Establishing knowledge gaps of health care workers calling the National HIV & TB Health Care Worker (HCW) Hotline between July 2013 and December 2013

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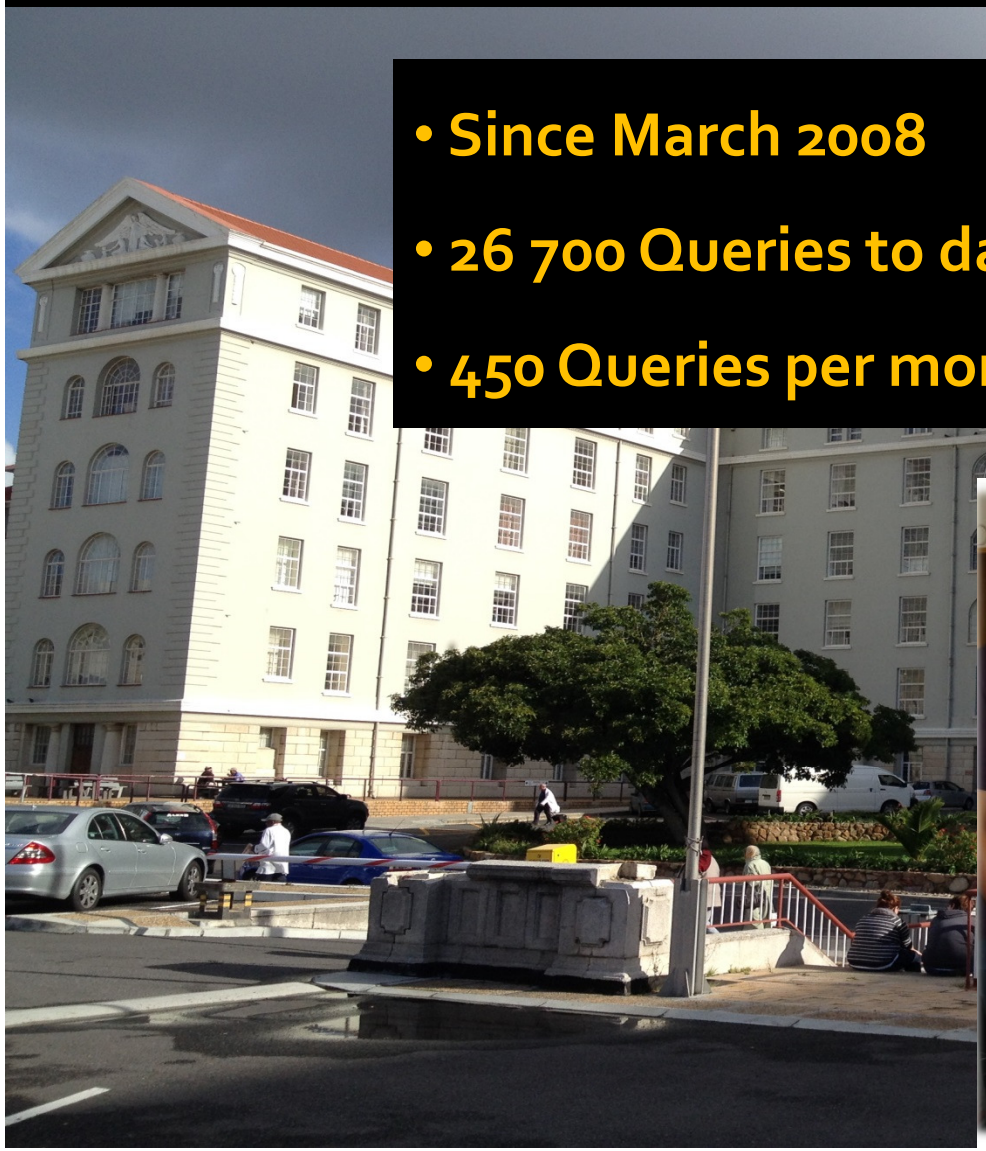
Introduction

- Since March 2008
- 26 700 Queries to date
- 450 Queries per month



Introduction

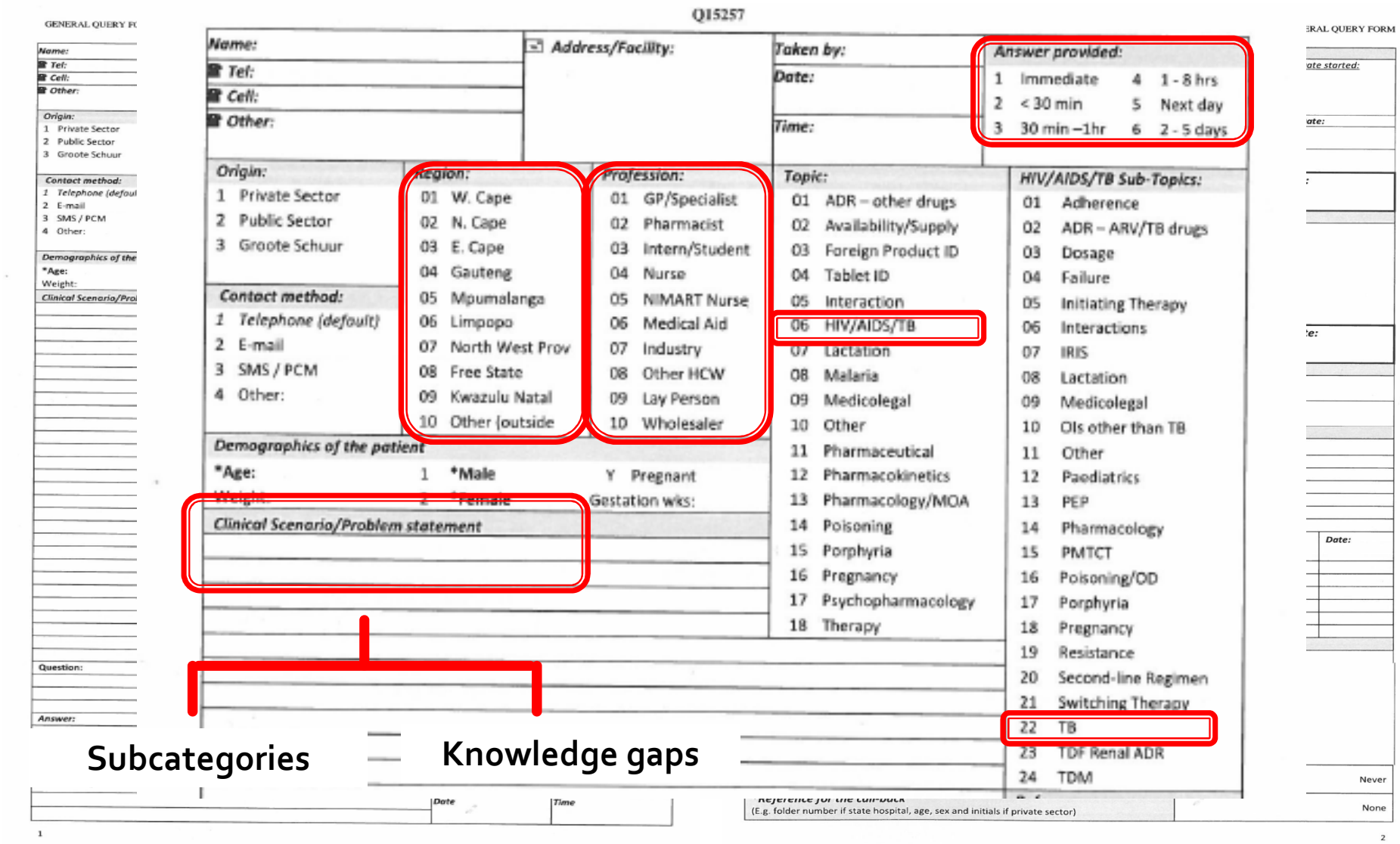
South Africa:

- Highes
- Pr
- Largest number of associat B cases

"Without **proper** treatment, up to two thirds of people ill with TB will die."

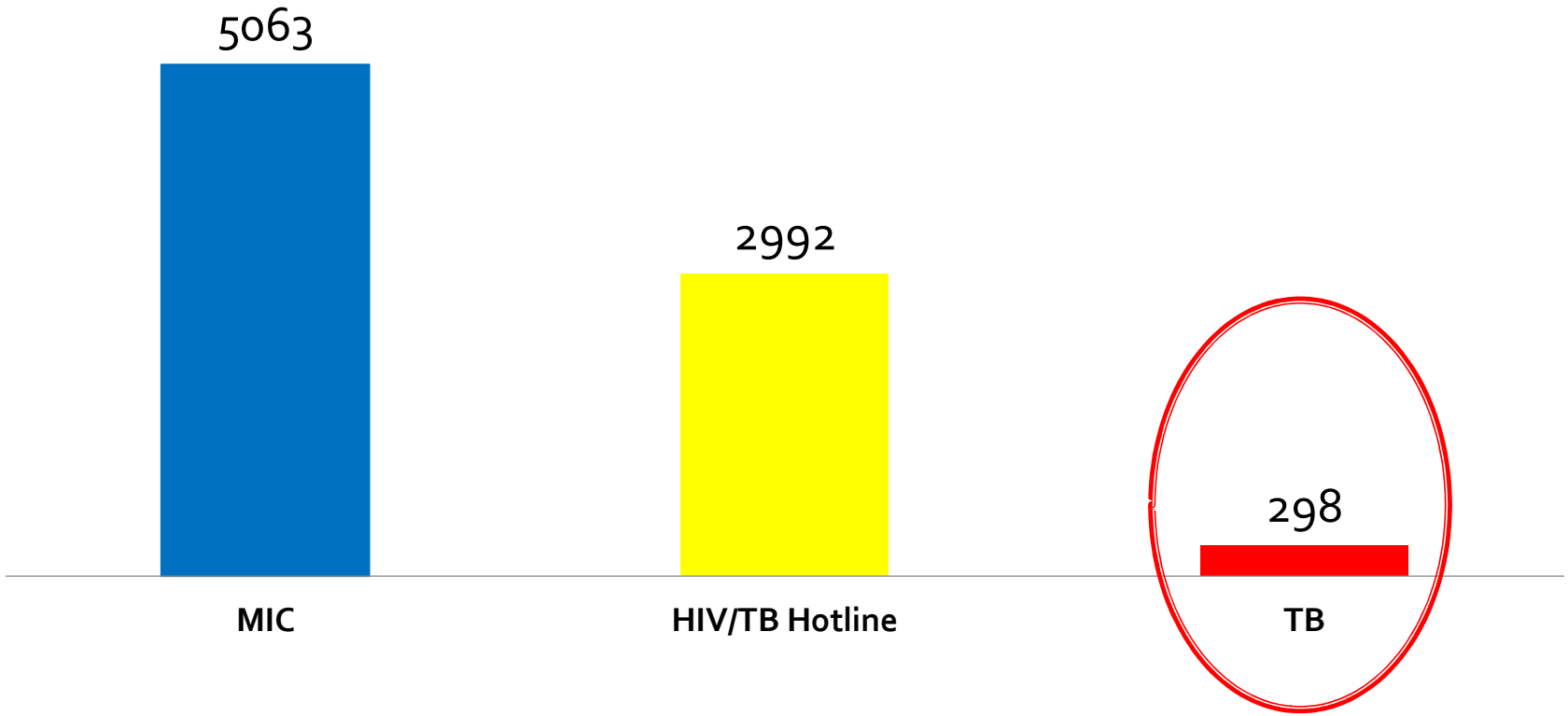
World Health Organization (WHO). Global tuberculosis report 2013. Geneva: WHO; 23 Oct 2013. Available from: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf (Accessed on 4 May 2014)

Methods


Q15257
Name:
Tel:
Cell:
Other:
Address/Facility:
Taken by:
Date:
Time:
Answer provided:
1 Immediate
2 < 30 min
3 30 min –1hr
4 1 - 8 hrs
5 Next day
6 2 - 5 days
Origin:
1 Private Sector
2 Public Sector
3 Groote Schuur
Contact method:
1 Telephone (default)
2 E-mail
3 SMS / PCM
4 Other:
Region:
01 W. Cape
02 N. Cape
03 E. Cape
04 Gauteng
05 Mpumalanga
06 Limpopo
07 North West Prov
08 Free State
09 Kwazulu Natal
10 Other (outside
Profession:
01 GP/Specialist
02 Pharmacist
03 Intern/Student
04 Nurse
05 NIMART Nurse
06 Medical Aid
07 Industry
08 Other HCW
09 Lay Person
10 Wholesaler
Topic:
01 ADR – other drugs
02 Availability/Supply
03 Foreign Product ID
04 Tablet ID
05 Interaction
06 HIV/AIDS/TB
07 Lactation
08 Malaria
09 Medicolegal
10 Other
11 Pharmaceutical
12 Pharmacokinetics
13 Pharmacology/MOA
14 Poisoning
15 Porphyria
16 Pregnancy
17 Psychopharmacology
18 Therapy
HIV/AIDS/TB Sub-Topics:
01 Adherence
02 ADR – ARV/TB drugs
03 Dosage
04 Failure
05 Initiating Therapy
06 Interactions
07 IRIS
08 Lactation
09 Medicolegal
10 OIs other than TB
11 Other
12 Paediatrics
13 PEP
14 Pharmacology
15 PMTCT
16 Poisoning/OD
17 Porphyria
18 Pregnancy
19 Resistance
20 Second-line Regimen
21 Switching Therapy
22 TB
23 TDF Renal ADR
24 TDM
Demographics of the patient
*Age:
1 *Male
Y Pregnant
Gestation wks:
Clinical Scenario/Problem statement
Question:
Answer:
Subcategories
Knowledge gaps
Date
Time
(E.g. folder number if state hospital, age, sex and initials if private sector)
Never
None

