Integrated and patient-selected care facilitates completion of isoniazid preventive therapy in Eswatini

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Setting: Five human immunodeficiency virus (HIV) care facilities in Eswatini.

Objective: To identify critical factors that enabled persons living with HIV to successfully complete a 6-month course of isoniazid preventive therapy (IPT) provided through a choice of facility-based or community-based delivery, coordinated with antiretroviral therapy (ART) refills.

Design: This was a mixed methods, retrospective cross-sectional study.

Results: Between June and October 2017, we interviewed 150 participants who had completed IPT in the previous year. Fourteen participants did not recall being offered a choice, and were excluded from the analysis. Of the remaining 136, 56.6% were female and 64.7% chose facility-based care; the median age was 42.5 years. Most participants reported that having a choice was important to their treatment completion (87.7%) and that linking IPT and ART refills facilitated undergoing IPT (98.5%). Participants were knowledgeable about the benefits of IPT and valued the education received from their providers. Participants also reported a high rate of IPT disclosure (95%) to friends and family members.

Conclusion: Offering patients a choice of IPT delivery, linking IPT with ART refills, emphasizing patient education and engagement with healthcare workers, and supporting disclosure of IPT are critical factors to enabling IPT completion. These interventions should be incorporated throughout Eswatini and in similar high tuberculosis and HIV burden settings.

In 2009, the Eswatini Ministry of Health adopted World Health Organization (WHO) recommendations to provide isoniazid preventive therapy (IPT) to all persons living with human immunodeficiency virus (PLWH) infection above 1 year of age and all child tuberculosis (TB) contacts under age five to reduce the incidence of TB-HIV co-disease.^{1–3} However, uptake, adherence and treatment completion were poor.

In a retrospective cohort review of IPT patient outcomes at four facilities in 2014, we found that less than 10% of eligible patients received IPT, and among those who started, only 47% completed treatment.⁴ In close collaboration with Eswatini's National TB Control Programme (NTCP) and the Eswatini National AIDS Programme (ENAP), we conducted a prospective cohort study in 2015–2016 to improve IPT uptake and outcomes at five HIV care facilities by basing IPT delivery on patient preferences. Our find-

ings showed that a model of self-selected IPT delivery, aligned with HIV care and ART refills achieved high rates of adherence (94.8% took at least 80% of their IPT) and treatment completion (89.4%).⁵ Outcomes were similar for both facility-based and community-based cohorts. There were no confirmed treatment failures and few patients discontinued IPT or were lost to follow-up.⁵

While these results were informative, the study collected only quantitative data and was not designed to identify the factors that most enabled patients to achieve high adherence and treatment completion rates. Review of evidence in the published literature suggests that several factors may influence adherence, including personal beliefs, relationships with providers and social support, and that social networks and stigma inform both illness perceptions, as well as treatment management.⁶

We conducted an immediate follow-up study to elucidate the critical factors that favorably influenced patient adherence and treatment completion in our Eswatini cohort.

STUDY POPULATION AND METHODS

We used a mixed-methods, retrospective, cross-sectional study design.

Population and sample size

We used purposive stratified sampling according to sex, age group (<18, 19–35, 36–49, >50 years), facility (1–5), and IPT delivery model (facility- or community-based) to select a total of 150 participants from the original study who completed treatment in the first IPT study. Only treatment completers were sampled due to a small number of non-completers who self-discontinued ($n = 24$), and their reasons for stopping isoniazid have been previously described.⁵ The enrollment target was based principally on a sampling matrix inclusive of subgroup representation, allowing up to four participants per domain. The total number was based secondarily on researcher judgment, informed by purposeful sampling priorities, as well as the goal of permitting descriptive comparisons between groups.^{7,8} The two IPT delivery models are described in detail elsewhere;⁵ briefly, treatment delivery followed patients' ART refill schedule (at 1-, 2- or 3-month intervals); community-based care was at a location selected by the patient (27 chose their home, four chose their workplace and the remainder chose a varying combination of community sites).

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Survey

The survey and an accompanying guide for interviewers were developed in coordination with in-country stakeholders and designed for an estimated fifth grade comprehension level (Flesch grade). These were first developed in English, translated to Siswati and back-translated to English to test for translation accuracy. The survey contained Likert scales, and multiple-choice questions, open-ended questions about what helped participants complete their treatment and closed-ended (yes/no/don't know) questions about whether the specific study interventions facilitated their treatment completion. Trained interviewers piloted the survey at two study sites with community members and clinic staff, and then with the first 10 interviewees.

Training

Quantitative and qualitative research training materials were developed in partnership with representatives from the key stakeholder groups, including the NTCP, ENAP, TB/HIV National Coordinating Committee and frontline clinical providers. Two researchers with backgrounds in health and social science were hired and trained through didactic lectures, role play, and discussion.

