Preprints.org

Article

Not peer-reviewed version

# A Geospatial Analysis of TPT Treatment Outcomes among PLHIV in Ethiopia, South Africa, and Zimbabwe

Joeri Sumina Buis *, Christiaan Mulder, Ahmed Bedru, Jozefien Groenendijk, Solomon Sisay, Israel Rabothata, Nicole Kawaza, Christopher J. Hoffmann, Violet Chihota, Sibuse Ginindza, Kenny Sithole, Kate Shearer, Lucy Chimoyi

Posted Date: 15 August 2025

doi: 10.20944/preprints202508.1144.v1

Keywords: people living with HIV (PLHIV); tuberculosis; preventive tuberculosis treatment; geospatial analysis; treatment outcomes

Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

*Article*

# A Geospatial Analysis of TPT Treatment Outcomes Among PLHIV in Ethiopia, South Africa, and Zimbabwe

**Joeri S. Buis [1,*], Christiaan Mulder [1,2], Ahmed Bedru [3], Jozefien Groenendijk [1], Solomon Sisay [3], Israel Rabothata [4], Nicole Kawaza [5] Christopher J. Hoffmann [6], Violet Chihota [4,7], Sibuse Ginindza [4], Kenny Sithole [5], Kate Shearer [6] and Lucy Chimoyi [4]**

[1] Prevention & Access, KNCV TB Foundation, The Hague, The Netherlands
[2] Amsterdam Institute for Global Health and Development, Amsterdam University Medical Centres, Amsterdam, The Netherlands
[3] KNCV TB Foundation, Addis Ababa, Ethiopia
[4] Aurum Institute, Johannesburg, South Africa
[5] Clinton Health Access Initiative, Harare, Zimbabwe
[6] John Hopkins University, United States of America
[7] University of Witwatersrand, School of Public Health, Johannesburg, South Africa
* Correspondence: joeri.buis@kncvtbc.org

**Abstract**

**Background:** Tuberculosis (TB) preventive treatment (TPT) is crucial in reducing the TB burden among people living with HIV (PLHIV), particularly in high TB/HIV burden countries like Ethiopia, South Africa, and Zimbabwe. Despite the availability of shorter TPT regimens, suboptimal treatment completion persists, and subnational variations remain poorly understood. **Methods:** This study utilized geospatial analyses of treatment completion data from the Opt4TPT study, a prospective cohort conducted in Ethiopia, South Africa, and Zimbabwe (2021–2023). Participants' demographic and clinical data were included, and geospatial patterns were assessed using QGIS and local indicators of spatial autocorrelation (LISA) to identify clusters of treatment outcomes. **Results:** Of the 1,320 participants enrolled, 1,076 (81.5%) had geolocated data, and 90.1% reported completing TPT. Treatment non-completion clustered near clinics in all three countries. LISA analysis identified spatial cold spots for low treatment completion near clinics in South Africa and Zimbabwe, but not in Ethiopia. Distribution of demographic and clinical factors did not align with treatment outcomes. **Conclusions:** Geospatial analyses revealed clustering of non-completion near clinics, warranting further research on contextual factors, including stigma and facility-switching behavior. These findings emphasize the potential of geospatial tools in optimizing TPT programs through locally tailored interventions.

**Keywords:** people living with HIV (PLHIV); tuberculosis; preventive tuberculosis treatment; geospatial analysis; treatment outcomes

## Introduction

The increased risk of developing tuberculosis (TB) disease among people living with HIV (PLHIV) is well-established, even in the presence of antiretroviral therapy (ART)[1]. According to the World Health Organization (WHO), PLHIV have a 16-times increased risk of progression to TB disease compared to people without HIV, making TB the most common cause of death within this group [2]. In 2022, 6.3% of the incidence of people developing TB lived with HIV, resulting in 167,000 deaths in this population [2]. TB preventive treatment (TPT) prevents the development of TB among people with TB infection (TBI) [3]. This underscores the importance of TPT in mitigating the impact

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



of TB among PLHIV, particularly in high TB/HIV burden countries like South Africa, Ethiopia, and Zimbabwe [4].

TPT is effective in preventing TB disease in PLHIV, with the WHO recommending isoniazid preventive treatment (IPT) for all children and adults living with HIV since 2011 [5]. Research among PLHIV showed that IPT reduces the risk of TB with 35% (RR = 0.65, 95% CI (0.51, 0.84)) and 52% among those who test positive on the tuberculin skin test (TST) (RR = 0.48; 95% CI (0.29, 0.82)) [3]. Despite IPT's effectiveness, the duration of 6, 9, or 36 months complicates treatment completion. Recently, the WHO updated guidelines to include the 3 month weekly regimen of rifapentine and isoniazid (3HP), which was shown to be non-inferior to IPT and increases completion rates [6]. The introduction of 3HP aims to enhance treatment adherence and outcomes.

