Special considerations in treating susceptible PTB and EPTB

Dr Kogie Naidoo - MBChB, PhD

Head: CAPRISA Treatment Research Programme
Honorary Lecturer - UKZN Department of Public Heath Medicine

Presentation Outline

- TB Disease Burden ≈ TB Morbidity and Mortality

- TB diagnostics in PTB and EPTB

- Clinical scenarios:
  - Treatment Interruption
  - DILI
  - Renal Impairment/Failure
  - SKIN ADR
  - TB-HIV coinfection
  - TB Prevention

2016 WHO Report - TB among Top 10 causes of Death Globally

With an estimated 480 000 new cases of MDR-TB and an additional 100 000 with rifampicin RR-TB

10.4 million people **FELL ILL FROM TB**

That's 28,500 people every day

1.8 million people **DIED FROM TB**

including 400,000 **WITH HIV + TB**

**60% of TB cases** worldwide occurred in just **SIX COUNTRIES**

CHINA   INDIA   INDONESIA   NIGERIA   PAKISTAN   SOUTH AFRICA

SOURCE: WHO GLOBAL TB REPORT 2016

Tuberculosis in SA

Estimates of TB burden,[a] 2015

	Number (thousands)	Rate (per 100 000 population)
Mortality (excludes HIV+TB)	25 (21–29)	46 (39–53)
Mortality (HIV+TB only)	73 (27–140)	133 (50–256)
Incidence (includes HIV+TB)	454 (294–649)	834 (539–1 190)
Incidence (HIV+TB only)	258 (165–370)	473 (303–680)
Incidence (MDR/RR-TB)[b]	20 (13–27)	37 (24–50)

Incidence (Rate per 100 000 population per year)

Legend: Notified (new and relapse) — Incidence — Incidence (HIV + TB only)
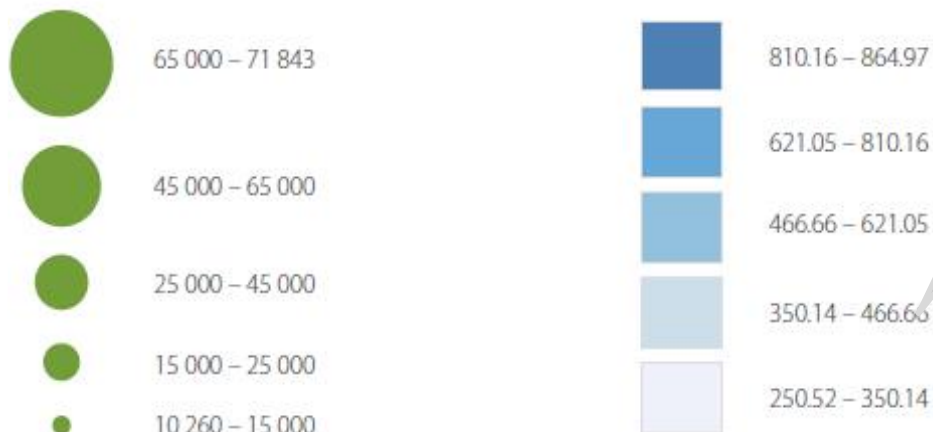
DS TB Incidence and Burden in SA (2015)
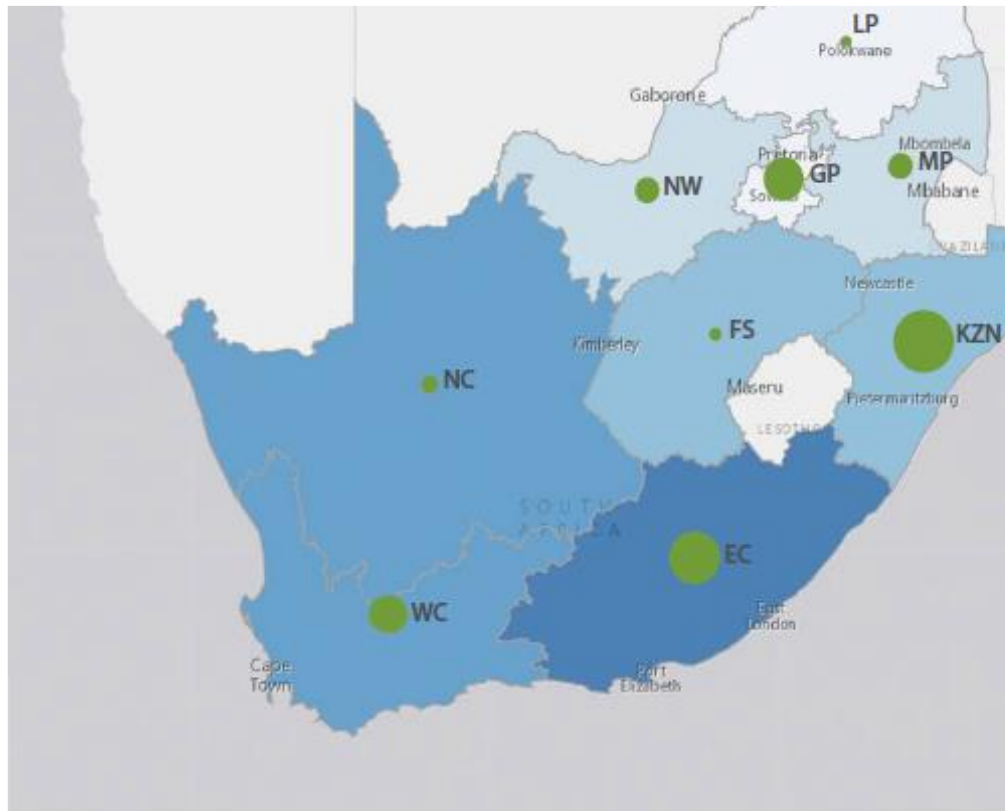
- EC, WC, KZN and Gauteng account for 74% of total case load
- TB Incidence reduction of 37% between 2011-2014 – showing sharpest decline nationally

