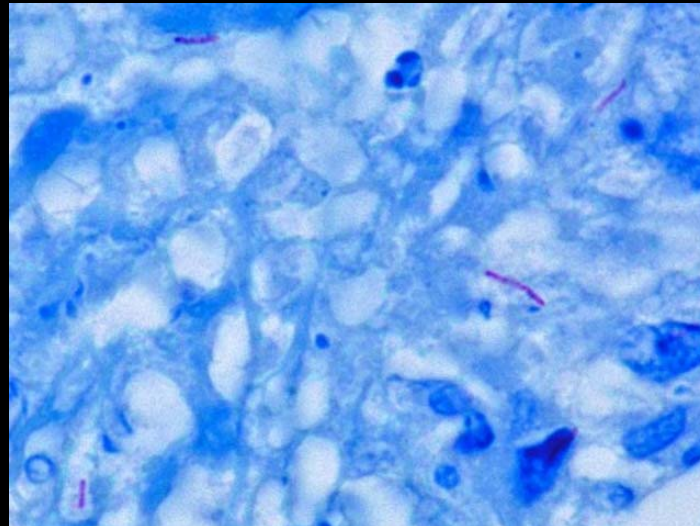


TUBERCULOSIS REVIEW

ACADEMIC HALF DAY 2016

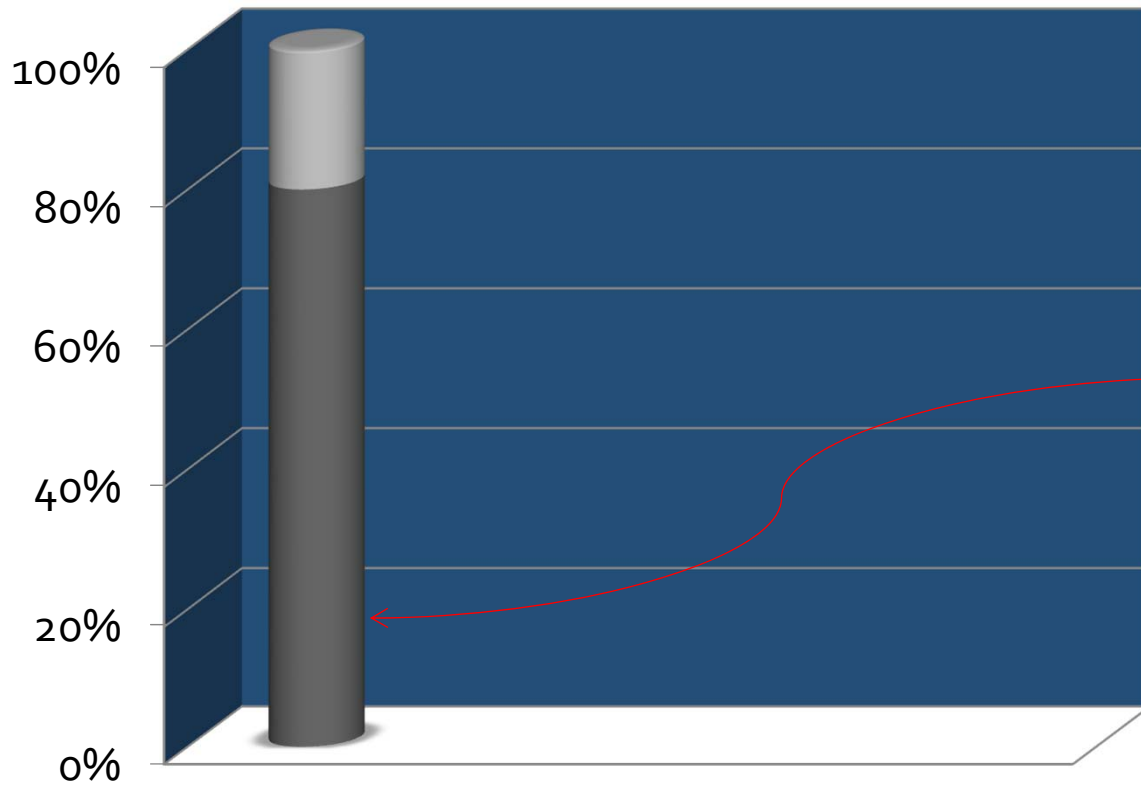


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Worldwide Statistics

- 2015 WHO Report
 - Good News
 - Mortality down by 47 %
 - 43 million lives saved between 2000-2014
 - We still have work to do
 - Second leading cause of death due to an infectious agent
 - 9.6 million new cases (2014)
 - 1.5 million deaths
 - 140,000 children
 - 400,000 HIV positive