Successful completion of TPT is dependent on various demographic and clinical factors besides treatment duration. Factors such as longer travel distances to clinics, being male, younger and older ages, non-adherence to ART clinic visits, and having side effects are associated with non-completion of TPT [7–12]. Additionally, being underweight or overweight may negatively impact treatment outcomes by increasing the risk of side effects and progression to active TB disease [13,14]. Understanding these factors is vital for policy makers and decision-makers when allocating resources for TPT programs [15,16].

South Africa, Ethiopia, and Zimbabwe are among the 30 high TB/HIV burden countries that have recently implemented and scaled up the new WHO-recommended shorter TPT regimen [4]. The WHO estimated in 2022, that of the 156,000 TB cases in Ethiopia, 6,100 (3.9%) were co-infected with HIV [17]. In South Africa, they estimated 280,000 TB cases of which 152,000 (54%) were co-infected with HIV and in Zimbabwe the estimates were 33,000 TB cases and 20,000 TB/HIV cases (61%) [18,19]. TPT initiation among – newly enrolled in care- PLHIV was 64% in Ethiopia, 62% in South Africa, and 67% in Zimbabwe [17–19]. In addition to the -relatively low- initiation percentages, treatment completion is vital in preventing progression to TB and preventing antimicrobial resistance (AMR). A study in Ethiopia found that 70.5% of PLHIV on TPT completed treatment [20], this was 52% in South Africa [21], and 94% in Zimbabwe [22]. None of these studies however, assessed for subnational differences between TPT treatment outcomes. Understanding TPT treatment outcomes on subnational level can support optimization of TPT programs and resource allocation.

Spatial analyses are increasingly used to identify health disparities within countries, aiding the development of locally tailored interventions to improve prevention and care [23,24]. To the researchers knowledge, no previous research has used spatial analyses to assess geospatial differences in TPT treatment outcomes among PLHIV. Understanding the geospatial heterogeneity in TPT completion can help generate new hypotheses about regional variations and identify regions needing targeted interventions. This study aims to show how geospatial analyses can enhance understanding of TPT completion by assessing and comparing geospatial patterns of treatment completion and demographic and clinical factors in Ethiopia, South Africa, and Zimbabwe.

## Materials and Methods

### *Study Design and Setting*

This secondary analysis utilized data from the Optimizing the delivery cascade for tuberculosis preventive treatment among PLHIV (Opt4TPT) prospective study, which aimed to optimize TPT delivery among PLHIV attending routine HIV services [25]. The Opt4TPT study followed PLHIV who attended primary healthcare facilities for routine HIV-related care, from eligibility for TPT (3HP or IPT) to initiation and completion of treatment in Ethiopia, South Africa, and Zimbabwe [16].

### *Participants*

Adult PLHIV (≥ 18 years of age) receiving HIV care at selected facilities in Ethiopia, South Africa, and Zimbabwe who consented to participate in the Opt4TPT study were included. Participants either received IPT or 3HP. Due to COVID-19 restrictions at the time of monitoring, most participants

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



received the full regimen at their first visit in Ethiopia and Zimbabwe. In South Africa, participants prescribed IPT were provided with a three-month prescription whereas those taking 3HP were prescribed at two time points. For one month followed by the remaining two months at the next clinic visit.

*Data Collection*

Between July 2021 and December 2023, data were collected from three primary healthcare facilities who distributed IPT and/or 3HP to PLHIV in each country. In Addis Ababa, Ethiopia, the selected health centres included Arada, Meri, and Yeka. Meri health centre only provided IPT and not 3HP. In Johannesburg and Tshwane, South Africa, we included the community health centres (CHC) Chiawelo, Soshanguve, and Stretford. Soshanguve centre solely provided IPT and not 3HP. In Gweru, Kwekwe and Beitbridge, Zimbabwe, the selected sites included Monomotapa and Mbizo clinics, and Beitbridge hospital, with the Mbizo clinic solely providing IPT.

*Treatment Completion*

Healthcare personnel assessed self-reported treatment completion through monthly phone calls or during participants' quarterly clinic visits. We followed WHO TPT guidelines for the definition of treatment completion as documented in clinical records [15]. This included ≥11/12 doses over a 16 week period for 3HP; ≥167/182 doses over a 32 week period for 6 months of IPT (6H) and ≥336/365 doses over a 64 week period for 12 months of IPT (12H).

