



health

Department:  
Health  
PROVINCE OF KWAZULU-NATAL

# Pre XDR and XDRTB

## *Current Management & Programmatic challenges*

Iqbal Master  
Clinical Manager  
KDHC

# DR-TB DEFINITIONS

| Type of DR-TB | Definition   |
|---------------|--|
| RR-TB         | Resistance to Rifampicin with or without resistance to other TB medicines  |
| MDR-TB        | Resistance to Rifampicin and INH, with or without resistance to other first line anti-TB drugs                             |
| XDR-TB        | MDR TB (HR) with Resistance to <u>any</u> Fluoroquinolone <b><u>AND</u></b> to any second line Injectable drugs (CM,KM,AM) |
| Pre- XDR TB   | MDR TB (HR) with Resistance to <u>either</u> any Fluoroquinolone <b><u>OR</u></b> to any second line Injectable drug       |

# WHAT DRUGS ARE USED TO TREAT XDR TB ?

1. INH & Rifampacin with Moxifloxacin and Kanamycin for 6 months
2. Kanamycin / Moxofloxacin / PZA / Ethionamide / Terizidone up to 18 months
3. Kanamycin / Moxifloxacin / Augmentin / Ethambutol / Rifampacin for 9 months
4. Bedaquiline based regimen as part of an individualized regimen for up to 18 months
5. Kanamycin , Moxifloxacin / PZA / Clofazimine / Ethionamide / Ethambutol for 9-12 months

# EVOLUTION OF SA DR-TB TREATMENT

- ◉ Before 1996 - Individualized MDR Rx
- ◉ 1997-2005 - Standardized MDR Rx (MRC Guidelines)
- ◉ 2006 - 2013 - DOH guidelines
  - Standardized treatment for MDR & XDR
- ◉ 2014 onwards (current)
  - MDR TB - Standard MDR Treatment
    - ◉ 6 months injectable (minimum)
      - ◉ **Kana or Amik / Moxi / Ethio / Terizidone / PZA**
    - ◉ 18 months continuation (minimum)
      - ◉ **Moxi / Ethio / Terizidone / PZA**
  - Pre-XDR / XDR - Individualized regimen
    - ◉ Regimens structured around Bedaquiline +/- Linezolid
- ◉ 2017 - The future
  - Shorter Regimen for most MDRs based on new WHO policy
  - Pre-XDRs / XDRS - individualized

# WHO - OLD GROUPING OF MDR-TB DRUGS

| GROUP  | DRUGS   |   |
|--|---|---|
| <b>Group 1</b> First-line oral drugs                                       | Ethambutol (E)  | Pyrazinamide (Z)                                |
| <b>Group 2</b><br>Injectable Anti-TB agents                                | Streptomycin (S)<br>Amikacin (Am)   | Kanamycin (Km)<br>Capreomycin (Cm)              |
| <b>Group 3</b><br>Fluoroquinolones   | Ciprofloxacin (Cfx)<br>Moxifloxacin (Mfx)<br>Levofloxacin (Lvx)   | Ofloxacin (Ofx)<br>Gatifloxacin (Gfx)           |
| <b>Group 4</b><br>Oral bacteriostatic 2 <sup>nd</sup> line anti-TB agents  | Ethionamide (Eto) ( Prothionamide) (Po)<br>Terizidone (Cyloserine (Cs))<br>Para-aminosalicylic acid (PAS )                            |   |
| <b>Group 5</b><br>Agents with unclear efficacy – not recommended routinely | Clofazimine (Cfz)<br>Amoxicillin/Clavulanate (Amx/Clv)<br>Clarithromycin (Clr)<br>Linazolid (Lzd)<br>Bedaquiline<br>Thiacetazone (Th) | High Dose INH<br>Azithromycin (Azr)<br>Imipenem |

|   |  |           |  |           |                                  |           |   |
|---|--|-----------|--|-----------|----------------------------------|-----------|---|
| <p><b>GROUP A</b></p> <p>Fluoroquinolones</p>   | <p>Levofloxacin<br/>Moxifloxacin<br/>Gatifloxacin</p>  |           |  |           |                                  |           |   |
| <p><b>GROUP B</b></p> <p>Second-line injectable agents</p>                                    | <p>Amikacin<br/>Capreomycin<br/>Kanamycin<br/>(Streptomycin)</p>   |           |  |           |                                  |           |   |
| <p><b>GROUP C</b></p> <p>Other Core Second-line Agents</p>                                    | <p>Ethionamide / Prothionamide<br/>Cycloserine / Terizidone<br/>Linezolid<br/>Clofazimine</p>  |           |  |           |                                  |           |   |
| <p><b>GROUP D</b></p> <p>Add-on agents</p> <p><i>(not core MDR-TB regimen components)</i></p> | <table border="1"> <tr> <td data-bbox="1062 714 1188 892"><b>D1</b></td> <td data-bbox="1188 714 1825 892"> <p>Pyrazinamide<br/>Ethambutol<br/>High-dose isoniazid</p> </td> </tr> <tr> <td data-bbox="1062 892 1188 1013"><b>D2</b></td> <td data-bbox="1188 892 1825 1013"> <p>Bedaquiline<br/>Delamanid</p> </td> </tr> <tr> <td data-bbox="1062 1013 1188 1306"><b>D3</b></td> <td data-bbox="1188 1013 1825 1306"> <p><i>p</i>-aminosalicylic acid<br/>Imipenem-Cilastatin<br/>Meropenem<br/>Amoxicillin-Clavulanate<br/>(Thioacetazone)</p> </td> </tr> </table> | <b>D1</b> | <p>Pyrazinamide<br/>Ethambutol<br/>High-dose isoniazid</p> | <b>D2</b> | <p>Bedaquiline<br/>Delamanid</p> | <b>D3</b> | <p><i>p</i>-aminosalicylic acid<br/>Imipenem-Cilastatin<br/>Meropenem<br/>Amoxicillin-Clavulanate<br/>(Thioacetazone)</p> |
| <b>D1</b>   | <p>Pyrazinamide<br/>Ethambutol<br/>High-dose isoniazid</p>   |           |  |           |                                  |           |   |
| <b>D2</b>   | <p>Bedaquiline<br/>Delamanid</p>   |           |  |           |                                  |           |   |
| <b>D3</b>   | <p><i>p</i>-aminosalicylic acid<br/>Imipenem-Cilastatin<br/>Meropenem<br/>Amoxicillin-Clavulanate<br/>(Thioacetazone)</p>  |           |  |           |                                  |           |   |

# INTERPRETING LPA RESULTS

| Mutation      | Meaning and Resistance Caused  | Drugs you can use                            |
|---------------|--|--|
| InhA          | low level INH resistance but usually confers resistance to Ethionamide                   | High Dose INH                                |
| KatG          | High level INH resistance confers resistance to INH, but Ethionamide should be sensitive | Ethionamide                                  |
| InhA and KatG | Confers resistance to Ethionamide and High Dose INH                                      | Neither INH nor Ethionamide<br>? May add PAS |
| Gyr A & GyrB  | Ofloxacin resistance   |  |
| RRS & EIS     | Injectable resistance  |  |

# MANAGEMENT PROTOCOL

- Counsel
- Sign consent for MDR treatment
- Baseline Audio
- Bloods
  - FBC
  - U&E
  - LFT
  - Ca/PO4/Mg (XDR)
  - HIV/CD4
  - TFT
- Baseline CXR
- Discuss at MDR Committee - Decide on MX
- Refer Social worker - where indicated
- Identify contacts (in ideal circumstances)
- Commence Treatment