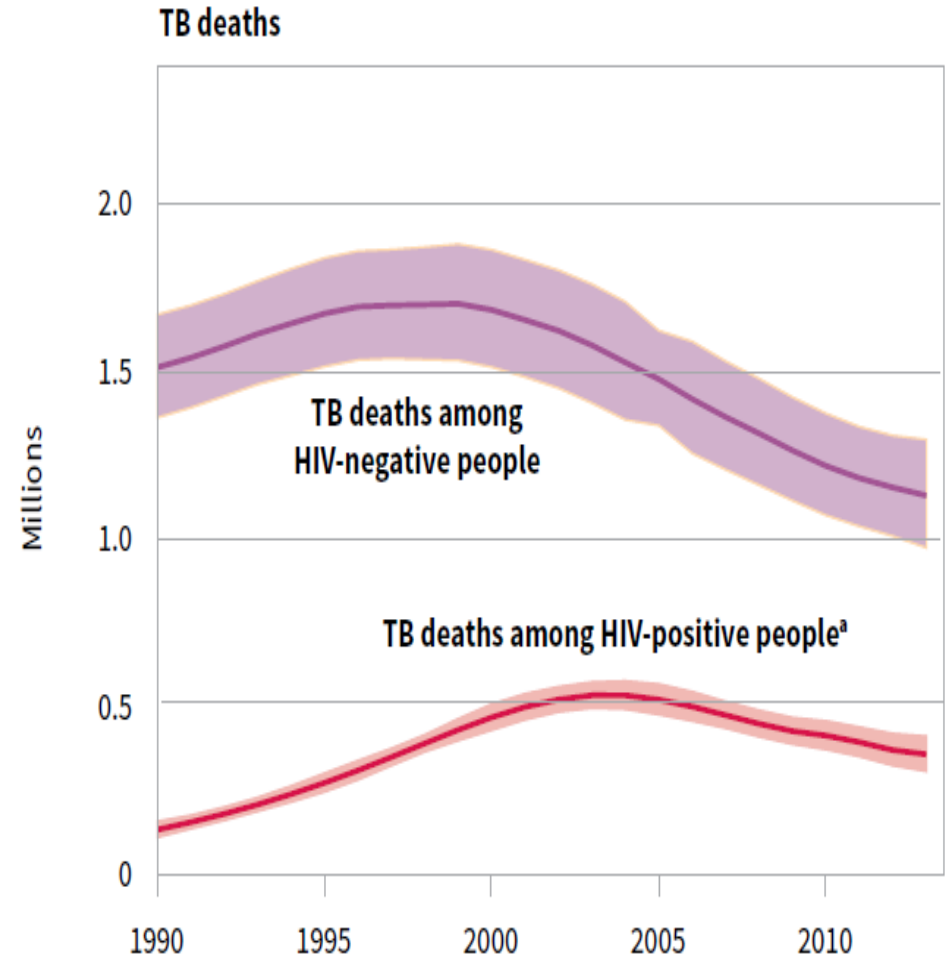
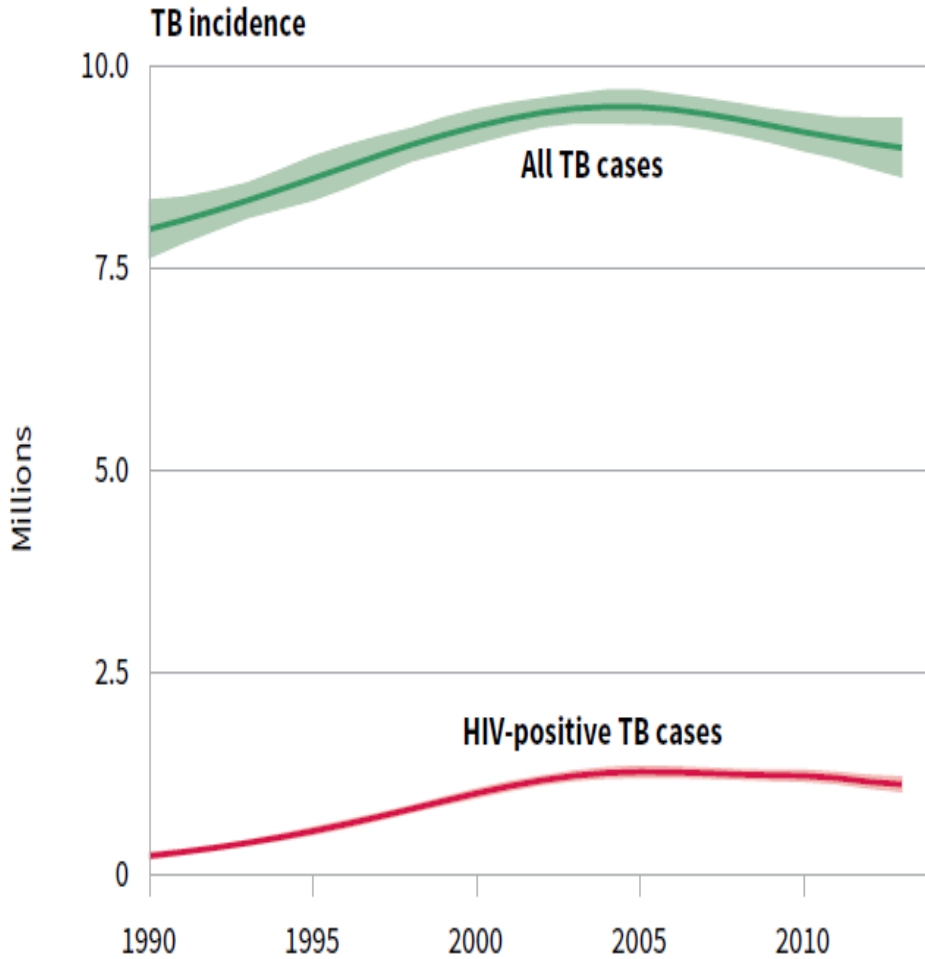
High Burden Countries (HBC)



% INCIDENT TB CASES WORLDWIDE

- Afghanistan
- Bangladesh
- Brazil
- Cambodia
- China
- DR of the Congo
- Ethiopia
- India
- Indonesia
- Kenya
- Mozambique
- Myanmar
- Nigeria
- Pakistan
- Philippines
- Russian Federation
- South Africa
- Thailand
- Uganda
- Tanzania
- Viet Nam
- Zimbabwe

