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# Impact of three empirical tuberculosis treatment strategies for people initiating antiretroviral therapy

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## Abstract

**Background—**Early mortality in people initiating antiretroviral treatment (ART) in Africa remains high. Empiric TB treatment strategies aim to reduce early mortality by initiating TB treatment in individuals without clinical suspicion of TB who are at high-risk of death from undiagnosed TB.

**Methods—**Using data from 16,913 individuals starting ART under programmatic conditions, we simulated the impact of three empiric treatment strategies on mortality and incident TB: two randomized clinical trials (REMEMBER and PrOMPT) and a pragmatic approach. The main analysis assumed that 50% of early deaths and 100% of incident TB is averted in those eligible and ignored outcomes in those lost to follow up.

**Results—**The increase in individuals eligible for TB treatment under empirical TB treatment strategies ranged from 4.4% to 31.4% as compared to those started on clinical or mycobacteriological grounds. The proportion of deaths averted by empiric treatment strategies ranged from 5.5% to 25.4%. The proportion of incident TB cases averted ranged from 10.9% to 57.3%. The proportion receiving any TB treatment during the first six months of ART increased from the observed 24.0% to an estimated 27.5%, 40.4% and 51.3% under the PrOMPT, REMEMBER and pragmatic approach, respectively.

**Conclusion—**The impact of empiric TB treatment strategies depends greatly on the eligibility criteria chosen. The additional strain placed on TB treatment facilities and the relatively limited impact of some empirical TB strategies raise the question whether the benefits will outweigh the risks at population level.

### Keywords

HIV; health systems; simulation; population impact; South Africa

## INTRODUCTION

Mortality in people initiating combination antiretroviral treatment (cART) in sub-Saharan Africa remains high, especially in the first months of cART[1]. Postmortem studies in Africa showed that TB is the cause of death in 32–45% of HIV-infected individuals in the pre-ART

era and 42–87% in the cART era[2–4], with the majority of cases not diagnosed before death or diagnosed too late to prevent death due to the poor sensitivity of smear microscopy and lack of symptoms suggestive of TB in up to 25% of individuals with culture-positive TB.[5, 6]

Empirical TB treatment strategies to reduce early mortality are premised on the hypothesis that a subset of people living with HIV is at high risk of undiagnosed TB such that the benefit of empirical TB treatment outweighs the risks[7]. It is important to note that, where empirical or clinical TB treatment refers to TB treatment initiation *upon clinical suspicion*, empirical TB treatment strategies start TB treatment in high-risk individuals *without clinical suspicion* of TB. Two randomized controlled trials (RCTs) and one cluster-randomized trial of empirical TB treatment strategies have been registered.[8–10]

The aim of this simulation study is to predict the population and health systems impact of empirical TB treatment strategies in an ART clinic population.

## METHODS

### Study site and clinical data

The Themba Lethu Clinic in Johannesburg, South Africa, is a public adult HIV clinic. Since 2004, over 21,000 people have initiated cART at the clinic[11]. Clients receive care according to South African Guidelines. TB symptom screening is performed at all visits by asking patients about prolonged (> 2 weeks) cough or fever, night sweats, weight loss. During the study period, smear microscopy was the initial diagnostic, in some complemented by chest X-ray, culture, histopathology, or a clinical decision to prescribe TB treatment. The proportion of individuals started on treatment without bacteriological confirmation is about 40%.[12, 13]

### Empirical TB treatment strategies

We identified the key characteristics of the REMEMBER (Reducing Early Mortality and Early Morbidity by Empiric Tuberculosis Treatment Regimens)[8] and PrOMPT (Prevention of Early Mortality by Presumptive Tuberculosis Treatment)[9] trials, and a pragmatic strategy suggested by Lawn.[7] Key eligibility differences between strategies relate to the level of immunosuppression (CD4 count <50 cells/mm$^3$ for REMEMBER and PrOMPT; < 100 cells/mm$^3$ for the pragmatic strategy) and body mass index (BMI <18 for PrOMPT, any BMI for REMEMBER and pragmatic strategy). All strategies limit eligibility to those not diagnosed (bacteriologically or clinically) with active TB, those without a TB treatment history (to avoid first line TB treatment in people at high risk of drug-resistant TB), and individuals without known liver disease (to reduce the risk of hepatotoxicity). In addition, each strategy has unique inclusion and exclusion criteria (Table 1).

