Management of MDR and XDR TB

By
Dr I H Master

01/10/2009

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Definitions

- **MDR TB** (multidrug resistance)

  Where there is resistance to both INH and Rifampacin

- **XDR TB** (extreme or extensively drug resistant TB)

  Where there is resistance to INH and Rifampacin as well as the quinalones in addition to one of the injectable TB agents (kanamycin and amikacin and capreomycin) but excluding streptomycin. .

- **Mono-resistance**

  Resistance to one of the first line TB drugs.

- **Poly-resistance**

  Resistance to more than one first line TB drug. (but not both INH and RIF)

MDR TB

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When to do DST (Drug Suceptability Testing)

- All retreatment cases
- TB patients still positive after 2 months or 5 months Rx.
- Symptomatic close contacts of MDR/XDR
- Symptomatic - High risk groups with TB
  - Health care workers
  - Laboratory workers
  - Prisoners
  - HIV infected patients
- On diagnosis of MDR – especially if result is old
  - DST may have changed
- All extra-pulmonary TB specimens (eg .aspirations and abscesses)
- All Biopsy specimens for AFB drug suscept. test (in saline)
  - (This is a golden opportunity to make a diagnosis of MDR/XDR)

Sputum Testing

- Smear
- Culture and Sensitivity
  - L- J method
  - MGIT
  - PCR
    - Rapid screening test for INH and Rif resistance
    - Results in days
    - Very promising results
    - How it will be incorporated is not apparent ?
    - Only validated currently on smear pos. sputum
    - Some labs are sending out PCR results on smear negative specimen and other body fluids – creating management problems.

MOTTs – Mycobacterium other than TB (NTM)

- Other mycobacterium similar toTB
- Some cause pathology
  - M.leprae (leprosy) , M.bovis (Abd. TB)
- Some are commensals or found in the environment
- Some may cause TB like pathology in HIV patients eg M.avium (MAC)
- If causing disease may need to treat
- Do not respond to standard TB treatment
  - often very resistant.
- Usually managed by Respiratory clinic (IALCH)
- Often use drugs like Ethambutol and Clarithromycin (Klacid) to treat

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Changes in MDR Management
(since March 2007)

- National Plan based on WHO Guidelines of 2006
  - (New version 2008)
- Intensive phase (with injectable) for a minimum of 6 months
  - least 4 months after culture conversion.
- Discharge patients only after culture conversion.
- Continuation phase - at least 18 months after culture conversion.
- Treat for at least 24 months depending on culture conversion.
- After completion of treatment follow up –
  6 monthly for at least 2 years

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MDR Treatment

- Intensive phase – Minimum 6 months
  - 5 drugs – at least 6 x per week
    - **Aminoglycoside (5 x weekly) (Kanamycin/Amikacin)**
    - **PZA**
    - **Ofloxacin**
    - **Ethionamide**
    - **Terizidone/Cycloserine**
    - **(Ethambutol currently out of favour)**
    - **Pyridoxine (B6) - 150mg daily with Terizidone/Cycloserine**
- Continuation Phase – Minimum 18 months
  - Drugs at least 6 x per week
    - **Ethionamide**
    - **Ofloxacin**
    - **Terizidone/Cycloserine**
    - **Continue PZA**

Management Protocol

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

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1. Drug Dosages for MDR TB

	Drug	< 33KG	33 – 50kg	51 – 70kg	>70 kg
	Pyrazinamide	**30-40 mg/kg**	**1g**	**1,5**	**2g**
	Kanamycin or Amikacin	**15-20 mg/kg**	**500mg (10-15mg/kg)**	**750mg to 1g (10-15mg/kg)**	**1g**
	Ethionamide	**15-20 mg/kg**	**500mg**	**750mg**	**750mg (1g)**
	Ofloxacin	**800mg**	**800mg**	**800mg**	**800mg**
	Cycloserine or Terizadone	**15-20 mg/kg**	**500mg**	**750mg**	**750mg (1g)**
	Ethambutol X **??On the way OUT**	**25 mg/kg**	**800mg**	**1.2g**	**1.6g (2g)**
	~~Ciprofloxacin (not drug of choice)~~	~~**1g**~~	~~**1,5g**~~	~~**1,5g**~~	~~**1,5g**~~

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Monitoring Complications

- Repeat U & E for patients on injectables
  - Monthly for amikacin/kanamycin
  - (more often if renal impairment)
  - Up to weekly on capreomycin
- Monitor Ca/PO4/Mg at intervals on Capreomycin
- Serial Audios
  - Especially if complaining of
    - buzzing, ringing and blocked ears
- Regular TFTs if on PAS/Ethionamide (6 monthly)

Monitoring Recovery

- Patients are monitored by
  - monthly sputa cultures
  - Monthly weights
  - Serial X Rays (6/12/24 months)
- Culture conversion
  - when 2 consecutive negative directs and cultures are achieved at least 30 days apart
  - Safety for outpatient Rx/work

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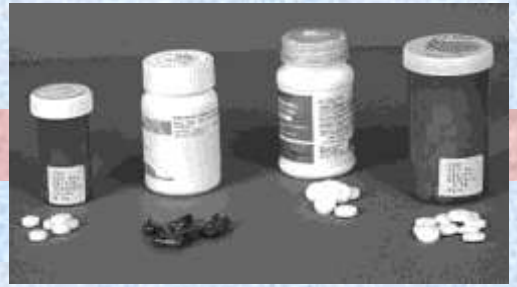
Treatment Costs

Drug Cost	Cost (per patient per month)
PAS	**R 2360 (R1600)**
Capreomycin	**R 1400 (R800)**
Moxifloxacin	**R 785**
Terizidone	**R 579 (R650)**
Cycloserine	**R 522 (R600)**
Klacid	**R 228**
Amikacin	**R 216 (R400)**
Kanamycin	**R 200 (R250)**
Ethionamide	**R 177 (R130)**

Drug Costs



Drug	Cost (per patient per month)
STD TB (intensive phase)	**R67**
STD TB (continuation phase)	**R43**
MDR (intensive phase)	**R1033**
MDR (continuation phase)	**R833**
XDR (intensive phase)	**R5300**
XDR (continuation phase)	**R3901**

Paediatric MDR

- Often Primary resistance.
  - Difficult to diagnose.
- Disease is often paucibacilliary
  - seldom culture pos.
- Limited international experience.
- Treated with adult drugs (including quinalones.)
- Every attempt to confirm diagnosis with sputum culture or gastric washings must be made
- If culture negative, symptomatic TB with MDR contact - treat according to contacts DST.

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Special Conditions

- Diabetes
  - Poorly control results in poorer outcomes
  - potentiates side effects eg. renal disease and heuropathy
  - Oral Diabetic agents not contra-indicated
  - Monitor renal function
- Liver Disease
  - 2nd Line Drugs
    - Ethionamide and PAS also hepatotoxic
    - Fluoroquinolones less often
  - If jaundice - stop all treatment
  - Rule out other causes (viral hepatitis / obstructive jaundice)
  - Restart with safer drugs (Strep / Emb)
  - Once Jaundice settles challenge with one drug at a time
    - Preferable not to restart – PZA
  - Monitor LFT's closely

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Renal Disease

- May be associated with diabetes on HIV disease
  - Monitor U&E and creatinine
  - Decrease frequency of MDR dosaging
    - PZA (25 –35 mg/kg) 3 x weekly
    - EMB (15 –25 mg/kg) 3 x weekly
    - Ciprofloxacin (1000 - 1500 mg) 3 x weekly
    - Ofloxacin (600 - 800 mg) 3 x weekly
    - Cycloserine (500 mg) 3 x weekly
    - Aminoglycoside (12-15 mg/kg) 3 x weekly
    - Capreomycin (12-15 mg/kg) 3 x weekly
    - PAS/Ethionamide – no change
- Estimated GFR = $\frac{(140 - \text{age}) \times (\text{ideal body weight in kg})}{72 \times (\text{serum creatinine})}$
    - Adjust in Women – Estimated GFR x 0.85
    - If GFR < 30ml/min adjust dosages

MDR in Pregnancy (WHO)

- Advocate contraception in all MDR Females
- Exclude Pregnancy B4 MDR Rx.
- Evaluation, counselling and informed decision.
- Defer Rx if patient well & slow disease progression.
- Treat after 2nd trimester (sooner if condition warrants)
- Start with 4 oral agents , add injectable after delivery
- Aminoglycosides - higher risk of ototoxicity to fetus.
- If using injectable - capreomycin preferred.
- Avoid ethionamide - nausea and teratogenic (animals).
- KGV has inadvertently treated pregnant MDRs (> 30).
  So far no adverse events found in babies.