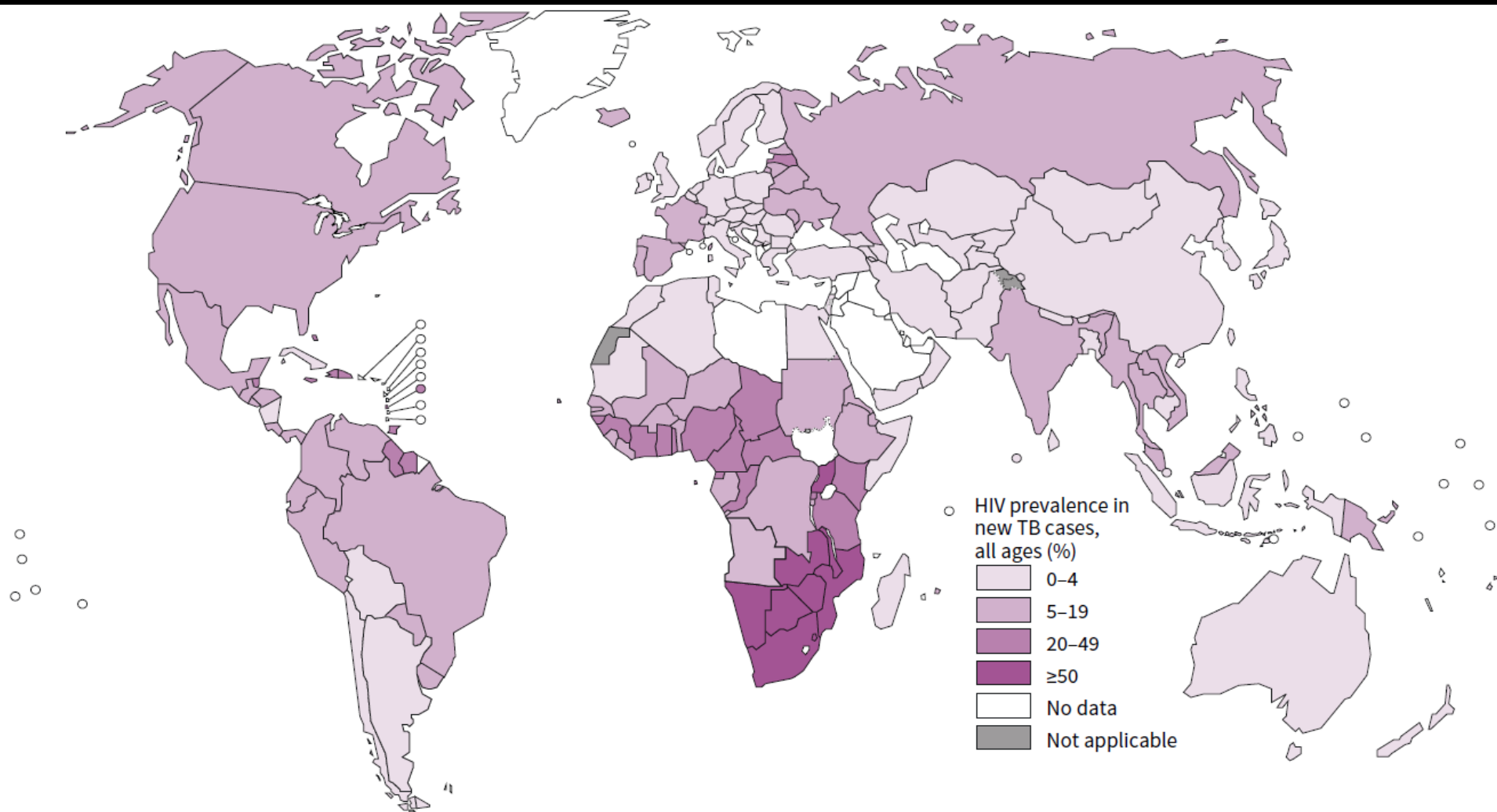
Global Impact of HIV on TB



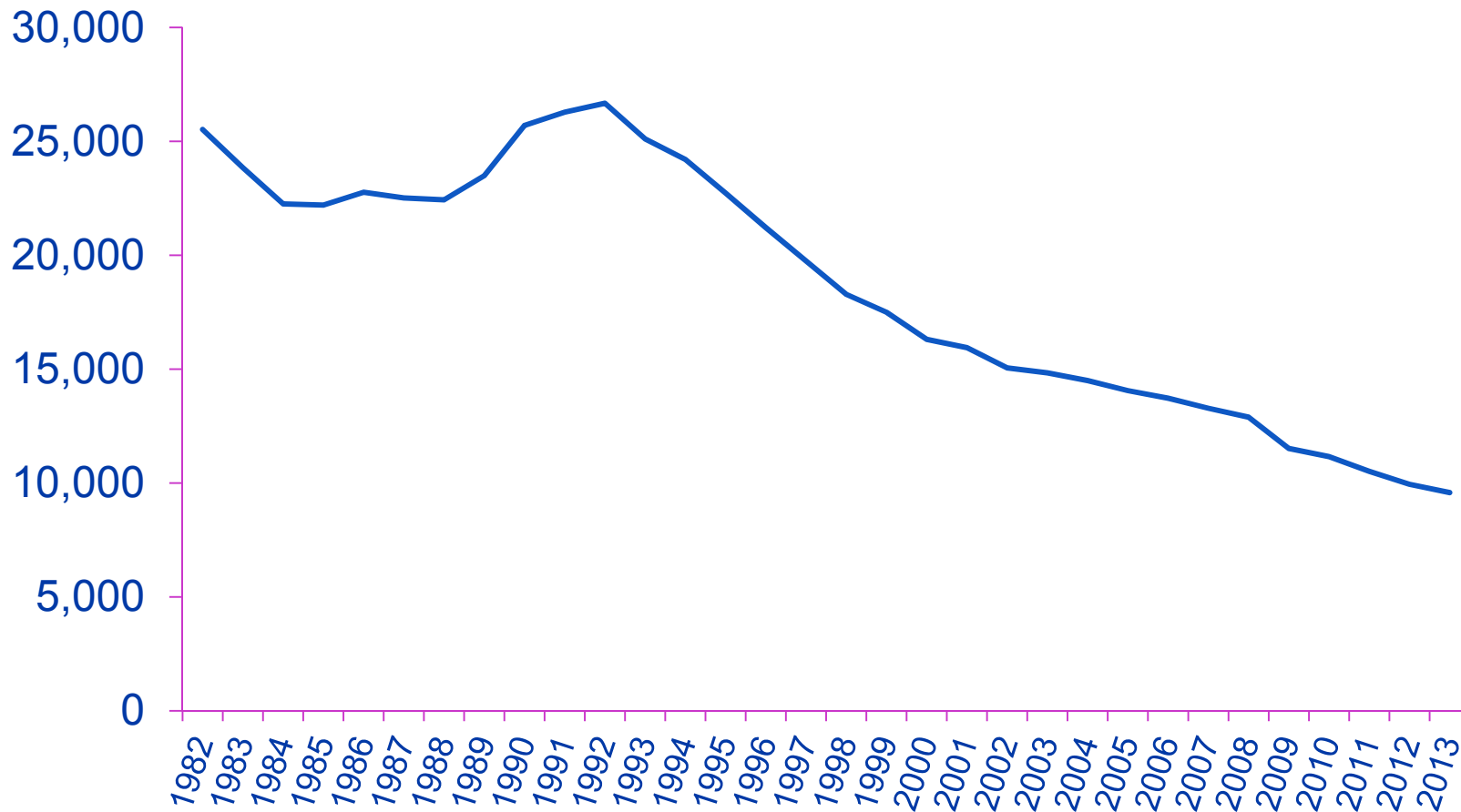
HIV/TB SYNDEMIC

- Urbanization
- Poverty
- Migration
- Increased susceptibility
- Accelerated Progression
- Increased mortality