Source: NICD 2017

TB Remains the No. 1 cause of death in SA

STATS SA
STATISTICS SOUTH AFRICA

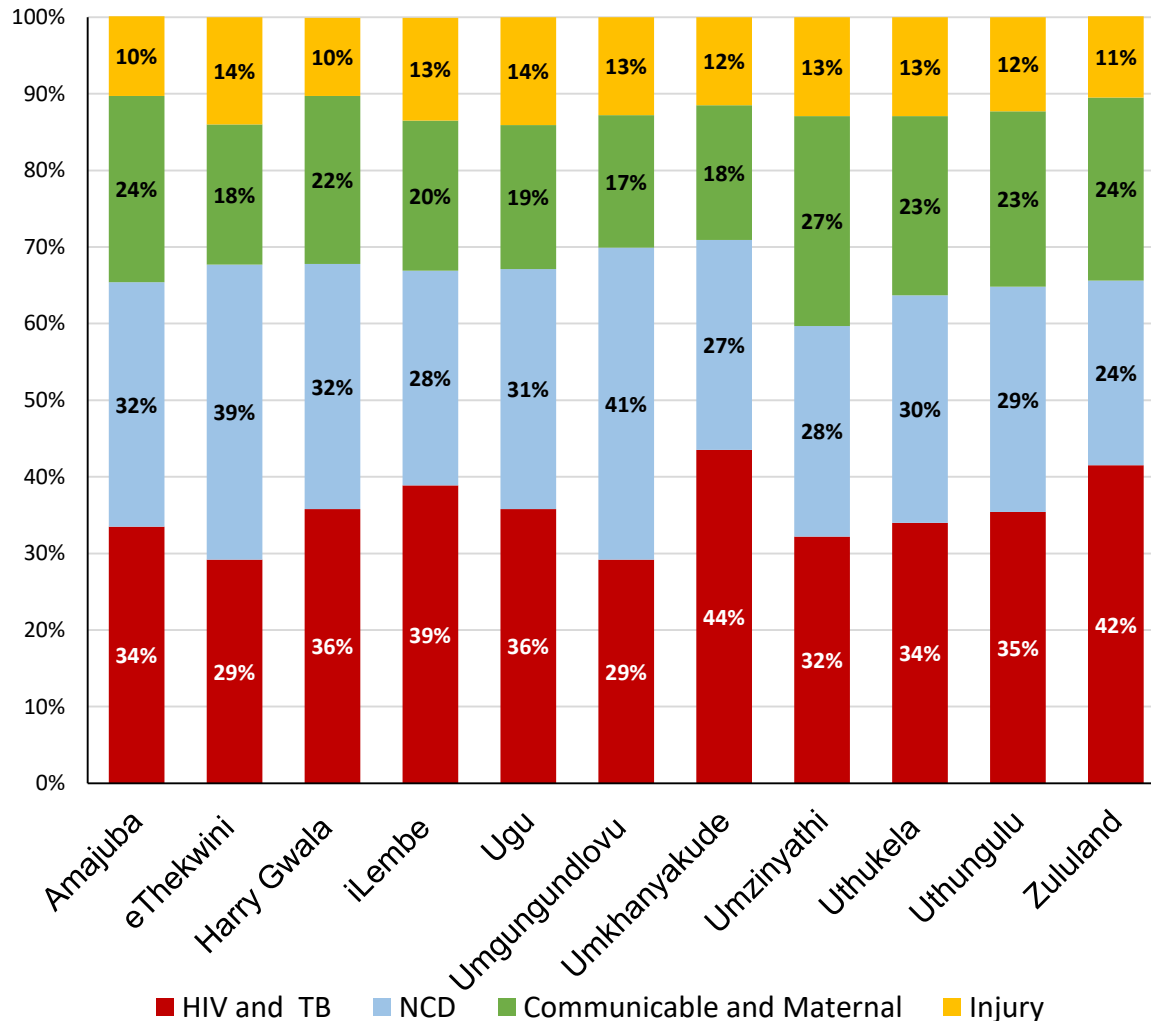| Causes of death (based on ICD-10)	2013			2014			2015		
	Rank	Number	%	Rank	Number	%	Rank	Number	%
Tuberculosis (A15-A19)**	1	41 904	8,8	1	39 495	8,3	1	33 063	7,2
Diabetes mellitus (E10-E14)	5	23 133	4,9	3	23 966	5,0	2	25 070	5,4
Cerebrovascular diseases (I60-I69)	4	23 158	4,9	2	24 131	5,1	3	22 879	5,0
Other forms of heart disease (I30-I52)	6	22 189	4,7	4	22 928	4,8	4	22 215	4,8
Human immunodeficiency virus [HIV] disease (B20-B24)	3	23 825	5,0	6	22 729	4,8	5	21 926	4,8
Influenza and pneumonia (J09-J18)	2	24 345	5,1	5	22 813	4,8	6	20 570	4,5
Hypertensive diseases (I10-I15)	7	17 104	3,6	7	18 319	3,9	7	19 443	4,2
Other viral diseases (B25-B34)	9	14 101	3,0	9	14 508	3,1	8	16 097	3,5
Chronic lower respiratory diseases (J40-J47)	10	12 384	2,6	10	12 690	2,7	9	12 667	2,8
Ischaemic heart diseases (I20-I25)							10	12 239	2,7
Intestinal infectious diseases (A00-A09)	8	16 163	3,4	8	14 795	3,1			
Other natural causes		207 523	43,6		207 593	43,7		202 840	44,1
Non-natural causes		49 681	10,4		50 692	10,7		51 227	11,1
All causes		475 510	100,0		474 659	100,0		460 236	100,0

*Data from 2013–2014 have been updated with late registrations/delayed death notification forms processed in 2015/2016.
** Including deaths due to *MDR-TB* and *XDR-TB*.

Mortality and causes of death in South Africa, 2015: Findings from death notification, released 28 February 2017