# MONITORING PATIENTS

## ◉ Monitor Bloods

- Repeat U & E for patients on injectables
  - (monthly if possible)
- Monitor Ca/PO<sub>4</sub>/Mg - on injectables
- TFTs - PAS + Ethionamide

## ◉ Serial Audios -

- Monthly if possible

## ◉ Side Effect monitoring program should be in place.

## ◉ Response to therapy is monitored by

- monthly cultures & weights
- Serial X Rays (6/12/24 months)

| <b>Drug Cost – 30 days - Cost</b> per patient per month) |       |        |       |                 |               |
|--|-------|--------|-------|-----------------|---------------|
|  | 2008  | 2009   | 2010  | 2012            | 2016          |
| <b>Imipenem ( 1g TDS)</b>                                |       |        |       | <b>R9000</b>    | <b>R9000</b>  |
| <b>PAS (4g BD)</b>                                       | R1600 | R 2360 | R2358 | <b>R 1853</b>   | <b>R 2600</b> |
| <b>Capreomycin (1g 5x)</b>                               | R800  | R 1300 | R2391 | <b>R 1742</b>   | <b>R 2340</b> |
| <b>Bedaquiline</b>                                       |       |        |       |                 | <b>R1750</b>  |
| <b>Linezolid (600mg od )</b>                             |       |        |       | <b>R 4-9000</b> | <b>R950</b>   |
| <b>Terizidone (250mg tds)</b>                            | R650  | R 579  | R566  | R 607           | R 791         |
| <b>Klacid (500mg BD)</b>                                 |       | R 228  | R123  | R 121           | R 696         |
| <b>Kanamycin (1g 5x)</b>                                 | R250  | R 200  | R239  | R 242           | R 241         |
| <b>Moxifloxacin (400mg OD)</b>                           |       | R 800  | R911  | R 114           | R 203         |
| <b>Laevofoxacin (1gram) OD</b>                           |       |        |       | R 210           | R 184         |
| <b>Amikacin (1g 5x)</b>                                  | R400  | R 216  | R223  | R 192           | R 178         |
| <b>Augmentin (1 g BD)</b>                                |       | R 112  | R74   | R 146           | R 170         |
| <b>Ethionamide (250mg tds)</b>                           | R130  | R 177  | R191  | R 138           | R 115         |
| <b>Rifafour (4 BD)</b>                                   | R80   | R 67   | R67   | R 57            | R108          |
| <b>Rifanah (300 – 2 BD)</b>                              |       | R 40   | R42   | R 45            | R58           |
| <b>EMB (1,2 OD)</b>                                      |       | R 38   | R43   | R 44            | R 57          |
| <b>PZA (1,5gm OD)</b>                                    | R50   | R 42   | R33   | R 44            | R 44          |
| <b>Clofazamine (100mg) OD</b>                            |       |        | R204  | R 200           | R37           |

# Drug Costs



| Drug (> 50KG)   | Cost (per patient per month) |                 |  |
|-----------------|------------------------------|-----------------|--|
|                 | 2010                         | 2012            | 2016   |
| STD TB (IP)     | R67                          | R57             | R108   |
| STD TB (CP)     | R42                          | R45             | R58  |
| MDR (IP)        | R1207                        | R1189           | R1400  |
| MDR (CP)        | R968                         | R947            | R1150  |
| XDR (IP)        | R6654                        | R5000 -R20 000  | <b>R6300- R20000</b><br><b>(BDQ-LZD)-IMI</b> |
| XDR (CP)        | R4263                        | R5000 - R10 000 | <b>R3500 - R4500</b>                         |
| Short Reg ( IP) |                              |                 | R880   |

# WHAT MDR DRUG CAN CAUSES PERIPHERAL NEUROPATHY , OPTIC NEURITIS , BONE MARROW SUPPRESSION ?

1. Clofazimine
2. Kanamycin
3. Linezolid
4. Bedaquiline
5. Moxifloxacin

# COMMON SIDE EFFECTS

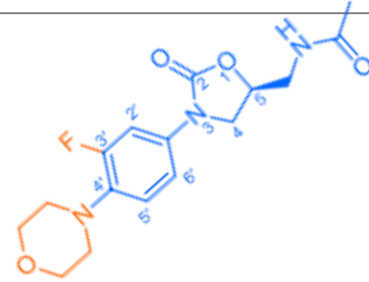
| Drug            | Common Side Effect                                      |
|-----------------|---|
| Rifampicin      | Hepatitis / Allergies / Thrombocytopenia                |
| INH             | Hepatitis / CNS   |
| Ethambutol      | Optic Neuritis  |
| PZA             | Arthralgia (Raised Uric acid) / Hepatitis               |
| Aminoglycosides | Ototoxicity / Nephrotoxicity                            |
| Capreomycin     | Ototoxicity / Nephrotoxicity + Electrolyte disturbances |
| Quinolones      | Myalgia / Arthralgia / QT / CNS                         |
| Terizidone      | Fits / Psychosis / Suicidal / Depression / Neuropathy   |
| Clofazamine     | Skin discolouration / QT                                |
| Ethionamide     | GIT / Hypothyroidism                                    |
| PAS             | GIT / Hypothyroidism                                    |
| Bedaquiline     | QT issues - prolongation                                |
| Linezolid       | Bone Marrow suppression / Neuropathy / Optic Neuritis   |

# CLOFAZIMINE(CFZ) (50MG/100MG)

- ⊙ Binds preferentially to mycobacterial DNA and inhibits mycobacterial replication and growth.
- ⊙ Teratogenic in animals
- ⊙ Long half life - months
- ⊙ Side effects:
  - ichthyosis, and dry skin
  - Darkening / discolouration of skin
  - anorexia
  - abdominal pain.
- ⊙ Use with caution in Liver DX
- ⊙ Currently a section 21 Drug

# LINEZOLID (ZYVOXID)

- Linezolid is an oxazolidinone
- Is a protein synthesis inhibitor
  - it stops growth of bacteria
  - Activity against *MTB*
- Long term usage is associated with serious A/E
  - bone marrow suppression
    - Thrombocytopaenia / Anaemia / Neutropaenia
  - Severe peripheral neuropathy
  - Optic neuritis - reversable if picked up early
  - Lactic acidosis - ? due to mitochondrial toxicity
- Linezolid - no effect on the QT interval



# LINEZOLID IN SA NEW DRUG GUIDELINES

- ⊙ Avoid if
  - severe anaemia (Hb < 8)
  - severe peripheral neuropathy
- ⊙ Dosage uncertain : Start at 600mg daily.
- ⊙ Used for 12 months in current program
- ⊙ Stop if toxicity , life threatening or worsens.
- ⊙ If bone marrow suppression -
  - Stop Linezolid - wait for a response and restart at a reduced dose ( 300mg) - if needed
  - May need transfusion



# DELAMINID

- ◉ Novel TB Drug related to Metronidazole (Otsuka)
- ◉ Bound by albumin
- ◉ Safety
  - Established in children
  - No ARV switch required
  - ECG monitoring required (QT issues)
  - Safety with BDQ not absolutely certain
- ◉ Mutations resulting in resistance already found
- ◉ Registered in Some countries ( Not SA)
- ◉ Available only via a Compassionate usage program
- ◉ SA TB program wants 100 courses to be made available via a DCAP program
- ◉ Still engaging with Otsuka and MCC