Breastfeeding

- **Lactating Mums**
  - If mother is sputa positive, separation is advised
  - If affordable - formula feed
  - If cannot avoid close contact – nurse in well ventilated area with N95 respirators.
  - Small amounts of drug are found in breast milk (not significant)

KGV – Current HIV Policy

- KGV - an acredited ARV site
- All patients offered VCT
- If pos. CD4s < 200 , patients - offered ARVs as soon as CD4 available.
  - Sooner if Stage 4
- Patients already on ARVs →MDR/XDR Rx is added
- ARVs often used - (D4T/3TC/EFV).
- On discharge patients continue ARV RX at KGV.
- HIV – MDR Drug interactions do occur
  - Rifampacin based regimens
  - Quinalones and DDI
  - Clarithromycin if used - many interactions
  - With Regimen 1a/1b often no need for treatment adjustment.
- Bactrim prophylaxis - 2 daily recommended
  - Until CD4 > 200 on 2 occasions
- New guidelines apparently advocate ARVs for MDRs with CD4 < 350
  - Draft guidelines not yet approved

IRIS

- Immune reconstitution inflammatory Syndrome
- Occurs in patients with low CD4 counts often recently commenced on ARV's (2 weeks onwards)
- Despite an immune response (increase in CD4) they may develop new or worsening disease
  - Active PTB
  - Worsening of PTB in patients already on TB treatment
- New or worsening TB does not automatically imply MDR TB
- Management
  - Treat the infections
  - May need steroids (Prednisone 1mg/kg for 2 weeks)
  - Advised to continue ARV and TB treatment
  - Send specimen for DST
  - Stop ARV’s only in rare circumstances. (life threatening)

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Surgery In MDR/XDR TB

- Primary treatment for MDR TB is medical
- Indications for Surgery
  - If localized disease (1 lung) and
    - Persistant sputa positive after 6 months treatment
    - Relapse after adequate treatment and good compliance
    - ? Extreme resistance – 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
- Preferable to have patient on intensive phase prior to surgery
- Continue treatment for at least 18-24 months post surgery

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Advice for Treatment Failures

- Ensure patient had supervised treatment
- Complete adequate course of treatment **(12-24 mths)**
- Consider Surgery
- It failing Rx (9–12mths) add what has not been used **(Capreomycin,PAS, Klacid Augmentin, Moxifloxacin + Clofazamine ?)**
- Stop all treatment **if** definite treatment failure.
- Suggestion palliative treatment, sanatorium or home based care

- KZN situation
  - We have many treatment failures (> 300)
  - They are being discharged home. (Some survive 5 years)
  - Expect more Rx failure with XDR TB
  - Often Retreat them but prognosis is poor
  - Patients resist stopping treatment

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MDR Contacts

- Routine prophylaxsis with 2nd line treatment not recommended.
- Assess all close contacts of MDR patients.
- Evaluate risk and exposure.
- Do sputa culture & DST on all symptomatic contacts.
- Emperical MDR regimen not routinely recommended.
  - Except in high burden areas like Tugela Ferry
- Screen neonatal contacts carefully for congenital TB
- Asymptomatic child contacts under 5 years – with positive mantoux not currently recommended for any prophylaxsis. Look for disease.
- Symptomatic Children with – MDR Contacts
  - **Evaluate with exam/skin test/CXR/sputa or gastric DST**
  - **If unable to prove TB but failure to respond to standard therapy**

    - then consider MDR TB treatment according to contact's DST
- Some centers were using their own emperic regimen in children with latent TB (high dose INH /PZA/Cipro)
  - not currently recommended by WHO/National

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Does every MDR result need to be treated ?

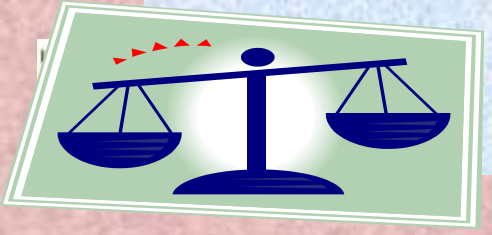
- NO !
  - Sputum results do not always correlate with patient's condition.
  - Patients with MDR results are sometimes well, improving with clear CXRays on standard Rx.
  - MDR treatment in the above situation exposes patients to toxic medication at high cost unnecessarily.
- Why?
  - **Lab Factors ?**
    - Lack of quality control
    - Human errors in recording
    - Errors in technique
    - Inherent difficulty in testing certain drugs - giving varying results
  - **Multiple strains** in same patient giving varying results.
  - Different response to drugs in vivo and in vitro

Surveillance Patients (to watch)

- Where we uncertain that Lab results are in keeping with the patients condition, symptoms, CXR.

  → KGV puts them on "**Surveillance".**

- These patients are continued on Standard RX.
- They are monitored monthly at the MDR clinic.
- **If at follow up they**
  - **Remain sputa positive**
  - **More results show MDR TB**
  - **Fail to convert**
  - **Then these patients will be commenced on MDR Rx.**
- **If Sputa remain negative a standard course of TB treatment will be completed.**



Medicolegal Aspects

Question 1. Can a patient refuse treatment ?

- YES ! - A patient has a right to refuse treatment.
  - You can get a court order to hold him in hospital but you can't force him to take medication.

Question 2 How long can you Keep him?

- Period is undefined. (years?)
  - Treatment failures remain alive & infectious for years.
  - We lack the capacity to keep them more than 6 months

Question 3 Who bears the responsibility of the patients commitments (house, subsidy, business)?

- **No one!**
  - **This does not encourage patients to be admitted!**

If you criminalize TB, patients will be reluctant to be treated.

We do not even have enough beds for those who are eager to be treated?

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Can you inform the employer ?

2 opinions

- MRC
  - **We can neither inform the employer nor a training institute without patient consent.**
  - **We could be held liable for breach of patient confidentiality.**
  - **The patient may lose his job**
- **Jerome Singh – UKZN**
  - **You are allowed to breach confidentiality under certain circumstancess when a defined 3rd party is at risk like a co-worker or husband.**
- **Until there is a test case there is no clear direction for doctors !**
- **There needs to be a clear written policy from national.**

XDR TB

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Principle of XDR Treatment

- With arrival of Capreomycin and PAS new regimens had to be designed.
- No absolute regimen (limited by available drugs)
- Use at least 4-6 drugs expected to work
- Must receive an injectable
    - Streptomycin if sensitive or Capreomycin
- Add other drugs based on susceptibility pattern, efficacy, side effects profile, availability and cost.
- Use Group 5 drugs if unable to make up an adequate regimen.
- **KZN using ffg regimen**
    - **PZA + EMB (if sensitive) + Ethionamide + Cycloserine/Terizidone + Capreomycin + PAS + Moxifloxacin (new patients)**
    - **Duration of treatment and injectable phase is same as for MDR**
    - **Add Group 5 drugs if regimen inadequate**

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WHO – Grouping of MDR-TB Drugs

GROUP	DRUGS
Group 1 First-line oral drugs	**Ethambutol (E)** **Pyrazinamide (Z)**
Group 2 Injectable Anti-TB agents	**Streptomycin (S)** **Kanamycin (Km)** **Amikacin (Am)** **Capreomycin (Cm)**
Group 3 Fluoroquinolones	**Ciprofloxacin (Cfx)** **Ofloxacin (Ofx)** **Moxifloxacin (Mfx)** **Gatifloxacin (Gfx)**
Group 4 Oral bacteriostatic 2nd line anti-TB agents	**Ethionamide (Eto)** **Cyloserine (Cs)** **Terizadone (Trd)** **Para-aminosalicylic acid (PAS)** **Thiacetazone (T)**
Group 5 Agents with unclear efficacy – not recommended routinely	**Clofazamine (Cfz)** **Amoxicillin/Clavulanate (Amx/Clv)** **Clarithromycin (Clr)** **Linazolid (Lzd)**

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1. Drug Dosages for XDR TB

Drug	< 33KG	33 – 50kg	51 – 70kg	>70 kg
Pyrazinamide	30-40 mg/kg	1g	1,5g	2g
Ethambutol	25 mg/kg	800mg	1.2g	1.6g (2g)
Ethionamide	15-20 mg/kg	500mg	750mg	750mg (1g)
Terizadone or Cycloserine	15-20 mg/kg	500mg	750mg	750mg (1g)
Capreomycin	15-20 mg/kg	500 to 750mg	750mg to 1g	1g
Para-amino salicylic acid	4g bd	4g bd	4g bd	4g bd
Moxifloxacin Selected cases		400mg	400mg	400mg
Salvage therapy – battling to make up a new regimen – add drugs below				
Clarithromycin (Klacid)	**500mg BD**	**500mg BD**	**500mg BD**	**500mg BD**
Augmentin	**2 BD**	**2 BD**	**2 BD**	**2 BD**
Klacid/Augmentin only added as a last resort				

WARNING

- Beware!
- There is no optimal regimen for XDR at present!
- There are no sensitivity results available for drugs being used
  - Sensitivity for most 2nd line drugs are unreliable

Thus

The patient may already be resistant to whatever drugs are being used!

There is no guarantee of a cure!

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Treatment for mono and poly resistant TB

Drug resistance pattern	Suggested regimen	Minimum duration of treatment (months)	Comments
H (+/-S or +/- Z or +/- E)	Add Ofloxacin and continue Regimen I or II initial phase treatment (except for H)	6 - 9	If patient on Regimen II, Streptomycin should be discontinued after 6 Months. If resistant to Streptomycin, discontinue it Immediately
R (+/- any other 1st line drug)	Standardized MDR-TB regimen	18	Notion of potential over treatment Use of Ethambutol in the MDR regimen
HEZ (+/- S)	Rifampicin, Ofloxacin, Ethionamide, plus Kanamycin for the first 2-3 months	18	Six months of Kanamycin may strengthen the regimen in patients with extensive disease

Side Effects

Aminglycosides

- Ototoxicity + Nephrotoxicity
- Poorly tolerated due to pain
- Ototoxicity is dose related and Irreversible
- Up to 25% have degree of hearing loss
- Do baseline and serial audios.
- If damage detected decrease frequency and dose
- Monitor U & E for nephrotoxicity
- May be given IVI

Terizidone/Cycloserine

- Causes severe CNS side effects
- May trigger convulsions (contraindicated)
- Presents with confusion/psychosis/anxiety attacks peripheral neuropathy and fits,
- Stop drug
- Antipsychotics, Sedation, Antidepressants can be used
- If mild problems try reduced dose.
- Occasionally Psychosis may persist.
- Use with high dose Pyridoxine to prevent neuropathy.