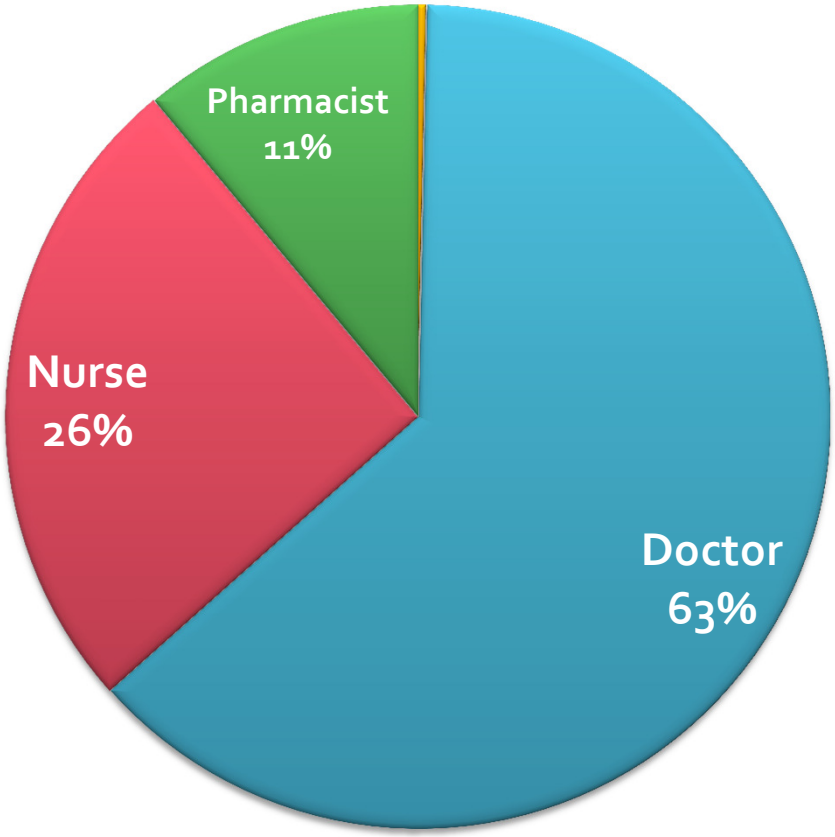
Results

Number of calls – July 2013 to December 2013

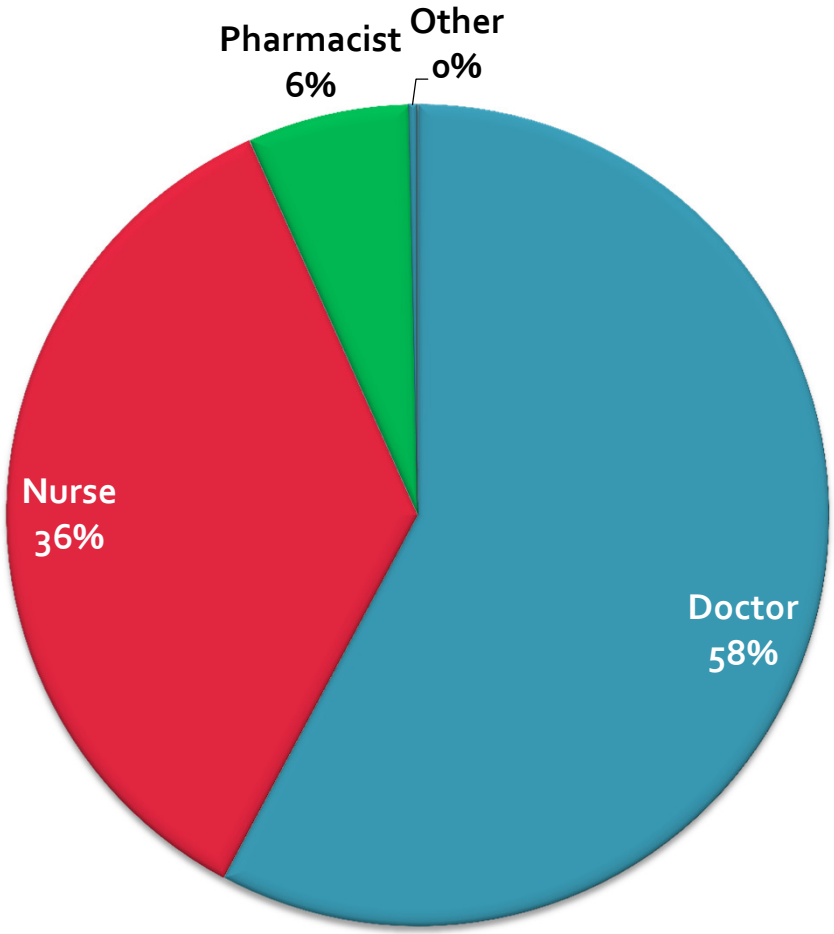


Who phoned us?