For simulation of the REMEMBER trial, we made three modifications; (1) limit to individuals age ≥ 18 years, (2) not exclude individuals in contact with MDR-TB as this information is not routinely collected, (3) exclude individuals with documented baseline peripheral neuropathy assuming that only grade 2[14] or higher is routinely recorded. Modifications to the eligibility criteria for simulation of the PrOMPT trial were: (1) operationalize “no breastfeeding” as no recorded pregnancy in last 12 months, (2) assume

that absence of documentation of cryptococcal disease, Kaposi sarcoma, lymphoma, or toxoplasmosis indicates absence of disease, and (3) pragmatically assume absence of danger signs in clients initiating cART at an ambulatory clinic. To simulate the impact of the pragmatic approach, we selected the cut-off of CD4<100 cells/mm$^3$, defined liver disease as documented liver function test (ALT) ≥ 2.5 times upper normal limit, and excluded pregnant women (in line with the other strategies).

### Assumptions and sensitivity analyses

We applied two key assumptions for the main analysis. First, all individuals receiving empiric TB treatment strategy are adherent to TB treatment such that 100% of incident TB is prevented. Second, 50% of early deaths (first 6 months of cART) are preventable by empirical TB treatment strategies.[2–4] In sensitivity analyses, we explored assumptions that 30% and 70% of early deaths are preventable by empirical TB treatment strategies.

In these simulations, we ignored potential deaths and incident TB in individuals lost to follow up. In a “best-case scenario” sensitivity analysis, we assumed that empirical TB treatment strategies prevent 50% of deaths in those lost to follow up (LTFU) under standard of care (SOC) and 100% of incident TB as people lost to HIV care may still continue TB treatment at their primary care clinic. We based the risk of death among people LTFU on a study performed at the same clinic, which observed the following 6-month risk of death among those LTFU: 33.0% if CD4 0 to 50 cells/mm$^3$, 6.4% if CD4 count 51 to 100 cells/mm$^3$, and 8.6% if CD4 count 101 and 200 cells/mm$^3$, and 24% among those with missing CD4 count[15]. The 6-month risk of incident TB among those LTFU was assumed to be 10%.

### Simulation of population and health systems impact of empirical TB treatment strategies

Using data on all adults initiating cART at TLC between 1 April 2004 and 30 September 2011, we first estimated the proportion of individuals starting cART eligible for empirical TB treatment strategies according to the strategy-specific inclusion and exclusion criteria. We then compared the proportion of deaths prevented (primary outcome of the RCTs) and proportion of incident TB cases prevented (secondary outcome of RCTs) by each empiric TB treatment strategy to what was observed under SOC. Next, we estimated the number of clients receiving any TB treatment during the first 6 months of cART, including prevalent TB cases (individuals on TB treatment at time of cART initiation), incident TB cases in the first 6 months of cART, and cases started on TB treatment under empiric TB treatment strategies. Finally, we calculated the number of people needed to treat (NNT) to prevent one case of incident TB or one death in the first 6 months of cART for each empiric TB treatment strategy.

### Ethics statement

The study was approved by the Institutional Review Boards of the University of the Witwatersrand, South Africa, and University of North Carolina, USA. Patients gave written informed consent for use of routine data for research purposes.