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ADVERSE REACTIONS AT KGV

For Period 01/04/2007 to 29/08/2008 = 17 months

Side Effect	*Patients*
Committed Suicide	**5**
Suicidal	**4**
Psychotic	**95**
Depressed	**22**
Confusion	**31**
Epileptic Fits	**14**
Violent	**8**
Anxiety Attacks	**3**
Memory Impairment	**4**
Miscellaneous (Headache/Dizziness/Neuropathy)	**6**
Total	**192**

- 1/3 of the patient are on ARVs
  - Effavirenz may be playing a role in these events
- Adverse events appear commoner in HIV positive patients
- ? Cycloserine contributed to these reactions

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Other Drugs

Quinalones and PZA

- Severe arthritis/arthralgia
- Try NSAID
- PZA may cause hyperuricaemia
- If very severe may have to stop drugs
- PZA implicated in hepatitis

Ethionamide

- Metallic taste
- Severe nausea/vomitting
- May have to take it daily/reduce dose

PAS

- Old TB Drug brought back for XDR TB (USA)
- This preparation requires a cold chain
- Must be taken with some acid drink or Maas for proper absorption
- Not well tolerated
- Causes severe GIT side effects like gastritis?loss of appetite/diarrhoea
- Side effects are worse if taken with ethionamide
- Outpatient treatment will be an issue due to the cold chain

Capreomycin

- Also an old TB drug brought back
- Side effects are similar to aminoglycosides.
- Severe electrolyte problem
- Causes hypokalaemia and hypomagnasaemia.
- Poor response to K+ supplementation.
- Need to correct Mg and K+ and Ca+
- May need to add aldactone (25mg)
- Monitor weekly U&E
- Do Ca , Mg. at intervals
- Have had > 10 deaths possibly linked to Capreomycin.

The KZN Program

A King George V Perspective

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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 ↓)
- Had a waiting list for admission – peaked at 150 patients
  - Currently 50 waiting and waiting period 3 to 6 weeks
- Satellite MDR Units operational since March 2008 who are keeping their own registers
  - Thulasizwe/Greytown/Murchison/Manguzi
  - Plans for future units in - Mosvold, Catherine Booth, Doris Goodwin
- We are also initiating outpatient Treatment in selected patients and referring most back to District hospitals, TB Centres
  - A few are pure outpatients
- **Planned Future MDR Bed State in KZN**
  - **320 Beds KGV**
  - **195 Beds FOSA**
  - **200 Beds at 8 satellite units**

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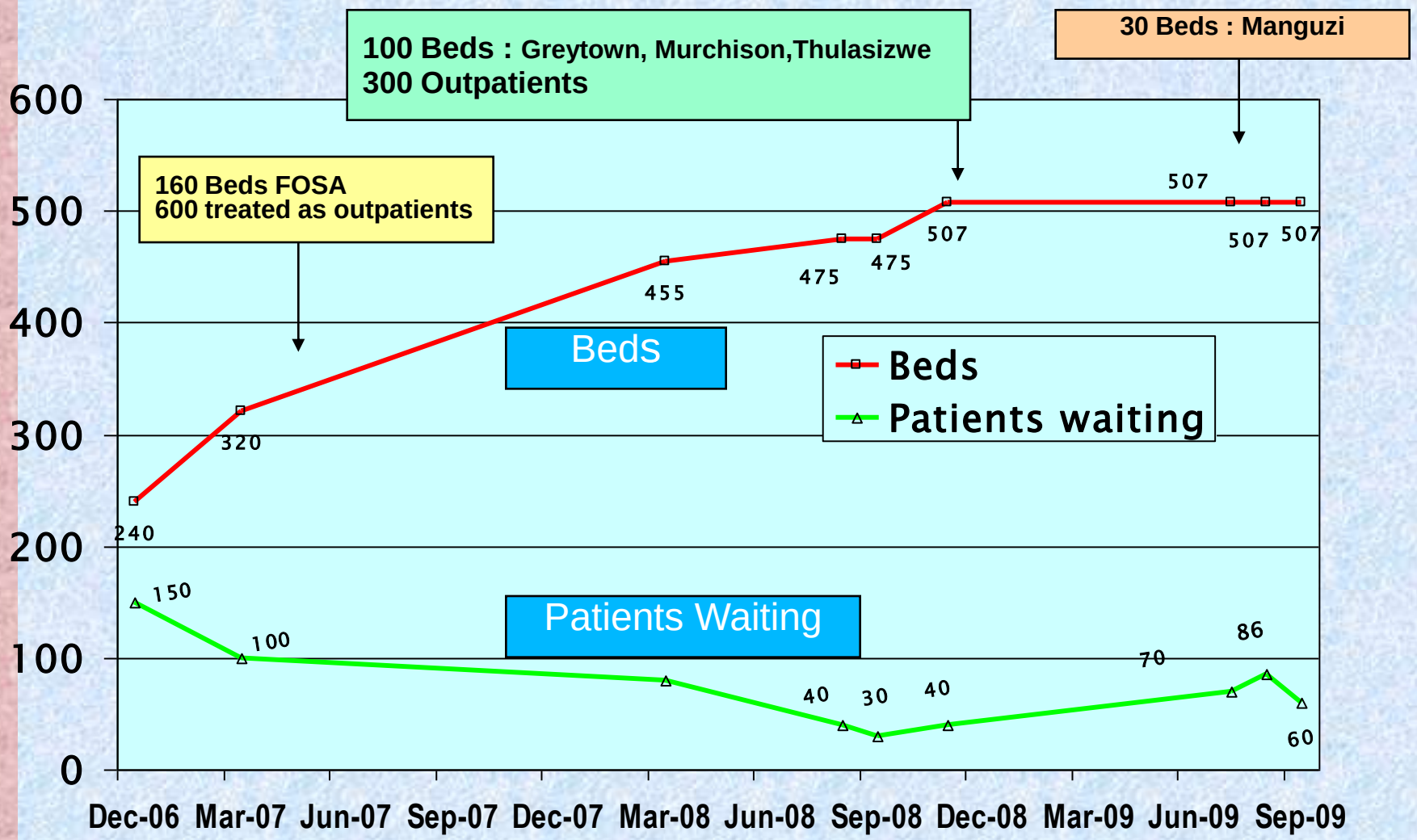
Bed State vs Waiting List



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KZN/KGV – Management policy

- National policy advocates all patients be kept until culture conversion
- In KZN we try to keep them for at least 6 months.
  - In special circumstances - allow early discharge
    - Urgent social issues
    - Aggressive patients
    - Extreme shortage/pressure on beds
  - Selected outpatients
    - Mainly admitted to district hospital
    - Treatment failures being given a 2nd chance
    - Absolute refusal to be admitted
- XDR and ill patients are prioritized
- Unfortunately with current bed pressures patients still having positive cultures at 6 months are being sent home on treatment
- Probably have at least 300 treatment failures in the community
- Tugela Ferry is piloting an outpatient program
- National is seriously considering outpatient programs for MDR TB
- **Pass outs** are granted – depending on need

Current KGV Patient Profile

- Almost exclusively MDR and XDR (99%)
- Currently 90 XDRs admitted
- +/- 70 % HIV positive
- MDRs from throughout KZN
- 50% of XDRs patients are from Tugela Ferry area

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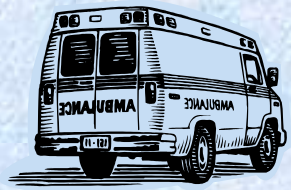
MDR TB Follow-up Clinic

- Discharged MDR patients attend monthly.
- Follow-up clinic operates twice weekly (Tue and Thur).
- Patients attend from through out KZN (& Transkei) .
- See up to 250 patients/clinic = 2000/month.
- New patients are seen on Mon/Wed/Fri
- Discharges are processed on Mondays
- Transport issues
  - Difficulty in reaching King George V
  - Insufficient transport
  - Move to decentralize MDR treatment makes absolute sense
- Currently using a new Ward as Clinic
  - Awaiting a new TB Outpatient complex to be built




Renovated multi-storey
For MDR TB
New star shaped ward

Infection Control - KGV

- **Patient education**
  - **Cough hygiene** (turn head/cover mouth)
  - **Surgical masks** – are used on patients coughing excessively or during transport.
- **Isolation of Patients –**
  - **Isolation of TB from MDR from XDR patients (in ideal circumstances)**
  - **Not always practical**
    - **Impacts on recruitment of staff**
    - **Insufficient beds for Isolation**
  - **Currently only able to separate patients within the same ward**
- Good ventilation
  - **Natural ventilation (open window policy) in multi-storey**
  - **Mechanical Ventilation - Negative pressure ventilation is in place**
  - **Still need to implement ongoing assessment of air exchanges.**
- **Individual Protection - N95 respirators**
  - **Respirators are available – (filter small enough to stop TB / need tight fit).**
  - **Have not as yet implemented fit test.**
- **Ultraviolet lights** none at King George V
  - **Require proper maintenance and monitoring**
    - **Cost implication**
    - **Certain risk to staff**