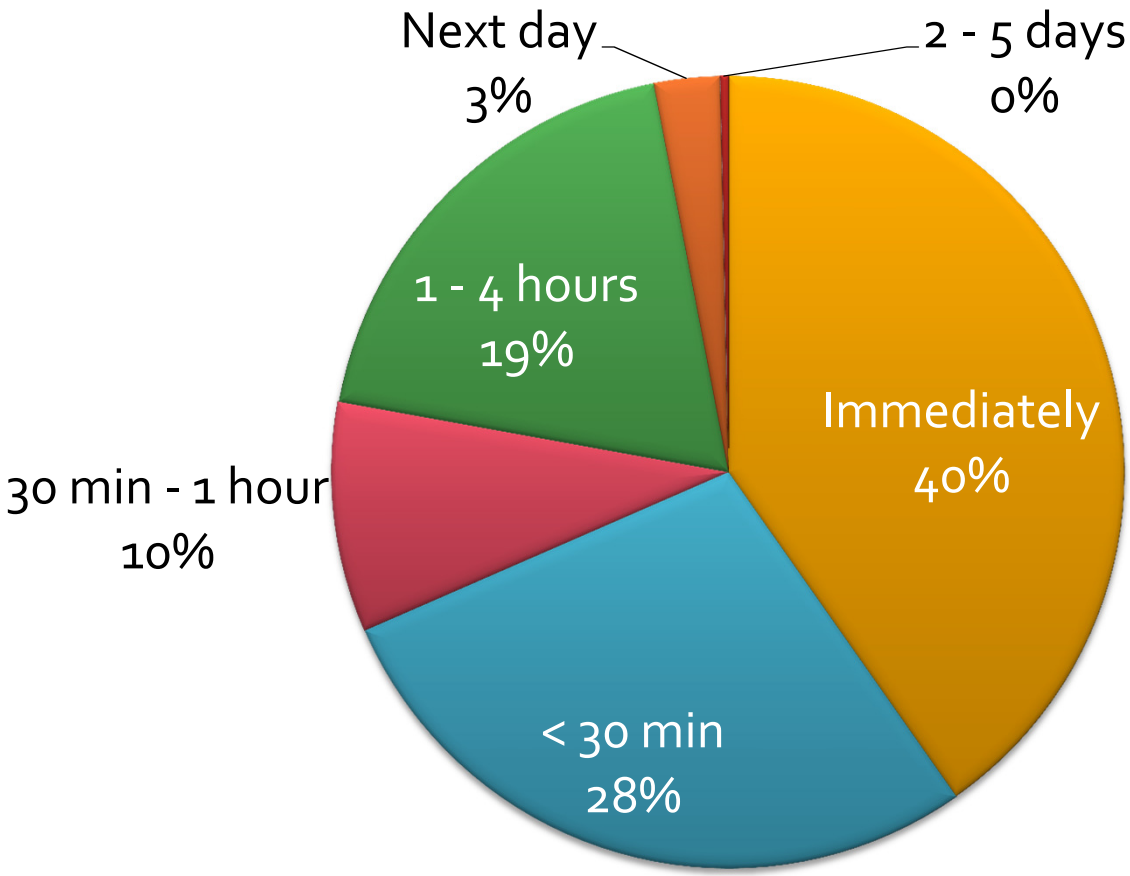
TB Queries
(n = 298)



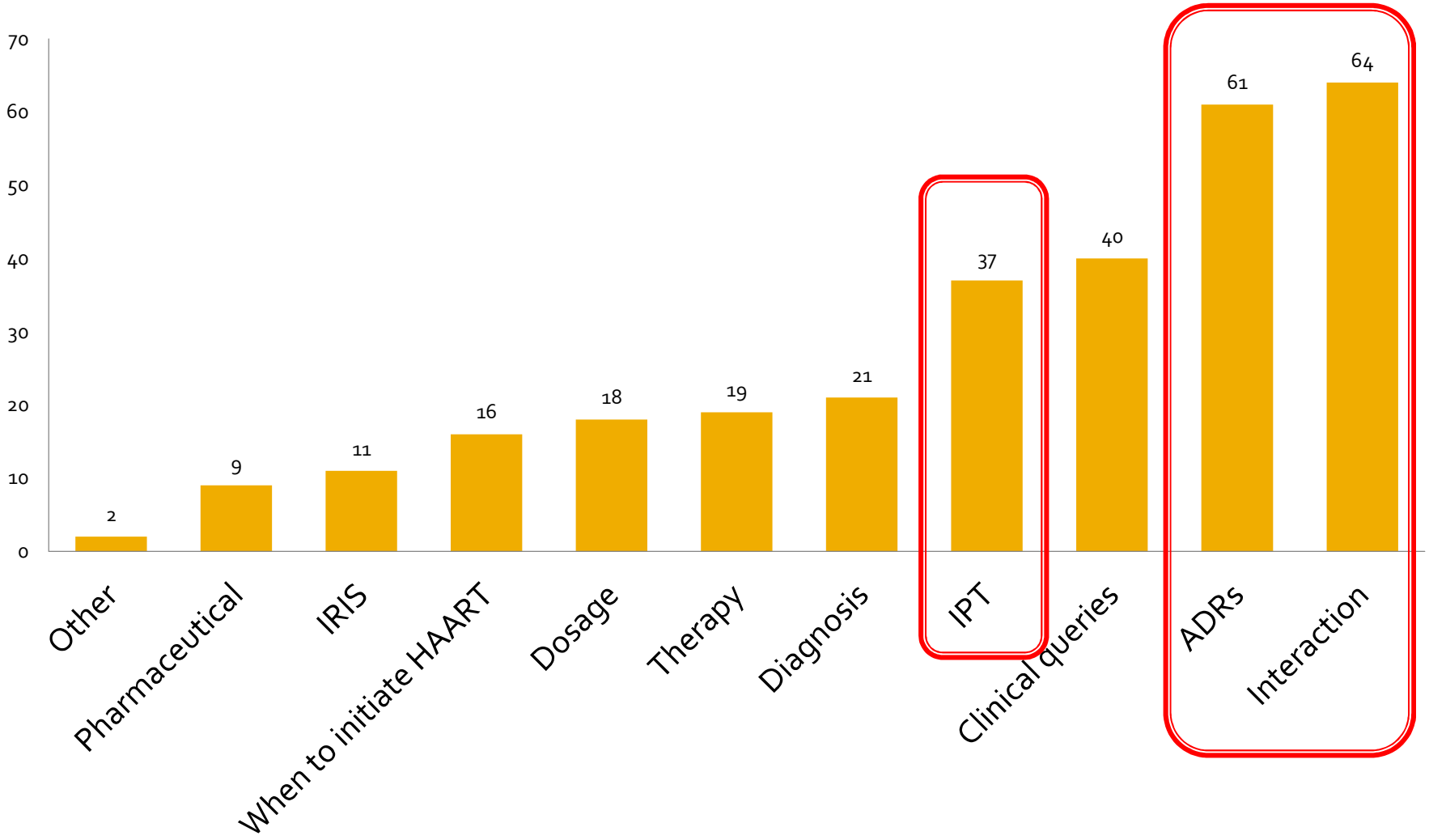
HIV & TB Hotline
(n = 2992)



Time until answer was provided



Subtopics of queries



Knowledge gaps identified

Question	Total	Doctor	Nurse
ARVs initiated before TB diagnosis	5	2	3
How to handle retreatment cases of TB	6	4	1
How to treat disseminated TB	6	4	2
How to treat MDR/XDR TB	6	5	0
Managing IRIS	8	5	1
When to initiate HAART after TB Rx	12	4	7
Diagnosing TB	13	8	4
Dosing of TB drugs	18	13	2
IPT	34	20	12
Managing ADRs	48	33	11
Drug Interactions	58	36	14
Other	84	54	19

Knowledge Gap - IPT

Knowledge Gap	Total	Doctor	Nurse
Would a patient who previously had IPT get it again?	1	1	0
Dosing of IPT in children?	2	0	2
Duration of IPT in children	2	2	0
Should IPT be initiated if there is no Mantoux available?	2	1	1
Do you give IPT in patients who previously had TB?	3	2	1
IPT - Managing ADRs	4	4	
Should IPT be initiated? (Adults)	10	6	4
Should IPT be initiated? (Peads)	10	4	4
Total	**34**	**20**	**12**