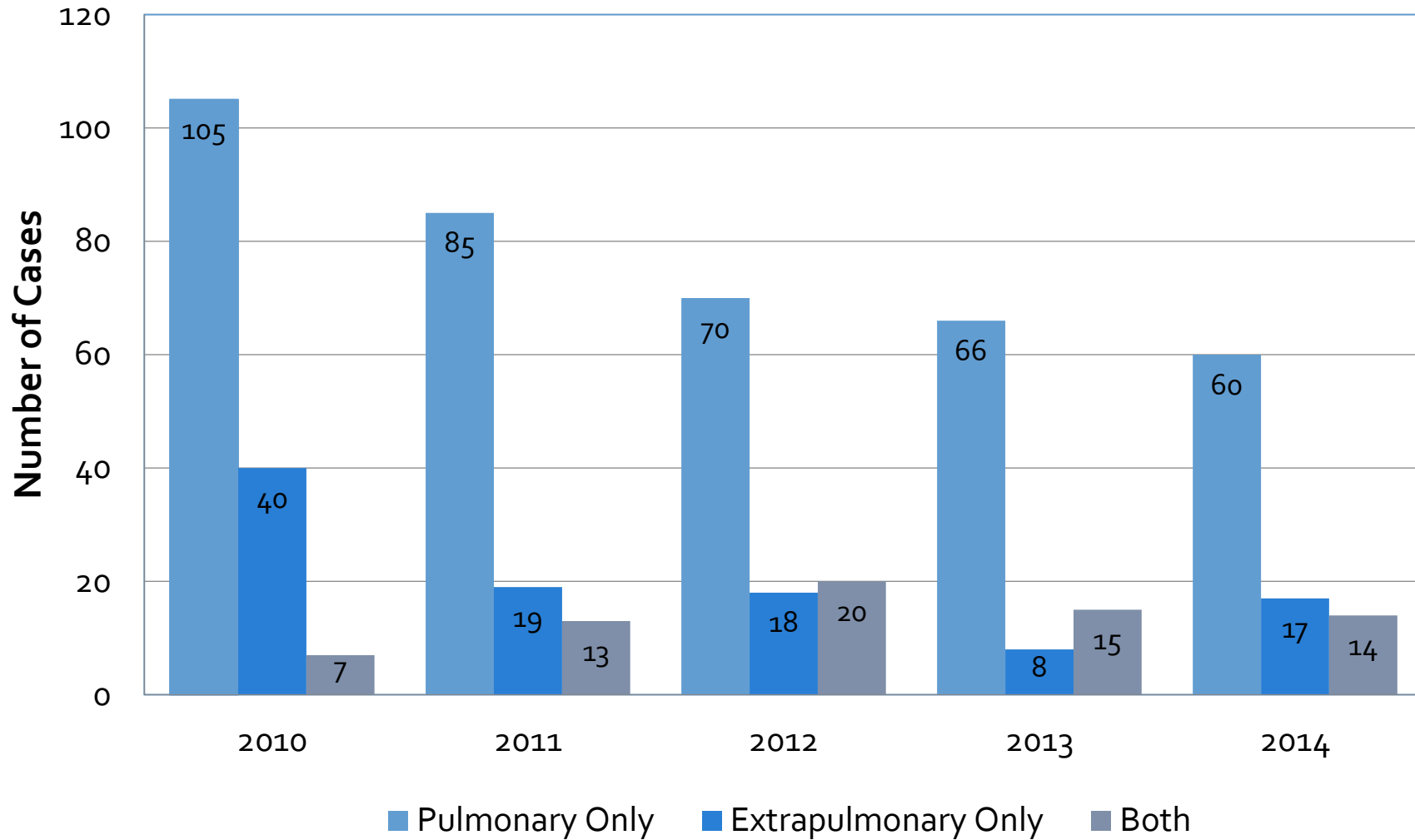
HIV Prevalence Among New TB Cases



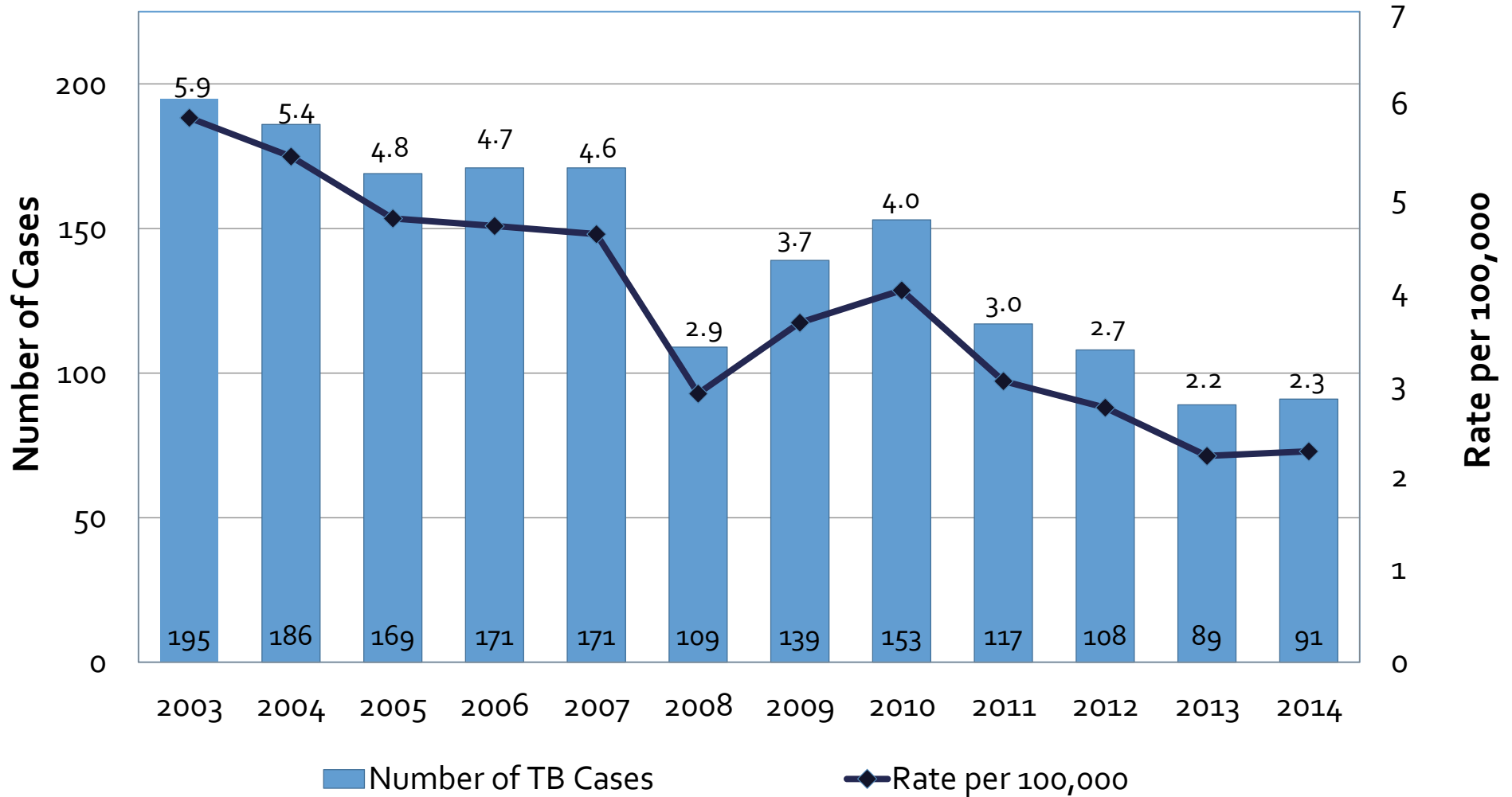