Understanding the problem: Health priorities in KZN
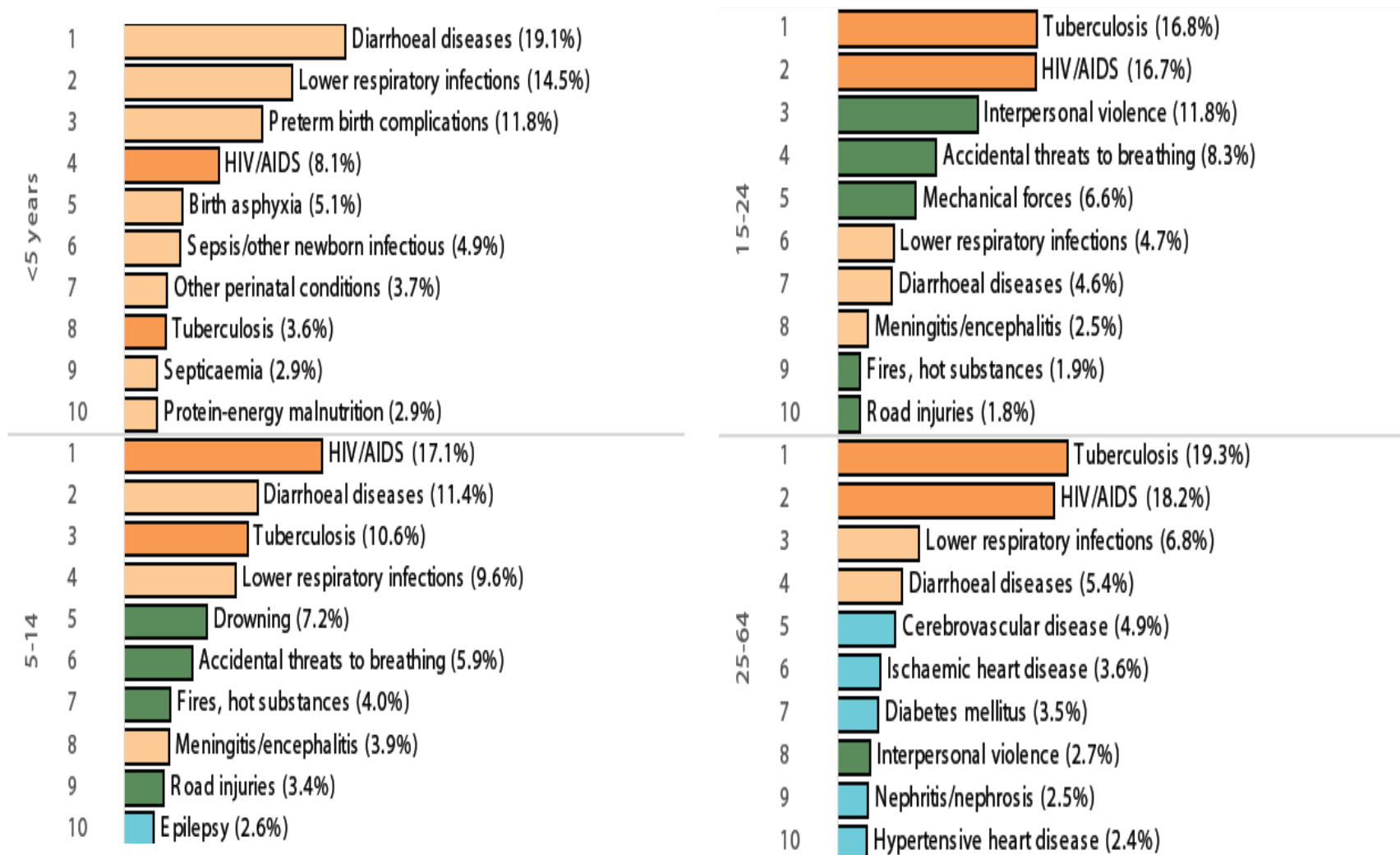## Leading causes of death by district in KZN

Chart — Leading causes of death by district in KZN (percentage, stacked bar)

District	HIV and TB	NCD	Communicable and Maternal	Injury
Amajuba	34%	32%	24%	10%
eThekwini	29%	39%	18%	14%
Harry Gwala	36%	32%	22%	10%
iLembe	39%	28%	20%	13%
Ugu	36%	31%	19%	14%
Umgungundlovu	29%	41%	17%	13%
Umkhanyakude	44%	27%	18%	12%
Umzinyathi	32%	28%	27%	13%
Uthukela	34%	30%	23%	13%
Uthungulu	35%	29%	23%	12%
Zululand	42%	24%	24%	11%

Legend: ■ HIV and TB ■ NCD ■ Communicable and Maternal ■ Injury

- TB leading underlying cause of death in 29 of the 52 districts in South Africa[1]

- 8 of 11 districts in KwaZulu-Natal were among the highest affected districts[1]

Understanding the problem:
Leading causes of death in one district by age

<5 years
1. Diarrhoeal diseases (19.1%)
2. Lower respiratory infections (14.5%)
3. Preterm birth complications (11.8%)
4. HIV/AIDS (8.1%)
5. Birth asphyxia (5.1%)
6. Sepsis/other newborn infectious (4.9%)
7. Other perinatal conditions (3.7%)
8. Tuberculosis (3.6%)
9. Septicaemia (2.9%)
10. Protein-energy malnutrition (2.9%)

15-24
1. Tuberculosis (16.8%)
2. HIV/AIDS (16.7%)
3. Interpersonal violence (11.8%)
4. Accidental threats to breathing (8.3%)
5. Mechanical forces (6.6%)
6. Lower respiratory infections (4.7%)
7. Diarrhoeal diseases (4.6%)
8. Meningitis/encephalitis (2.5%)
9. Fires, hot substances (1.9%)
10. Road injuries (1.8%)

5-14
1. HIV/AIDS (17.1%)
2. Diarrhoeal diseases (11.4%)
3. Tuberculosis (10.6%)
4. Lower respiratory infections (9.6%)
5. Drowning (7.2%)
6. Accidental threats to breathing (5.9%)
7. Fires, hot substances (4.0%)
8. Meningitis/encephalitis (3.9%)
9. Road injuries (3.4%)
10. Epilepsy (2.6%)

25-64
1. Tuberculosis (19.3%)
2. HIV/AIDS (18.2%)
3. Lower respiratory infections (6.8%)
4. Diarrhoeal diseases (5.4%)
5. Cerebrovascular disease (4.9%)
6. Ischaemic heart disease (3.6%)
7. Diabetes mellitus (3.5%)
8. Interpersonal violence (2.7%)
9. Nephritis/nephrosis (2.5%)
10. Hypertensive heart disease (2.4%)

Meta-analysis of Sensitivity & Specificity of Xpert MTB/RIF in Pulmonary TB

- Meta-analysis of 27 unique studies with 9,558 participants
  - Initial diagnostic test replacing AFB smear: Pooled sensitivity 88%; specificity 99%
  - Add-on test following negative AFB smear: Pooled sensitivity 68%; specificity 99%
  - Detecting true RIF resistance: pooled sensitivity 95%; specificity 98%

Parameter	Pooled Sensitivity	95% CrI
Smear (+)/Culture (+)	98%	97-99%
Smear (-)/Culture (+)	68%	61-74%
HIV (+)	79%	70-86%
HIV (-)	86%	76-92%