# HIV + MDR TB

## ⊙ HIV + MDR

- Adverse events are commoner
- Mortality is higher
  - (advanced HIV , advanced TB disease and OIs)
- Often smear neg. making diagnosis difficult

## ⊙ HIV + MDR/XDR- add ARVs in $\pm$ 2 weeks on (90%)

## ⊙ On ARVs – just add MDR treatment

## ⊙ Cure rates appear to be better with ARVs

## ⊙ Some prefer to change TDF to either AZT /ABC in injectable phase

## ⊙ Complicating Treatment

- Drug-drug interactions;
- Overlapping toxicities;
- Adherence to multiple medicines

# SURGERY IN MDR/XDR TB

- ◉ Primary treatment for MDR TB is medical
- ◉ Indications for Surgery
  - If localized disease (1 lung) and
    - ◉ Failing treatment
    - ◉ Relapse after initial conversion and good compliance
    - ◉ ? Extreme resistance (XDR) - where chance of cure is poor
    - ◉ Residual cavitation - where relapse is anticipated
- ◉ Decision for Surgery based on
  - ◉ High Resolution CT Scan
  - ◉ Assessment/Decision by Cardio-thoracic Surgeon
  - ◉ Adequate Lung Function
- ◉ Keep on intensive phase prior to surgery
- ◉ Continue treatment 18-24 months post surgery

# ADVICE FOR TREATMENT FAILURES

## ○ KZN situation

- We have many treatment failures (10% per year)
- They were being discharged home/into the community
- Some survive >5 years

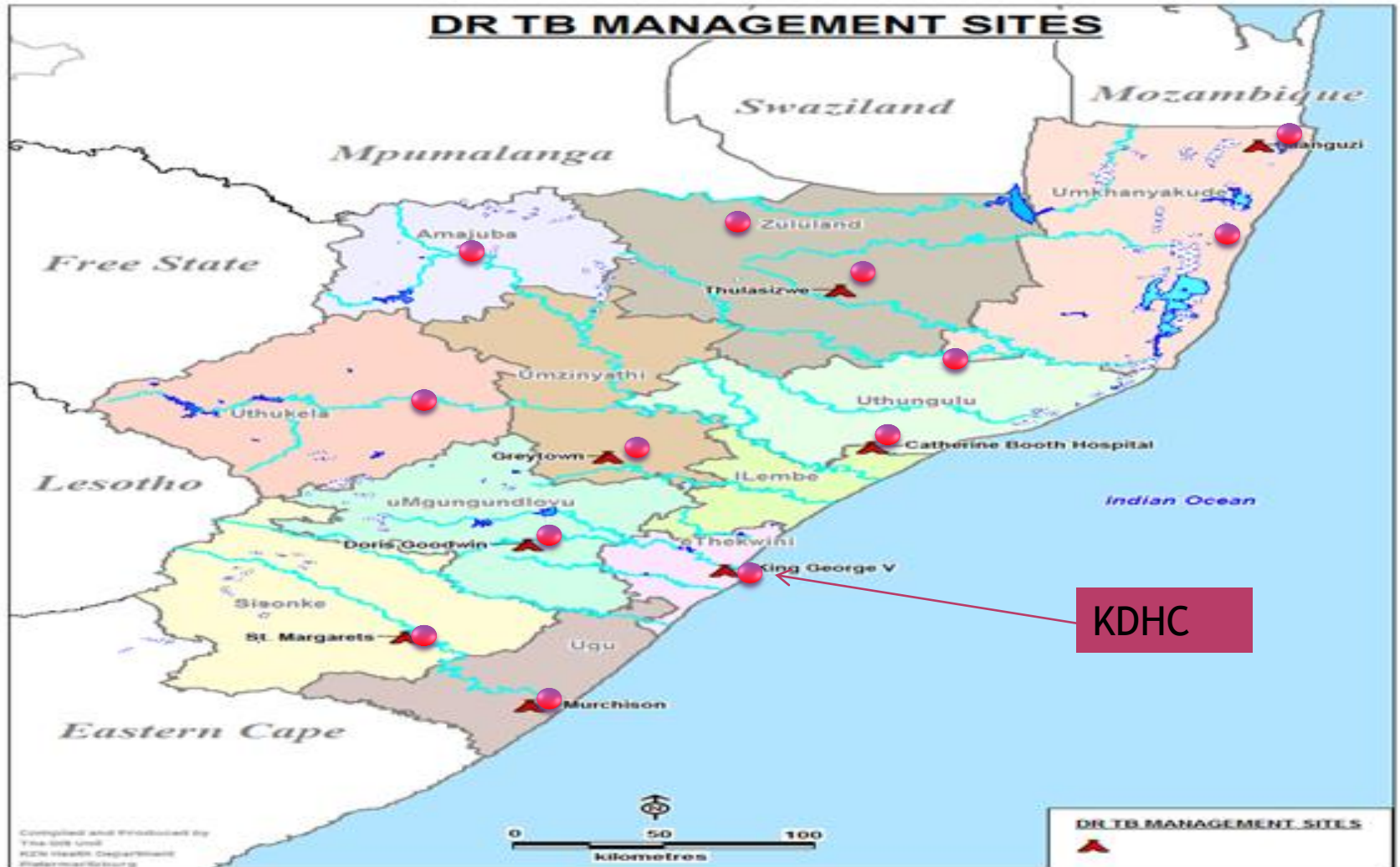
## ○ Plan For Failures

- Assess & reinforce Adherence
- Complete adequate course of treatment (12-24 mths)
- It failing Rx - Consider salvage regimen - new Drugs
- If definite Rx. Failure with no treatment options then consider stopping Rx
- Palliative treatment, sanatorium or home based care. (limited current capacity)



**The  
KZN  
Program**  
A King George V  
Perspective

# KWAZULU NATAL MAP - SHOWING MDR UNITS



# The Future of KDHC

- King Dinuzulu Hospital Complex (KDHC)
- The Hospital complex :
  - District Hospital – 400 Beds
  - MDR/XDR TB Unit - 320 Beds
  - TB Spinal & Thoracic Unit – 80 Beds
  - Psychiatric Hospital – 130 Beds



New District Hospital



Star Shaped MDR Wards



Multistorey MDR Wards



- Initially the only provincial site treating MDR TB
- Traditionally there have been long waiting lists but key policies implemented by National , Province and District have had a positive impact
- Key interventions from 2006 were
  - National Decentralization Plan (based on Tugela Ferry)
  - Opening an MDR unit in every district
  - Treating stable MDRs as outpatient
  - Rapid diagnostics (Gene Xpert)
  - National Goal is treat MDR TB within 5 days
  - Next step is to Make MDR Rx available PHC level
- National hopes for improved outcomes and access to care



# KDHC - ADMISSION POLICY

- KDHC (256 beds)
  - MDRs from Ethekwini District
  - All provincial XDRs, Pre-xdrs & complex MDR cases
  - All paediatric cases
  - Recently - Patients for new drug program
- 2 streams of care at KDHC for new patients
  - Inpatient Care (up to 6 months)
    - XDR, Ill and complex MDR cases
    - Patients living to far from a clinic
  - Outpatient Care - (without admission)
    - Initiated on treatment as outpatients on MDR
    - Stable / MDRs
- KDHC has Surgical Depts which offer
  - Thoracic surgery - pneumonectomy
  - Spinal Surgery