# RESULTS

## TLC cohort characteristics

Between 1 April 2004 and 30 September 2011, 16,913 individuals initiated cART, of which 2,856 (17%) received TB treatment at cART initiation (prevalent TB) (Table 2). The majority (62%) were women, median age was 36 (interquartile range [IQR] 31, 43), 52% had a CD4 count ≤100 cells/mm$^3$ and median BMI was 21.6 (IQR 19.1, 24.9). In total, 1019 deaths were recorded in the first 6 months, corresponding to 6.0% of those initiating cART. The 6-month risk of death decreased with increasing CD4 count: 11.3% if CD4 count 0 to 50 cells/mm$^3$, 5.7% if CD4 count 51 to 100, and 3.0% if CD4 count 101 to 200. Among the 14,057 individuals not receiving TB treatment at cART initiation, 1194 cases of incident TB were recorded, corresponding to an 8.5% 6-month risk. The risk of incident TB decreased with increasing CD4 count: 13.8% if CD4 count 0 to 50 cells/mm$^3$, 9.6% if CD4 count 51 to 100, and 5.3% if CD4 count 101 to 200. Overall, 94.7% were retained in care during the first 6 months of cART, 95.2% of those with and 94.6% of those without prevalent TB at cART initiation.

## Impact of empirical TB treatment strategies

Of the 16,913 individuals initiating cART, 5311 (31.4%) were eligible for empirical TB treatment when implementing the pragmatic strategy, 3205 (19.0%) according to the REMEMBER strategy, and 736 (4.4%) when using the PrOMPT strategy (Table 3).

Under SOC, 1019 deaths were recorded in the first 6 months of cART: 198 in those with and 821 among those without prevalent TB at start cART. Of these 1019 deaths, 518 (50.8%) occurred in those eligible for empirical TB treatment under the pragmatic strategy, 346 (34.0%) in those eligible for REMEMBER and 112 (11.8%) in those eligible for PrOMPT. Under the assumption that 50% of early deaths in those eligible are preventable by strategy-based empiric TB treatment, the proportion of all deaths observed among the 16,913 individuals initiating cART that are averted would be 25.4% for the pragmatic strategy, 17.0% for REMEMBER, and 5.5% for PrOMPT (figure 1). Consequently, 74.6% (n=760) of all 1019 deaths observed under SOC would still occur under the pragmatic strategy, 83.0% (n=846) under REMEMBER, and 94.5% (n=963) under PrOMPT. The proportion of deaths averted under the alternative assumption that 30% of early mortality can be prevented by empiric TB treatment strategies would be 15.3% for the pragmatic strategy, 10.2% for REMEMBER, and 3.3% for PrOMPT. When 70% of early mortality can be prevented by strategy-based empiric TB treatment, 35.6% of early deaths would be averted by the pragmatic strategy, 23.8% by REMEMBER, and 7.7% by PrOMPT.

Under SOC, 1194 incident TB cases were recorded in the first 6 months of cART among the 14,057 judged free of TB at start of cART (table 3), of which 684 (57.3%) occurred in those eligible for empirical TB treatment under the pragmatic strategy, 431 (36.1%) eligible for REMEMBER and 130 (10.9%) eligible for PrOMPT. Based on the assumption that 100% of all incident TB cases are prevented, the proportion of the 1194 incident TB cases recorded under SOC averted would be 57.3% for the pragmatic strategy, 36.1% for REMEMBER, 10.9% for PrOMPT strategy (Figure 2). Consequently, 42.7% (n=510) of all 1194 incident

TB cases observed under SOC would still occur under the pragmatic strategy, 63.9% (n=763) under REMEMBER, and 89.1% (n=1064) under PrOMPT.

The proportion of clients receiving any TB treatment during the first 6 months of cART was lowest for SOC (24.0%), increased to 27.5% for PrOMPT, 40.4% for REMEMBER, and 51.3% for the pragmatic strategy (Figure 1).

For every 100 people started on strategy-based empiric treatment according to the pragmatic, REMEMBER or PrOMPT strategy, an estimated 4.9, 5.4 and 7.6, deaths would be averted, corresponding to a NNT of 20.5, 18.5 and 13.1 to avoid one death (table 3). For every 100 people started on strategy-based empiric treatment according to the pragmatic, REMEMBER or PrOMPT strategy, an estimated 12.9, 13.4, and 17.7 cases of incident TB would be averted, corresponding to a NNT of 7.8, 7.4 and 5.7 to avoid one case of incident TB.

In sensitivity analyses the proportion of deaths averted and NNT to prevent one death were highly sensitive to the alternative assumptions of effectiveness of the empirical TB treatment strategies (Table 2).