WHO Xpert MTB/RIF Policy Update-2014

Meta-analysis of Sensitivity & Specificity of Xpert MTB/RIF in Extrapulmonary TB

Specimen Type	Median Pooled Sensitivity (95% CrI)	Median Pooled Specificity (95% CrI)
Lymph Node Bx/Asp	84.9% (72-92)	92.5% (80-97)
CSF	79.5% (62-90)	98.6% (96-100)
Pleural Fluid	43.7% (25-65)	98.1% (95-99)
Gastric Lavage/Asp	83.8% (66-93)	98.1% (92-100)
Other tissue	81.2% (68-90)	98.1% (87-100)

WHO Xpert MTB/RIF Policy Update-2014

Urine Lipoarabinomannin (LAM) in HIV-Infected Patients

- Meta-analysis of LAM studies (Flores LL, et al. Clin Vaccine Immunol 2011; 18:1616-27; Lawn S, et al. AIDS 2009; Shah M, et al. JAIDS 2009; Nakiyingi L et al JAIDS 2014)

    – Pooled sensitivity 47% in HIV(+) vs. 14% in HIV(-); specificity 96%-97%

    – Highest sensitivity in those with CD4 < 50 (67%-85%)

- Urine LAM + sputum smear microscopy → sensitivity 53.7% overall and 67.9% in persons with CD4 $\leq$ 100

    – In HIV-infected patients & CD4 $\leq$ 100, urine LAM may detect with accuracy more than half of those with TB in < 30 min

Clinical Presentation of TB

CNS
-Headache
-Subacute meningism
-Confusion
-Drowsiness
-Coma
-Focal neurological deficits

General
-Weight loss
-Malaise
-Fever
-Night sweats
-Lymphadenopathy
-Erythema nodosum
-Abscess formation

Skeletal
-Bone pain (spine most common)
-Stiffness
-Pathological fractures/collapse

Pulmonary
- Cough
- Haemoptysis
- Chest pain

Cardiovascular
-Pericarditis

Gastrointestinal
-Abdominal pain
-Diarrhoea
-Malabsorption
-Ulcers
-Localising symptoms e.g. dysphagia, haematochezia
-Anorexia
-GI obstruction

Genitourinary
-Dysuria
-Pyuria (with negative cultures)
-Loin pain
-Epididymitis
-Salpingitis
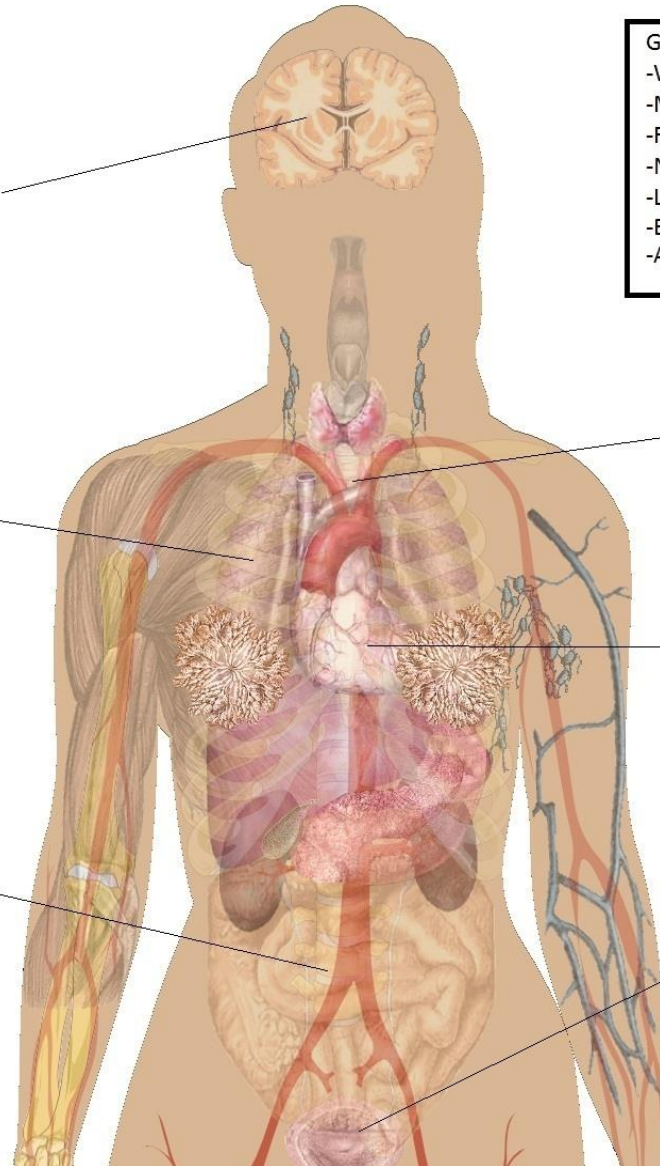
Clinical and Lab diagnosis of Extrapulmonary TB

Clinical Diagnosis

- High index of suspicion

- Risk stratify each patient

- Definitive microbiological diagnosis not always possible

Laboratory Diagnosis: unique diagnostic approach by site

- Lymph Node Biopsy / Aspirate (97% yield - TB adenitis)

- CSF/ Blood culture

- Liver Biopsy - (20-60% yield)

- Peritoneal/Pleural Fluid ADA – Sensitivity and specificity → 90%

- Bone Marrow Aspirates

- Biopsy with histology, cytology and culture

TB Diagnostics in Pleural TB

- Paucibacilliary form of TB
- Gold standard: demonstration of TB in pleural fluid
- Pleural fluid ADA levels over 40U/L with > 50% lymphocyte proportion suggest pleural TB
- Sensitivity 90.7% , Specificity of 97.7%→ justifies treatment initiation in high TB burden settings
- False negative: early disease, elderly and smokers
- False positive:bacterial empyema, lung cancer, parapneumonic effusions, haematologic malignancies
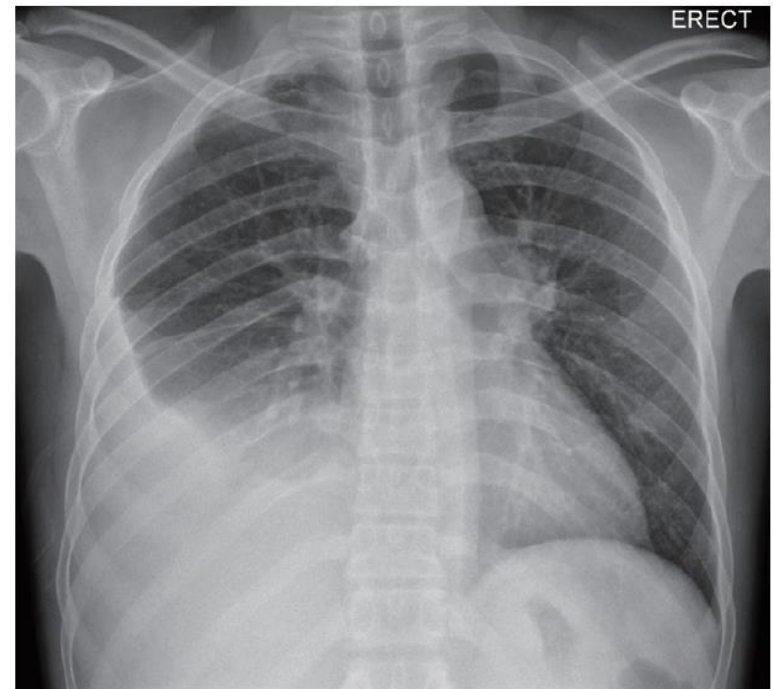
- Pericardial and abdominal ultrasonography valuable and cost effective supplementary investigations in diagnosing EPTB or disseminated TB