Current Lab Susceptablilty done

- All provincial sputa sensitivity testing in KZN is done at IALCH
- Drugs tested for are
  - *INH*
  - *RIFAMPACIN*
  - *ETHAMBUTOL*
  - *STREPTOMYCIN*
  - *KANAMYCIN*
  - *CIPROFLOXACIN*

- ***NB No Testing done for***

PZA ETHIO TERIZIDONE CAPREOMYCIN & PAS

MDR and XDR at KGV

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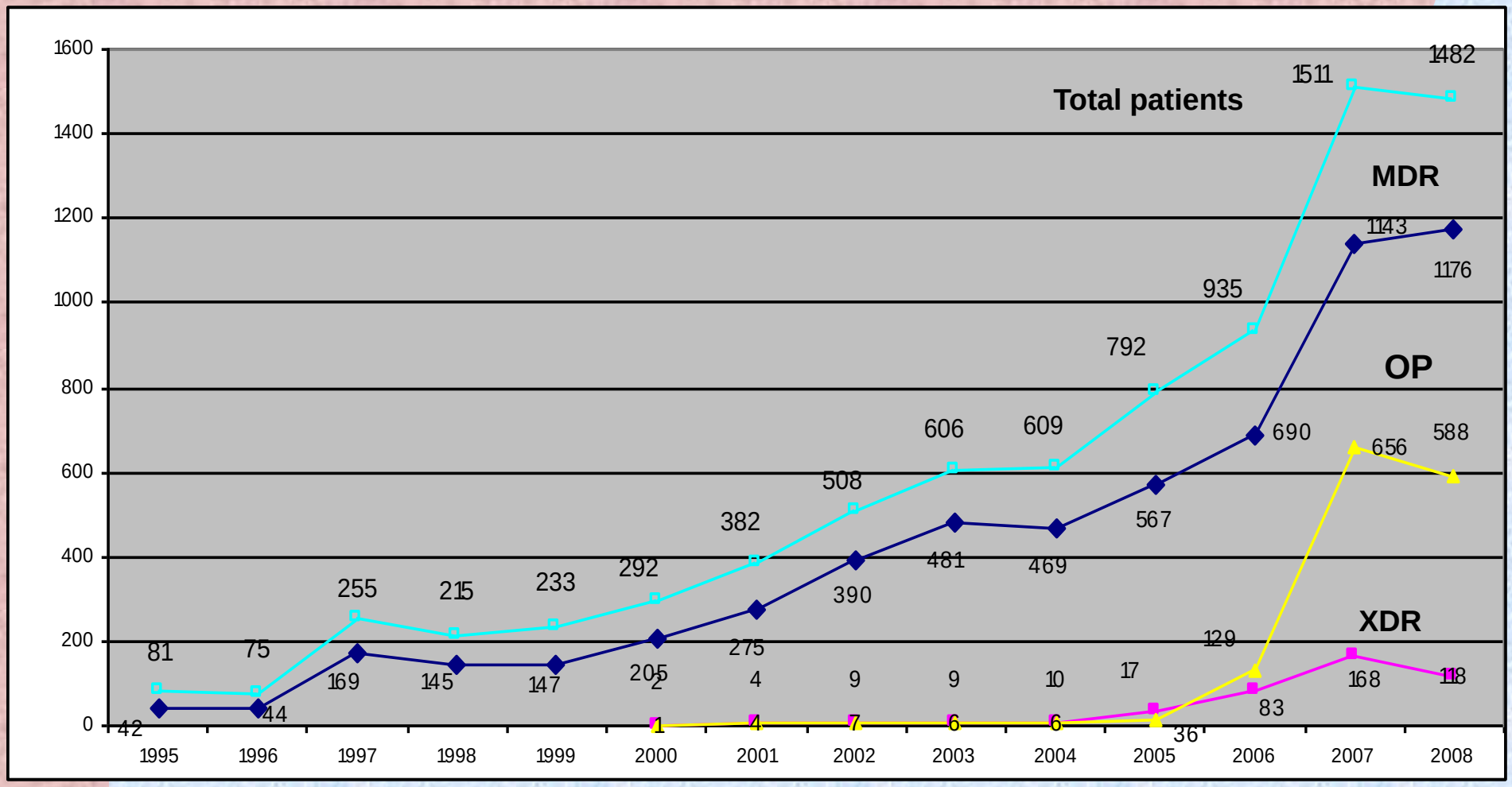

- MDR has been increasing since 1995
- XDR has been here since year 2000
- Outpatients on treatment increased

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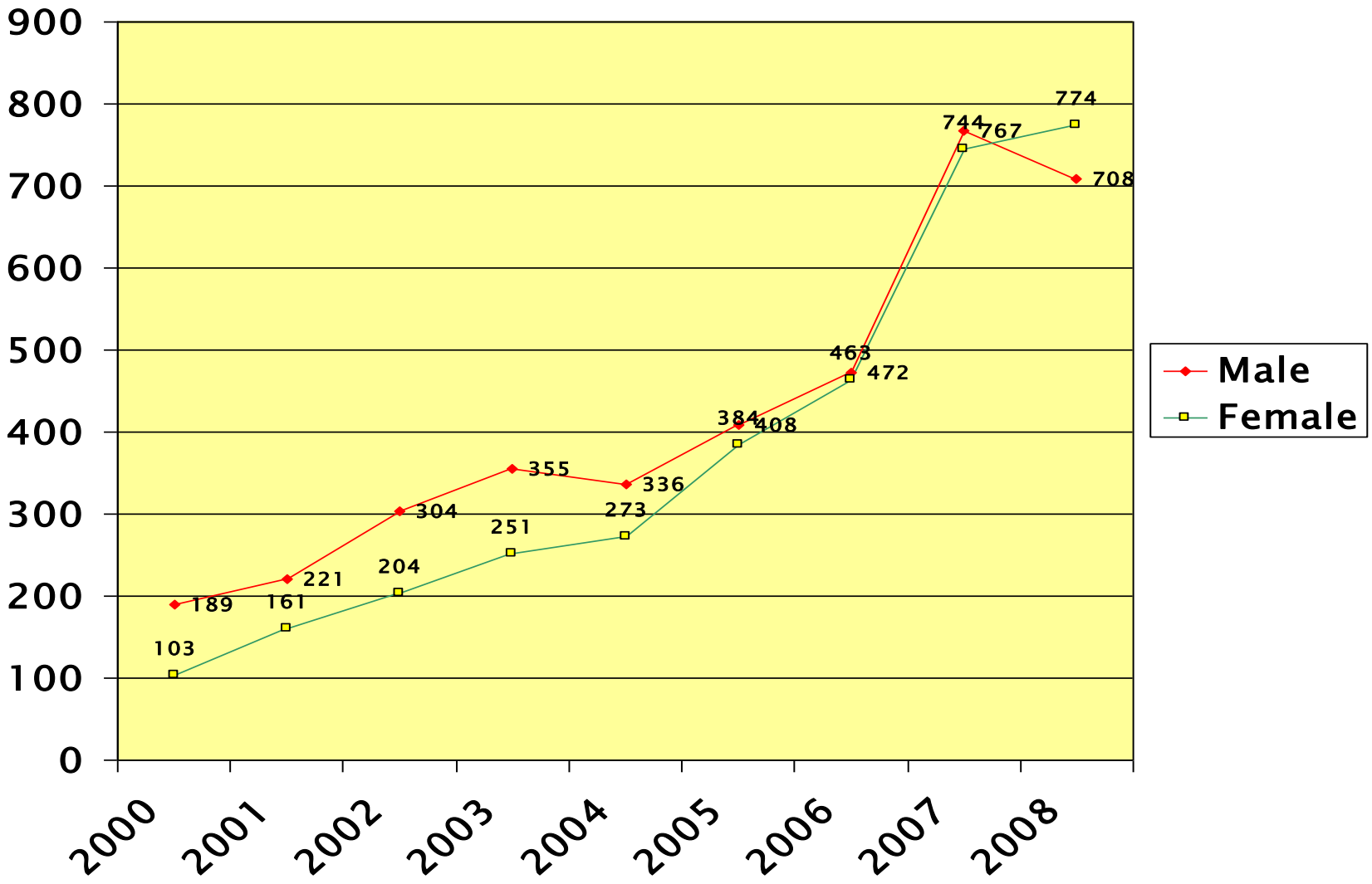
Stats from 2000 to 2006 for KGV

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
MDR	205	275	390	481	469	567	690	1143	1176	700
XDR	1	4	7	6	6	36	83	168	118	72
OP	2	4	9	9	10	17	129	656	588	400
Mono Poly	69	85	96	105	83	85	84	111	92	66
Surveillance	2	4	22	39	53	66	71	105	57	26