Informed consent

Written consent was provided by all adult participants, and by a parent/caregiver of participants aged <18 years. Children between the ages of 15 and 17 years provided verbal assent and were interviewed with the parent/caregiver present. For children aged <15 years selected to participate, the parent/caregiver who administered the IPT in the initial study was interviewed.

Data collection

Between June and October 2017, staff at the five study clinics called potential participants to inform them about the study. Research team members then contacted potential participants to obtain consent and schedule interviews on the day of their next routine HIV care appointment. Dedicated interview appointments were made for participants whose next appointment was beyond the study period. With participants' consent, researchers audio-recorded interviews that were conducted in the participants' native language and lasted 30–45 min. Directly after the interview, the researchers prepared field notebooks from their observations and created summary memos and transcripts from the tapes.

Data analysis

Quantitative data were analyzed using STATA v14 (StataCorp, College Station, TX, USA). *P* values were calculated using Fisher's exact test. Qualitative data were analyzed using multi-step data reduction and verification method for thematic analysis on the qualitative data as described by Corbin and Strauss.⁹ Survey data were maintained on a secure, shared online database and a password-protected computer.

Ethical approval

The study was approved by the Eswatini National Health Research Review Board (Mbabane, eSwatini),

the University Research Co., LLC's Institutional Review Board (IRB; Chevy Chase, MD, USA), the IRB for Human Subject Research at Baylor College of Medicine and Affiliated Hospitals (Houston, TX, USA), the IRB for Baylor College of Medicine Children's Foundation-Eswatini (Eswatini) and Dartmouth College's Committee for the Protection of Human Subjects (Dartmouth, NH, USA).

RESULTS

We interviewed 150 participants who had completed IPT in the original IPT feasibility study. Fourteen participants did not recall being offered a delivery choice and were excluded from the analysis. Of the remaining 136, 56.6% were female; the median age was 42.5 years (interquartile range 26.5–42.5). Demographic characteristics of the remaining 136 (88 of whom chose facility-based care) are shown in Table 1.

Most participants viewed their healthcare facility favorably. Despite acknowledgement of long wait times and concerns about access/travel times, most participants felt that being able to see a doctor and access a wider array of services (compared to community-based models) overcame these challenges. One participant stated,

All the services we need are there and we get the help we need. (Male, age 51 years, facility-based model)

TABLE 1 Demographic and other characteristics of participants (*n* = 136)

Variable	<i>n</i> (%)
Female sex	77 (56.6)
Age distribution, years	
1–17	22 (16.1)
18–35	42 (30.8)
36–49	47 (34.6)
≥50	25 (18.3)
IPT delivery model at study conclusion	
Community-based	48 (35.3)
Facility-based	88 (64.7)
Switched between models	
Yes	11 (8.0)
No	125 (92.0)
Facility-based model	
Mode of transportation to IPT delivery site	
Walk	14 (15.9)
Bus or Kombi van	66 (75.0)
Own car	3 (3.4)
Walk and Kombi van	5 (5.7)
Received IPT at home	0
Community-based model	
Mode of transportation to IPT delivery site	
Walk	4 (8.3)
Bus or Kombi van	14 (29.2)
Own car	3 (6.3)
Walk and Kombi van	0
Received IPT at home	27 (56.3)

IPT = isoniazid preventive therapy.

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TABLE 2 Participant assessment of quality of tuberculosis care services ($n = 136$)

	IPT delivery model		Total ($n = 136$, 100%)	<i>P</i> value*
	Facility-based ($n = 88$, 64.7%)	Community-based ($n = 48$, 35.3%)		
Quality of health services in your healthcare facility				
Very good	34 (38.6)	22 (45.8)	56 (41.2)	>0.05
Good	53 (60.2)	25 (52.1)	78 (57.4)	>0.05
Bad	0	1 (2.1)	1 (0.7)	>0.05
Very bad	1 (1.1)	0	1 (0.7)	>0.05
What most people in your community think about the quality of care in your healthcare facility				
Very good	22 (25.0)	15 (31.3)	37 (27.2)	>0.05
Good	50 (56.8)	17 (35.4)	67 (49.3)	>0.05
Bad	7 (8.0)	14 (29.2)	21 (15.4)	<0.01
Very bad	1 (1.1)	10 (0.0)	1 (0.7)	>0.05
Don't know	8 (9.1)	2 (4.2)	10 (7.4)	>0.05
Availability and access to facility-based health services in your community				
Very good	18 (20.5)	14 (29.2)	32 (23.5)	>0.05
Good	50 (56.8)	19 (39.6)	69 (50.7)	>0.05
Bad	15 (17.0)	12 (25.0)	27 (19.9)	>0.05
Very bad	2 (2.3)	3 (6.3)	5 (3.7)	>0.05
Don't know	3 (3.4)	0	3 (2.2)	>0.05

*Calculated using Fisher's exact test.