*Geospatial Descriptive Analysis*

We assessed the geospatial distribution of treatment completion and investigated whether the geospatial distribution of the demographic and clinical variables showed a similar pattern. We highlighted geographic patterns of treatment completion using descriptive visualizations in QGIS 3.32 LIMA [26]. Separate maps were created for treatment completion and the outcome variables: sex (male/female), age (<30y, between >30 and <50y, and >50y), TPT regimen (3HP or IPT), interruption of antiretroviral treatment (ART) since enrolment, and BMI (underweight: <18, normal: 18.5-24.9, overweight: 25-29.9, and obese: 30+). [1] Geographic data (shapefiles) including administrative boundaries, were obtained through www.diva-gis.org. Participants' addresses were geolocated with street names, landmarks and additional descriptions using Google Maps. When exact addresses were unavailable, neighbourhood approximations were used or GPS coordinates of participants with a similar address. By doing this, certain participants' GPS coordinates were overlapping. Therefore, we separated the GPS points in QGIS 3.32 LIMA by creating 80m buffer zones around each point. We used the function '*random points inside polygon*' to create a new point within the buffer zone with the limitation that points cannot overlap and ensured that data points did not cross their original administrative boundaries.

Participants without a treatment completion outcome or a GPS coordinate were excluded. Descriptive results were visualized as point data. For the South African and Zimbabwean maps, we zoomed in on the regions surrounding the hospital as the land cover was to large to show the regions further removed. For Ethiopia, the map zoomed in on Addis Ababa so that the data points could be clearly viewed and potential geospatial trends could be identified. Variables with insufficient data were not visualized. ART interruption since enrolment was not geospatially mapped due to the low numbers of participants interrupting treatment (n≤5 per country). All BMI data was missing for the Mbizo health centre and the numbers were considerably low for Monomotapa clinic (3 in total). Therefore, BMI was not geospatially visualized for these two clinics in Zimbabwe. Additionally, TPT regimen data was not spatially visualized for the clinics that provided all participants with either IPT

[1] We did not find any identifiable patterns in the maps created with these demographic variables and therefore, these maps are not included in this article.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



or 3HP as this would not provide a geospatial distribution that could be compared with the geospatial distribution of treatment completion.

*Spatial Autocorrelation*

Next, we calculated local indicators of spatial autocorrelation (LISA) for each administrative area with data points in each country. LISA's were used to identify significant spatial clusters (hot- and cold spots) and spatial outliers with high or low treatment completion rates. A hotspot was defined as an area in which the administrative areas with high treatment completion rates were significantly nearer to each other (clustered) than expected with random distribution. A cold spot had administrative areas with low treatment completion rates that are significantly near to each other (clustered) compared to random distribution. A spatial outlier occurred when an administrative area with high treatment completion rates neighbours an administrative area with low completion rates and vice versa. We used the coordinates of the raw data to calculate the LISA statistic [27]. We took the number of participants who completed treatment and divided it by the total number of participants per administrative area to generate a numeric z-value. Administrative level 3 was used for Ethiopia (woreda level) and Zimbabwe (wards) and administrative level 4 was used for South Africa (wards). The LISA analysis was conducted in GeoDa [28]. In GeoDa, the empirical bayes estimator was calculated to account for outliers caused by low denominator values within the sample size. The empirical smoothed rates were log transformed to normalize the data. We used the Queen Contiguity in the weight manager. The maps visualized the presence of significant spatial clusters of high or low completion rates as well as any existing spatial outliers.

*Post-hoc Analysis*

We conducted a post-hoc sensitivity analysis of treatment completion based on the data collected using the EvriMED1000 Medication Event Reminder Monitors (MERM, Wisepill Technologies, Cape Town, South Africa) [29]. The EnvriMED1000 is a pillbox with a SIM-card that records and sends date and time information to a central server every time the box is opened. The number of times the pillbox was opened was used as a proxy to measure treatment completion. The device was given to a subsample of people who initiated TPT. The boxes could accommodate one month supply of 3HP or IPT.

*Ethical Statement*

The Human Research Ethics Committees of the University of the Witwatersrand, South Africa granted the initial ethical approval (Ref No: 210212). In addition, we received approval from the independent review boards for Johns Hopkins University (Ref No: IRB00280677), Medical Research Council, Zimbabwe (Ref No:MRCZ/A/2727) and Addis Ababa Health Bureau (Ref No: A/A/145/227). We received further approval from Johannesburg Metropolitan Health District and City of Tshwane (South Africa). Respective health facilities gatekeepers were approached for permission before data collection. All participants interviewed provided written informed consent.

## Results

The Opt4TPT study collected data from 1,319 participants who initiated TPT starting from enrolment, with 125 in Ethiopia, 520 in South Africa, and 674 in Zimbabwe. A GPS coordinate could be identified for 1,076 (81.5%) participants. This resulted in 83 (66.4%) data points in Ethiopia, 484 (93%) in South Africa, and 509 (75.5%) for Zimbabwe. Overall, 50.6% of the geo-located participants received 3HP and 90.1% completed TPT as documented in clinical records. Most of the participants were between 30 and 50 years old (62.5%) female (71.4%) and reported a BM1≥ 25 (55.5%). Table 1 shows the demographic and clinical factors of the participants with a GPS coordinate.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

**Table 1.** Descriptives of people living with HIV (PLHIV) enrolled in the *Optimizing the delivery cascade for tuberculosis preventive treatment* (Opt4TPT) study for whom a GPS coordinate could be identified in the designated hospitals in South Africa, Ethiopia, Zimbabwe, 2021.

