

Determinants of isoniazid preventive therapy among people living with HIV in Kasai-Oriental Province, Democratic Republic of the Congo: a cross-sectional study

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Abstract

Background

Tuberculosis (TB) remains the leading infectious cause of illness and death among people living with HIV (PLHIV) in sub-Saharan Africa. Isoniazid preventive therapy (IPT), is a core component of the package of HIV care recommended by the World Health Organization (WHO) is delivered alongside antiretroviral therapy (ART), yet it remains substantially underused in high-burden countries despite the strong supporting evidence.

Methods

We conducted an analytical cross-sectional using the records of 1,176 people living with HIV (PLHIV) who received care between January 2020 and December 2022 at the main HIV care facilities in Kasai-Oriental, DRC. Sociodemographic, clinical and programmatic variables were extracted from HIV registers and patient charts. Bivariate and multivariable binary logistic regression were used to estimate adjusted odds ratios (aOR) with 95% confidence intervals (95% CI). The ability of the final model to distinguish patients who did and did not initiate IPT was assessed with the area under the receiver operating characteristic curve (AUC).

Results

Of the 1,176 PLHIV included, 61.6% were female and the median age was 38 years (IQR: 30–46). At enrolment, 63.7% were at WHO clinical stage III. The Overall 245 patients (20.8%; 95% CI: 18.5–23.2) initiated IPT. Among the who started treatment, 106 discontinued it before reaching six months, that is 43.3% of initiators and 9.0% of the whole cohort, and documented six-month completion was found for only 2 patients (0.2%; 95% CI: 0.02–0.7). After multivariable adjustment, four factors remained independently associated with IPT initiation: urban residence (aOR = 7.89; 95% CI: 1.03–60.71; $p = 0.047$); TDF+3TC + DTG ART regimen (aOR = 5.43; 95% CI: 2.76–10.69; $p < 0.001$); WHO clinical stage I or II (aOR = 2.19; 95% CI: 1.61–2.99; $p < 0.001$); and being active in HIV care at the time of analysis (aOR = 2.06; 95% CI: 1.22–3.46; $p = 0.007$).

Conclusions

IPT uptake among PLHIV in Mbuji mayi remains far below WHO and UNAIDS targets, and the near-absence of documented treatment completion is particularly alarming. Priority actions to close this implementation gap in a setting with a high HIV/TB co-epidemic include strengthening TB/HIV service integration, securing the supply of isoniazid and pyridoxine, providing continuous training for frontline

providers, scaling up patient therapeutic education and progressively introducing shorter rifapentine-based regimens (3HP, 1HP) within differentiated service delivery models.

Introduction

Globally, tuberculosis (TB) remains one of the leading causes of death from an infectious disease and is the most common lethal opportunistic infection in people living with HIV (PLHIV). In its Global Tuberculosis Report 2024, the World Health Organization (WHO) estimated 10.8 million new TB cases in 2023, about 6.1% of them in people co-infected with HIV; TB caused 1.25 million deaths that year, including 161,000 among PLHIV (1, 2). TB mortality in PLHIV has fallen steadily since 2010, but progress is still too slow to reach the End TB Strategy milestones and the UNAIDS 95-95-95 targets by 2030 (2, 3). HIV multiplies the risk that latent TB infection progresses to active disease by 20 to 30 times, which makes TB/HIV co-infection one of the heaviest challenges facing health systems in sub-Saharan Africa (4, 5).

Isoniazid preventive therapy (IPT), has been part of international policy for more than three decades, and remains the reference intervention for stopping the progression from latent TB infection to active TB in PLHIV (6, 7). Randomized trials and systematic reviews have shown that 300 mg of isoniazid taken daily for six to nine months lowers the incidence of active TB by 32% to 62% in PLHIV, and that the effect is greater when IPT is combined with antiretroviral therapy (ART) (6, 8, 9). A meta-analysis of twelve randomized trials found an overall 35% reduction in TB risk (RR = 0.65; 95% CI: 0.51–0.84), with the largest benefit in patients with a positive tuberculin skin test (RR = 0.48; 95% CI: 0.29–0.82) (9). The benefits also extend beyond TB prevention patients who complete the full course show a sustained reduction in all-cause mortality, that persists for several years after treatment stops (10, 11).

On this evidence, WHO has recommended since 2011, and reiterated in its 2018 consolidated guidelines and the 2024 second edition, that every PLHIV in whom active TB has been reasonably ruled out should receive TB preventive treatment, regardless of CD4 count, clinical stage, or ART status (1, 12). Shorter rifapentine-based regimens now complement the classical six-month course, three months of weekly isoniazid and rifapentine (3HP) and one month of daily isoniazid and rifapentine (1HP) are non-inferior to longer regimens, are better tolerated, and achieve higher completion rates, including in patients taking dolutegravir (13–15). The evidence is therefore solid, yet IP scale-up of IPT still lags behind in most high burden countries. Globally, only about half of eligible PLHIV had started any form of TB preventive treatment in 2023, far below the 90% target of the end TB Strategy and the UNAIDS 2025 roadmap (2, 3, 16).

National coverage is equally uneven. A cohort in Bulawayo, Zimbabwe, reported 52% initiation and 94% completion (17); and in Mbarara, Uganda, differentiated service delivery models pushed completion rates 80% (18, 19). At the other end of the range, initiation was 18% in Zambia (20), 29.8% in Nepal (21), and 11% in Nigeria before a continuous quality improvement intervention (22). Across Ethiopian regions and facilities, reported rate vary from 13% to 79% which points to programmatic factors and local service

availability as the dominant influences (23–26). The same barriers recur in the literature: stock-outs of isoniazid and pyridoxine, providers' fear of promoting isoniazid resistance, weak integration of TB and HIV services, stigma, patients' limited knowledge of the benefits of IPT, and the absence of dedicated monitoring tools (27–30).