Knowledge gap – Managing ADRs

	Total	Doctor	Nurse
Gynaecomastia	1	1	0
Leg cramps	1	0	1
Liver and Cutaneous	1	1	0
Peripheral Neuropathy	2	1	1
Visual disturbances	3	2	1
Gastrointestinal side effects	4	2	2
Renal impairment	4	3	1
Cutaneous reaction	10	8	1
Liver toxicity	22	15	4
Total	**48**	**33**	**11**

ADR – Cutaneous reaction

	Mild reaction	Severe reaction
Systemic symptoms		√
Extensive skin involvement		√
Mucosal involvement		√
Deranged liver funtions		√

Treatment:

Mild reaction

- Anti-histamines
- Skin moisturizing
- Observation

Severe reaction

- Hospitalization
- Specialist

Knowledge gap – Managing ADRs

	Total	Doctor	Nurse
Gynaecomastia	1	1	0
Leg cramps	1	0	1
Liver and Cutaneous	1	1	0
Peripheral Neuropathy	2	1	1
Visual problems	3	2	1
Gastrointestinal side effects	4	2	2
Renal impairment	4	3	1
Cutaneous reaction	10	8	1
Liver toxicity	22	15	
Total	**48**	**33**	

ALT > 200

Western Cape Antimicrobial Guidelines for Tertiary Hospitals, 2013

TB drug hepatotoxicity	TB drug-induced hepatitis is over-diagnosed: the case definition is transaminases more than 5-fold elevated or more than 3-fold elevated with symptoms/jaundice. Antituberculosis therapy should be discontinued. The basis for the TB diagnosis should be reviewed. If the grounds for diagnosing TB were reasonable then commence three antituberculosis drugs with low/no hepatotoxic potential (see background therapy below). Selected patients may then be rechallenged once symptoms of hepatitis have resolved, bilirubin levels return to normal and transaminases have decreased to <100. Rechallenge is NOT recommended for those who have had fulminant hepatitis (defined as hepatic encephalopathy with coagulopathy). The rechallenge regimen of the American Thoracic Society (Am J Respir Crit Care Med 2006;174:935–52) have been followed as these are simple and quick. Rechallenge with PZA was previously not recommended, but a recent trial has shown that most patients tolerate it. PZA rechallenge should be considered in patients with severe TB (e.g. miliary, meningitis) or with drug resistance. ALT should be monitored frequently (e.g. three times weekly) during rechallenge and every two weeks for a month following rechallenge.	
	If possible all patients with a drug induced liver injury should have their TB isolates sent for drug susceptibility testing. Do not rechallenge with an agent to which the isolate is resistant.	
rechallenge regimen:	Background therapy	Ethambutol, amikacin/kanamycin and moxifloxacin
	day 1	Rifampicin 450 or 600 mg daily depending on weight
	day 3	Check ALT
	day 4-6	Add INH 300mg daily
	day 7	Check ALT
	day 8	Consider PZA rechallenge (see text)

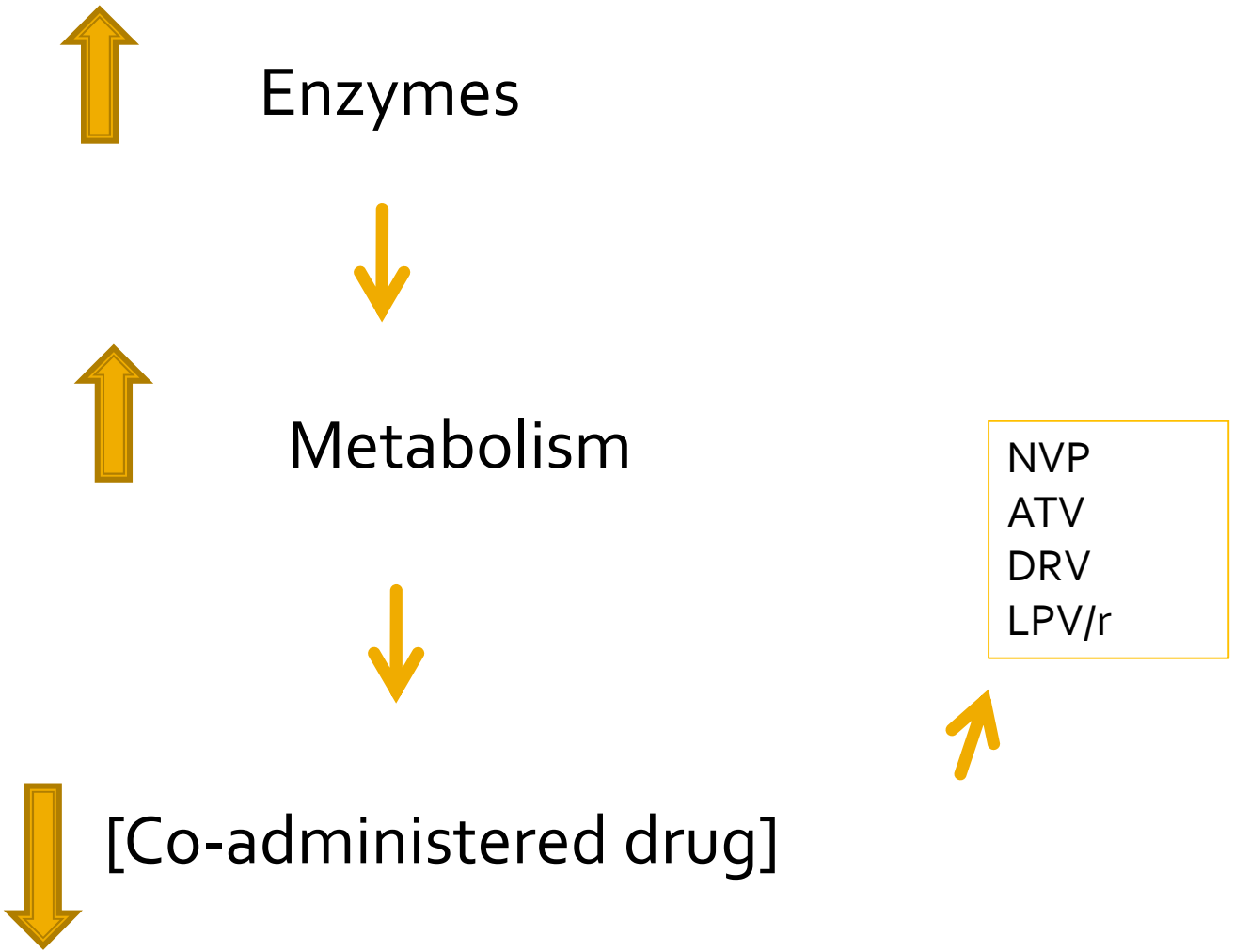
NB: Duration of therapy should be individualised after rechallenge – consult ID for advice. The following are guidelines, which may be modified depending on how far into TB therapy hepatitis occurred:

- Pyrazinamide not rechallenged/not tolerated: stop moxifloxacin and amikacin/kanamycin, continue isoniazid, rifampicin and ethambutol for total duration 9 months
- Rifampicin not tolerated: continue amikacin/kanamycin (for 2 months) and moxifloxacin, isoniazid, and ethambutol for total duration of 18 months
- Isoniazid not tolerated: stop amikacin/kanamycin. Continue moxifloxacin, rifampicin and ethambutol for total duration 12 months
- Rifampicin and isoniazid not tolerated or no rechallenge attempted due to fulminant hepatitis: treat with MDR regimen

Knowledge gap – Drug interactions

	Total	Doctor	Nurse
ATV	3	1	0
NVP	4	4	0
FDC (TDF/FTC/EFV)	5	1	2
Other	6	4	1
TDF and aminoglycoside	7	4	2
Aluvia (Lopinavir/Ritonavir)	33	22	8
Total	**58**	**36**	**14**

Rifampicin



Rifampicin + Aluvia

- Initiate TB treatment
- 1st week: Aluvia 2 bd, Monitor ALT
- 2nd week: Aluvia 3 bd, Monitor ALT
- 3rd week: Aluvia 4 bd, continue until 2 weeks after completing TB treatment

Rifampicin + ATV or DRV

- CONTRAINDICATED!!
- Use: Rifabutin 150 mg on alternate days

Recommendations

Future training needs identified:

- IPT
- ADR
- Drug interactions

Monitoring & Management of Common Adverse Effects of MDR/XDR-TB Treatment

Nausea & Vomiting - Ethionamide, PAS

Management:
Counsel patient regarding the high likelihood of this side effect – awareness of the cause and the probability of the symptoms abating over time may help the patient to tolerate it
1. Take the medication with a non-fatty meal or before going to bed
2. Assess for dehydration and rehydrate if indicated
IF STEP 1 NOT EFFECTIVE:
3. Initiate anti-emetics 30 min prior to administering MDR-TB drugs
IF STEP 3 NOT EFFECTIVE:
4. Administer ethionamide in two (250 mg am and 500 mg nocte) or three separate doses
IF NONE OF ABOVE EFFECTIVE:
6. Lower dose of offending drug agent
AS A LAST RESORT:
7. Discontinue use of offending drug and discuss substitution with an expert

- Nausea and vomiting is common in the early weeks of treatment and usually abates with time on treatment or supportive therapy. Monitor. If no response, investigate for liver toxicity and other causes of vomiting
- Electrolytes should be monitored and replenished if vomiting is severe
- Reversible upon discontinuation of suspected agent

Hearing Loss / Ototoxicity - Streptomycin, Kanamycin, Amikacin, Capreomycin

Monitoring:
Audiometry at baseline, monthly during injectable phase and 3 months after completion of the injectable therapy
Management:
Conduct audiometry and compare with baseline
- Is there significant hearing loss? I.e. 20 db or more increase at one frequency; 10db in at least 2 adjacent frequencies; or complete loss of response at any frequency?
- Is the hearing loss a new change when compared to the baseline or previous audiograms?

If abnormal audiometry screening test, refer to tertiary audiology services if possible for diagnostic testing to determine the type of hearing loss i.e. sensori-neural or conductive
Investigate for other causes of hearing loss (i.e. wax, middle ear infection) and treat appropriately
If significant sensori-neural hearing loss has occurred after commencing ototoxic treatment:
1. Consider reducing the frequency of the drug administration to 3 times per week
2. Discontinue suspected drug if hearing loss continues to deteriorate on repeated screening, and refer patient to expert for advice on how to tailor regimen

- Patients with prior exposure to aminoglycosides may have baseline hearing loss
- Patients may develop hearing loss due to other causes while receiving an injectable
- Aminoglycoside-induced sensori-neural hearing loss is permanent and generally not reversible; it is also usually bilateral and progressive, affecting the higher frequencies first.
- The risk of further hearing loss should be weighed against the risk of stopping the drug in the regimen and potentially compromising the chance of cure
- Patients with pre-existing vestibulo-cochlear impairment should be counselled on the risk of further hearing loss
- Informed consent should be obtained before use in any patient
- Concomitant use of furosemide may exacerbate ototoxic effects of these medications

Peripheral Neuropathy - Terizidone, High dose INH, Linezolid

Monitoring:
Findings occur most commonly in the lower extremities: Sensory disturbances (e.g. numbness, tingling, burning, pain, loss of temperature sensation), difficulty walking, weakness, and decreased or absent deep tendon reflexes
Management:
Always exclude other causes i.e. d4T, HIV
1. Increase pyridoxine dose – usually 50 mg for each 250 mg of terizidone but may need to be higher (200 mg daily) if on other neurotoxic drugs AND
2. Begin exercise regimen, focus on affected regions
IF STEPS 1 AND 2 NOT EFFECTIVE:
3. First check electrolytes if on injectable drug. Initiate therapy with tricyclic antidepressant drugs. Start with 25 mg/day for one week. If no response, the dose may be increased to 75 mg/day.
IF NONE OF ABOVE STEPS EFFECTIVE:
4. Lower dose of suspected drug
AS LAST RESORT:
5. Discontinue suspected drug and discuss substitution with an expert

- Patients with co-morbid disease e.g., diabetes, HIV and alcoholism are more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the offending TB drugs
- It may be possible to re-introduce drug at a later stage at a lower dose if PN pains resolved, especially if drug is essential in regimen

Optic Neuritis / Impaired Vision - Ethambutol, Linezolid

Monitoring:
Do eye test at baseline and when indicated
Use Ishihara colour test for retrobulbar neuritis caused by ethambutol, and standard visual acuity tests for optic neuropathy caused by linezolid
Management:
1. Stop agent
2. Refer patient to ophthalmologist

- Avoid in patients with impaired vision other than due to nearsightedness, farsightedness or old age (needs reading glasses)
- Usually reverses with cessation of the drug
- Not detectable by funduscopy

This service is brought to you as a result of the generous support of the American people through USAID/PEPFAR

Electrolyte Disturbances e.g. hypokalaemia, hypomagnesaemia, hypocalcaemia - Capreomycin (most frequent), Amikacin, Kanamycin, Streptomycin