Among the 895 individuals LTFU, an estimated 215 deaths and 76 cases of incident TB occurred. Extending effectiveness of empiric TB treatment to individuals lost to cART under SOC slightly reduced the NNT to prevent one death (16.6, 15.2 and 11.4 for pragmatic, REMEMBER and PrOMPT, respectively) whereas the NNT to prevent one case of incident TB remained almost identical (7.4, 7.1 and 5.5 for pragmatic, REMEMBER and PrOMPT, respectively).

## DISCUSSION

The high burden of TB and HIV in sub-Saharan Africa demands innovative interventions. Empirical TB treatment strategies aim to start TB treatment without diagnostic delay in people initiating cART who are at high risk of dying from undiagnosed TB. While awaiting results of RCTs, we simulated the population level effect of such strategies using data from a large cohort of individuals starting cART under programmatic conditions.

Our results demonstrate that eligibility criteria greatly determine the impact of empirical TB treatment strategies at population level, with the proportion of deaths averted ranging from 6% to 25%, and the proportion of incident TB cases averted ranging from 11% to 57%. Different strategies also have variable health care system effects, with the proportion of ART clinic clients receiving any TB treatment during the first six months of ART being similar to more than doubling compared to the standard of care.

The proportion of deaths averted by empirical treatment strategies will remain unknown until the publication of RCT results. Enrollment in the REMEMBER trial was completed in May 2014. The PrOMPT trial was prematurely closed due to insufficient enrolment, in line with our results that only 4.4% of people initiating ART are eligible for this strategy. We therefore performed a sensitivity analysis exploring plausible effectiveness estimates. As expected, the proportion of deaths averted increases and number needed to treat decreases

with increased effectiveness of empiric TB treatment strategies. However, even if 70% of early deaths in those eligible can be averted, 64 to 92% of all deaths still occur and all strategies result in high numbers of people placed on “unnecessary” TB treatment as most individuals would not have died or developed incident TB under standard of care.

We simulated a “best case scenario” of empirical treatment strategies, with 100% of incident TB prevented. Our assessment of effects on the health care system was limited to the single measure of the number of people receiving TB treatment. Available data did not allow simulating the risk of other potential adverse effect such as increased rates of drug toxicity, adverse effects on adherence due to high pill burden, failure to diagnose other infections, and delay in cART initiation when first starting TB treatment, factors that could result in less favorable outcomes of empirical TB treatment strategies. We also did not explore potential operational challenges, effects on the quality of care for HIV-negative TB patients, or impact of isoniazid preventive therapy. We could not simulate the rapidly changing landscape of TB diagnostics. The Xpert MTB/RIF assay on a sputum sample can detect all sputum smear-positive TB, about 70% of sputum smear-negative TB, rifampicin resistance, and when used on a blood sample, about 20% of blood-culture positive cases[16, 17]. The point-of-care urine Determine TB-LAM, which is not yet endorsed by the WHO, has high sensitivity in those with low CD4 count[18]. Implementation of Xpert MTB/RIF, Determine TB-LAM and future novel TB diagnostics have the potential to reduce the impact of empiric TB treatment strategies. A cluster-randomized trial, TB Fast Track[10], which uses low BMI and anemia as criteria for empiric TB treatment in cART-naïve individuals will be the first “second generation empirical treatment strategy”, evaluating the use of empiric TB treatment in the setting where Determine TB-LAM is available for same-day decision-making and Xpert for assessment of sputum at centralized laboratories.

In conclusion, the important advances in rapid diagnostics, the strain empirical TB treatment strategies is likely to place on already overburdened health centers, and the relatively limited impact of some empirical TB strategies on the total mortality and TB incidence at an ART clinic population level raise the question whether the benefits of empirical TB treatment strategies will outweigh its risks at population level. If the RCTs demonstrate high efficacy, then Departments of Health will need to carefully consider inclusion and exclusion criteria in order to maximize risk reduction at individual level, limit the effects of potential unnecessary exposure to TB drugs in a substantial proportion of the ART clinic population, and limit the negative impact an empirical treatment strategy may have on already overburdened TB treatment services.