The Democratic Republic of the Congo (DRC) is one of the 30 countries that WHO classifies as bearing a high burden of TB, TB/HIV co-infection, and multidrug-resistant TB (1). In 2022, the country notified more than 200,000 TB cases, of which some 6.5% were also HIV-positive (1, 31). An investigation at Mbuji-Mayi central prison documented a focal outbreak of TB and multidrug-resistant TB, which argues for systematic screening at entry and intensified active case finding, and highlights the vulnerability of the populations concentrated in this province (32, 33). The National Tuberculosis Control Program (PNLT) and the National Multisectoral HIV/AIDS Control Program (PNMLS) adopted the WHO recommendations on IPT in 2017, within a strengthened TB/HIV collaboration policy supported by several international technical and financial partners. How IPT is actually delivered in routine facilities is, however, poorly documented, particularly in provinces outside the Kinshasa–Lubumbashi corridor (34, 35)

Kasai-Oriental province combines a high prevalence of HIV and TB, a heavy reliance on external financing for priority health programs and a health system weakened by logistical and economic constraints (36). In this context, we set out to measure the use of isoniazid preventive therapy and to identify its determinants among PLHIV followed in the province.

Methods

Study design and setting

We carried out an analytical cross-sectional study in Mbuji-Mayi, the capital of Kasai-Oriental province, DRC, covering the period from January 2020 to December 2022.

Study population and eligibility criteria

The study population comprised all adults living with HIV (≥ 15 years) who received care at HIV care facilities in Mbuji-Mayi between January 2020 and December 2022. Patients were included if they had (i) serological confirmation of HIV infection, (ii) an active registration in the HIV care cohort of one of the selected facilities, and (iii) a clinical chart containing all the sociodemographic, clinical and programmatic information needed for the analysis. We excluded patients with incomplete charts and those who had developed active TB before IPT eligibility was assessed, in line with the WHO screening algorithm that must precede the start of TB preventive treatment (1, 12).

Sampling and sample size

Sampling was exhaustive: every patient who met the inclusion criteria during the study window was enrolled, giving a total of 1,176 PLHIV. This number far exceeds the minimum sample size obtained with Cochran's formula ($n \approx 384$ for 5% precision at 95% confidence level), which gives the study high power to detect modest associations. Exhaustive enrolment also avoids the selection bias that a probability sample drawn from an already bounded cohort could introduce.

Variables and data collection

Trained investigators used a standardized form to extract data from HIV registers, patient charts (clinical follow-up forms) and programmatic tools. The primary dependent variable was IPT initiation (yes/no), defined as documented intake of at least one dose of isoniazid together with pyridoxine, in line with national and international guidance (1, 12). IPT completion was defined as documented intake of six months (180 days) of isoniazid. Independent variables were grouped into three blocks:

- Sociodemographic variables: sex, age, marital status, education level, occupation, and place of residence;
- Clinical variables: WHO clinical stage at enrolment, CD4 count at inclusion when available, body mass index, nutritional status, comorbidities, cotrimoxazole prophylaxis, ART regimen, duration on ART, viral load when documented, and clinical outcome;
- Programmatic variables: care facility, year of enrolment, IPT dispensing by a dedicated member of the clinical team, presence of community support (mentor or peer educator), and delay between enrolment in HIV care and IPT initiation.

Statistical analysis

Data were entered in Epi Info™ version 7.2 (CDC, Atlanta, USA) and analyzed in SPSS™ version 27.0 (IBM Corp., Armonk, NY, USA). Quantitative variables are described as mean and standard deviation or as median and interquartile range (IQR), depending on the distribution assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Qualitative variables are presented as absolute and relative frequencies. Groups were compared with the chi-square test or Fisher's exact test for qualitative variables, and with Student's t test or the Mann-Whitney U test for quantitative variables, depending on whether parametric assumptions held (37).

Binary logistic regression was used to identify factors associated with IPT initiation. In bivariate analysis, the crude odds ratio (cOR) and its 95% confidence interval were computed for each variable. Variables associated with initiation at $p < 0.20$ together with variables judged clinically relevant a priori, were entered into the multivariable model. Adjusted odds ratios (aOR) with their 95% CI were estimated to identify factors independently associated with IPT initiation. Discrimination of the final model was assessed with the receiver operating characteristic (ROC) curve and the area under the curve (AUC), and calibration with the Hosmer-Lemeshow test. Statistical significance was set at $p < 0.05$.

Ethical considerations

Ethical authorization was granted by the ethics committee of the Official University of Mbujimayi, registered in number 001/2024/CERUOM/NKL. Informed consent to participate was obtained from all participants, in both in both French and Tshiluba (the local national language), ensuring that they were fully aware of the study’s purpose, potential risks, and benefits. For participants under 18 years of age, informed consent was obtained from a parent and/or legal guardian. The ethical principles outlined in the Declaration of Helsinki were followed throughout the study. The data were stored on a laptop computer with a password-protected and locked cabinet, and only the lead investigator and study supervisor had access to the data.

Results

Sociodemographic characteristics of the cohort

A total of 1,176 PLHIV were included in the analysis. The cohort was predominantly female (61.6%; n = 724). The median age was 38 years (IQR: 30–46), and the largest age group was 35–44 years (32.1%). As regards marital status, 40.0% of participants were married. Nearly all participants (98.5%) lived in urban areas. The Table 1 presents the full set of characteristics.

Table 1
Sociodemographic characteristics of the patients
included (n = 1,176).