| | | **Ethiopia** | | | | **South Africa** | | | | **Zimbabwe** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Overall total | Total | Arada | Meri | Yeka | Total | Soshan-guve | Chiawelo | Stretford | Total | Mono-motapa | Mbizo | Beitbridge |
| Nr. Of participants (%) | 1,076 (100) | 83 (100) | 28 (33.7) | 13 (15.7) | 42 (50.6) | 484 (100) | 61 (12.6) | 208 (42.9) | 215 (44.4) | 509 (100) | 203 (39.9) | 206 (40.5) | 100 (19.7) |
| TPT treatment completion as documented in clinical records (%) | | | | | | | | | | | | | |
| Completed | 969 (90.1) | 69 (83.1) | 23 (82.1) | 8 (61.5) | 38 (90.5) | 424 (87.6) | 50 (82) | 190 (91) | 184 (85.6) | 476 (93.5) | 190 (93.6) | 193 (93.7) | 93 (93) |
| Not completed | 107 (9.9) | 14 (16.9) | 5 (7.9) | 5 (38.5) | 4 (9.5) | 60 (12.4) | 11 (18) | 18 (9) | 31 (14.4) | 33 (6.5) | 13 (6.4) | 13 (6.3) | 7 (7) |
| Age groups (%) | | | | | | | | | | | | | |
| <30 years | 164 (15.2) | 13 (15.6) | 6 (21.4) | 4 (30.8) | 3 (7.1) | 55 (11.4) | 15 (24.6) | 30 (14.4) | 10 (4.6) | 96 (18.9) | 41 (20.2) | 46 (22.3) | 9 (9) |
| >30 <50 years | 673 (62.5) | 51 (61.5) | 14 (50) | 8 (61.5) | 29 (7) | 299 (61.8) | 42 (68.9) | 133 (63.9) | 124 (57.7) | 323 (63.5) | 123 (60.6) | 127 (61.7) | 73 (73) |
| >50 years | 239 (22.3) | 19 (22.9) | 8 (28.6) | 1 (7.7) | 10 (23.8) | 130 (26.9) | 4 (6.6) | 45 (21.6) | 81 (37.7) | 90 (17.7) | 39 (19.2) | 33 (16) | 18 (18) |
| Gender (%) | | | | | | | | | | | | | |
| Female | 768 (71.4) | 54 (65) | 17 (60.7) | 7 (53.9) | 30 (71.4) | 342 (70.7) | 42 (68.9) | 157 (75.5) | 143 (66.5) | 372 (73) | 134 (66) | 174 (84.5) | 64 (64) |
| Male | 308 (28.6) | 29 (35) | 11 (39.3) | 6 (46.1) | 12 (28.6) | 142 (29.3) | 19 (31.1) | 51 (24.5) | 72 (33.5) | 137 (27) | 69 (34) | 32 (15.5) | 36 (36) |

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

| TPT regimen (%) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3HP | 545 (50.6) | 66 (79.5%) | 23 (82.1%) | 1 (7.7%) | 42 (100%) | 311 (64.3%) | 0 | 115 (55.3%) | 196 (91.2%) | 168 (33%) | 95 (46.8%) | 0 | 73 (73%) |
| IPT* | 531 (49.4) | 17 (20.5%) | 5 (17.9%) | 12 (92.3%) | 0 | 173 (35.7%) | 61 (100%) | 93 (44.7%) | 19 (8.8%) | 341 (67%) | 108 (53.2%) | 206 (100%) | 27 (27%) |
| ART interrupted since enrolment (%)[1] | | | | | | | | | | | | | |
| Yes | 11 (1) | 4 (5.2) | 1 (4.2) | 0 | 3 (7.5) | 4 (1) | 1 (1.9) | 1 (0.5) | 2 (1) | 3 (1) | 3 (1.5) | 0 | 0 |
| No | 1,027 (99) | 73 (94.8) | 23 (95.8) | 13 (100) | 37 (92.5) | 453 (99) | 53 (98.1) | 207 (99.5) | 193 (99) | 501 (99) | 196 (98.5) | 205 (100) | 100 (100) |
| BMI categories (%)[2] | | | | | | | | | | | | | |
| <18.5 | 39 (6.1%) | 11 (14.3%) | 7 (25.9%) | 1 (7.7%) | 7 (18%) | 17 (3.7%) | 3 (4.9%) | 3 (1.4%) | 16 (7.6%) | 3 (20%) | 0 | - | 2 (2.7%) |
| 18.5-24.9 | 246 (38.6%) | 48 (62.3%) | 16 (59.3%) | 11 (84.6%) | 25 (64.1%) | 146 (32%) | 32 (52.5%) | 54 (26%) | 79 (37.3%) | 5 (33.3%) | 2 (66.7%) | - | 27 (36%) |
| 25-29.9 | 175 (27.4%) | 14 (18.2%) | 4 (14.8%) | 1 (7.7%) | 4 (10.3%) | 149 (32.7%) | 16 (26.2%) | 89 (42.8%) | 36 (17%) | 5 (33.3%) | 1 (33.3%) | - | 24 (32%) |
| 30+ | 178 (27.9%) | 4 (5.2%) | 0 | 0 | 3 (7.7%) | 144 (31.6%) | 10 (16.4%) | 62 (29.8%) | 81 (38.2%) | 2 (13.3%) | 0 | - | 22 (29.3%) |