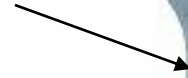
# KDHC MDR TB FOLLOW-UP CLINIC

- ◉ Discharged MDR patients attend monthly.
- ◉ Follow UP Clinic twice weekly
  - See up to 200-350 follow up patients per clinic > 2000/month.
- ◉ In Past on average - 150 new MDRs/per month
  - > 1500 new DR TB cases initiated per annum
- ◉ District / Provincial Plan
  - Decant patients from this site (KDHC)
  - Opened more decentralized units to take load away (Don Mackenzie & Charles James)
  - Initiate MDR care at District Hospitals and Clinic level (in keeping with the National TB program policy)
- ◉ Move to get KDHC to focus more on the new drug program
- ◉ Progress
  - Patients being seen at KDHC have reduced
  - waiting lists disappeared
  - However patients are more complex , need more investigations, counselling and monitoring and take more time

# MANAGEMENTS OF PATIENTS AWAITING CARE

- ◉ Waiting list has reduced drastically
- ◉ Ideal Goal is to commence treatment as soon as possible ( 5 days )
- ◉ If you have an understanding of MDR care and its issues - you could start Rx based on advice while awaiting a bed.
- ◉ An Obligation is to understand
  - Baseline testing required
  - Confirmatory tests needed
  - Audio tests and monitoring required
  - Reporting and recording required
- ◉ It is better not to start RX then to start a suboptimal regimen as you may compromise the drugs used