Variables	n	%	Median (IQR)
Age (years)	—	—	38 (30–46)
15–24	169	14.4	
25–34	285	24.2	
35–44	378	32.1	
45–54	226	19.2	
55–64	85	7.2	
≥ 65	33	2.8	
Sex			
Female	724	61.6	
Male	452	38.4	
Marital status			
Single	438	37.2	
Divorced/separated	144	12.2	
Married	470	40.0	
Widowed	124	10.5	

Clinical and therapeutic characteristics

At enrolment, most PLHIV (63.7%; n = 749) were at WHO clinical stage III, and cotrimoxazole prophylaxis coverage reached 89.6%. As regards ART, 62.3% of patients (n = 733) were on the first-line regimen TDF+3TC + DTG (tenofovir/lamivudine/dolutegravir). When data collection closed, 55.5% of PLHIV were still active in care, 26.6% had been lost to follow-up, 9.4% had been transferred, and 8.4% had died. Over the study window, 245 patients (20.8%; 95% CI: 18.5–23.2%) initiated IPT. Of these 245 patients, 106 discontinued treatments before the six-month endpoint, that is 43.3% of initiators and 9.0% of the whole cohort, and only 2 of the 1,176 patients (0.2%; 95% CI: 0.02–0.7%) had documented six-month completion (Table 2).

Table 2
Clinical and therapeutic characteristics of the patients (n = 1,176)

Variables	n	%	Median (IQR)
WHO clinical stage at enrolment			
Stage I	182	15.5	
Stage II	186	15.8	
Stage III	749	63.7	
Stage IV	59	5.0	
Pregnant at ART initiation			
No	1089	92.6	
Yes	87	7.4	
Cotrimoxazole prophylaxis			
No	122	10.4	
Yes	1054	89.6	
IPT initiation			
No	931	79.2	
Yes	245	20.8	
IPT outcome			
Not assessed	1068	90.8	
Treatment completed	2	0.2	
Treatment interrupted	106	9.0	
Newly enrolled on ART			
Yes	1089	92.6	
No	87	7.4	
ART regimen			
TDF+3TC + DTG	733	62.3	
Other regimens	443	37.7	
Viral load documented			
No	1026	87.2	
Yes	150	12.8	

Variables	n	%	Median (IQR)
Viral suppression (n = 150)			
No	24	16.0	
Yes	126	84.0	
Duration on ART (years)			
0–3 years	866	73.6	3 (2–3)
> 3 years	310	26.4	
Clinical outcome			
Active in care	653	55.5	
Deceased	99	8.4	
Lost to follow-up	313	26.6	
Transferred/out-migrated	111	9.4	

Factors associated with IPT initiation

In bivariate analysis, several variables were significantly associated with IPT initiation: urban residence, earlier WHO clinical stage (I or II), TDF+3TC + DTG-based ART, being active in HIV care and being married. After multivariable logistic regression with adjustment for potential confounders, four factors remained independently associated with IPT initiation (Table 3): Urban residence, showed the strongest association (aOR = 7.89; 95% CI: 1.03–60.71; $p = 0.047$). A TDF+3TC + DTG regimen, was also strongly associated with initiation (aOR = 5.43; 95% CI: 2.76–10.69; $p < 0.001$) compared with other regimens, as was WHO clinical stage I or II (aOR = 2.19; 95% CI: 1.61–2.99; $p < 0.001$), which corresponds to more than twice the odds of initiation relative to advanced stages. Finally, being active in HIV care, doubled the odds of having initiated IPT (aOR = 2.06; 95% CI: 1.22–3.46; $p = 0.007$) (Table 3).

Table 3

Factors associated with initiation of isoniazid preventive therapy (bivariate and multivariable analysis; n = 1,176)

Variables	Initiation IPT		cOR [95% CI]	p	aOR [95% CI]	p
	Yes	No				
	n (%)	n (%)				
Sex						
Female	161 (22.2)	563 (77.8)	1.25 [0.93– 1.68]	0.133	1.08 [0.78– 1.48]	0.656
Male	84 (18.6)	368 (81.4)	Ref		Ref	
Marital status						
Living alone	131 (18.6)	575 (81.4)	Ref		Ref	
Married	114 (24.3)	356 (75.7)	1.41 [1.06– 1.87]	0.018	1.28 [0.94– 1.75]	0.113
Place of residence						
Rural	1 (5.3)	18 (94.7)	Ref		Ref	
Urban	244 (21.1)	913 (78.9)	4.81 [0.64– 36.21]	0.127	7.89 [1.03– 60.71]	0.047
Clinical outcome						
Active in care	211 (32.3)	442 (67.7)	6.87 [4.68– 10.08]	< 0.001	2.06 [1.22– 3.46]	0.007
Deceased/other	34 (6.5)	489 (93.5)	Ref		Ref	
Treatment status						
Newly on ART	238 (21.9)	851 (78.1)	3.20 [1.46– 7.01]	0.002	1.01 [0.41– 2.49]	0.980
Already on ART	7 (8.0)	80 (92.0)	Ref		Ref	
WHO stage						
Stage I/II	123 (33.4)	245 (66.6)	2.82 [2.11– 3.77]	< 0.001	2.19 [1.61– 2.99]	< 0.001
Stage III/IV	122 (15.1)	686 (84.9)	Ref		Ref	
ART regimen						

Variables	Initiation IPT		cOR [95% CI]	p	aOR [95% CI]	p
	Yes	No				
	n (%)	n (%)				
TDF+3TC + DTG	228 (31.1)	505 (68.9)	11.31 [6.80–18.83]	< 0.001	5.43 [2.76–10.69]	< 0.001
Other regimens	17 (3.8)	426 (96.2)	Ref		Ref	
TB status						
Positive	1 (4.5)	21 (95.5)	Ref		Ref	
Negative	244 (21.5)	910 (78.9)	5.63 [0.75–42.06]	0.058	1.71 [0.20–14.48]	0.624

The final model showed acceptable discrimination, with an AUC of 0.762 (95% CI: 0.732–0.791; standard error 0.015; $p < 0.001$) (Fig. 1). The value means that for a randomly chosen pair of patients, one who initiated IPT and one who did not, the model assigns the higher predicted probability of initiation to the former in about 76% of pairs. The curve sits well above the diagonal reference line and rises steeply at low false-positive rates: sensitivity approaches 0.60 when 1- specificity is about 0.24, so the retained predictors separate initiators from non-initiators reasonably well while producing a moderate number of false positives. The Hosmer-Lemeshow test did not reject the hypothesis of adequate model fit ($p = 0.28$), with indicates acceptable calibration. These predictors should be read as markers of programmatic and clinical patterning rather than as the basis of an individual risk score: the model is explanatory rather than predictive.