Reported TB Cases US 1982-2013



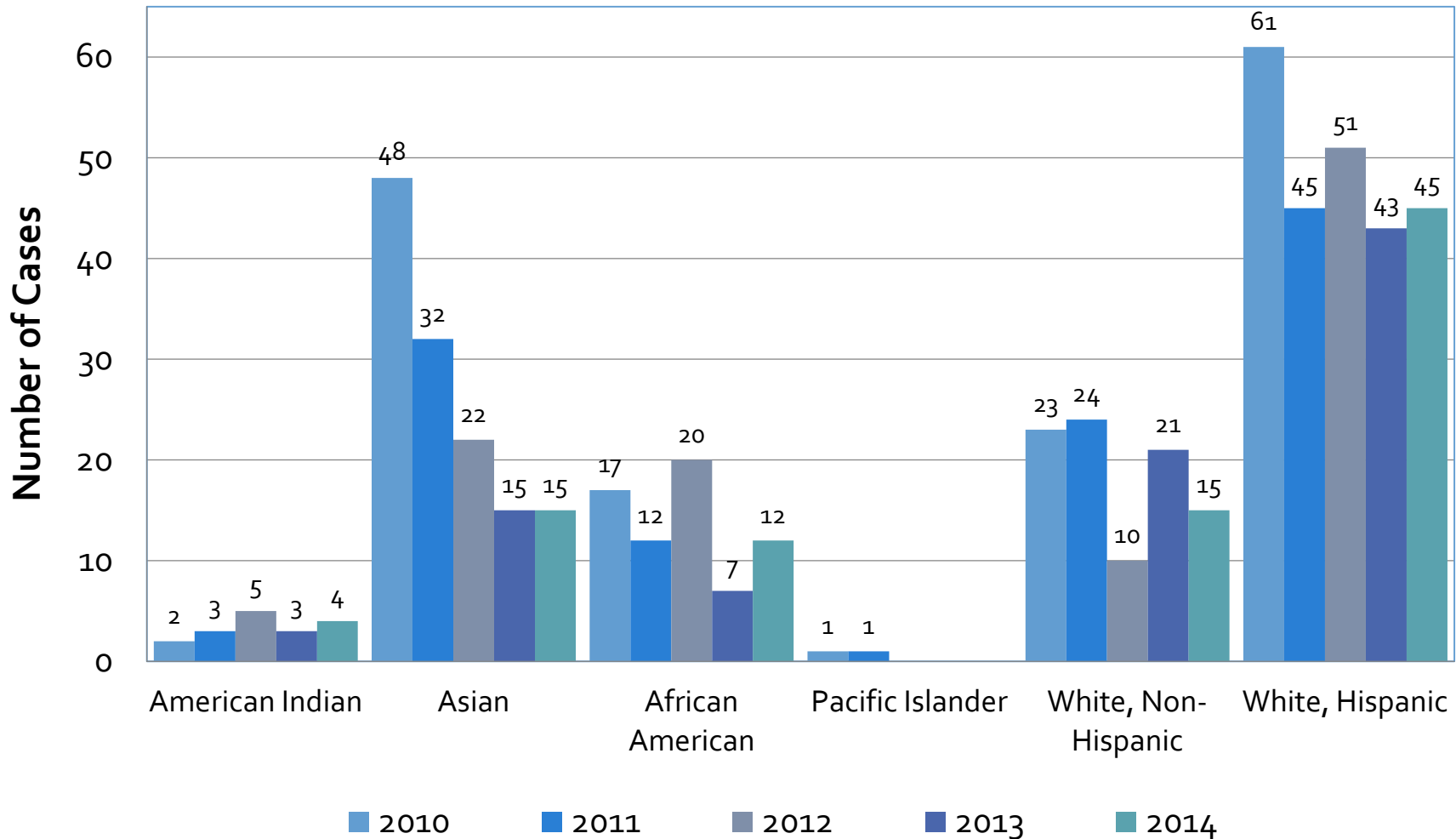
TB Cases by Site of Disease, Maricopa County, 2010 - 2014