Male vs female for All TB KGV



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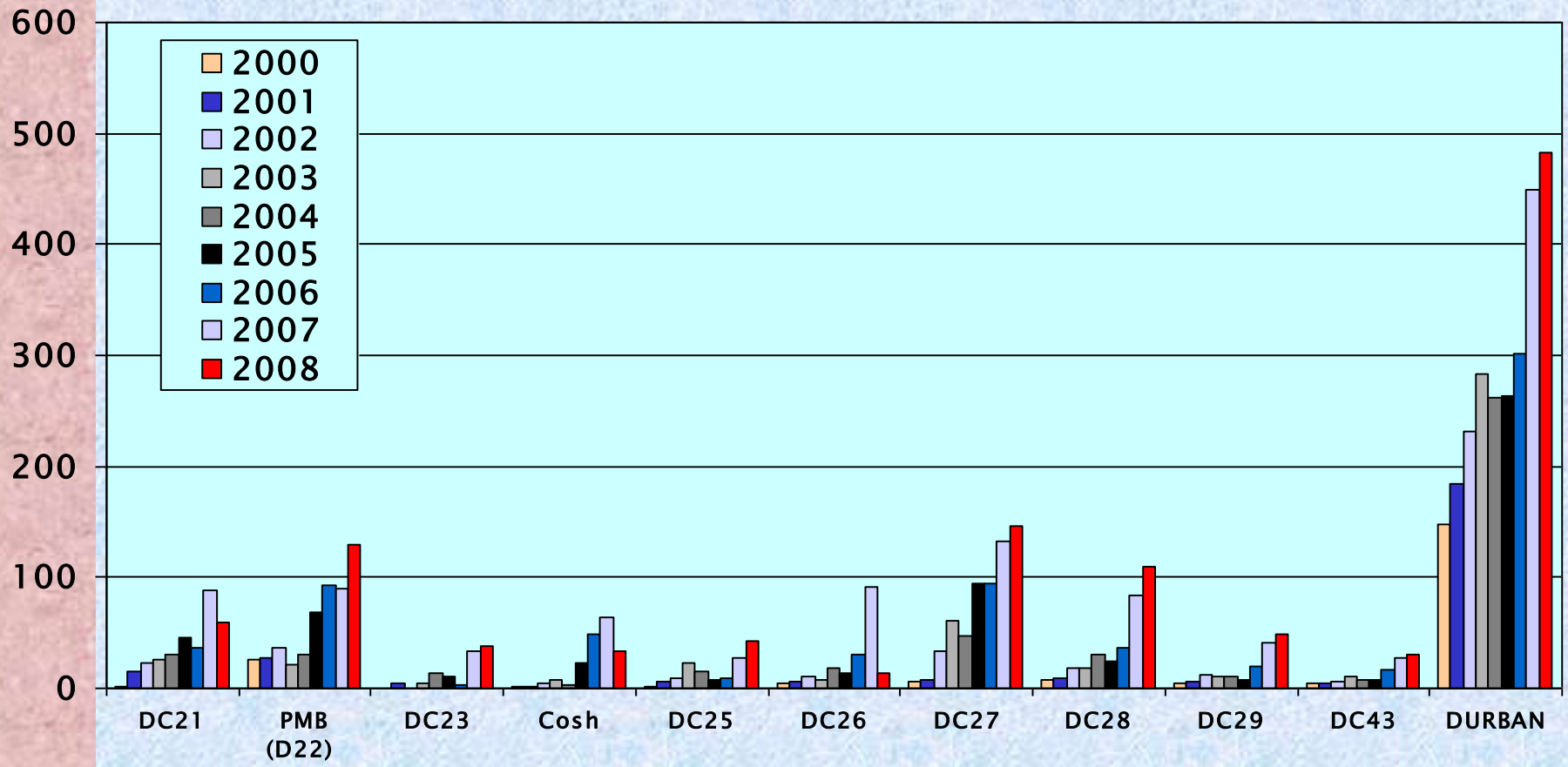
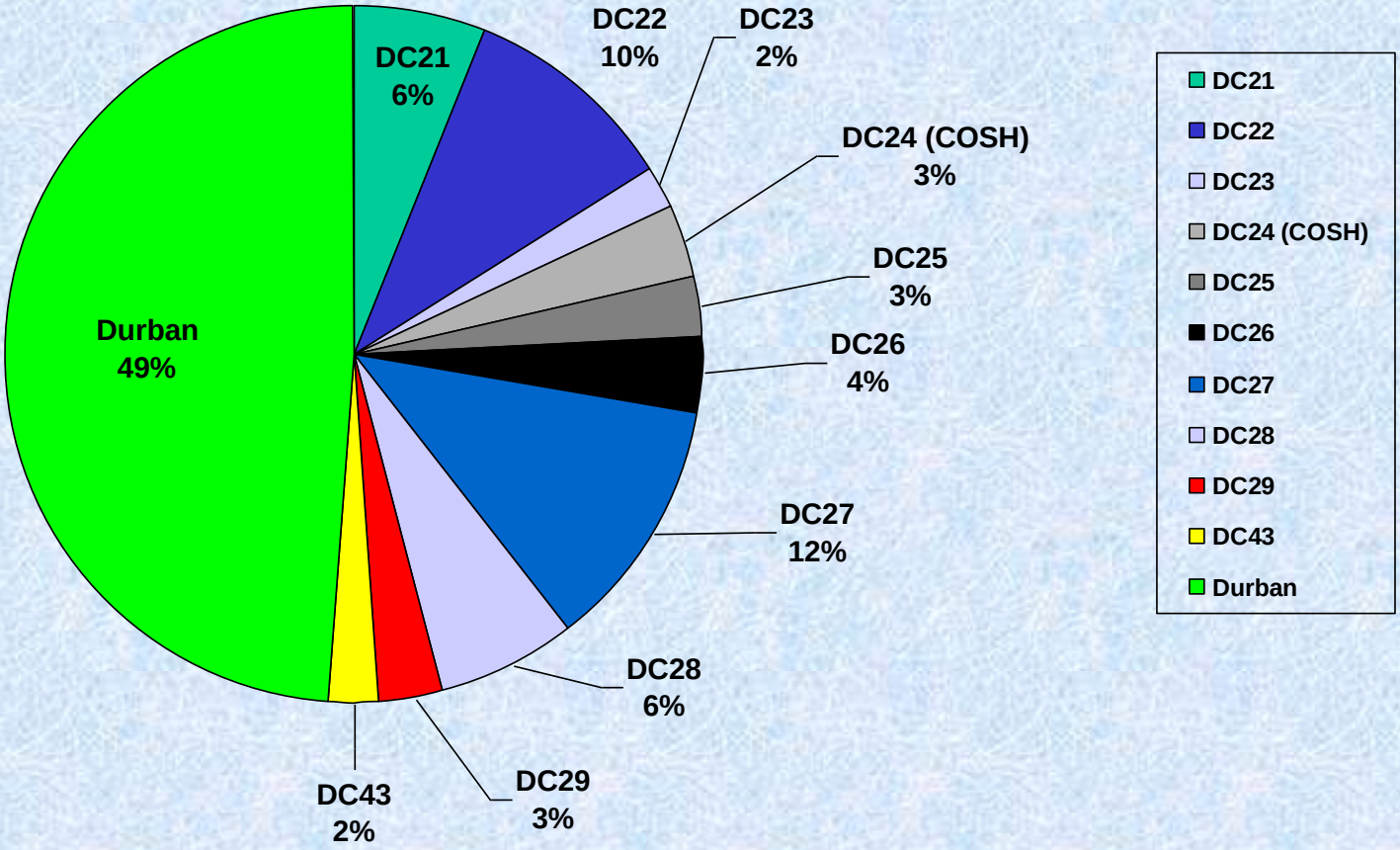
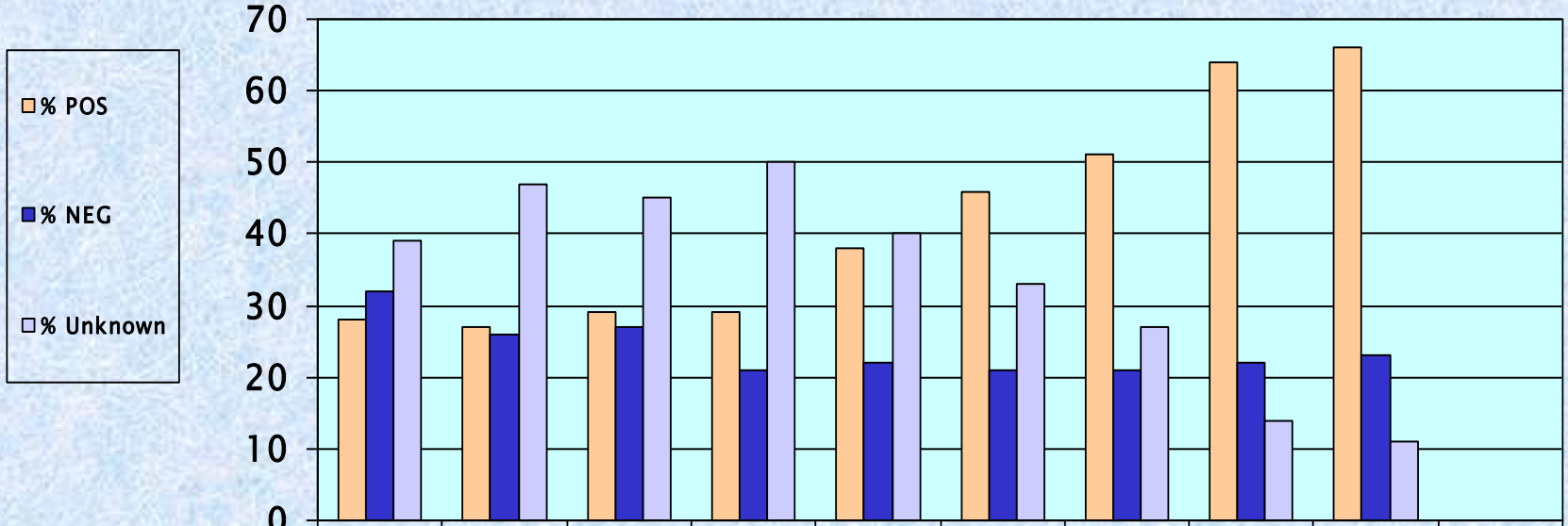
Distribution of MDR by district