Discussion

This study provides operational data on how isoniazid preventive therapy is used among PLHIV followed in Mbujimayi, DRC. Three findings stand out: a modest IPT initiation rate (20.8%); a near-absence documented completion rate (0.2%); and a set of programmatic and clinical determinants dominated by the recent TDF+3TC + DTG ART regimen, earlier WHO clinical stage, urban residence and being active in HIV care. Taken together, these results fit into a heterogeneous sub-Saharan African landscape and argue for a repositioning of operational priorities.

The initiation rate observed in Mbujimayi is close to the 18% reported in Zambia (20) and the 29.8% reported in Nepal (21), but well below the 52% documented in Bulawayo, Zimbabwe (17), the 62.1% reported from Tigray (23), and the 78% recently reported from Kenya among newly enrolled adolescents and young adults (37). A systematic review covering 15,640 Ethiopian PLHIV found utilization rates ranging from 13% to 79% across regions and facilities (24, 25). In Nigeria, IPT initiation was 11%, before a structured Plan-Do-Study-Act (PDSA) cycle and rose above 50% afterwards (22). A study in Kinshasa among adolescents and adults living with HIV reported completion rates above 80% in a structured

academic setting (38, 39), which shows how much can be gained when service organization is rigorous. The gap between our findings and those from the capital points to disparities in implementation within the same country.

The completion rate we observed (0.2%) is strikingly low and is the most concerning finding of this analysis. It contrasts sharply with rates reported elsewhere: 94.3% in Nepal (21), 94% in Bulawayo (17), 95.4% after a quality improvement intervention in Nigeria (22), 82.4% in Tanzania (27), 88.2% among adults in Kinshasa (38), 81.6% in Uganda within a differentiated care model (18), 62.1% in Tigray (23), and approximately 61.5% on average in a recent multi-country cohort (40). A prospective study conducted between 2021 and 2023 in Ethiopia, South Africa and the DRC confirmed same completion deficit, with the authors attributed to fragmented care pathways and weak adherence support (40). Several mechanisms plausibly explain the gap in Mbuji-Mayi: recurrent stock-outs of isoniazid and pyridoxine, a problem widely documented in the WHO African Region supply chain (30, 41); weak programmatic documentation of dispensing and follow-up, as described in Zambia, where the absence of interoperability between clinical and logistics information systems compromises traceability (20, 28); a substantial proportion of patients lost to follow-up (26.6% of the cohort), which mechanically interrupts prophylaxis; and the absence of a structured community-based adherence support system dedicated to IPT, in contrast with what now exists for ART (18, 19).

When completion is this low, most of the expected benefit of the intervention is lost. Beshaw and colleagues showed in northwest Ethiopia that IPT completion combined with ART conferred near-complete protection against incident TB in PLHIV (AHR = 0.08; 95% CI: 0.02–0.37) (42). Geremew and colleagues reported a TB incidence of 8.4% among IPT users versus 21.3% among non-users (AOR = 2.8; 95% CI: 1.3–5.9) (43, 44), and Mebratu and colleagues confirmed in a 2022 Ethiopian retrospective cohort a significantly lower TB incidence among isoniazid users than among non-users (45). Conversely, recent work indicates that TB can still occur in 2% to 6% of PLHIV who have completed IPT (46), which underscores the need for prolonged clinical surveillance after treatment ends. Patients who do not complete IPT are therefore deprived of the most of the potential benefit.

Our analysis identified four major determinants of IPT initiation. First, the TDF+3TC + DTG regimen was strongly associated with initiation (aOR = 5.43; $p < 0.001$). This probably reflects the recency of this regimen's introduction in the DRC's therapeutic optimization strategy, which coincided with an intensified IPT rollout supported by technical and financial partners (PEPFAR, the Global Fund). Patients assigned to this regimen were managed by clinicians recently trained in TB preventive therapy, which mechanically favors IPT prescription. Recent pharmacological data also support the safety of co-administering dolutegravir with isoniazid-pyridoxine and with rifapentine-based short regimens, which allays earlier concerns about drug–drug interactions (14, 47).

Second, earlier WHO stages (I and II) were independently associated with initiation (aOR = 2.19; $p < 0.001$). This result aligns with evidence from Ethiopia, where PLHIV at WHO stage I or II were significantly more likely to start IPT (42, 43). It also reflects clinicians' reluctance to initiate IPT in

patients at advanced stages, for whom active TB must be excluded with particular rigor and in whom differential diagnosis is more complex. Wider access to rapid screening tests such as the lateral flow urine lipoarabinomannan (LF-LAM) assay, together with broader availability of digital chest radiography, could help overcome this hesitation (1, 2, 48).

Third, urban residence was associated with nearly eight-fold higher odds of initiation (aOR = 7.89; $p = 0.047$). The confidence interval is very wide because the rural subgroup is small ($n = 18$), so this estimate should be interpreted with caution; the result nevertheless highlights inequalities in access to preventive services between urban and rural settings, as observed in other African contexts (25, 28, 41). Most HIV care facilities in Mbujimayi are concentrated in urban areas, where drug availability, trained providers, and diagnostic platforms are stronger. This spatial concentration calls for decentralized strategies such as differentiated service delivery (DSD), whose effectiveness in improving IPT coverage has been demonstrated in several East African countries (18).