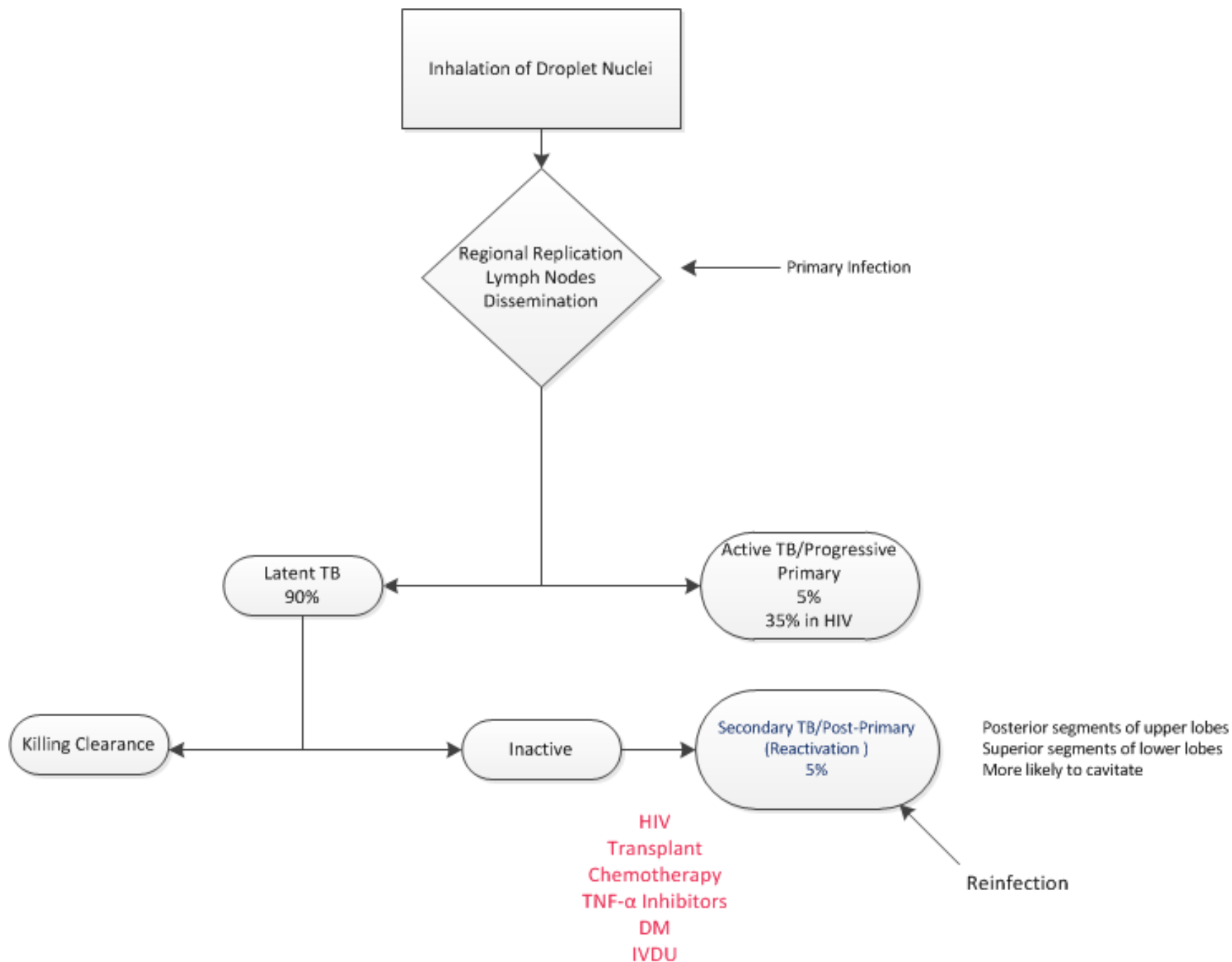


TB Cases and TB Case Rates, Maricopa County, 2003 - 2014



TB Cases by Race/Ethnicity, Maricopa County, 2010 - 2014





LATENT TB

Tuberculin Skin Test (TST)

- PPD = purified protein derivative
- Dose
 - 5 TU in 0.1 mL
- Intradermal injection
- Measure induration in mm (not redness)
 - Delayed Type IV hypersensitivity reaction (48-72 hours)
- Cut-off Points*
 - 5mm -HIV+, Immunosuppression (equivalent of ≥ 15 mg/d of prednisone for at least one month), recent contact to active case, fibrotic changes on cxr, TNF- α
 - 10mm
 - 15mm -low risk for TB for whom testing not generally indicated
- Anergy testing not recommended

*MMWR June 9, 2000

Interferon-Gamma Release Assay (IGRA)

- Blood tests that measure T-cell release of interferon- γ after exposure to M. tb specific antigens