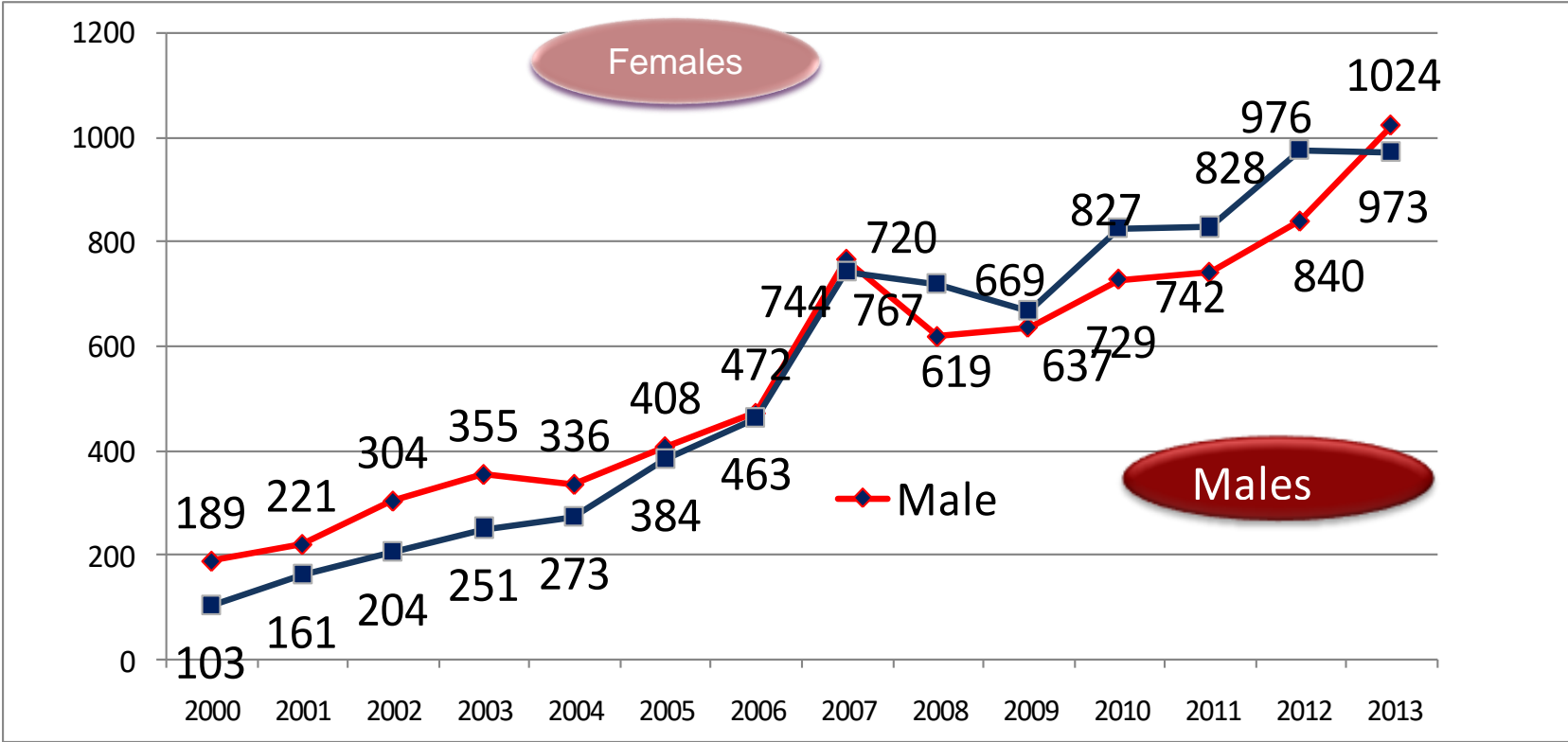
**Renovated multi-storey  
For MDR TB**



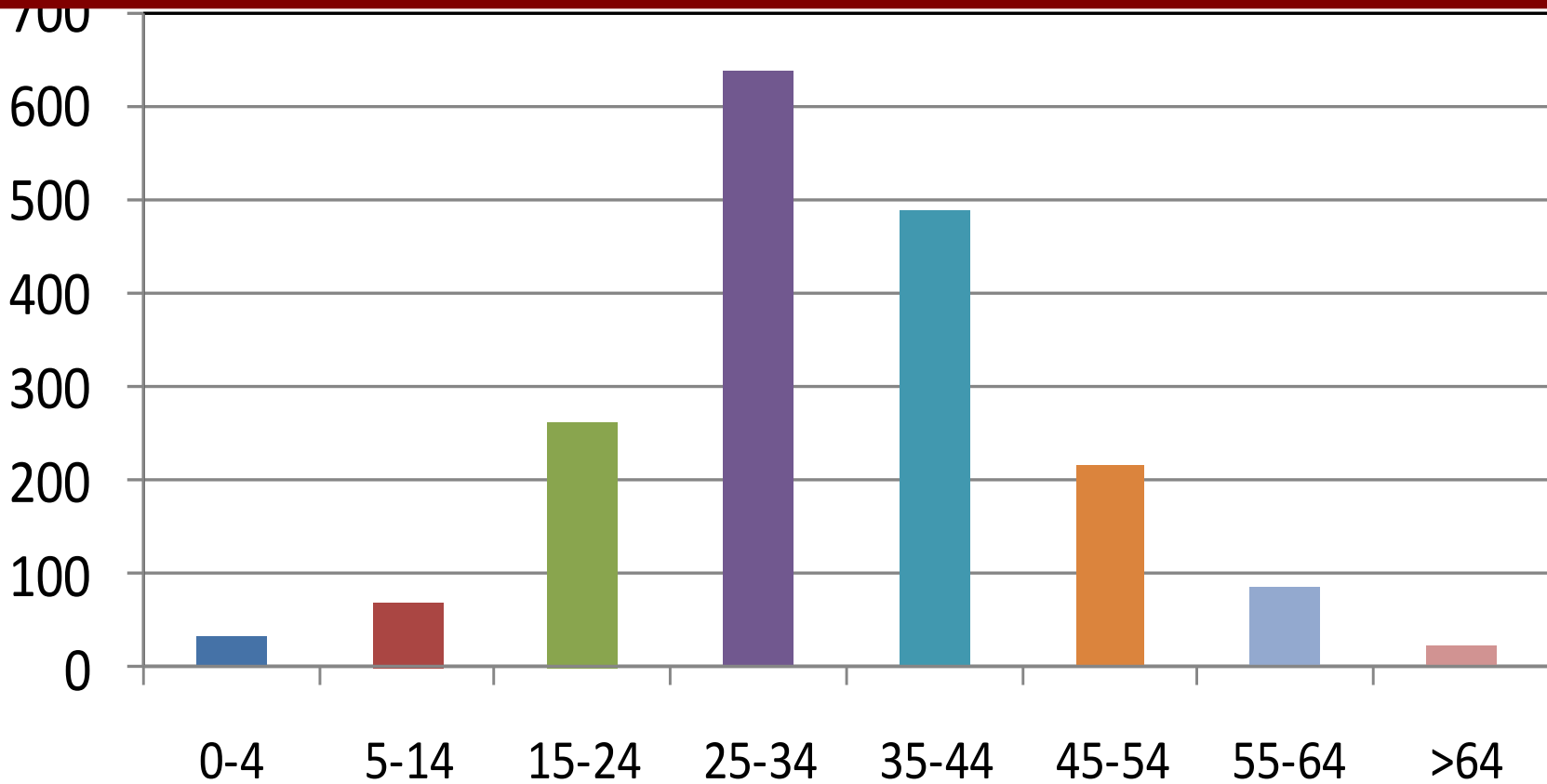
**New star shaped ward**



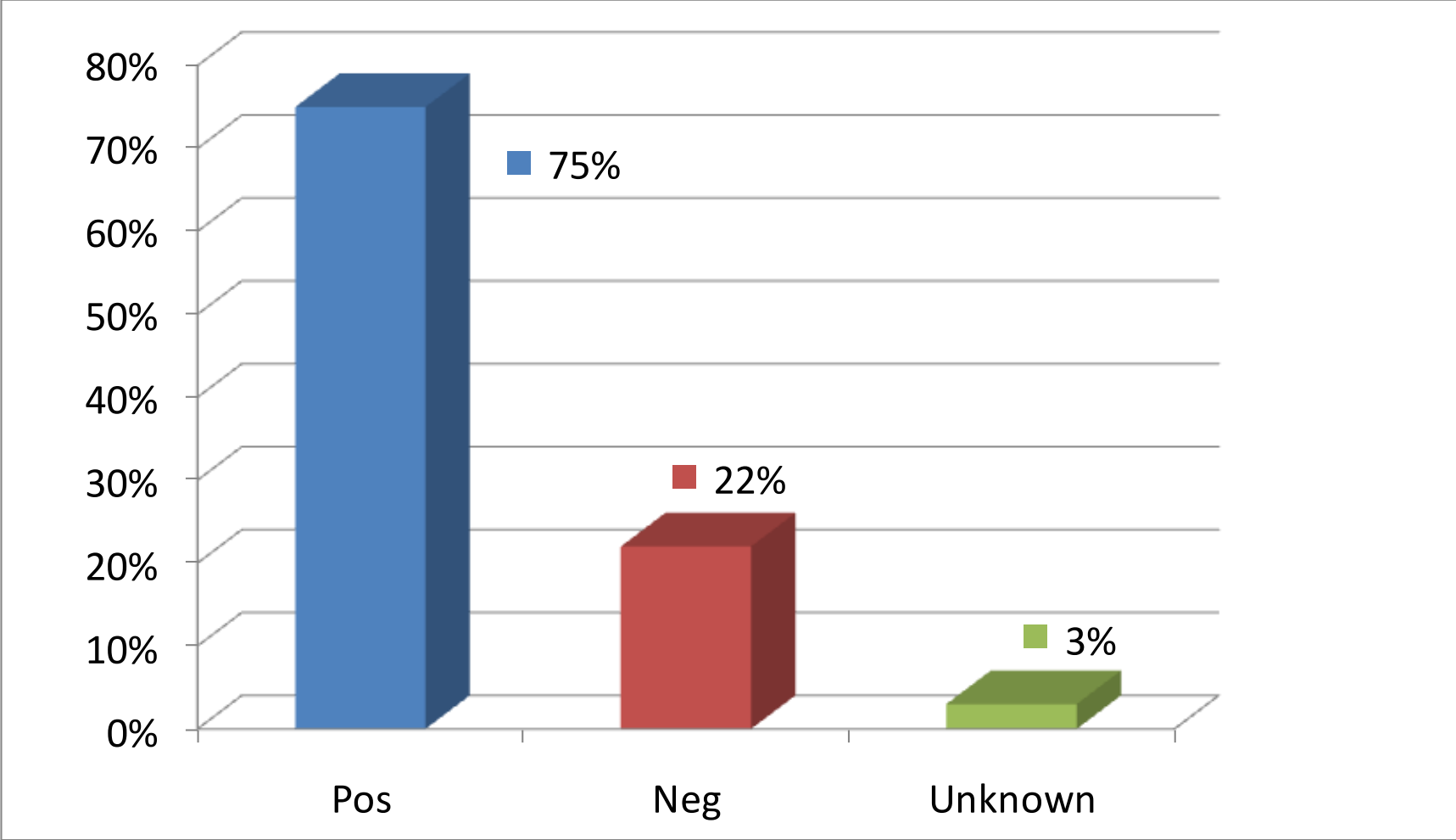
# Male vs Female for All TB KGV



# MDR/XDR Age Distribution KGV 2013

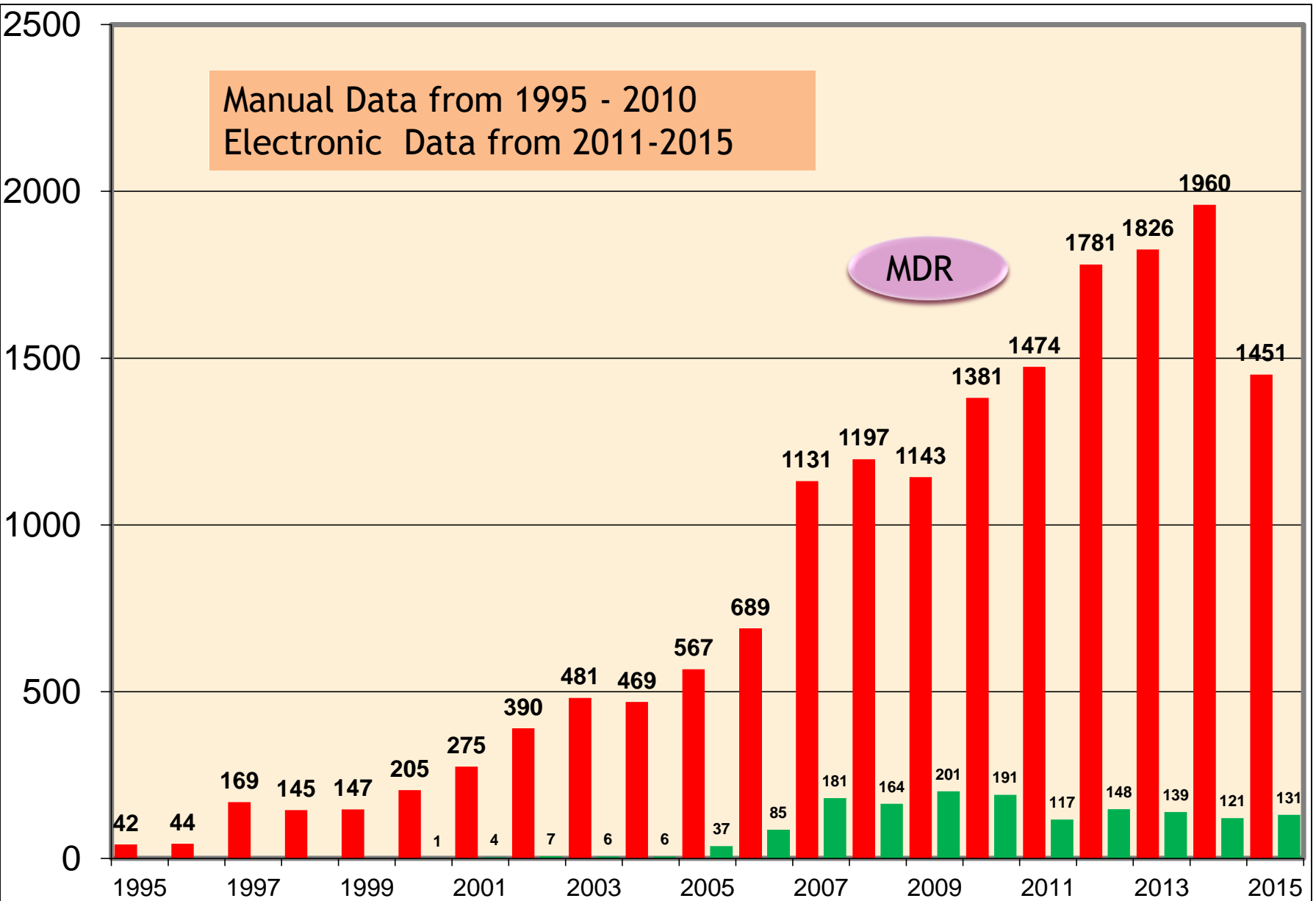


# HIV IN KING DINUZULU PATIENTS 2013-2015



84% of HIV Pos were reported as being on ARVs