Fourth, being active in HIV care doubled the odds of IPT initiation (aOR = 2.06; $p = 0.007$). This association is expected: patients who attend regularly have more contacts with their providers, which creates more opportunities to prescribe preventive treatment and to sustain adherence. Tram and colleagues previously reported in Uganda that the regularity of clinical visits was a strong predictor of IPT completion (49). This underscores the value of retention strategies such as multi-month dispensing, scheduled appointments, and SMS reminders, whose impact on care retention is now well documented (16, 18).

The barriers to IPT implementation in Mbujimayi are multidimensional and mirror the broader pattern observed in high HIV/TB co-burden countries. At the health system level, stock-outs of isoniazid and pyridoxine, insufficient TB/HIV integration at facility level, and the lack of dedicated IPT monitoring tools all contribute to weak coverage, as documented in Zambia (20), Ethiopia (24, 25), and across the WHO African Region (30). On the provider side, persistent but unfounded fears the risk of isoniazid resistance, hepatotoxicity, and repeated exposure to TB limit prescribing, even though the meta-analysis by Balcells and colleagues did not show a significant increase in isoniazid resistance attributable to IPT (50). A recent qualitative survey of nursing staff confirmed that perceived pill burden, training gaps, and limited time for counseling are first-order impediments (29, 51). On the biological side, the incidence of severe hepatotoxicity remains low ($< 1\%$) with short-course IPT and with modern ART, which should reassure prescribers and call for pragmatic transaminase monitoring (52, 53). On the patient side, limited awareness the IPT benefits and the stigma associated with sustained tablet intake, as described by Akamike and colleagues in Nigeria (54) and Nyarubamba and colleagues in Tanzania (28), remain important barriers to adherence.

Several improvement levers emerge from our findings and the recent literature. First, securing the supply chain for isoniazid and pyridoxine is essential: this requires integrating these products into the national stock management system, closely monitoring consumption and progressively introducing fixed-dose combinations (isoniazid + pyridoxine $\pm$ cotrimoxazole) to reduce pill burden and simplify dispensing (12,

30). Second, continuous training and coaching of providers on TB screening algorithms, correct IPT prescribing and the management of adverse events must be reinforced. The Nigerian experience shows that a structured PDSA cycle can raise IPT initiation from 11% to over 50% and completion from 53% to 95% within six months (22). Third, patient therapeutic education, community-based peer support and simplification of the preventive regimen notably by introducing 3HP (three months of weekly rifapentine plus isoniazid) or 1HP (one month of daily rifapentine plus isoniazid) should be considered in the Congolese context (8, 13–15). Fourth, deploying of a digital monitoring framework (electronic IPT register, indicator dashboards) is essential to steer the program, as urged by the second edition of the WHO consolidated guidelines published in 2024 (12, 16). Finally, IPT should be embedded within differentiated service delivery models through multi-month dispensing and community adherence groups in line with calls from international experts (41).

Beyond Mbuji mayi, our findings have implications for the entire national TB and HIV response in the DRC. They argue for setting provincial targets for IPT coverage and completion, integrating them into annual programmatic reviews, and strengthening pharmacovigilance and drug-resistance surveillance. The UNAIDS 2025 roadmap sets a target of 90% of eligible PLHIV receiving TB preventive treatment (3, 16); reaching this objective will require sustained engagement of national and provincial decision-makers and greater integration with existing funding streams (PEPFAR, the Global Fund). The Kinshasa experience (38, 39) and the lessons from Mbuji mayi central prison (32, 33) provide relevant foundations for designing interventions adapted to the Congolese health system.

Strengths and limitations

This study has several strengths. The large sample size ($n = 1,176$) gives the model high statistical power, and exhaustive recruitment over the study period limits selection bias. The analysis relies, based on adjusted multivariable models combined with an explicit assessment of discrimination using the ROC curve, which supports robust inferences. To our knowledge, this is the first study to systematically document IPT use among PLHIV in Mbuji mayi.

Several limitations should, however, be acknowledged. First, the retrospective medical-record-based design carries a risk of under-documentation of dispensed doses and adverse events, which may have led us to underestimate the true rates of initiation and completion. Second, biological variables (CD4 count, viral load, transaminases) were not consistently available, which limited our ability to examine fine-grained clinical determinants. Third, the small rural subgroup ($n = 18$) explains the wide confidence interval attached to the residence variable and warrants a cautious interpretation, in line with methodological recommendations on small strata. Fourth, the cross-sectional design does not allow causal inference between the factors identified and IPT initiation, nor direct estimation of TB incidence. Finally, findings should be generalizing beyond Mbuji mayi only with caution, given the urban and organizational specificities of the study site. A prospective multicenter study, ideally combined with cohort follow-up of at least two years, would be warranted to confirm the external validity of these observations.

Conclusions

This cross-sectional study of 1,176 PLHIV followed in Mbuji mayi shows that IPT uptake remains well below international targets: only 20.8% of eligible individuals had initiated IPT, and six-month completion was documented in only 0.2%. The principal determinants of initiation were the TDF+3TC + DTG ART regimen, earlier WHO clinical stage, urban residence, and being active in HIV care. These findings call for urgent programmatic action along four axes: securing the supply chain, strengthening provider competencies, scaling up patient therapeutic education and improving operational monitoring through dedicated digital tools. The deployment of shorter rifapentine-based preventive regimens (3HP, 1HP), embedded within differentiated service delivery models, offers a particularly promising path to bring the Congolese context closer to the WHO and UNAIDS targets for 2030.