1.ART total missing values= 38, of which Stretford clinic missed 20 values, Soshanguve Community Health Centre (CHC) 7, Arada health centre and Monomotapa clinic both missed 4 values, Yeka health centre 2, and Mbizo clinic 1. 2. BMI total missing values= 438, all BMI values were missing for Mbizo health centre, Monomotapa clinic missed 200, Beitbridge hospital 25, Stretford CHC, Yeka health centre both missed 3 values, and Arada health centre missed 1.*IPT regimen in South Africa is given for 12 months to PLHIV, In Ethiopia and Zimbabwe, IPT is prescribed for 6 months.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



*Descriptive Mapping*

In Ethiopia, participants not completing treatment as documented in clinical records seemed to be more concentrated in the areas close to the health centres, with little non-completion among participants living outside the municipalities of the health centres (see supplementary material A, Figure 1-2). There was no similarity between the distribution of participants who did not complete treatment and the distribution of demographic and clinical variables. Notably, the same pattern could be discerned in South Africa (see supplementary material B, Figure 1-3). In Chiawelo and Stretford CHC, participants who did not complete treatment lived relatively close to the CHC and there was no similarity between the distribution of treatment completion and the distribution of the demographic and clinical variables, except in the CHC in Stretford (see supplementary material B, Figure 4). In Stretford, the participants who received IPT seemed to be living closer to the CHC similar to the clustering of non-completion in the area close to the centres. In Zimbabwe, similar to Ethiopia and South Africa, non-completion seemed to be clustered close to the clinics in Mbizo and Monomotapa clinic (see supplementary material C, Figure 1-3). Around Beitbridge Hospital treatment non-completion did not seem to cluster spatially (see supplementary material C, Figure 4). Additionally, the distribution of treatment completion was not similar to the distribution of the demographic and clinical variables for any of the three facilities in Zimbabwe.

*Geospatial Aut#ocorrelation*

The geospatial maps showing the LISA statistics with the identified significant clusters can be found in the supplementary D, Figure 1 and 2. There were no significant hot and/or cold spots or outliers identified in Ethiopia. In all three locations of the CHC in South Africa, there were significant spatial clusters of low values (cold spots), which were close to the CHC, especially in the area of Soshanguve CHC (supplementary D, Figure 1). This suggests that treatment completion as documented in clinical records in those areas are consistently lower relative to the surrounding areas. In Zimbabwe (supplementary material D, Figure 2), we identified a few significant spatial cold spots in Mbizo and Monomotapa area. Notably, one of these cold spots is close to the clinic, the other two are further removed from the clinic. In Beitbridge there were no significant hot- or cold spots nor outliers found.

*Post-hoc Analysis*

The number of PLHIV enrolled in the Opt4TPT study using the EvriMed1000 and for whom a GPS coordinate could be identified, was smaller than the dataset with treatment outcomes as documented in clinical records. In total treatment completion was considerably lower (around 50%) based on the clinical records (Table 2). Using the EvriMed1000 data, we did not find a pattern of clustering close to the clinics, CHC, hospitals (supplementary material E, Figure 1-9). The LISA statistics only identified one cold cluster close to the health center in Monomotapa, Zimbabwe (supplementary material F).

**Table 2.** Treatment outcomes based on the Evrimed1000 data of people living with HIV (PLHIV) enrolled in the *Optimizing the delivery cascade of preventive treatment* (Opt4TPT) study ) for whom a GPS coordinate could be identified and who initiated preventive treatment (TPT) in Ethiopia, South Africa, and Zimbabwe, 2021.

| | Ethiopia | South Africa | Zimbabwe |
|---|---|---|---|
| Total participants (%) | 98 | 302 | 302 |
| Participants who completed treated (%) | 50 (51) | 179 (59) | 146 (48) |

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



## Discussion

We investigated the utility of geospatial analyses in understanding TPT treatment completion using treatment outcome data, as well as demographic and clinical factors, collected during the prospective Opt4TPT cohort study in Ethiopia, South Africa, and Zimbabwe between 2021-2023. The reported treatment completion as documented in clinical records was high and we did not find similarities between the distribution of treatment outcomes and the demographic and clinical factors across the study sites.