# MDR AND XDR IN KDHC FROM 1995 -2015

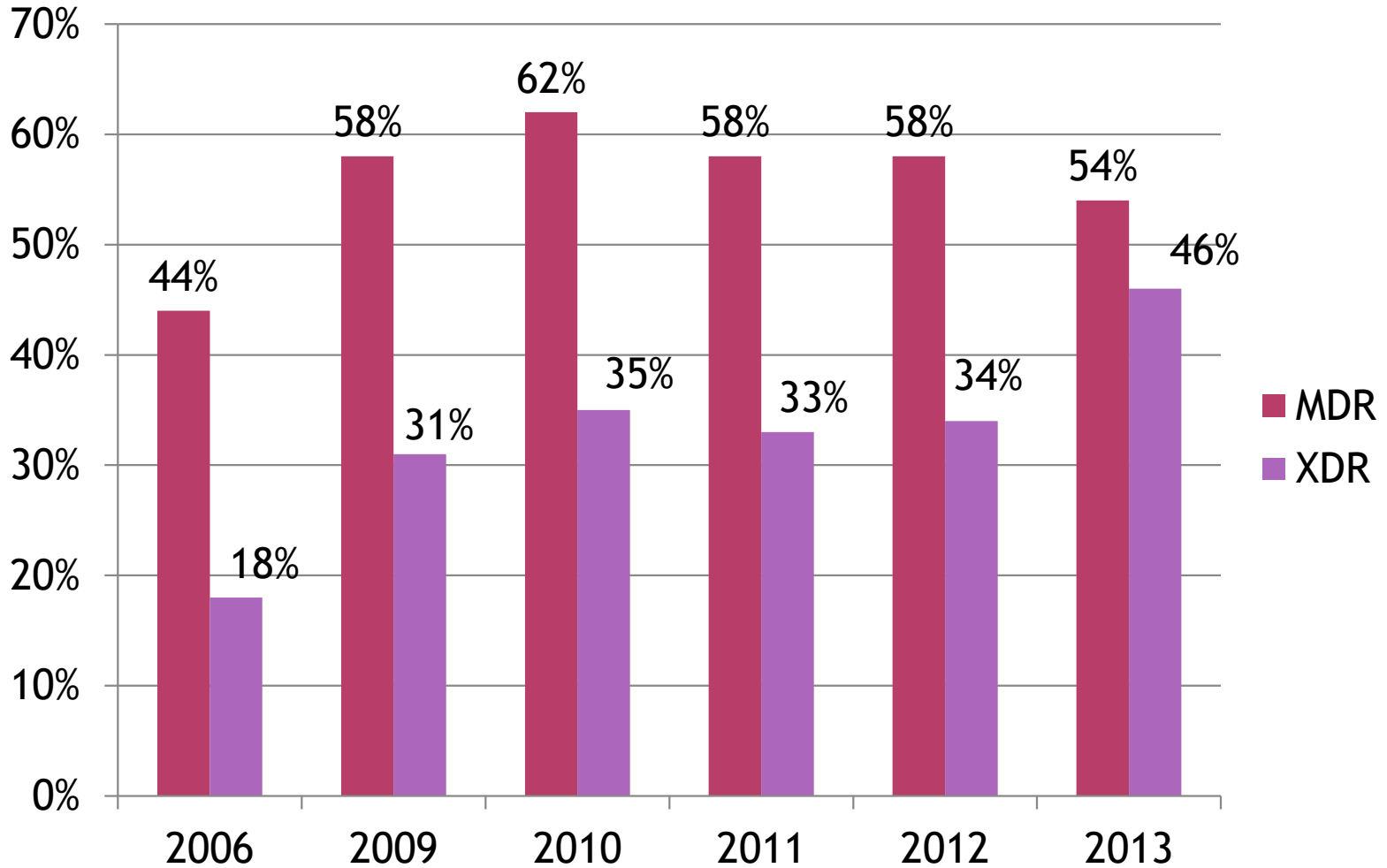




# WHAT ARE NATIONAL TREATMENT SUCCESS RATES FOR MDR AND XDR TB

1. 80% for MDR and 60% for XDRs
2. 70% for MDRs and 50% for XDRs
3. 55% for MDRs and 35% for XDRs
4. 40% for MDRs and 20% for XDRs
5. 30% for MDRs and 10% for XDRS