Abbreviations

aOR
adjusted odds ratio
ART
antiretroviral therapy
AUC
area under the curve
CI
confidence interval
cOR
crude odds ratio
DSD
differentiated service delivery
DRC
Democratic Republic of the Congo
IPT
isoniazid preventive therapy
IQR
interquartile range
OR
odds ratio
PDSA
Plan-Do-Study-Act
PLHIV
people living with HIV
ROC
receiver operating characteristic
RR

risk ratio
TB
tuberculosis
WHO
World Health Organization.

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Ethics Committee of the Official University of Mbujimayi, registered in number 001/2024/CERUOM/NKL. Because the study was retrospective and used only anonymized routinely collected data, the committee granted a waiver of individual informed consent. All procedures complied with the Declaration of Helsinki as revised in 2013.

Consent for publication: Not applicable.

Availability of data and materials: The de-identified datasets analyzed during the current study are available from the corresponding author on reasonable request, subject to approval by the relevant health authorities.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: DB, LN, AM and PL designed the study; DB, LN, GN, and EB supervised data collection; DB and CKM performed the statistical analysis; DB, BMN, and PMC drafted the manuscript; AM and PL critically revised it for important intellectual content. All authors read and approved the final version submitted for publication and agree to be accountable for the work

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References

1. World Health Organization. Global Tuberculosis Report 2024. Geneva: World Health Organization. 2024. Licence: CC BY-NC-SA 3.0 IGO.; 2024.
2. Goletti D, Meintjes G, Andrade BB, Zumla A, Shan Lee S. Insights from the 2024 WHO Global Tuberculosis Report – More Comprehensive Action, Innovation, and Investments required for achieving WHO End TB goals. International Journal of Infectious Diseases.2025;150.
3. UNAIDS. AIDS, crisis and the power to transform: UNAIDS Global AIDS Update 2025. Geneva: Joint United Nations Programme on HIV/AIDS. Licence: CC BY-NC-SA 3.0 IGO.; 2025.

4. Martinson NA, Hoffmann CJ, Chaisson RE. Epidemiology of tuberculosis and HIV: recent advances in understanding and responses. *Proc Am Thorac Soc*. 2011;8(3):288–93.
5. Aberg J, Powderly W. HIV: primary and secondary prophylaxis for opportunistic infections. *BMJ Clin Evid*. 2010;2010.
6. Briggs MA, Emerson C, Modi S, Taylor NK, Date A. Use of isoniazid preventive therapy for tuberculosis prophylaxis among people living with HIV/AIDS: a review of the literature. *J Acquir Immune Defic Syndr*. 2015;68(Suppl 3):S297–305.
7. Zar HJ, Cotton MF, Strauss S, Karpakis J, Hussey G, Schaaf HS, et al. Effect of isoniazid prophylaxis on mortality and incidence of tuberculosis in children with HIV: randomised controlled trial. *BMJ*. 2007;334(7585):136.
8. Sterling TR, Scott NA, Miro JM, Calvet G, La Rosa A, Infante R, et al. Three months of weekly rifapentine and isoniazid for treatment of *Mycobacterium tuberculosis* infection in HIV-coinfected persons. *Aids*. 2016;30(10):1607–15.
9. Ayele HT, Van Mourik M, Debray T, Bonten 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.
10. Badje A, Moh R, Gabillard D, Guéhi C, Kabran M, Ntakpé JB, et al. Effect of isoniazid preventive therapy on risk of death in west African, HIV-infected adults with high CD4 cell counts: long-term follow-up of the Temprano ANRS 12136 trial. *Lancet Glob Health*. 2017;5(11):e1080–9.
11. Rangaka MX, Wilkinson RJ, Boulle A, Glynn JR, Fielding K, van Cutsem G, et al. Isoniazid plus antiretroviral therapy to prevent tuberculosis: a randomised double-blind, placebo-controlled trial. *Lancet*. 2014;384(9944):682–90.
12. World Health Organization. WHO consolidated guidelines on tuberculosis. Module 1: prevention – tuberculosis preventive treatment. second edition ed. Geneva: World Health Organization. 2024. Licence: CC BY-NC-SA 3.0 IGO.; 2024.
13. Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. *N Engl J Med*. 2011;365(23):2155–66.
14. Swindells S, Ramchandani R, Gupta A, Benson CA, Leon-Cruz J, Mwelase N, et al. One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis. *N Engl J Med*. 2019;380(11):1001–11.
15. Podany AT, Cramer Y, Imperial M, Rosenkranz SL, Avihingsanon A, Arduino R, et al. Twice-Daily Dolutegravir–Based Antiretroviral Therapy With 1 Month of Daily Rifapentine and Isoniazid for Tuberculosis Prevention. *Clin Infect Dis*. 2024;79(4):983–9.
16. Rabkin M, Howard AA, Ehrenkranz P, Fernandez LG, Preko P, Singh V, et al. Leveraging differentiated HIV service delivery to expand tuberculosis preventive treatment: a call to action. *Int J Tuberc Lung Dis*. 2020;24(2):165–9.
17. Nyathi S, Dlodlo RA, Satyanarayana S, Takarinda KC, Tweya H, Hove S, et al. Isoniazid preventive therapy: Uptake, incidence of tuberculosis and survival among people living with HIV in Bulawayo,

Zimbabwe. PLoS ONE. 2019;14(10):e0223076.