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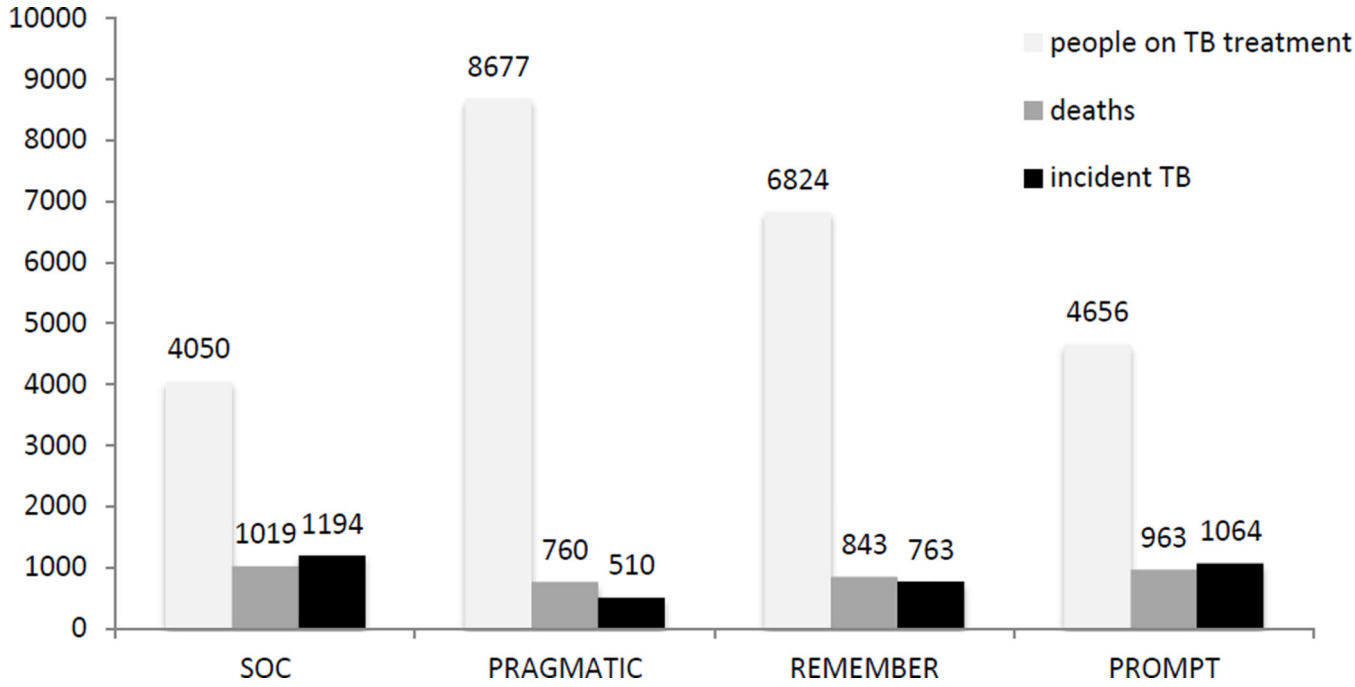


**Figure 1.**

Number people receiving any TB treatment (for prevalent TB, incident TB or initiation per empirical treatment strategy) experiencing death, and developing incident TB in the first six months of cART, observed under standard of care (SOC) and predicted for three empiric TB treatment strategies (pragmatic, REMEMBER, PrOMPT)

