XDR-TB patients and patients with unsuitable social circumstances will be admitted until they achieve TB culture conversion.
Challenges in current KGV program

- Delays in Admission
  - 6 weeks (currently)
- Transport Problems - unable to access KGV
  - Long distances, not enough transport
- Contact tracing – not optimum
- Defaulter tracing – not optimum
- DOT/treatment supporters – not optimum
- Discharge of culture positive patients - lack of beds
- No solution for treatment failures (in excess of 300)
- Refusal of patients to be admitted/isolated
- Frequent passouts taken by patients for
  - Grants/social problems/cultural functions
- Shortages or Erratic Supply of Drugs at times
  - PZA, Ofloxacin, Ethionamide, PAS and Pyridoxine, kanamycin in the past
  - Currently out of EMB (twice in August 2008)
- Side effects of medication
  - Cycloserine / Capreomycin
- Legal Issues
  - Confidentiality / Incarceration / Duration
Acknowledgements

Dr Njeka & Department of Health, District Office & Management + Staff of KGV &

A Special Thanks to All the Health Care workers who tirelessly continue the fight against TB & MDR TB & HIV often at great risk to themselves.

Thank You

iqbal.master@kznhealth.gov.za