18. Tram KH, Mwangwa F, Chamie G, Atukunda M, Owaraganise A, Ayieko J, et al. Predictors of isoniazid preventive therapy completion among HIV-infected patients receiving differentiated and non-differentiated HIV care in rural Uganda. *AIDS Care*. 2020;32(1):119–27.
19. Amany 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(8):e0277739.
20. Kagujje M, Mubiana ML, Mwamba E, Muyoyeta M. Implementation of isoniazid preventive therapy in people living with HIV in Zambia: challenges and lessons. *BMC Public Health*. 2019;19(1):1329.
21. Dhungana GP, Thekkur P, Chinnakali P, Bhatta U, Pandey B, Zhang W-H. Initiation and completion rates of isoniazid preventive therapy among people living with HIV in Far-Western Region of Nepal: a retrospective cohort study. *BMJ Open*. 2019;9(5):e029058.
22. Ogunsola OO, Ajayi O, Ojo O, Adeyeye O, Akinro Y, Oke O, et al. Improving coverage and completion rate of isoniazid preventive therapy among eligible HIV patients using quality improvement approaches: a case study of State Hospital, Ijebu Ode, Ogun State, Nigeria. *Pan Afr Med J*. 2019;34:193.
23. Legese H, Degefa H, Gebrewahd A, Gebremedhin H. Utilization of isoniazid prophylaxis therapy and its associated factors among HIV positive clients taking antiretroviral therapy at Fre Semaetat primary hospital, Hawzien districts, Tigray, Northern Ethiopia. *Tropical Diseases, Travel Medicine and Vaccines*. 2020;6(1):11.
24. Assefa DG, Zeleke ED, Bekele D, Ejigu DA, Molla W, Woldeesenbet TT, et al. Isoniazid Preventive Therapy for Prevention of Tuberculosis among People Living with HIV in Ethiopia: A Systematic Review of Implementation and Impacts. *Int J Environ Res Public Health*. 2023;20(1):621.
25. Matakanye H, Mboweni S. Factors Influencing the Uptake of Isoniazid Tuberculosis Preventive Therapy among Eligible HIV Patients in Africa: A Systematic Review. *Open Public Health J*. 2024;17.
26. Semu M, Fenta TG, Medhin G, Assefa D. Effectiveness of isoniazid preventative therapy in reducing incidence of active tuberculosis among people living with HIV/AIDS in public health facilities of Addis Ababa, Ethiopia: a historical cohort study. *BMC Infect Dis*. 2017;17(1):5.
27. Hunter OF, Kyesi F, Ahluwalia AK, Daffé ZN, Munseri P, von Reyn CF, et al. Successful implementation of isoniazid preventive therapy at a pediatric HIV clinic in Tanzania. *BMC Infect Dis*. 2020;20(1):738.
28. Nyarubamba RF, Silumbwe A, Jacobs C, Maritim P, Mdoe P, Zulu JM. Assessment of contextual factors shaping delivery and uptake of isoniazid preventive therapy among people living with HIV in Dar es salaam, Tanzania. *BMC Infect Dis*. 2022;22(1):884.
29. Müller P, Velez Lapão L. Mixed methods systematic review and metasummary about barriers and facilitators for the implementation of cotrimoxazole and isoniazid—Preventive therapies for people living with HIV. *PLoS ONE*. 2022;17(3):e0251612.
30. Mhazo AT, Miyango S, Palani L, Maponga CC. Tuberculosis commodities supply chain performance in the WHO African region: A scoping review. *PLOS Global Public Health*. 2024;4(5):e0003219.

31. Centers for Disease Control and Prevention. HIV and TB overview: Democratic Republic of the Congo. Atlanta: CDC; 2023.
32. Kayomo MK, Hasker E, Aloni M, Nkuku L, Kazadi M, Kabengele T, et al. Outbreak of Tuberculosis and Multidrug-Resistant Tuberculosis, Mbuji-Mayi Central Prison, Democratic Republic of the Congo. *Emerg Infect Dis*. 2018;24(11):2029–35.
33. Kalonji GM, De Connick G, Okenge Ngongo L, Kazumba Nsaka D, Kabengele T, Tshimungu Kandolo F, et al. Prevalence of tuberculosis and associated risk factors in the Central Prison of Mbuji-Mayi, Democratic Republic of Congo. *Trop Med Health*. 2016;44(1):30.
34. Programme National de Lutte contre la Tuberculose (PNLT). Plan stratégique national de lutte contre la tuberculose 2020–2023. In: Publique MdIS, editor. Kinshasa, République Démocratique du Congo. 2020.
35. Andre K, Tshilonda J, Mukendi J, Cilumba R, Mutombo A, Nsenda M, et al. Rate and Associated Factors of Discontinuation of Anti-Tuberculosis Treatment in Patients with Pulmonary Tuberculosis at Positive Microscopy in the City of Mbuji Mayi, DR Congo—Case of the HDTC of Muya and Lubilanji Health Zones. *OALib*. 2020;07:1–12.
36. Programme National Multisectoriel de Lutte contre le Sida (PNMLS). Rapport d'activités annuel 2022. République Démocratique du Congo: PNMLS; Kinshasa; 2023.
37. Black D, LaCourse S, Njuguna I, Beima-Sofie K, Mburu C, Mugo C et al. Tuberculosis preventative therapy initiation and completion among adolescents and young adults with HIV in Kenya. *J Acquir Immune Defic Syndr* (1999). 2023;Publish Ahead of Print.
38. Bidashimwa D, Ditekemena J, Sigwadhi L, Nkuta L, Engetele E, Kilundu A, et al. Completion of isoniazid preventive therapy for latent tuberculosis infection among children and adolescents compared to adults living with HIV in Kinshasa, Democratic Republic of the Congo. Volume 29. *Tropical Medicine & International Health*; 2023.
39. Yotebieng M, Edmonds A, Lelo P, Wenz LK, Ndjibu PT, Lusiana J, et al. High completion of isoniazid preventive therapy among HIV-infected children and adults in Kinshasa, Democratic Republic of Congo. *Aids*. 2015;29(15):2055–7.
40. Chimoyi L, Ginindza S, Nonyane B, Mulder C, Bedru A, Kawaza N et al. High initiation but sub-optimal completion of tuberculosis preventive treatment among people living with HIV on ART, persistent tuberculosis incidence and programmatic implications: Findings from a two-year multi-country cohort study. *medRxiv*. 2026:2026.01.16.26344254.
41. Johnson A, Chimoyi L, Charalambous S, Kawaza N, Hoffmann CJ, Davis JL et al. Differentiated HIV Service Delivery vs Conventional Care: Tuberculosis Preventive Therapy Outcomes for People Living with HIV in Sub-Saharan Africa. *medRxiv*. 2025.
42. Beshaw M, Balcha S, Molla A. Effect of Isoniazid Prophylaxis Therapy on the Prevention of Tuberculosis Incidence and Associated Factors Among HIV Infected Individuals in Northwest Ethiopia: Retrospective Cohort Study. *HIV/AIDS - Research and Palliative Care*. 2021;13:617 – 29.