In summary, participants who did not complete their treatment lived relatively close to the clinics in all three countries. This finding was substantiated with the LISA statistics, which identified cold spots in areas around the clinics in South Africa and partly in Zimbabwe but not in Ethiopia. Previous research showed that distance negatively impacts TB and TPT treatment completion [9,11], although findings vary and are complex [30]. During the time of this study participants received their full regimens upon initiation and additional clinic visits were not needed due to COVID-19 measures, which may explain the absence of a clear geospatial pattern of non-completion in areas further away from the clinics. Providing full regimens upon initiation is a model within the differentiated service deliveries (DSD). Several countries have strengthened the implementation of DSD during the COVID-19 lockdowns because it alleviates the burden on the health facilities and limits traveling [31]. Some research has shown increase treatment completion rates[32] however, more monitoring and evaluation research is necessary to understand the impacts of DSD on TPT delivery.

It is unclear why we are seeing the opposite in South Africa and Zimbabwe. Stigma remains a significant factor in HIV care [33] and it could be that PLHIV prefer to visit facilities further away from their residences as they may fear inadvertent disclosure of their HIV positive status [34]. Some of the participants who initiated TPT and were living close to the facility may have changed healthcare facility and terminated contact with the initial healthcare facility. This warrants further exploration through qualitative research.

Participants who received IPT and those who did not complete treatment seemed to live in the same areas based on the descriptive mapping in the area of Stretford CHC. It is unclear whether the longer duration of IPT compared to 3HP might explain the lower treatment outcomes in Stretford CHC in South Africa, proximity to the health centre, or other factors [6]. It is not clear, why this result was only found in the community centre of Stretford. As our study did not identify similarities between the distribution of the demographic and clinical factors, factors that were not included in this study, may have influenced treatment completion. Other factors associated with TPT completion include marital status, counselling, and health education as [7,9,35]. Additional research using inferential statistics is needed to further explore these relationship in the context of Ethiopia, South Africa, and Zimbabwe.

The post-hoc analysis using the EvriMed1000 data did not find clustering close to the clinics, CHC, hospitals. Additionally, treatment completion was considerably lower compared to the treatment completion as recorded in clinical records, indicating a potential overestimation of treatment completion based on self-reporting.

### *Implications and Limitations*

The interpretation and application of this study warrant careful consideration. The healthcare facilities were not randomly sampled, which limits the generalizability of our findings. Additionally, the GPS coordinates were derived from information provided in the informed consent forms, which made geolocating and verification of the addresses challenging. This may have introduced some bias in our results. Additionally, we could not find a GPS coordinate for all participants. For the descriptive mapping, we used point data instead of choropleths due to the non-representative nature of our sample. While this approach allowed us to assess overlap in geospatial patterns for various variables, it necessitates cautious interpretation, especially given the low number of participants, the large land cover, and the complexity of mapping multiple factors. Similarly, the LISA statistics

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1



provided valuable insights but would benefit from a random sample to strengthen the evidence for decision-making.

Another consideration is the interpretation of the relatively high treatment completion percentages. Treatment completion as documented in clinical records was based on participants' self-reporting during phone calls by study staff. This may have led to an overestimation of treatment completion. This is further supported by the lower treatment completion percentages found within the Evrimed1000 data. Self-reported data can be subject to recall bias, social desirability bias, or (un)intentional misreporting. While convenient, relying solely on self-reports may not provide a complete picture of treatment completion, especially in the context of remote monitoring during the COVID-19 pandemic. Using a more objective measure will be necessary as it ensures a more accurate assessment of adherence and treatment completion, which is crucial for evaluation and improving TPT programs. An objective assessment of TPT completion could include a combination of pill counts or electronic monitoring devices to track medication intake, periodic clinical visits or home visits to verify treatment adherence, or for example, testing for biological metrics in blood or urine samples.

*Strengths*

To our knowledge, this is the first study to assess the utility of geospatial analyses in understanding TPT treatment outcomes in Ethiopia, South Africa, and Zimbabwe. We demonstrated that geospatial maps can highlight the need for further targeted research such including additional factors potentially influencing treatment completion, and monitoring and evaluating DSDs, Stronger interpretations require random sampled data, accurate geolocated addresses, and a more objective measure or combination of measures to assess treatment completion.

## Conclusions

Future geospatial research should prioritize randomized samples, improved data accuracy, and objective outcome measures. Our findings suggest a need to explore the role of stigma in TPT completion and to include additional demographic variables. Integrating TPT care in differentiated service delivery models (DSD) and geospatial data in M&E systems may improve monitoring of treatment and increase initiation and completion of TPT among PLHIV. This combined approach can inform health facilities and local TB programs, enhancing the overall care provided by the TPT programs.

**Author contribution:** L.C., K.S., V.C., C.M., and J.S.B. conceptualized and designed the study protocol. J.S.B. and J.G. geolocated the participants' coordinates. J.S.B. performed the spatial mapping, conducted the data analysis, and drafted the initial version of the manuscript. L.C. supervised the spatial mapping and together with C.M. supported the interpretation of results and revised and edited the manuscript. All authors reviewed and approved the final manuscript.