Distribution of MDR by district

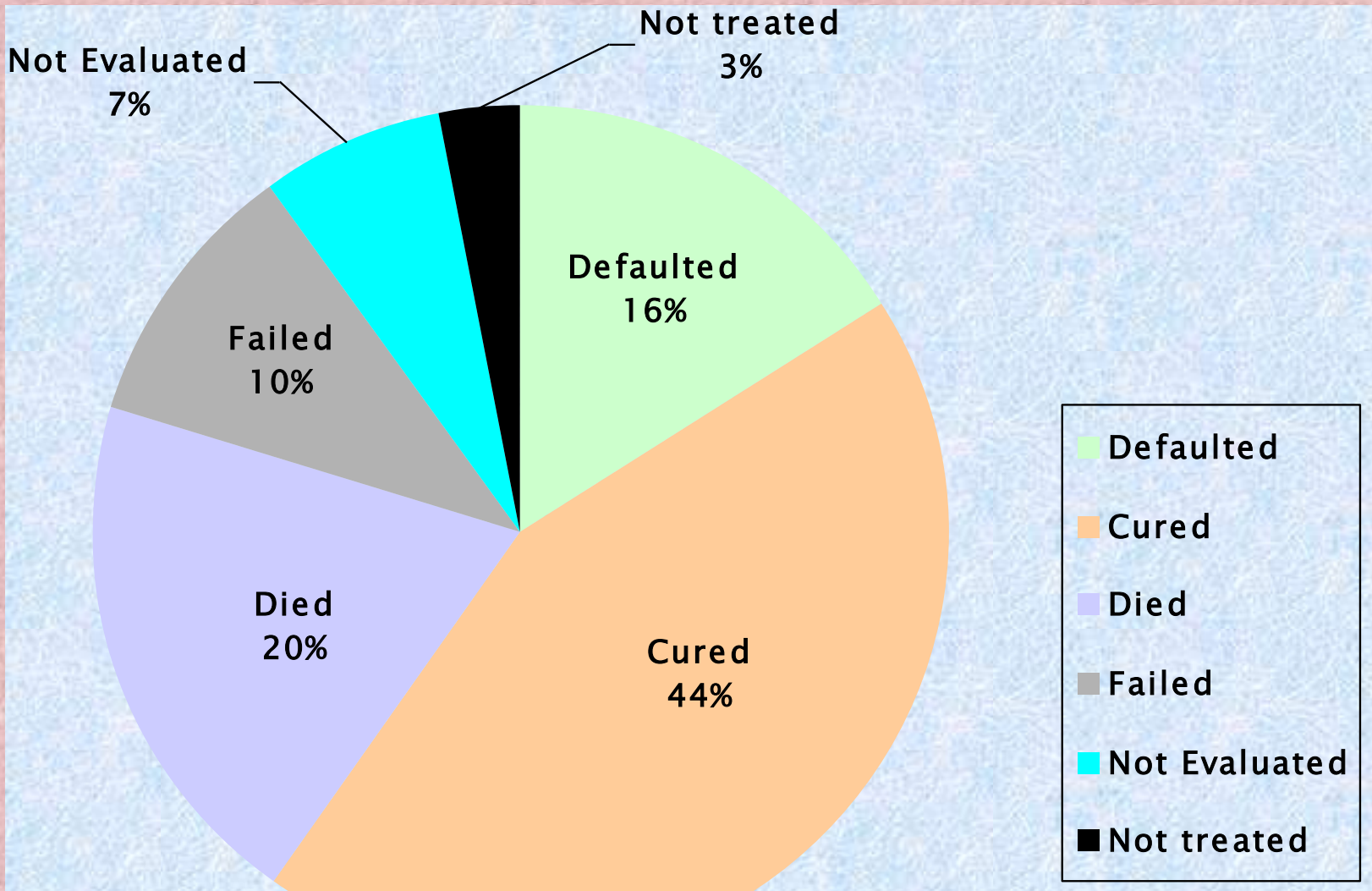


HIV percent year on year



	2000	2001	2002	2003	2004	2005	2006	2007	2008
% POS	28	27	29	29	38	46	51	64	66
% NEG	32	26	27	21	22	21	21	22	23
% Unknown	39	47	45	50	40	33	27	14	11

MDR OUTCOMES 2000 TO 2006



XDR TB

Church of Scotland - COSH

- COSH has a high incidence of XDR.
- Since 2005, 250 of 400 MDRs were XDR **(55%)**
- **80% of COSH XDRs are late.**
- Little community spread of XDR TB.
- Suspicion of nosocomial spread.
- Infection control has been improved.

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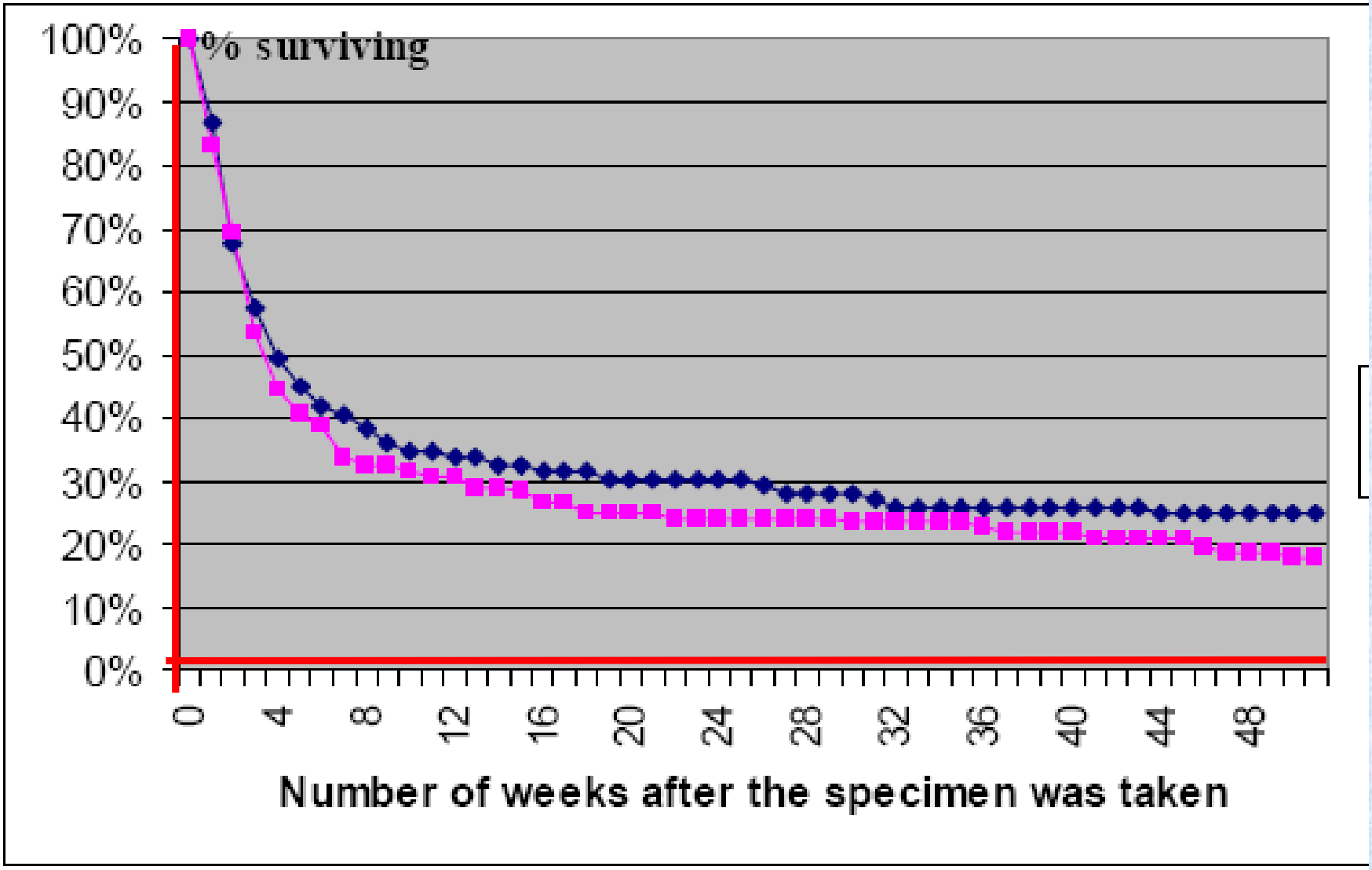
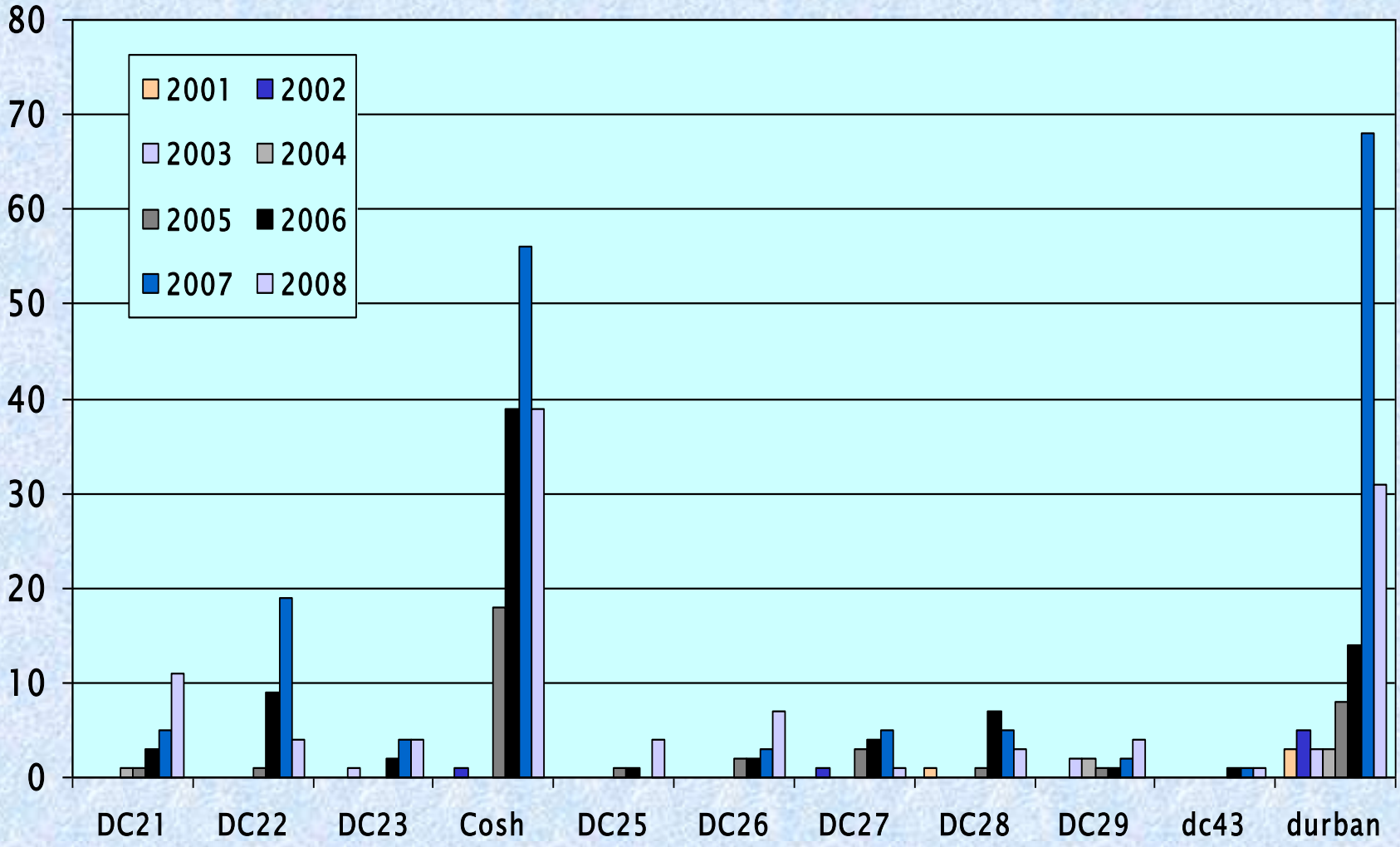
Survival of MDR & XDR at COSH (Jan 05-Jun 06)