Monitoring:
Do serum potassium and magnesium at least monthly during injectable phase or in patients with significant GI losses
Management:
Look for other causes of hypokalaemia e.g. diarrhoea, vomiting, diuretics etc.
1. Treat associated vomiting or diarrhoea
2. Control hypoglycaemia – this causes a rise in insulin which then pushes potassium into the cells and leads to low serum potassium
3. Replenish potassium po or IV e.g. oral Slow K 2 tabs BD when $K^+ < 3.5$. Oral potassium supplements are relatively well tolerated (do cause some GI effects), are absorbed readily and can be given in fairly high doses safely (therefore more appropriate in outpatient setting). IV supplementation can irritate the veins and is less well tolerated. Smaller doses need to be given, and in an inpatient setting
4. Check magnesium levels if potassium levels do not improve as refractory hypokalaemia may be due to low magnesium levels. Occasionally, extracellular magnesium levels on blood monitoring may still appear to be normal even in the presence of intracellular hypomagnesaemia, and so it may be worth supplementing magnesium anyway if there is persistent refractory hypokalaemia which is not responding to potassium supplementation. If Mg^{2+} <0.6, supplement with oral Slow Mag (2 – 4 tabs BD), or if <0.4 may consider IM $MgSO_4$ every 4-6 hours. If levels get this low, patient may need admission to inpatient facility to correct electrolyte levels
5. Discontinue arrhythmogenic drugs e.g. digoxin, amytriptyline, cisapride, and haloperidol, if patient is taking them.
Discontinue other drugs which may cause electrolyte depletion if possible e.g. salbutamol, diuretics (change to potassium sparing diuretics)
6. Discontinue aminoglycosides if condition is severe i.e. if patient is symptomatic or has seizures and discuss patient with expert

- Although sometimes asymptomatic, may present with fatigue, myalgias, cramps, paresthesias, lower extremity weakness, behaviour or mood changes, somnolence and confusion
- More severe disturbances can lead to tetany, paralysis and life-threatening cardiac arrhythmias
- Amiloride 5-10 mg qid or spironolactone 25 mg qid may decrease the potassium and magnesium wasting and is useful in refractory cases
- Is reversible once the injectable is suspended
- Commonly associated with GI disturbances

Renal Toxicity - Capreomycin, Kanamycin, Amikacin, Streptomycin

Monitoring:
Do serum creatinine at baseline and monthly during injectable phase and use these values to estimate the creatinine clearance, which indicates degree of renal function/dysfunction. Various formulae can be used. Below find the simplified formula recommended by the South African Renal Society:

$$\frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine (}\mu\text{mol/L)}}$$

For females multiply by 0.85

Management:
Consider other causes of renal impairment and other nephrotoxic drugs
1. If creatinine clearance (GFR) < 30, stop likely offending agent(s) and consult hospital or hotline for further advice. If GFR 30 – 60, reduce doses of renally cleared drugs and monitor clearance closely (e.g. 1 – 2 times a week). If worsening, may need to withdraw injectable, but if stable on reduced dose, could continue with weekly monitoring
2. Consider use of capreomycin if patient was on aminoglycoside and if injectable cannot be avoided i.e. if regimen is compromised by too few effective drugs and no others available

- History of diabetes or renal disease is not a contraindication to the use of the offending TB drugs, although patients with co-morbidities may be at increased risk for developing renal failure
- Renal impairment may be permanent
- Symptomatic cases may present with any of the following: oliguria or anuria, edema, shortness of breath or uremic symptoms such as mental status changes
- Avoid other nephrotoxic drugs, e.g. tenofovir

Arthralgia / Arthritis / Osteo-articular Pain - Pyrazinamide, Fluoroquinolones

Management:
1. Initiate therapy with non-steroidal anti-inflammatory drugs
2. Initiate physiotherapy where necessary
IF STEPS 1 AND 2 NOT EFFECTIVE:
3. Lower dose of offending drug, if this will not compromise the regimen. Consider intermittent administration of pyrazinamide
AS LAST RESORT:
4. Discontinue offending drug and discuss substitution with expert

- Symptoms of arthralgia/ arthritis generally diminish over time, even without intervention
- Uric acid levels may be elevated in some patients but are of little therapeutic relevance
- Anti-gout treatment e.g. allopurinol, colchicine does not correct the uric acid levels in these cases

Depression - Terizidone

Management:
1. Rule out side effects of concomitant medications or drug or alcohol dependence or hypothyroidism
2. Refer to psychologist or psychiatrist for assessment and treatment

- Importance of personal socioeconomic conditions and confinement to hospital should not be underestimated as contributing factor to depression
- Depression and depressive symptoms may fluctuate during treatment
- History of prior depression is not a contraindication to the use of the offending TB drugs; however, these patients may be at increased risk for developing depression during MDR-TB treatment
- The need to discontinue an anti-TB agent due to refractory depression is extremely rare

PLEASE NOTE:
When we state lower the dose, it seems to the appropriate mg/kg
One of the principles of DR-TB drug management is to try and keep at least 4 likely effective drugs in the regimen (one of them an injectable for at least the first 6 months) if possible

Skin Reactions - Could be several agents

Treatment can be continued if rash is mild, but should be stopped for a severe reaction e.g. blistering, mucosal involvement, fever, and patient referred to hospital for re-introduction

- Frequent in patients with HIV infection
- True allergic reactions are uncommon

Liver Toxicity / Hepatitis - Pyrazinamide, Ethionamide, PAS, INH, Fluoroquinolones

Monitoring:
Screen with ALT every 3 months, and if abnormal, do full LFT
Management:
1. If ALT/AST > 5 times the upper limit of normal or more than 3-fold elevated with symptoms or patient is jaundiced, stop all medicines and consult specialist. If patient is unwell, stop treatment, refer to hospital and re-introduce agents as inpatient
2. Rule out other potential causes of hepatitis, such as viral hepatitis, CMV, alcohol use, other medications
3. After resolution, monitor liver function every 1-2 months

- History of prior hepatitis should be carefully analysed to determine the most likely causative drug(s), these should be avoided in future regimens
- Generally reversible upon discontinuation of offending drug
- Hepatitis is characterized by nausea, vomiting, jaundice, sclera yellow, tea-colored urine, pale stool and diminished appetite
- Tuberculosis itself may cause hepatitis
- Mild transient raised serum ALT may be observed in the first months of therapy
- Clinically significant hepatitis is almost invariably symptomatic and the diagnosis is confirmed by an elevation in serum transaminases (ALT/AST) or direct bilirubin greater than 5 times normal

Seizures - Terizidone, Fluoroquinolones, High dose INH

Management:
1. Rule out other likely causes e.g. electrolyte disturbances, sub-therapeutic levels of current antiepileptics
2. Treat any suspected causes or adjust doses of current antiepileptics. May need to stop terizidone in patients on antiepileptics who experience an increase in seizures
3. Refer patient to hospital to initiate anticonvulsant treatment if not a known epileptic. Only valproic acid/ lamotrigine can be used in patients on ARVs. Monitor levels as drug interactions are common
4. Increase pyridoxine to 200 mg daily

- Clinical evaluation is generally sufficient unless there is high suspicion of infectious, malignant, vascular or metabolic cause
- Anticonvulsant must be continued until MDR-TB treatment completed or suspected agent discontinued
- History of prior seizure disorder is not a contraindication for the use of the offending TB drugs if the patient's seizures are well-controlled and/ or the patient is receiving anticonvulsant treatment
- Patients with history of prior seizures may be at increased risk for development of seizures during MDR-TB treatment