- Role of US in diagnosing EPTB/pericardial TB

Table II. Abdominal ultrasound findings

Ultrasound findings	Active TB by smear or culture				
	OR	95% CI	p-value	Frequency	
Lymphadenopathy	2.63 ←	1.51 - 4.60	0.0002	55.3%	(94/170)
Hepatomegaly	0.63	0.34 - 1.19	0.128	18.8%	(32/170)
Splenomegaly	1.65	0.66 - 4.24	0.242	12.9%	(22/170)
Splenic lesions	1.89	1.04 - 3.46	0.024	37.1%	(63/170)
Ascites	2.24 ←	1.22 - 4.15	0.005	38.2%	(65/170)
Pericardial effusion	2.83 ←	1.62 - 4.96	0.00008	55.9%	(95/170)
Splenic lesions + lymphadenopathy	2.02 ←	1.07 - 3.82	0.019	32.9%	(56/170)
Splenic lesions + ascites	2.43	0.96 - 6.41	0.041	15.9%	(27/170)
Splenic lesions + lymphadenopathy + ascites	2.86	1.07 – 8.07	0.02	15.9%	(27/170)

Current DSTB Treatment Strategies

PTB

- 2 months - RIF/ INH/ PZA/etham

- 4 months - RIF/INH

- Intensive phase: 7 times/week

  - New patient - 2 months

  - retreatment TB- 3 months

- No difference in TB outcomes between HIV+ and HIV- patients

EPTB

- 6 month regimen as per PTB except:

  - 9–12 months treatment recommended for TB meningitis since high risk of disability & mortality.

  - Adjuvant corticosteroids recommended for drug susceptible TB meningitis and pericarditis

  - 9 months of treatment :

    - TB bone/ joints

TB Treatment if unable to treat with standard first line Rx

Missing drug	Possible regimen	Duration of treatment
INH	Moxifloxacin/ rifampicin/ ethambutol	12 months ±PZA in intensive phase
Rifampicin	Moxifloxacin/ INH/ ethambutol	18 months(PZA or streptomycin in intensive phase)
Rifampicin/INH	Moxifloxacin/ ethambutol/ streptomycin	18 months
PZA	Rifampicin/INH/ ethambutol	Nine months

TB Treatment Interruption

BMC
Infectious Diseases

RESEARCH ARTICLE   **Open Access**

Factors associated with mortality in patients with drug-susceptible pulmonary tuberculosis

Payam Nahid[1,2*], Leah G Jarlsberg[1], Irina Rudoy[1,2], Bouke C de Jong[3], Alon Unger[4], L Masae Kawamura[2,1], Dennis H Osmond[1], Philip C Hopewell[1,2], Charles L Daley[5]

----- HIV- with adequate intensive phase therapy

—— HIV+ with adequate intensive phase therapy

---- HIV- with inadequate therapy in the intensive phase

▬▬ HIV+ with inadequate therapy in the intensive phase
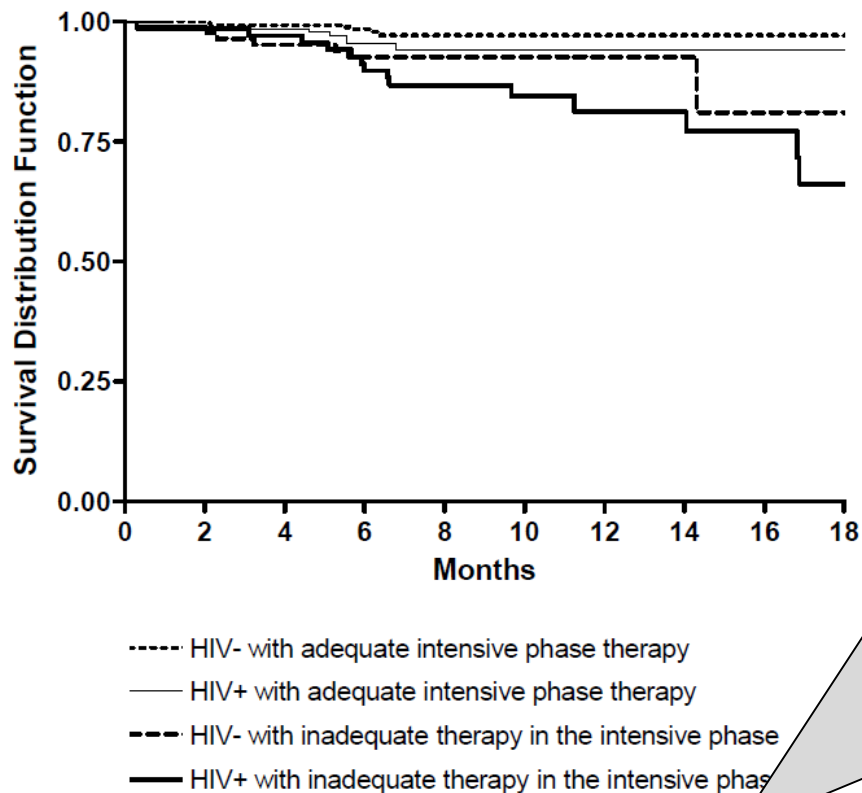
Figure 1 Kaplan-Meier survival curves showing time to death by HIV status & treatment adequacy during the intensive phase of therapy.