Italian Co-operation, Issue 16 Epidemiology Bulletin, Sept 2007

Distribution of XDR by District



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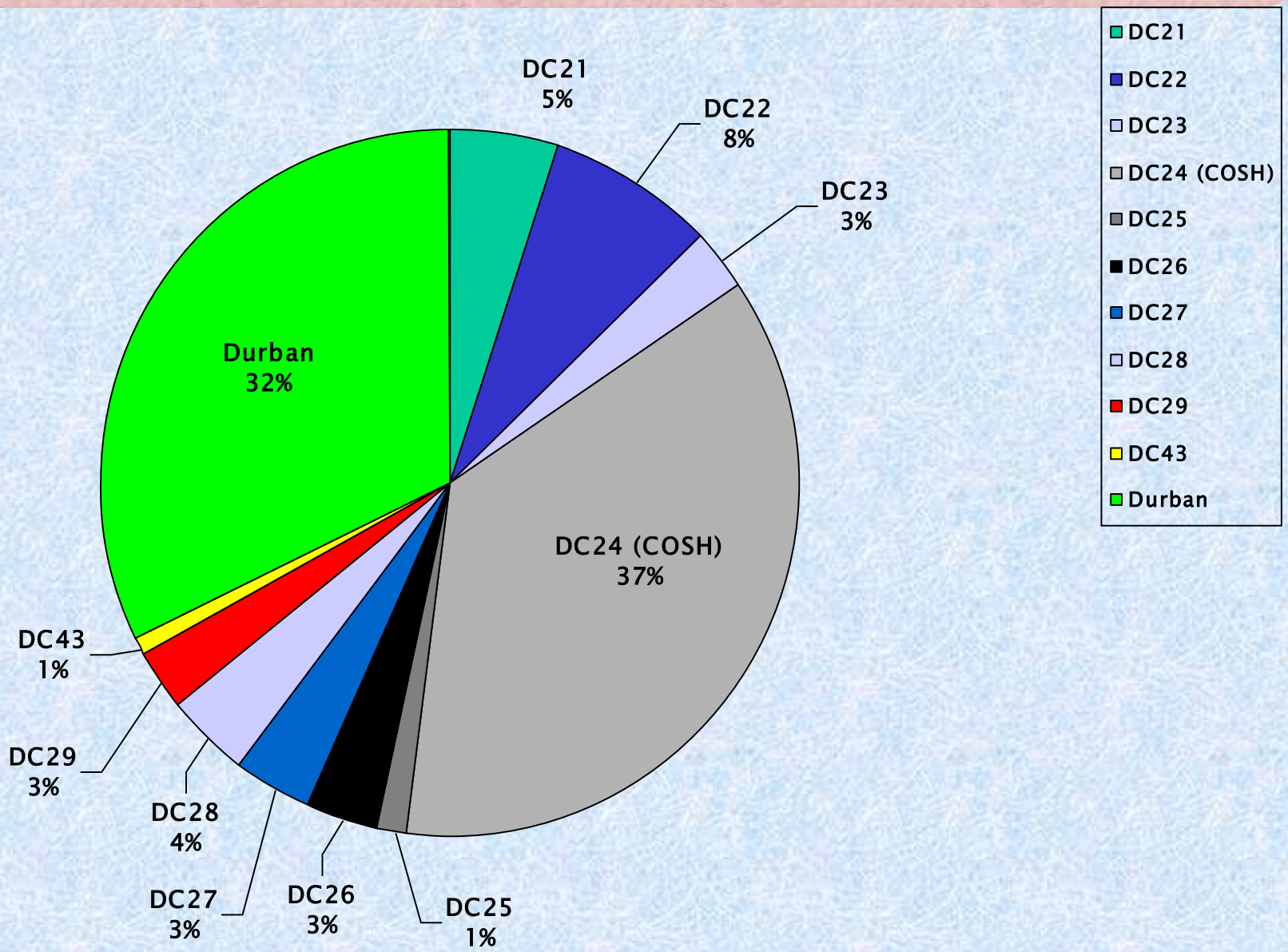
Distribution of XDR by district over years