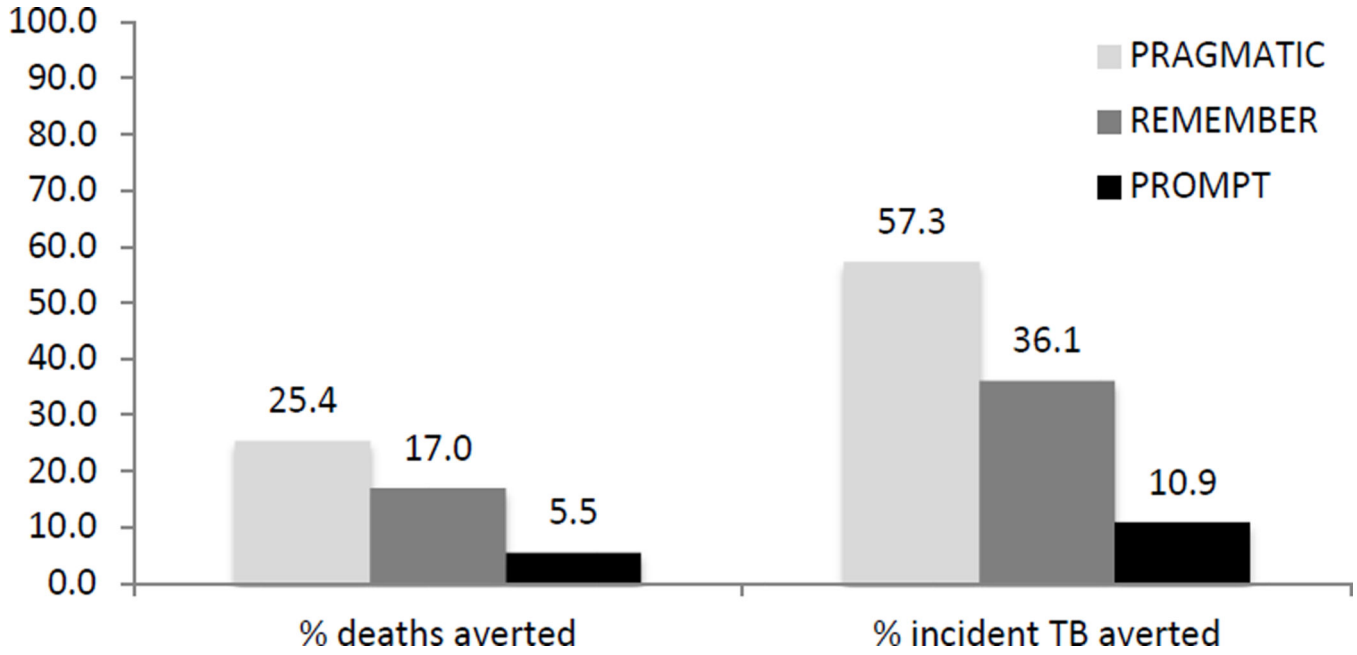


**Figure 2.**

Proportion of deaths and incident TB cases occurring under standard of care (SOC) in the first 6 months of antiretroviral treatment that are averted by implementation of three empirical TB treatment strategies.

**Table 1**

Inclusion and exclusion criteria for three empirical TB treatment strategies

| | REMEMBER[8] | PrOMPT[9] | Lawn et al.[7] |
|---|---|---|---|
| **INCLUSION CRITERIA** | | | |
| Age | ≥ 13 years | ≥ 18 years | |
| CD4+ cell count | < 50 | < 50 | < 100 or < 50 * |
| Body mass index | | <18 | |
| **EXCLUSION CRITERIA** | | | |
| Diagnosis of active TB | ✓ | ✓ | ✓ |
| History of TB treatment | Within 96 weeks | Ever | Ever |
| IPT for >30 days in last 48 weeks | ✓ | ✓ | |
| Exposure to MDR TB | ✓ | ✓ | |
| Renal insufficiency | Creat. clearance <30 mL/min | | |
| Abnormal liver function | > 2.5 ULN | ≥ 5 ULN | Known acute liver disease |
| Hepatitis B | Surface Ag neg. | | |
| Pregnant | ✓ | ✓ | |
| Breastfeeding | | ✓ | |
| Seriously ill:<br>- Karnofsky performance score < 30 | ✓ | | |
| - Severe illness (disseminated KS; malignant lymphoma; toxoplasmosis) | | ✓ | |
| - Danger signs (respiratory rate > 30/min, pulse > 120/min, temp > 39°C) | | ✓ | |
| Current Grade ≥2 peripheral neuropathy | ✓ | | |
| Cryptococcal meningitis (CrAG positive) | | ✓ | |

* In the simulation study, we used <100 cells/mm$^3$

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**Table 2**

Baseline characteristics of 16,913 individuals initiating ART, overall and by outcomes of death and incident TB in first 6 months of ART.