- Mortality among TB patients associated with:
  - HIV co-infection (HR = 2.57),
  - older age at TB diagnosis (HR = 1.52 per 10 years)
  - initial sputum smear AFB positive (HR = 3.07); and
  - TB Rx interruption (HR = 3.15)

- Among HIV infected patients:
12 month survival in adequate Intensive phase Rx compared to inadequate intensive phase Rx - 97% vs 81%

Managing TB treatment Interruption

- **Less than 1 month: extend treatment for the number of days that patient did not take treatment**

- **1-2 months missed: do geneXpert**
  - Sensitive: add number of days that patient did not take treatment.
  - Resistant: stop treatment: refer to MDR-TB unit

- **More than 2 months missed (loss to follow up) do geneXpert**
  - Sensitive : restart treatment
  - Resistant : refer MDR-TB

CAPRISA

Mechanism of TB treatment associated DILI

Drug	Mechanism	Clinical picture
RIF	Cholestatic: Dose-dependent interference with bilirubin uptake ±hypersensitivity reaction	• Onset: Transient, early in treatment • Subclinical, Jaundice without hepatocellular damage, • ↑Unconj Bil. May potentiate hepatotoxic effects of other drugs
PZA	Directly heptatotoxic Dose-dependent and idiosyncratic hepatotoxicity	• Hypersensitivity reactions with eosinophilia and liver injury or granulomatous hepatitis. • More damage in liver with pre-existing disease.
INH	Hepatitis: Free radical generation: toxic to hepatocytes	• Onset: Within weeks to months. • Re-challenge does not always elicit a rapid recurrence of hepatotoxicity

**Alcohol consumption doubles rate of probable INH hepatitis

CAPRISA

Definition of DILI

SA HIV Clinician's Society DILI guidelines:

ALT level > 120 IU/L **and** symptomatic (Nausea, vomiting, abdominal pain, jaundice) **or**

ALT level >200 IU/L **and** asymptomatic **or**

Total serum bilirubin concentration > 40 umol/L

American Thoracic Society Documents

An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy

Jussi J. Saukkonen, David L. Cohn, Robert M. Jasmer, Steven Schenker, John A. Jereb, Charles M. Nolan, Charles A. Peloquin, Fred M. Gordin, David Nunes, Dorothy B. Strader, John Bernardo, Raman Venkataramanan, and Timothy R. Sterling, on behalf of the ATS Hepatotoxicity of Antituberculosis Therapy Subcommittee

APRISA
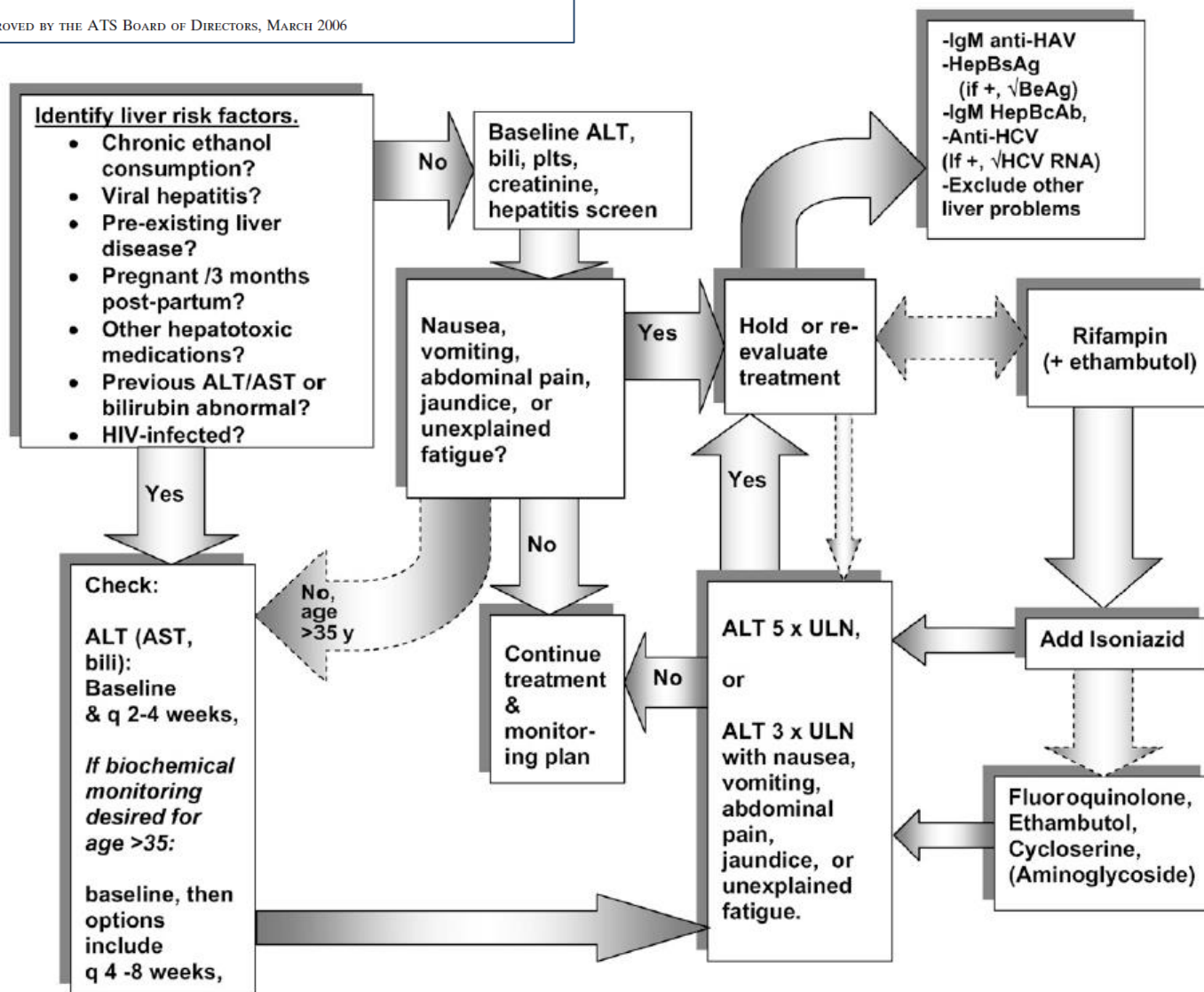
TB Regimen selection with DILI :

- INH and RIF crucial → warrants their use and retention in regimen, even in pre-existing liver disease