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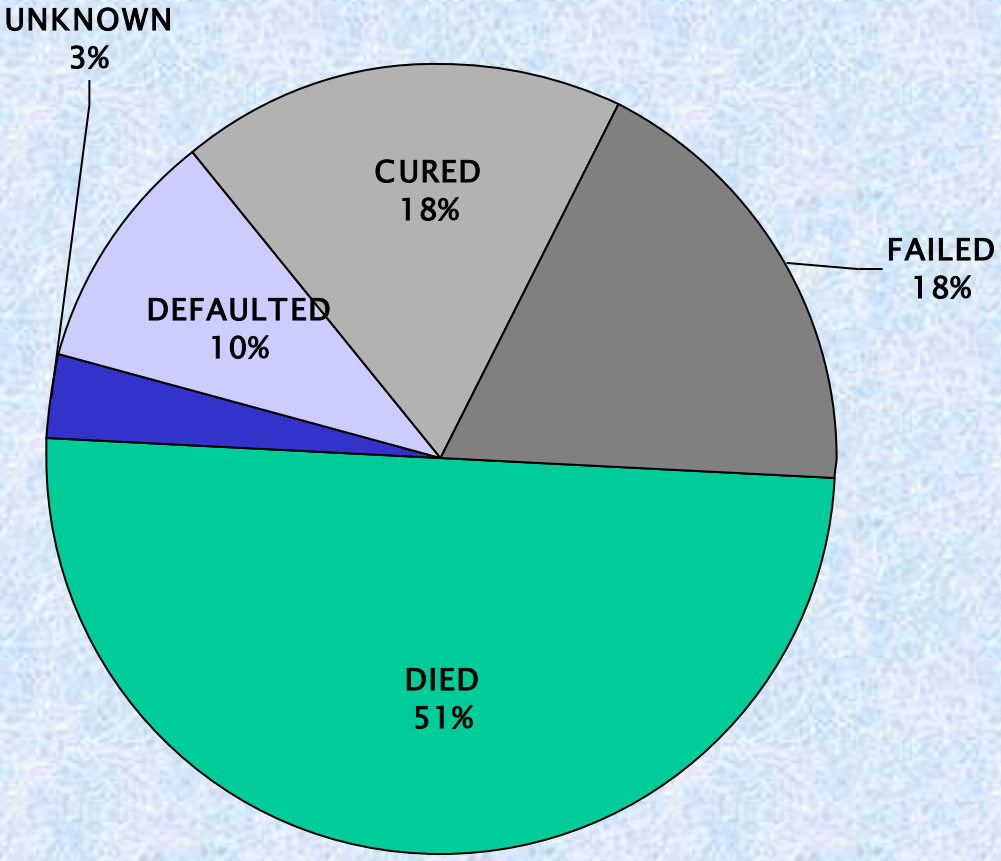
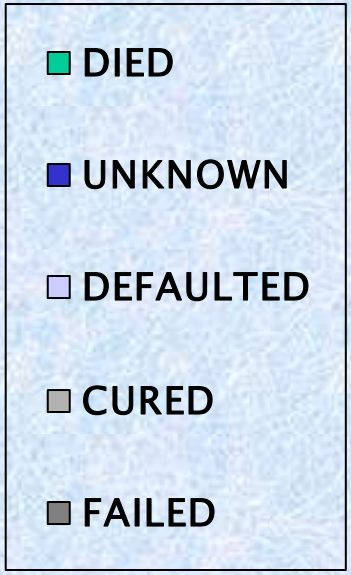
Progress of XDR Cohort (60) since 2006





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 dissussion with KGV doctors)

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How to refer to King George

- Contact Dr Pala and discuss patient.
  - He will contact you when there is a bed available.
- MDR beds are being increased but *the reality is that there may never be enough beds!*
- If you need advice – contact the MDR clinic, or any of the other KGV TB doctors.
- The odd patient may be considered for outpatient treatment
  - Book outpatients with the MDR Follow up Clinic. (Do not just send them)

STAFF and TB

Risk to STAFF

- Staff exposed to TB, MDR TB and XDR TB are at a potential risk of developing TB.
- It is important to take precautions to avoid unnecessary exposure.
- Infection control measures must be in place.
- If you are immunocompromised it is preferable not to work in a TB hospital/high risk settings.
- Take up the offer for confidential VCT and if positive ask for redeployment

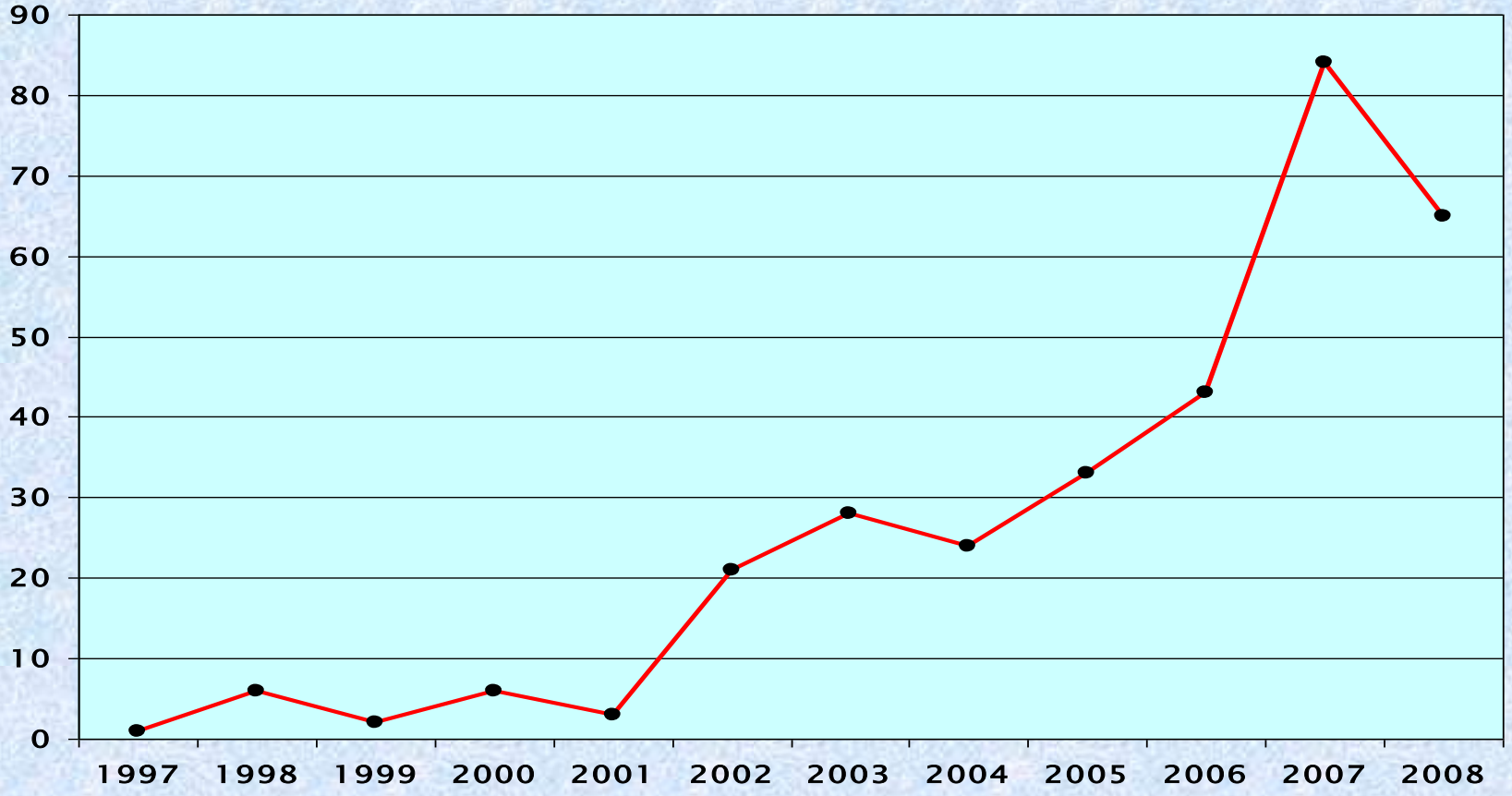
Workmans Compensation

- All staff who develop TB during employment and have been exposed to TB patients in the course of their work must have WCA forms filled.
- TB has been accepted as an occupational disease.
- If you develop TB what are you entitled to ?
  - IOD - Sick leave until you are fit to work
  - If you are unfit for work then WCA may compensate you on loss of lung function.
  - This in practical terms is very hard to obtain.

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
- Provision of confidential ARVs for Staff
- Offer Relocation or Transfer to staff at risk

Health Care workers treated at KGV for Resistant TB



- 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

Challenges in current KGV program

- Delays in Admission
  - 2 to 4 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 in the past
  - Currently out of Kanamycin (twice in August 2008)
- Side effects of medication
  - Cycloserine / Capreomycin
- Legal Issues
  - Confidentiality / Incarceration / Duration

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Issues to Ponder

1. **Problem of PCR results**
   - Practitioners are acting on PCR results from smear negative and extrapulmonary specimens.
     - Some of these patients are clinically well.
     - PCR has not yet been validated for above specimens
     - Discussion needed on the implication and applicability of these PCR tests.
2. **KGV is being pressurized to commence patients on outpatient Rx**
   - Patients agree to outpatient therapy just to get on to therapy earlier.
   - Facilities/Doctors want patient to start treatment at any cost
   - The problem
     - Some are too sick for outpatient treatment.
     - There are inadequate arrangements for supervision of outpatient Rx.

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Issues to Ponder

3. **Should XDRs be prioritized?**
   - By admitting an XDR before MDRs it is delaying the admission of MDRs
   - Some MDRs die before they can get a bed.
   - We have a better chance of cure with MDR
   - MDRs(45% cure) vs XDRs (less than 20% cure) o
   - It makes more sense to prioritize MDR patients as they have a better chance of cure?
4. **Should XDR Rx be freely available?**
   - Some satellite units want to treat their own XDRs
   - Concerns
     - Cost of XDR Rx is high – R5500
     - Possibility of …
       - Abuse of the drugs
       - Inappropriate usage
       - Worsening Resistance patterns in the community

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Acknowledgements

- Bruce Margot – Provincial TB Technical advisor
- Department of Health
- Executive Management of KGV
  - Dr K Naidu, Dr S Maharaj, Matron Ngubane
- Staff of King George V & Fosa
  - MDR Doctors of King George V and FOSA
  - Nursing, Paramedical & Support Staff of KGV & FOSA
    - MDR clinic, MDR wards, TB register unit , Audiology & Pharmacy
- Dr Osborne & Mrs V. Raman – for Database & Data
- Doctors and Staff of the Decentralized & Satellite units
- MRC (Dr Alex Pym + Marion Loveday)
- Capresa/TBTC (Dr Padayatchi)
- Dept of Psychiatry + Thoracic Unit – for assistance
- Italian Cooperation

iqbal.master@kznhealth.gov.za