## References

1. Dheda, K.; Barry, C.E.; Maartens, G. Tuberculosis (HIV). *The Lancet* **2016**, *387*, 1211–1226, doi:10.1016/S0140-6736(15)00151-8.
2. Global Tuberculosis Report 2023 Available online: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023 (accessed on Feb 19, 2024).
3. Ayele, H.T.; Mourik, M.S.M. van; Debray, T.P.A.; Bonten, M.J.M. Isoniazid Prophylactic Therapy for the Prevention of Tuberculosis in HIV Infected Adults: A Systematic Review and Meta-Analysis of Randomized Trials. *PLoS One* **2015**, *10*, e0142290, doi:10.1371/journal.pone.0142290.
4. WHO releases new global lists of high-burden countries for TB, HIV-associated TB and drug-resistant TB Available online: https://www.who.int/news/item/17-06-2021-who-releases-new-global-lists-of-high-burden-countries-for-tb-hiv-associated-tb-and-drug-resistant-tb (accessed on Jun 13, 2024).

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1




5. New WHO guidelines: TB prevention for people with HIV Available online: https://www.who.int/news/item/28-01-2011-new-who-guidelines-tb-prevention-for-people-with-hiv (accessed on Jun 12, 2024).
6. Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection | New England Journal of Medicine Available online: https://www.nejm.org/doi/full/10.1056/NEJMoa1104875 (accessed on Jun 12, 2024).
7. Lwevola, P.; Izudi, J.; Kimuli, D.; Komuhangi, A.; Okoboi, S. Low level of tuberculosis preventive therapy incompletion among people living with Human Immunodeficiency Virus in eastern Uganda: A retrospective data review. *J Clin Tuberc Other Mycobact Dis* **2021**, *25*, 100269, doi:10.1016/j.jctube.2021.100269.
8. Musaazi, J.; Sekaggya-Wiltshire, C.; Okoboi, S.; Zawedde-Muyanja, S.; Senkoro, M.; Kalema, N.; Kavuma, P.; Namuwenge, P.M.; Manabe, Y.C.; Castelnuovo, B.; et al. Increased uptake of tuberculosis preventive therapy (TPT) among people living with HIV following the 100-days accelerated campaign: A retrospective review of routinely collected data at six urban public health facilities in Uganda. *PLoS One* **2023**, *18*, e0268935, doi:10.1371/journal.pone.0268935.
9. Amanya, I.; Muhoozi, M.; Aruhomukama, D.; Ssebagereka, A.; Mugambe, R. Isoniazid preventive therapy completion and factors associated with non-completion among patients on antiretroviral therapy at Kisenyi Health Centre IV, Kampala, Uganda. *PLOS ONE* **2023**, *18*, e0277739, doi:10.1371/journal.pone.0277739.
10. Uptake and completion of tuberculosis preventive therapy among people living with HIV on antiretroviral therapy in Uganda, 2020–2023 - UNIPH 2024.
11. McNabb, K.C.; Bergman, A.J.; Patil, A.; Lowensen, K.; Mthimkhulu, N.; Budhathoki, C.; Perrin, N.; Farley, J.E. Travel distance to rifampicin-resistant tuberculosis treatment and its impact on loss to follow-up: the importance of continued RR-TB treatment decentralization in South Africa. *BMC Public Health* **2024**, *24*, 578, doi:10.1186/s12889-024-17924-0.
12. Ngugi, S.K.; Muiruri, P.; Odero, T.; Gachuno, O. Factors affecting uptake and completion of isoniazid preventive therapy among HIV-infected children at a national referral hospital, Kenya: a mixed quantitative and qualitative study. *BMC Infectious Diseases* **2020**, *20*, 294, doi:10.1186/s12879-020-05011-9.
13. Choun, K.; Thai, S.; Pe, R.; Lorent, N.; Lynen, L.; Van Griensven, J. Incidence and risk factors for tuberculosis in HIV-infected patients while on antiretroviral treatment in Cambodia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **2013**, *107*, 235–242, doi:10.1093/trstmh/trt001.
14. Njagi, L.N.; Nduba, V.; Mureithi, M.W.; Mecha, J.O. Prevalence and predictors of tuberculosis infection among people living with HIV in a high tuberculosis burden context. *BMJ Open Respiratory Research* **2023**, *10*, e001581, doi:10.1136/bmjresp-2022-001581.
15. World Health Organization *WHO operational handbook on tuberculosis: module 1: prevention: tuberculosis preventive treatment*; World Health Organization: Geneva, 2020; ISBN 978-92-4-000290-6.
16. IMPAACT4TB - IMPAACT4TB Available online: http://impaact4tb.org/ (accessed on Feb 19, 2024).
17. TB profile Ethiopia Available online: https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&iso2=%22ET%22&lan=%22EN%22 (accessed on Jun 13, 2024).
18. TB profile SA Available online: https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&iso2=%22ZA%22&lan=%22EN%22 (accessed on Jun 13, 2024).
19. TB profile Zimbabwe Available online: https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&iso2=%22ZW%22&lan=%22EN%22 (accessed on Jun 13, 2024).
20. Gebreegziabher, S.B.; Ashuro, A.A.; Kumssa, T.H.; Teferi, M.Y.; Alemayue, E.A.; Datiko, D.G.; Yimer, S.A.; Shagre, M.B. Tuberculosis preventive treatment uptake among people living with HIV during COVID-19 period in Addis Ababa, Ethiopia: a retrospective data review. *BMC Infect Dis* **2024**, *24*, 499, doi:10.1186/s12879-024-09403-z.
21. Naidoo, P.; Theron, G.; Rangaka, M.X.; Chihota, V.N.; Vaughan, L.; Brey, Z.O.; Pillay, Y. The South African Tuberculosis Care Cascade: Estimated Losses and Methodological Challenges. *The Journal of Infectious Diseases* **2017**, *216*, S702–S713, doi:10.1093/infdis/jix335.


© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2025 doi:10.20944/preprints202508.1144.v1




22. Nyathi, S.; Dlodlo, R.A.; Satyanarayana, S.; Takarinda, K.C.; Tweya, H.; Hove, S.; Matambo, R.; Mandewo, W.; Nyathi, K.; Sibanda, E.; et al. Isoniazid preventive therapy: Uptake, incidence of tuberculosis and survival among people living with HIV in Bulawayo, Zimbabwe. *PLOS ONE* **2019**, *14*, e0223076, doi:10.1371/journal.pone.0223076.
23. The KIT MATCH Approach for Enhancing TB Care Coverage Available online: https://www.kit.nl/institute/project/the-kit-match-approach-for-enhancing-tb-care-coverage/ (accessed on Jun 9, 2024).
24. Mergenthaler, C.; Gurp, M.; Rood, E.; Bakker, M. The study of spatial autocorrelation for infectious disease epidemiology decision-making: a systematized literature review. *CABI Reviews* **2022**, *2022*, doi:10.1079/cabireviews202217018.
25. OPT4TPT Study. *IMPAACT4TB*.
26. Benvenuto in QGIS! Available online: https://www.qgis.org/it/site/ (accessed on May 3, 2024).
27. Anselin, L. Local Indicators of Spatial Association—LISA. *Geographical Analysis* **1995**, *27*, 93–115, doi:10.1111/j.1538-4632.1995.tb00338.x.
28. GeoDa on Github Available online: https://geodacenter.github.io/ (accessed on May 3, 2024).
29. evriMED1000 Pillbox Available online: https://www.wisepill.com/evrimed (accessed on Dec 23, 2024).
30. Robsky, K.O.; Hughes, S.; Kityamuwesi, A.; Kendall, E.A.; Kitonsa, P.J.; Dowdy, D.W.; Katamba, A. Is distance associated with tuberculosis treatment outcomes? A retrospective cohort study in Kampala, Uganda. *BMC Infect Dis* **2020**, *20*, 406, doi:10.1186/s12879-020-05099-z.
31. Nhari, L.G.; Dzobo, M.; Chitungo, I.; Denhere, K.; Musuka, G.; Dzinamarira, T. Implementing effective TB prevention and treatment programmes in the COVID-19 era in Zimbabwe. A call for innovative differentiated service delivery models. *Public Health in Practice* **2020**, *1*, 100058, doi:10.1016/j.puhip.2020.100058.
32. Tran, C.H.; Moore, B.K.; Pathmanathan, I.; Lungu, P.; Shah, N.S.; Oboho, I.; Al-Samarrai, T.; Maloney, S.A.; Date, A.; Boyd, A.T. Tuberculosis treatment within differentiated service delivery models in global HIV/TB programming. *Journal of the International AIDS Society* **2021**, *24*, e25809, doi:10.1002/jia2.25809.
33. Earnshaw, V.A.; Chaudoir, S.R. From Conceptualizing to Measuring HIV Stigma: A Review of HIV Stigma Mechanism Measures. *AIDS Behav* **2009**, *13*, 1160–1177, doi:10.1007/s10461-009-9593-3.
34. Pellowski, J.A. Barriers to Care for Rural People Living With HIV: A Review of Domestic Research and Health Care Models. *Journal of the Association of Nurses in AIDS Care* **2013**, *24*, 422–437, doi:10.1016/j.jana.2012.08.007.
35. Cola, J.P.; Nascimento do Prado, T.; Alves, K.B.A.; Lapa E Silva, J.R.; Trajman, A.; Golub, J.E.; Chaisson, R.E.; Maciel, E.L.N. Factors associated with non-completion of TB preventive treatment in Brazil. *Int J Tuberc Lung Dis* **2023**, *27*, 215–220, doi:10.5588/ijtld.22.0571.


**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.