- Alternate regimens recommended if ALT > 3 X ULN and TB Liver excluded
  - Treatment without pyrazinamide using isoniazid, rifampicin and ethamutol for 9 months, confirm *MTB* DST
  - Cirrhosis: rifampicin and ethambutol, with levofloxacin, moxifloxacin, gatifloxacin, or cycloserine, for 12 to 18 months may be considered.
  - Encephalopathic liver disease, ethambutol combined with a fluoroquinolone, cycloserine, and capreomycin or aminoglycoside for 18 to 24 months may be an option.
  - Clinicians may avoid aminoglycosides in severe, unstable liver disease due to concerns about renal insufficiency, or bleeding from injected medication in patients with thrombocytopenia and/or coagulopathy

CAPRISA

Principles of TB DILI management

- Moderate to severe liver damage STOP drugs

- Investigate for other causes of hepatitis

- Confirm the diagnosis of TB
  - Green card
  - Intensive phase/ continuation phase
  - Search for pending TB culture results
  - Re-investigate for TB

CAPRISA

TB Drug Rechallenge in DILI

- If patient presented in liver failure:
    - **TB drug re-challenge is not recommended**

- Otherwise, re-challenge
    - Rates of DILI recurrence in re-challenge is 12 %

- Rechallenge method: Regimen Rechallenge vs Sequential Drug Rechallenge - latter in full doses vs incremental doses

- RCT data on Rates of DILI recurrence by type of Rechallenge method: Regimen Rechallenge (14%) vs Sequential Drug Rechallenge in full (10%) vs incremental (9%) doses

Mild DILI
Clinically well
ALT <200 and Total Bili <40

- Continue TB drugs

- Continue ART if already initiated

- Repeat ALT and Bili in 1 week

- If ALT and bili improving or normal then stop Lab monitoring

- If ALT and Bili continue to rise, treat as moderate or severe DILI

Moderate DILI
Clinically well
ALT > 200 irrespective of Total Bili

- Stop TB regimen
- Discontinue cotrimoxazole prophylaxis and other hepatotoxic drugs
- Start ETH/ MOX/ STR if treatment necessary
- Stop ART unless on a stable ART regimen for > 6 months
- Repeat ALT and Bili in 3 (Inpt) or 7 (Outpt) days
- When ALT < 100 and Bili is normal, attempt rechallenge

CAPRISA

TB Drugs in Renal failure

- INH, rifampicin, PZA : biliary excretion → normal doses

- Streptomycin and ethambutol : can maintain at reduced dose – monitor for uveitis

- Safest regimen: INH, Rifampicin, pyrazinamide X 4 months followed by INH and Rifampicin x 2 months

Lichenoid drug reaction to antituberculosis drugs treated through with topical steroids and phototherapy

Rannakoe J. Lehloenya[1,2]*, Gail Todd[1],
Lesiba Mogotlane[3], Nomphelo Gantsho[1], Carol Hlela[1,4]
and Keertan Dheda[2,4]

Necessary to balance the interruption of therapy against treating through the ADRs:
- Limited number of effective anti-TB drugs,
- Stopping TB drugs is associated with
  - a higher mortality,
  - increases risk of drug resistance,
  - longer duration of therapy and
  - public health concerns – ongoing transmission

(a) (b) (c)

Integration of TB HIV Services

- **Screening for TB and HIV**
- **Early initiation of ARVs and management of adherence to both regimen**
- **Co-management of Drug toxicities common to both**
- **Consideration of Drug interactions**
- **Early detection and management of TB IRIS**
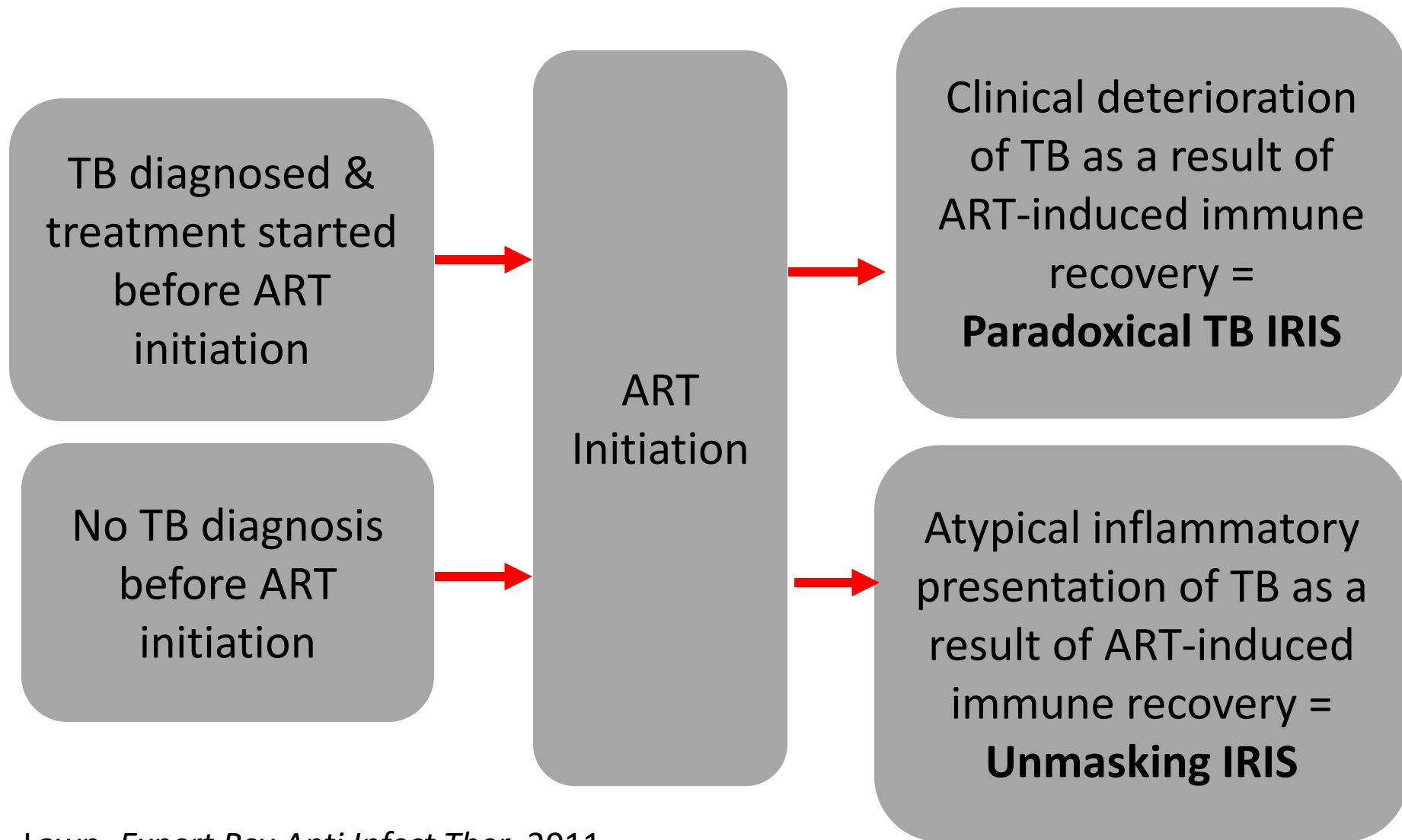- **Initiation and completion of IPT as per guidelines**

Drug Interactions: RIF and EFV

- Previously reported that Rif caused a 30% decrease in EFV trough concentrations, particularly in patients >50kg.