| | All | | Early death n=1019 | | Incident TB n=1194 | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Gender | | | | | | |
| Male | 6385 | 38 | 473 | 46 | 584 | 49 |
| Female – not pregnant | 9852 | 58 | 535 | 53 | 596 | 50 |
| Female - pregnant | 474 | 4 | 11 | 1 | 14 | 1 |
| Age‡ | 36 (31, 43) | | 38 (32, 45) | | 36 (31, 42) | |
| CD4 count | | | | | | |
| ≤ 50 cells/mm3 | 5066 | 32 | 572 | 59 | 540 | 49 |
| 51–100 | 3133 | 20 | 179 | 19 | 235 | 21 |
| 101–200 | 5545 | 35 | 166 | 17 | 254 | 23 |
| > 200 | 1971 | 13 | 49 | 5 | 69 | 6 |
| Missing | 1198 | | 53 | | 96 | |
| Body mass index | | | | | | |
| < 18.0 kg/m2 | 2487 | 16 | 288 | 35 | 266 | 26 |
| ≥ 18.0 kg/m2 | 13228 | 84 | 537 | 65 | 776 | 74 |
| Missing | 1198 | | 194 | | 152 | |
| Hemoglobin | | | | | | |
| Normal† | 7400 | 47 | 198 | 21 | 263 | 24 |
| Low | 7329 | 46 | 601 | 62 | 696 | 63 |
| Very low (<8g/dl) | 1069 | 7 | 163 | 17 | 147 | 13 |
| Missing | 1115 | | 57 | | 88 | |
| WHO stage | | | | | | |
| I or II | 8149 | 56 | 317 | 36 | 329 | 32 |
| III | 4375 | 30 | 328 | 37 | 444 | 44 |
| IV | 1963 | 14 | 242 | 27 | 247 | 24 |
| Missing | 2426 | | 132 | | | |
| Prevalent TB | | | | | | |
| Yes | 2856 | 17 | 198 | 19 | 0 | 0 |

| | All | | Early death n=1019 | | Incident TB n=1194 | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| No | 14057 | 83 | 821 | 81 | 1194 | 100 |
| History of TB treatment | | | | | | |
| Yes | 1945 | 12 | 110 | 11 | 118 | 10 |
| No | 14968 | 88 | 909 | 89 | 1076 | 90 |
| IPT in past year | | | | | | |
| Yes | Unknown* | | | | | |
| No | | | | | | |
| Liver function | | | | | | |
| Normal or missing | 16177 | 95 | 909 | 89 | 1089 | 91 |
| LFT > 2.5× UNL | 736 | 4 | 109 | 11 | 105 | 9 |
| LFT > 5 × UNL | 129 | 1 | 18 | 2 | 19 | 2 |
| Renal function | | | | | | |
| Normal or missing | 16875 | 100 | 1015 | 100 | 1189 | 100 |
| Creatinine clearance < 30ml/min | 38 | 0 | 4 | 0 | 5 | 0 |
| Peripheral neuropathy | | | | | | |
| Yes | 100 | 1 | 14 | 1 | 7 | 1 |
| No | 16813 | 99 | 1005 | 99 | 1187 | 99 |
| Severe illness present** | | | | | | |
| Yes | 29 | 0 | 4 | 0 | 3 | 0 |
| No | 16884 | 100 | 1015 | 100 | 1191 | 100 |

‡Median (interquartile range).

†Lower limit of normal defined as >12.35 g/dL in men; >11.35 g/dL in women; >10.35 g/dL in pregnant women.

*IPT was not yet implemented and not systematically recorded

**Defined as documented of cryptococcal disease, Karopsi sarc, lymphoma, or toxoplasmosis.

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**Table 3**

Predicted population and health systems impact of empiric TB treatment strategies in the first 6 months of antiretroviral treatment (cART) among 16913 individuals starting ART at a clinic in Johannesburg, South Africa