# KDHC - MDR / XDR RX SUCCESS RATES 2006 -2013



# WHAT ARE CURRENT DR-TB DEFAULTER RATES AT KDHC ?

1. 24 %

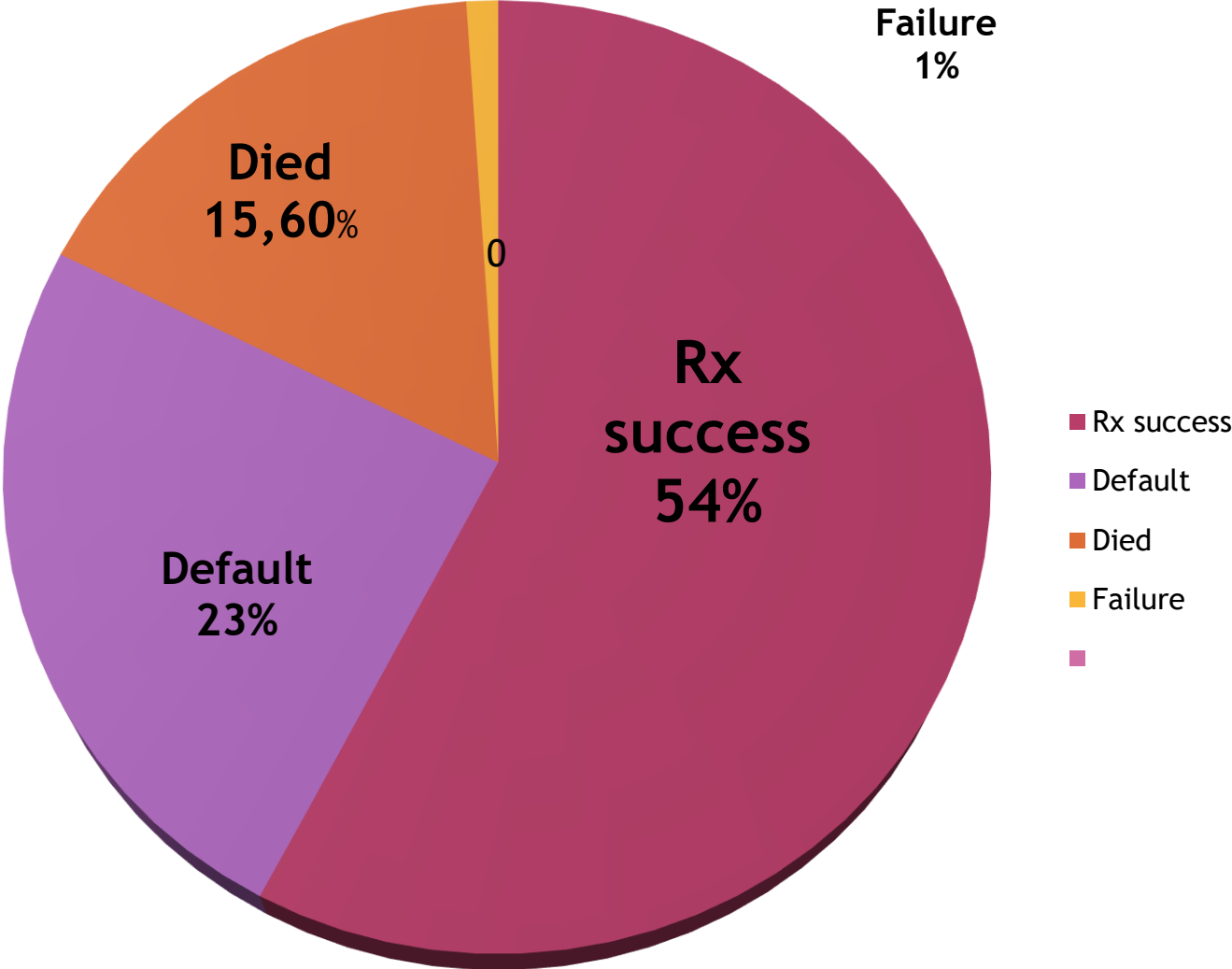
2. 11%

3. 16%

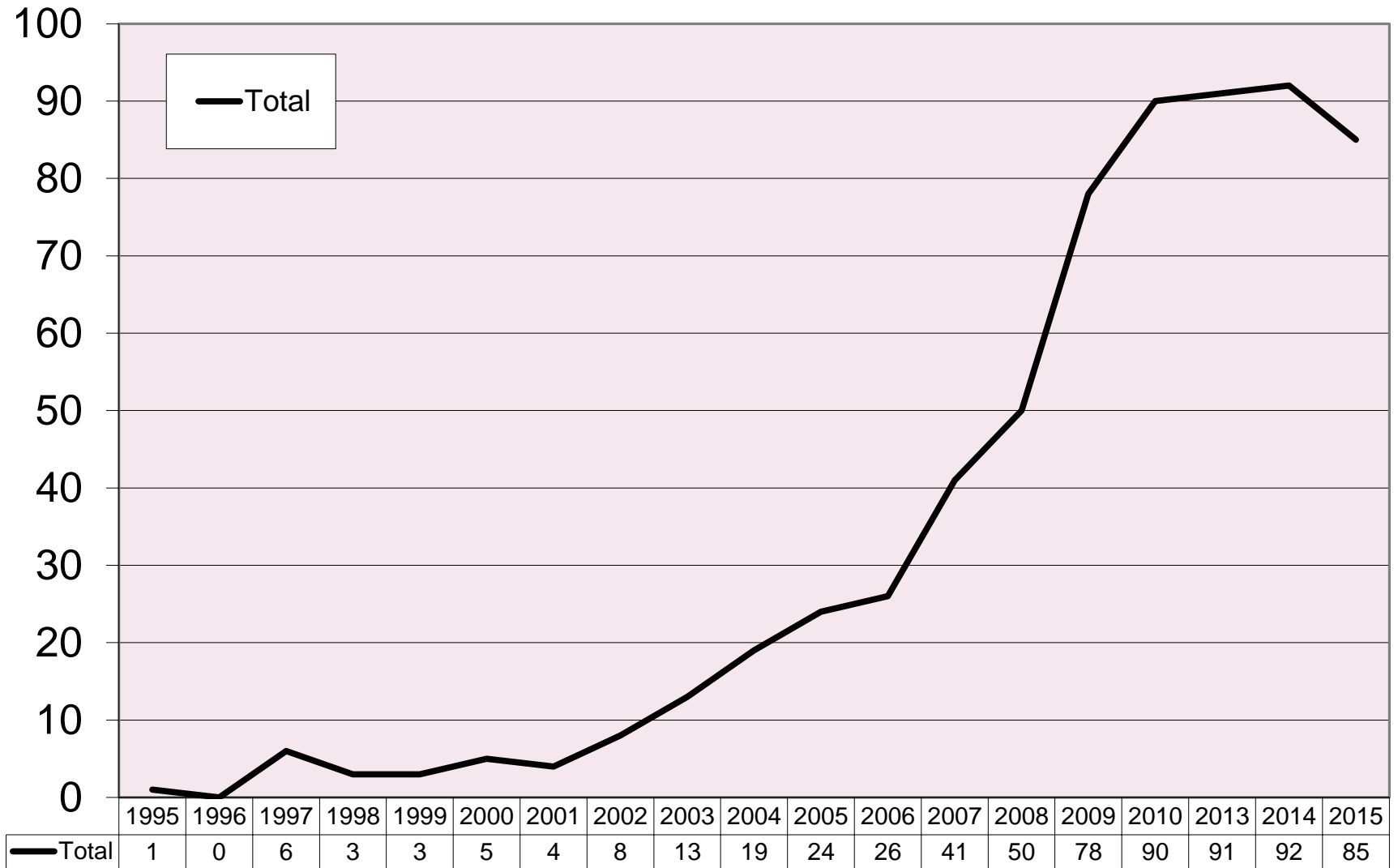
4. 31%

5. 6%

# KDHC - MDR OUTCOMES 2013



# Paediatric MDR Patients treated from 1998



KZN Team

BEDAQUILINE  
PROGRAM  
KZN

# TREATMENT

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## ⊙ Bedaquiline -

- Long half life ( 5 months)
- 400 mg (daily) for 2 weeks
- 200 mg (3 times a week) for 22 weeks
- Background regimen (BR) of 2nd line drugs (XDR/Pre-XDR ) to be continued (duration of course)
- C

# BDQ PROGRAM

- Initial Bedaquiline Clinical Access Program (BCAP) started in 2013 in South Africa
  - Ended - 6/2/2015 -
  - 72 patients recruited in KZN
- New National Program commenced in Feb 2015
  - KZN started in July 2015
  - Submission to National or Provincial committee