- An increase in EFV dose recommended by FDA (USA)

- No increase in EFV dose recommended in SA

  - Later reports → clearance of EFV is reduced in black African patients, due to CYP enzyme polymorphisms (therefore drug levels actually increased by 30-50%)

CAPRISA

2. RIF and PI

- PI metabolized by CYP 3A4: induced by Rifampicin and inhibited by Ritonavir

- Significant reduction of plasma drug levels of most PI's, except Ritonavir

- LPV/r (Aluvia): Ritonavir boosted Lopinavir (400/100mg)

- **Increase Ritonavir to 400mg daily to overcome the enzyme induction – double Aluvia dose**

  - **Usual 2T BD, increased to 3T BD for 1 wk then 4T BD**

  - **Maintain escalated dose of PI until 2 wks after TB Rx completion**

- **Rif accelerated Atazanavir/r metabolism, cannot be overcome by boosting with Ritonavir**

  - Referral to higher centre to change PI or change Rifampicin to Rifabutin

CAPRISA

TB IRIS

TB diagnosed & treatment started before ART initiation → ART Initiation → Clinical deterioration of TB as a result of ART-induced immune recovery = **Paradoxical TB IRIS**

No TB diagnosis before ART initiation → ART Initiation → Atypical inflammatory presentation of TB as a result of ART-induced immune recovery = **Unmasking IRIS**

Lawn. *Expert Rev Anti Infect Ther*, 2011.

TB IRIS incidence, risk factors and outcomes

- Unmasking TB IRIS Incidence 4.8%

- Paradoxical TB-IRIS Incidence 18%

- Onset 14 days after ART initiation in 48%

- Hospitalisation 25%

- Mortality 7%, death attributed to TB IRIS 2%

- Increased mortality in CNS IRIS

- Risk Factors: Low CD4 count, Short interval between TB treatment and ART, Disseminated TB

TB IRIS Management

Randomized placebo-controlled trial of prednisone for paradoxical TB-associated immune reconstitution inflammatory syndrome

Graeme MEINTJES[1,2,3], Robert J WILKINSON[4,1,2,3,5], Chelsea MORRONI[1,6], Dominique J PEPPER[1,2,3], Kevin REBE[2,3], Molebogeng X RANGAKA[1], Tolu ONI[1,4], and Gary MAARTENS[1,7]

- Double-blind, placebo-controlled RCT
- Intervention: Prednisone 1.5mg/kg/day x 2 wks then 0.75mg/kg/day x 2 wks
- Primary outcome = hospital days
- Findings: Steroid arm - fewer days in hospital and fewer procedures. IRIS associated mortality same in both arms, except CNS disease
- Excl other causes of patient deterioration: MDR TB etc

Evidence of IPT and ART

- **Retrospective data from South Africa* and Brazil****

- **South Africa: 2778 HIV-infected patients, 4287 person-years,**

- **267 TB incident cases (IR 6.2/100 pyrs)**
  - Without IPT or ART   IR 7.1 (95% CI 6.2–8.2)
  - ART alone   IR 4.6 (95% CI 3.4–6.2)
  - IPT alone   IR 5.2 (95% CI 3.4–7.8)
  - ART and IPT   IR 1.1 (95% CI 0.02–7.6)

- **Compared to treatment-naive patients:**

  - ART-only patients had a 64% decreased risk of TB (aHR 0.36; 95% CI 0.25–0.51)
  - Patients receiving ART after IPT had a 89% decreased risk of TB (aHR 0.11; 95% CI 0.02–0.78)

- **Brazil**: 11 026 HIV-infected patients between 1 Sep 2003 and 1 Sep 2005**
  - Compared to treatment-naive patients those on ART had a 76% reduced TB risk (aHR 0.24) after starting IPT

*Golub JE, AIDS 2009, 23:*631–636*
**Golub JE,* AIDS 2007, 21:1441–1448

Evidence from Recent RCT's

- RCT 2056 patients
- Ivory Coast
- Early vs deferred ART with and without IPT

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

Risk of death or severe HIV-related illness was 35% and 39% lower with IPT than with no IPT among patients with baseline CD4 ≥ 500 and < 500 cells/mm^3

INH Prophylaxis

Patients on ART (Adolescent/Adult)	• TST positive: 36 months • TST negative: 12 months • TST not available: 6 months • If later TST becomes positive – extend IPT to 36 months	• All eligible for IPT regardless of CD4 count • If TST negative, re-assess TST status and IPT eligibility 1 year after completing IPT

Summary

- Despite being preventable and curable, TB is the number one cause of death in SA

- Extremely high TB incidence – driven by HIV

- Standard approach to managing TB irrespective of site, except for TB bone/meningitis

- Enhanced diagnostic capacity for TB yet ongoing TB transmission

- Strong policies and guidelines for improved TB outcomes in HIV – vast majority of patients don't require special considerations, however, non-adherence to guidelines!!!!

- TB Prevention: key strategy for reducing TB related morbidity and mortality

Acknowledgements

TB-HIV studies are funded by:

- DAIDS, NIAID, National Institutes of Health
- President's Emergency fund for AIDS Relief (PEPFAR)
- US Centers for Disease Control and Prevention (CDC)
- Fogarty International Center, NIH
- Doris Duke Charitable Foundation (DDCF)
- Howard Hughes Medical Institute (HHMI)
- The Global Fund to fight AIDS, Tuberculosis and Malaria
- EDCTP
- MRC
- MRC-SHIPP
- USAID through BroadReach Health Care Africa

CAPRISA gratefully acknowledges:

- University of KwaZulu-Natal & Columbia University
- South African National Department of Health
- KwaZulu-Natal Provincial Department of Health
- eThekwini Metro & staff of Prince Cyril Zulu clinic staff
- King DinuZulu Hospital staff
- CAPRISA eThekwini and Vulindlela Treatment teams