| | Eligible | Death | | | | Incident TB | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Deaths averted among eligible | | Deaths in total clinic population (n=16913) | Deaths averted in clinic population | NNT to prevent 1 death | Incident TB averted in eligible | | Incident TB in clinic population free of TB at start cART (n=14057) | Incident TB averted in clinic population free of TB at start cART | NNT to prevent 1 case of TB | People on any TB treatment in 1st 6 months of cART | |
| | | N | % | N | % | N | % | N | N | % | N | | % |
| **Standard of care** | | | | 1019 | | | | | 1194 | | | 4050 | 24.0 |
| **Main analysis** | | | | | | | | | | | | | |
| Pragmatic | 5311 | 50 | 259 | 760 | 25.4 | 20.5 | 100 | 684 | 510 | 57.3 | 7.8 | 8677 | 51.3 |
| REMEMBER | 3205 | 50 | 173 | 846 | 17.0 | 18.5 | 100 | 431 | 763 | 36.1 | 7.4 | 6824 | 40.4 |
| PrOMPT | 736 | 50 | 56 | 963 | 5.5 | 13.1 | 100 | 130 | 1064 | 10.9 | 5.6 | 4656 | 27.5 |
| **Sensitivity analysis 1** | | | | | | | | | | | | | |
| Lower efficacy of empiric TB treatment for prevention of early death, no change in efficacy for prevention of incident TB | | | | | | | | | | | | | |
| Pragmatic | 5311 | 30 | 155 | 864 | 15.2 | 34.2 | 100 | 684 | 510 | 57.3 | 7.8 | 8677 | 51.3 |
| REMEMBER | 3205 | 30 | 104 | 915 | 10.2 | 30.9 | 100 | 431 | 763 | 36.1 | 7.4 | 6824 | 40.4 |
| PrOMPT | 736 | 30 | 34 | 985 | 3.3 | 21.9 | 100 | 130 | 1064 | 10.9 | 5.6 | 4656 | 27.5 |
| **Sensitivity analysis 2** | | | | | | | | | | | | | |
| Higher efficacy of empiric TB treatment for prevention of early death, no change in efficacy for prevention of incident TB | | | | | | | | | | | | | |
| Pragmatic | 5311 | 70 | 363 | 656 | 35.6 | 14.6 | 100 | 684 | 510 | 57.3 | 7.8 | 8677 | 51.3 |
| REMEMBER | 3205 | 70 | 242 | 777 | 23.8 | 13.2 | 100 | 431 | 763 | 36.1 | 7.4 | 6824 | 40.4 |
| PrOMPT | 736 | 70 | 78 | 941 | 7.7 | 9.4 | 100 | 130 | 1064 | 10.9 | 5.6 | 4656 | 27.5 |
| **Sensitivity analysis 3** | | | | | | | | | | | | | |
| Efficacy for prevention of early death and prevention of incident TB extended to individuals lost to follow up under SOC * | | | | | | | | | | | | | |
| SOC ** | | | | 1234 | | | | | 1270 | | | 4126 | 24.4 |
| Pragmatic | 5311 | 50 | 319 | 1074 | 25.9 | 16.6 | 100 | 720 | 550 | 56.7 | 7.4 | 8717 | 51.5 |

| | Eligible | Death | | | | Incident TB | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Deaths averted among eligible | | Deaths in total clinic population (n=16913) | Deaths averted in clinic population | NNT to prevent 1 death | Incident TB averted in eligible | | Incident TB in clinic population free of TB at start cART (n=14057) | Incident TB averted in clinic population free of TB at start cART | NNT to prevent 1 case of TB | People on any TB treatment in 1st 6 months of cART | |
| | | N | % | N | % | N | % | N | N | % | N | | % |
| REMEMBER | 3205 | 50 | 212 | 1182 | 15.2 | 15.2 | 100 | 454 | 816 | 35.8 | 7.1 | 6877 | 40.7 |
| PrOMPT | 736 | 50 | 65 | 1329 | 5.3 | 11.4 | 100 | 135 | 1135 | 10.6 | 5.5 | 4727 | 27.9 |

*Conservative assumption that individuals lost to follow up under SOC experience the same protective effect of empiric treatment as those remaining in care for 6 months under SOC, those lost to follow up but not eligible for empiric TB treatment do not initiate TB treatment.

**Number for SOC includes estimated deaths and cases of incident TB among those LTFU under SOC



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