Psychosis - Terizidone, High dose INH, Fluoroquinolones, Ethionamide

Management:
1. Refer to a psychiatrist for assessment or phone the hotline for assistance
2. Discontinue suspected agent for short period of time (1-4 weeks) while psychotic symptoms are brought under control

- Some patients will need to continue antipsychotic treatment throughout MDR-TB treatment
- Prior history of psychiatric disease is not a contraindication to the use of the offending TB drugs, but may increase the likelihood of development of psychotic symptoms
- Psychotic symptoms are generally reversible upon MDR-TB treatment completion or discontinuation of the offending agent

Hypothyroidism - PAS, Ethionamide

Monitoring:
Do thyroid stimulating hormone (TSH) at baseline and then ideally, once between months 6 and 9 of treatment, if receiving ethionamide and / or PAS. Monitor monthly for signs/symptoms of hypothyroidism e.g. fatigue, somnolence, cold intolerance, dry skin, coarse hair, constipation as well as depression and psychosis
Management:
1. Exclude other causes, including iodine deficiency, medications e.g. lithium, amiodarone, previous radioiodine therapy, pregnancy-associated thyroid dysfunction, and Hashimoto's disease
2. Initiate thyroxine if TSH > 10 IU/mL. Start with 50 mcg OD and repeat TSH in one month. If still >10, increase dose by another 50 mcg and repeat again in one month. Continue until TSH levels controlled below 10

- Completely reversible upon discontinuation of offending drug
- The use of PAS and ethionamide in combination is more frequently associated with hypothyroidism than their individual use

Need Help?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 / 021 406 6782

Alternatively send an SMS or "Please Call Me" to 071 840 1572

www.hivhotline.uct.ac.za

Suspect an adverse drug reaction in a TB/HIV patient?
For advice and/or to report phone 080 1111 452 toll free.

	Interaction	Management
Zidovudine	No interaction reported.	No dosage adjustment required.
Propafenone		
Abacavir	No interaction reported.	No dosage adjustment required.
Didanosine	No interaction reported.	No dosage adjustment required.
Efavirenz	Efavirenz theoretically can increase or decrease propafenone levels.	Closely monitor response and adjust dose accordingly.
Lamivudine/Emtricitabine	No interaction found.	No dosage adjustment required.
Lopinavir/Atazanavir+ritonavir	Propafenone levels may be increased. In addition, propafenone may increase ritonavir levels.	Do not coadminister.
Nevirapine	Theoretically nevirapine may lower propafenone levels via enzyme induction.	Monitor response and increase dose of propafenone if required.
Ritonavir	Propafenone levels may be increased. In addition, propafenone may increase ritonavir levels.	Do not coadminister.
Stavudine	No interaction reported.	No dosage adjustment required.
Tenofovir	No interaction reported.	No dosage adjustment required.
Zidovudine	No interaction reported.	No dosage adjustment required.
Propranolol		
Abacavir	No interaction reported.	No dosage adjustment required.
Didanosine	No interaction reported.	No dosage adjustment required.
Efavirenz	No interaction reported.	No dosage adjustment required.
Lamivudine/Emtricitabine	No interaction reported.	No dosage adjustment required.
Lopinavir/Atazanavir+ritonavir	Ritonavir may increase propranolol levels. Potential for additive PR prolongation.	Clinical monitoring recommended.
Nevirapine	No interaction reported.	No dosage adjustment required.
Ritonavir	Ritonavir may increase propranolol levels. Potential for additive PR prolongation.	Clinical monitoring recommended.
Stavudine	No interaction reported.	No dosage adjustment required.
Tenofovir	No interaction reported.	No dosage adjustment required.
Zidovudine	No interaction reported.	No dosage adjustment required.
Pyrazinamide		
Abacavir	No interaction reported.	No dosage adjustment required.
Didanosine	No interaction reported.	No dosage adjustment required.
Efavirenz	No clinically significant interaction.	No dosage adjustment required.
Lamivudine/Emtricitabine	No interaction reported.	No dosage adjustment required.
Lopinavir/Atazanavir+ritonavir	No interaction reported.	No dosage adjustment required.
Nevirapine	No clinically significant interaction.	No dosage adjustment required.
Ritonavir	No clinically significant interaction.	No dosage adjustment required.
Stavudine	No interaction reported.	No dosage adjustment required.
Tenofovir	No interaction reported.	No dosage adjustment required.

	Interaction	Management
Zidovudine	Limited evidence suggests that zidovudine may lower pyrazinamide levels.	Clinical significance unknown.
Pyridoxine		
	No interaction reported.	No dosage adjustment required.
Quetiapine		
Abacavir	No interaction reported.	No dosage adjustment required.
Didanosine	No interaction reported.	No dosage adjustment required.
Efavirenz	Possible increase or decrease in quetiapine levels.	Monitor response and toxicity.
Lamivudine/Emtricitabine	No interaction reported.	No dosage adjustment required.
Lopinavir/Atazanavir+ritonavir	Theoretically quetiapine levels may be raised due to inhibition of CYP3A4-mediated quetiapine metabolism by protease inhibitors. Serious quetiapine adverse effects have been reported.	Use with caution and reduce quetiapine dosage.
Nevirapine	Possible decrease in quetiapine levels.	Monitor response.
Ritonavir	Theoretically quetiapine levels may be raised due to inhibition of CYP3A4-mediated quetiapine metabolism by protease inhibitors. Serious quetiapine adverse effects have been reported.	Use with caution and reduce quetiapine dosage.
Stavudine	No interaction reported.	No dosage adjustment required.
Tenofovir	No interaction reported.	No dosage adjustment required.
Zidovudine	No interaction reported.	No dosage adjustment required.
Quinapril		
	No interaction reported.	No dosage adjustment required.
Quinidine		
Abacavir	No interaction reported.	No dosage adjustment required.
Didanosine	No interaction reported.	No dosage adjustment required.
Efavirenz	Theoretically efavirenz can increase or decrease quinidine levels.	Monitor response.
Lamivudine/Emtricitabine	No interaction reported.	No dosage adjustment required.
Lopinavir/Atazanavir+ritonavir	Coadministration may result in increased quinidine levels and an increase of the associated cardiac adverse effects.	Caution is warranted and therapeutic concentration monitoring is recommended when available.
Nevirapine	Theoretically nevirapine can lower quinidine levels.	Monitor response.
Ritonavir	Effects of quinidine may be substantially increased.	Do not coadminister.
Stavudine	No interaction reported.	No dosage adjustment required.
Tenofovir	No interaction reported.	No dosage adjustment required.
Zidovudine	No interaction reported.	No dosage adjustment required.
Quinine		
Abacavir	No interaction reported.	No dosage adjustment required.

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