43. Geremew D, Geremew H, Tamir M, Adem M, Tegene B, Bayleyegn B. Tuberculosis and isoniazid prophylaxis among adult HIV positive patients on ART in Northwest Ethiopia. *PLoS ONE*. 2022;17(4):e0266803.
44. Geremew D, Endalamaw A, Negash M, Eshetie S, Tessema B. The protective effect of isoniazid preventive therapy on tuberculosis incidence among HIV positive patients receiving ART in Ethiopian settings: a meta-analysis. *BMC Infect Dis*. 2019;19(1):405.
45. Mebratu W, Wedajo S, Mohammed S, Endawkie A, Damtew Y. Prevalence and associated factors of tuberculosis among isoniazid users and non-users of HIV patients in Dessie, Ethiopia. *Sci Rep*. 2022;12(1):13500.
46. Sekayi W, Namyalo E, Namayanja J, Kungu JM. Prevalence and predictors of tuberculosis among HIV patients who completed isoniazid preventive therapy (IPT) at Reach out Mbuya community health initiative. *Sci Rep*. 2023;13(1):17602.
47. Podany AT, Leon-Cruz J, Hakim J, Supparatpinyo K, Omoz-Oarhe A, Langat D, et al. Nevirapine pharmacokinetics in HIV-infected persons receiving rifapentine and isoniazid for TB prevention. *J Antimicrob Chemother*. 2021;76(3):718–21.
48. Bjerrum S, Schiller I, Dendukuri N, Kohli M, Nathavitharana RR, Zwerling AA, et al. Lateral flow urine lipoarabinomannan assay for detecting active tuberculosis in people living with HIV. *Cochrane Database Syst Rev*. 2019;10(10):Cd011420.
49. Howard AA, El-Sadr WM. Integration of tuberculosis and HIV services in sub-Saharan Africa: lessons learned. *Clin Infect Dis*. 2010;50(Suppl 3):S238–44.
50. Balcells ME, Thomas SL, Godfrey-Faussett P, Grant AD. Isoniazid preventive therapy and risk for resistant tuberculosis. *Emerg Infect Dis*. 2006;12(5):744–51.
51. Grammatico MA, Moll AP, Ahmed A, Grau LE, Nsele S, Makhunga P, et al. And the stick to fight TB is TPT': nurse-identified barriers and facilitators of tuberculosis preventive therapy implementation in rural South Africa. *BMJ Open Respiratory Res*. 2025;12(1):e002663.
52. Hahn JA, Ngabirano C, Fatch R, Emenyonu NI, Cheng DM, Adong J, et al. Safety and tolerability of isoniazid preventive therapy for tuberculosis for persons with HIV with and without alcohol use. *Aids*. 2023;37(10):1535–43.
53. Ngongondo M, Miyahara S, Hughes MD, Sun X, Bisson GP, Gupta A, et al. Hepatotoxicity During Isoniazid Preventive Therapy and Antiretroviral Therapy in People Living With HIV With Severe Immunosuppression: A Secondary Analysis of a Multi-Country Open-Label Randomized Controlled Clinical Trial. *J Acquir Immune Defic Syndr*. 2018;78(1):54–61.
54. Akamike I, Okedo-Alex I, Agu A, Alo C, Ogbonnaya L. Knowledge and adherence to isoniazid preventive therapy among people living with HIV (PLHIV) in multilevel health facilities in South-East, Nigeria: baseline findings from a quasi-experimental study. *Pan Afr Med J*. 2020;36.

Figures

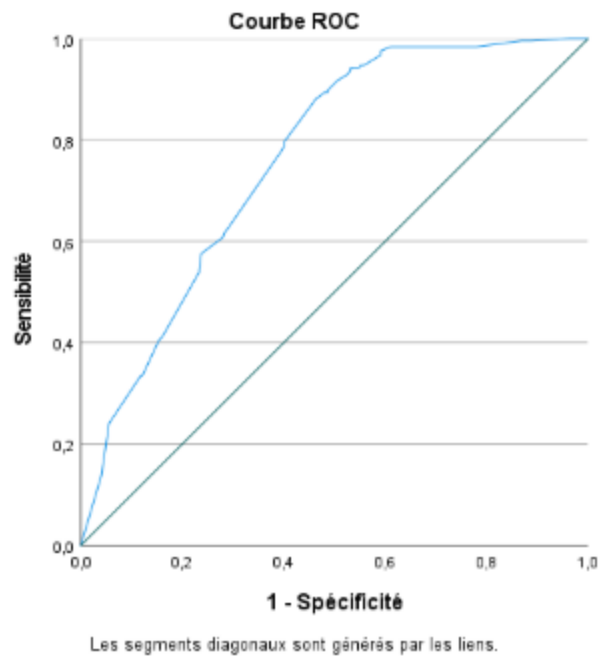


Figure 1

ROC curve of the final multivariable model predicting IPT initiation (area under the curve: 0.762; 95% CI: 0.732-0.791]; Standard error: 0.015; $p < 0.001$).