- Two commercially available tests
 - T-SPOT
 - Quantiferon-TB Gold
- Advantages
 - Less crossreactivity
 - No second visit needed
 - Results can be available within 24 hours
- Disadvantages
 - Susceptible to collection and transporting errors leading to false results
 - Expense
 - Limited data in children under 5 years of age (generally not recommended)

LATENT TB TREATMENT

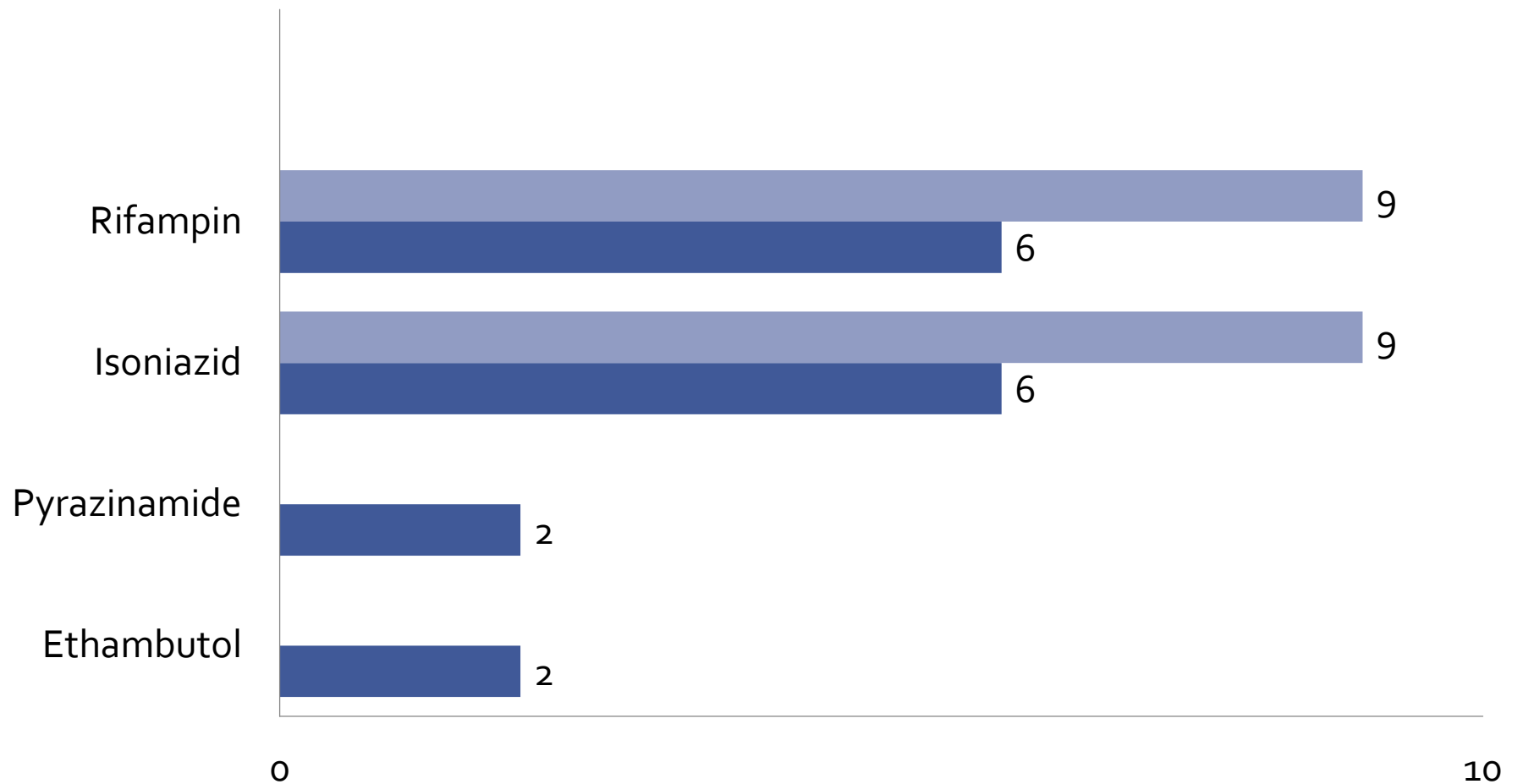
| Drug(s) | Duration | Interval | Minimum Doses |
|-------------------------|----------|--------------|---------------|
| Isoniazid | 9 months | Daily { | 270 |
| | | Twice weekly | 76 |
| | 6 months | Daily | 180 |
| | | Twice weekly | 52 |
| Isoniazid & Rifapentine | 3 months | Once weekly | 12 |
| Rifampin | 4 months | Daily | 120 |