# CRITERIA FOR PROVINCIAL APPROVAL

- XDR or Pre- XDR
- MDR TB ( including RR TB )
  - MDR - Both inhA and KatG mutation
  - MDR with known intolerance or developed intolerance to 2<sup>nd</sup> line Rx Drug Toxicities
  - Surgical candidate for pneumonectomy / Lobectomy
- Regardless of HIV status (or CD 4 count)
- Inclusive of extrapulmonary TB
- Must have a least 2 core drug thought to be effective or sensitive
  - Bedaquiline
  - Linezolid
  - Injectable TB agent
  - Fluroquinolones

REQUIRES APPLICATION TO PROVINCIAL COMMITTEE

# CRITERIA FOR NATIONAL APPROVAL

- ◉ Pre-XDR or XDR - with fewer than 2 core drugs thought to be effective, sensitive and available
  - ◉ Linezolid - Cannot consider if previously used
  - ◉ Bedaquiline - Cannot consider if Clofazimine used for > 3 month
  - ◉ Quinolones - Cannot consider if Not proven sensitive
  - ◉ Injectable - Cannot consider if Not proven sensitive
- ◉ Age < 18 years
  - Pre-XDR , XDRs , Treatment Failure , Drug toxicities
- ◉ Pregnancy
- ◉ MDR Rx failures (without proven XDR/Pre-XDRs)

REQUIRES APPLICATION TO NATIONAL COMM.

# BDQ INTERACTIONS & ISSUES

- ◉ Levofloxacin preferred to moxifloxacin (QTC risk)
- ◉ Monitoring
  - ECG Weekly for 1<sup>st</sup> month thereafter monthly till BDQ completed
  - Blood monitoring monthly (depending on drugs used)
- ◉ ARV switch often required
  - Current Primary regimen is TDF/3TC/EFV
  - Need to Switch EFV (Apparently decreases BDQ levels)
  - Often switched - EFV to NVP or occasionally to Alluvia (Lopinavir/Ritonovir)
  - If not suppressed may require 2 drug switch
- ◉ BDQ is used for 6 months
- ◉ If Linezolid used - for 12 months (if tolerated)

| <b>KZN Bedaquiline Program Data</b> | <b>17/8/16</b> |
|-------------------------------------|----------------|
| Patients screened                   | 1037           |
| Required National approval          | 90             |
| Patients approved                   | 937            |
| Applications being processed        | 15             |
| <b>Patients actually commenced</b>  | <b>778</b>     |
| About to start                      | 40             |
| Approximate Deaths confirmed        | 58             |
|                                     |                |
|                                     |                |

# CHALLENGES

- KDHC has filled up with BDQ patients
  - Difficulty tracking a Fast tracked program
  - Pharmacovigilance is weak and needs to be strengthened
  - Numbers are increasing & decentralization is next step
- We have made great strides in rapidly rolling out a new drug program in a short period
  - Need to expand access
  - Need to analyze data , and outcomes to judge the impact
  - Need to review and strengthen the program.
  - Need to look at the morbidity and mortality & A/E

# WAY FORWARD

- ⊙ **Expand Bedaquiline access**
  - Doris Goodwin already initiating BDQ
  - Currently working with Murchison to get them started
- ⊙ **Sites also being evaluated**
  - Escourt Hospital
  - Greytown
  - Madadeni
  - Don Mackenzie
- ⊙ **Requirements to expand**
  - Knowledge , understanding & training on issues
  - ECG machine
  - Adequate recording & reporting
  - Demonstrateable Competence in managing MDRs
  - Regular , competent MDR-Staff in unit

# NEW SHORTENED REGIMEN TO BE IMPLEMENTED IN RSA

*November 2016 / January 2017*

# MAIN OBJECTIVES

- ◉ Align MDR-TB guidelines in South Africa with the newly published WHO MDR-TB guidelines
- ◉ Align MDR-TB treatment guidelines with the SA Drug-Resistance Survey (DRS) results



# CURRENT AND FUTURE DEFINITIONS

- ⦿ Definitions of a cure - (long regimen)
  - MDR patient (Cat IV) , received 18 months Rx , culture converted , clinically stable and has 3 or more consecutive negative cultures after injectable phase
- ⦿ Definitions of a cure - ( shortened Regimen)
  - MDR-TB patient (CAT IV) who has culture converted, received 9 months (or more) , clinically stable and has 3 or more consecutive negative cultures after the injectable phase.

# WHAT IS NEEDED TO IMPLEMENT THE SHORTER REGIMEN IN KZN ? - (BY 1/1/2017)

1. More Training & Support
2. We Ain't never gonna be ready!
3. We are ready to implement
4. More Time to prepare before implementation
5. We should wait for more results (Stream) before full implementation

# SUMMARY OF MDR MANAGEMENT

- ⦿ Currently all MDRS are being started on an existing regimen of 18-24 months
- ⦿ There is a National Plan to implement a 9-12 month regimen in Most MDRs - (except for a certain group) by 1/1/2017
- ⦿ All Pre-XDRs , XDRS , Both INH mutations and MDRs with Adverse Events are currently getting A BDQ based regimen & this will continue

# ACKNOWLEDGEMENTS

- We are in for some interesting times.
- More clarity is needed on shorter regimens.
- We will have to adapt as we go along

Thanks to the organisers of the conference for the invitation

To All Health Care workers  
working in HIV and TB  
For your Sacrifice and  
commitment a Big

**Thank You !**



# 1. DRUG DOSAGES FOR MDR TB <sup>Rx</sup>

| Drug                     | < 33KG      | 33 – 50kg          | 51 – 70kg                | >70 kg     |
|--------------------------|-------------|--------------------|--------------------------|------------|
| Pyrazinamide             | 30-40 mg/kg | 1g                 | 1,5                      | 2g(2.5g)   |
| Kanamycin<br>or Amikacin | 15-20 mg/kg | 500mg<br>(15mg/kg) | 750mg to 1g<br>(15mg/kg) | 1g         |
| Ethionamide              | 15-20 mg/kg | 500mg              | 750mg                    | 750mg (1g) |
| Moxifloxacin             | 400mg       | 400mg              | 400mg                    | 400mg      |
| Terizidone               | 15-20 mg/kg | 500mg              | 750mg                    | 750mg (1g) |

# OTHER DRUG USED

R<sub>x</sub>

| Drug                      | < 33KG   | 33 – 50kg    | 51 – 70kg   | >70 kg           |
|---------------------------|--|--------------|-------------|------------------|
| <b>Ethambutol</b>         | <b>25 mg/kg</b>  | <b>800mg</b> | <b>1.2g</b> | <b>1.6g (2g)</b> |
| Para-amino salicylic acid | 4g bd  | 4g bd        | 4g bd       | 4g bd            |
| Clofazamine               | 50 mg  | 100mg OD     | 100mg OD    | 100mg OD         |
| Augmentin                 |  | 1 g bd       | 1 g bd      | 1 g bd           |
| High Dose INH             | 15 mg/kg   | 15 mg/kg     | 600mg/900mg | 600mg/900mg      |
| Clarithromycin            |  | 500mg bd     | 500mg bd    | 500mg bd         |
| Imipenam/<br>Meropenam    | ?  | ?            | 1 gram tds  | 1 gram tds       |
| Linezolid                 | <b>300mg</b>   | 600mg        | 600mg       | 600mg            |
| Bedaquiline               | <b>400mg for 2 weeks followed by 200mg 3 times a week for 22 weeks</b> |              |             |                  |
| Delaminid                 | ?  | ?            | ?           | ?                |