ACTIVE TB

ACTIVE TB

- Diagnosis
 - Presumptive
 - Consistent clinical syndrome + radiographic pattern
 - AFB smears & Culture
 - The gold standard
 - Sputum (expectorated or induced)
 - Can detect 5,000-10,000 bacteria per mL of sputum
 - Bronchoscopy
 - Gastric aspirate
 - Nucleic Acid Amplification
 - GeneXpert MTB/RIF
 - Sensitivity for smear - and culture + → 90%
 - Can be used in nonrespiratory samples but decreased sensitivity (70%)

Active TB Treatment



Active TB Treatment

| Initial Phase | | | | Continuation Phase | | | |
|---------------|-----------------|--|-----------------|--------------------|---------|---|-----------------|
| Regimen | Drugs | Dosing Interval | Number of Doses | Sub-regimen | Drugs | Dosing Interval | Number of Doses |
| 1 | INH-RIF-PZA-EMB | 7 day/wk (8 wk) or 5 day/wk (8 wk) | 56 or 40 | a | INH-RIF | 7 day/wk (18 wk) or 5 day/wk (18 wk) | 126 or 90 |
| | | | | b | INH-RIF | Twice weekly (18 wk) | 36 |
| | | | | c | INH-RPT | Once weekly (18 wk) | 18 |
| 2 | INH-RIF-PZA-EMB | 7 day/wk (2 wk), then twice weekly (6 wk); or 5 day/wk (2 wk), then twice weekly (6 wk) | 26 or 22 | a | INH-RIF | Twice weekly (18 wk) | 36 |
| | | | | b | INH-RPT | Once weekly (18 wk) | 18 |
| 3 | INH-RIF-PZA-EMB | 3 times/wk (8 wk) | 24 | — | INH-RIF | 3 times/wk (18 wk) | 54 |
| 4 | INH-RIF-EMB | 7 day/wk (8 wk) or 5 day/wk (8 wk) | 56 or 40 | a | INH-RIF | 7 day/wk (31 wk) or 5 day/wk (31 wk) | 217 or 155 |
| | | | | b | INH-RIF | Twice weekly (31 wk) | 62 |

EMB: ethambutol; INH: isoniazid; PZA: pyrazinamide; RIF: rifampin; RPT: rifapentine.
Source: References 1, 9, 10.

Treatment Duration

- Pulmonary
 - Uncomplicated: 6 months
 - Complicated: 9 months
- Extrapulmonary
 - Usually 6 months
 - Bone and joint 6 to 9 months
 - CNS 9 to 12 months
 - Steroids used in the treatment of CNS and pericardial disease
- MDR
 - Resistant to INH and Rifampin
 - XDR (MDR+ flouroquinolones + second-line injectable)
 - 18 to 24 months

TB MEDICATIONS

- First Line Agents
 - Isoniazid (1952)
 - Rifampin (1970)/Rifabutin
 - Ethambutol
 - Pyrazinamide
- Second line agents
 - Streptomycin (1946)
 - Amikacin
 - Capreomycin
 - Kanamycin
 - Cycloserine
- Para-aminosalicylic acid
- Ethionamide
- Clofazimine
- Levofloxacin/Moxifloxacin
- Linezolid
- New agents
 - Bedaquiline
 - Delamanid

INFECTION PREVENTION

INFECTION PREVENTION

- Any case where TB is being ruled should be placed in respiratory isolation
- Particulate respirator masks (N95)
- Powered Air Purifying Respirators (PAPR)
- When can we discontinue respiratory isolation
 - TB is considered unlikely AND:
 - Alternate diagnosis made that explains clinical syndrome
OR
 - Three consecutive sputum smears negative
 - At least one early morning specimen
 - 8-24 hours apart
 - NAAT increases the negative predictive value