IPT = isoniazid preventive therapy.

Another commented,

Here there is everything [and] doctors are easily accessible. (Female, age 43 years, facility-based model)

Others stated a preference for facility-based care based on their previous illness experience,

I first got treated for TB in this hospital, so decided to take [IPT] treatment here too. (Female, age 31 years, facility-based model).

A majority rated availability and accessibility to health services at the study sites as good or very good (respectively 50.7% and 23.5%; Table 2). Proximity to their home or work and trust in the healthcare workers were the two key drivers for participants' choice of a health facility to receive their HIV care; roughly half (52.9%) chose based on proximity and a quarter (27.0%) based on their trust in the clinicians at the facility. The majority of the participants (67%) said it was important that a clinician is friendly, and an additional 8.0% combined friendly with another attribute, such as respectful or competent (Table 3). More than half of the participants (63.2%) said availability of services mattered most to them when receiving health services (Table 3).

The following three key themes emerged from our thematic analysis of the qualitative data to describe interventions that aided treatment completion:

1) tailoring treatment delivery facilitated completion. Almost all participants (98.5%) said it was important to link IPT with ART pick-up, regardless of their IPT delivery model ($P > 0.05$) (Table 4). Most participants (89.7%) felt being offered a choice in models was important (Table 4). One participant emphasized this by saying:

I was glad to be given the choice because often times I am not [given a choice] and I leave early in the morning and return late in the evening. (Male, age 40 years, community-based model)

For others, being offered a choice provided the flexibility to choose their mode of delivery based on personal circumstances,

such as financial issues, transportation, or family/childcare needs. One participant stated:

Because I would not have money to go to the hospital and this resulted in me defaulting sometimes, [the community options were better] because the nurse was always on time. (Female, age 53 years, community-based model)

A greater proportion of those receiving community-based care (98.0% vs. 85.2%) felt that being offered a choice of delivery helped them complete IPT ($P = 0.03$). More than half (52.1%) of the participants in the community-based model felt they received special treatment by their healthcare team compared to 43.2% in the facility-based model ($P = 0.04$).

2) Participants valued TB education and resulting knowledge: participants were knowledgeable about the benefits of IPT and valued the education received from their providers. One patient commented:

TABLE 3 Participants' preferred clinician characteristics ($n = 136$)

Preferred characteristics	<i>n</i> (%)
Most important clinician characteristic when talking about your health/treatment*	
Friendly	91 (66.9)
Respectful	16 (11.8)
Competent	17 (12.5)
Friendly and competent	7 (5.1)
Friendly and respectful	4 (2.9)
Absence of language barrier	1 (0.7)
What matters most when receiving care from a clinic	
Availability of services	86 (63.2)
Short waiting times	44 (32.4)
Availability of services and short waiting times	6 (4.4)

*Participants were asked for the single most important characteristic, but some felt they could not decide so we allowed a combination of two characteristics.

TABLE 4 Critical factors enabling IPT treatment completion

Factor affecting IPT completion	IPT delivery model		Total (<i>n</i> = 136, 100%)	<i>P</i> value*
	Facility-based (<i>n</i> = 88, 64.7%)	Community-based (<i>n</i> = 48, 35.3%)		
Linking IPT with ART refills				
Yes	88 (100)	46 (96.0)	134 (98.5)	>0.05
No	0	1 (2.0)	1 (0.7)	
Don't know	0	1 (2.0)	1 (0.7)	
Being offered a choice of delivery helped me complete IPT				
Yes	75 (85.2)	47 (98.0)	122 (89.7)	0.03
No	4 (4.5)	1 (2.0)	5 (3.7)	
Don't know	9 (10.2)	0	9 (6.6)	
I received special treatment from clinic staff compared to other patients not on IPT				
Yes	38 (43.2)	25 (52.1)	63 (46.3)	0.04
No	48 (54.5)	18 (37.5)	66 (48.5)	
Don't know	2 (2.3)	5 (10.4)	7 (5.2)	

*Calculated using Fisher's exact test.

IPT = isoniazid preventive therapy; ART = antiretroviral therapy.

They explained, and I understood clearly how it is going to help me. (Male, age 50 years, facility-based model)

Nearly all participants (97.1%) reported taking IPT because they did not want to get TB, while the remainder (2.9%) took it because their clinician advised it. Afraid of a TB recurrence, one participant described how this reasoning was reinforced by her providers:

The nurse from the clinic already knew that I had suffered from TB before, so he advised me to participate in the study and take IPT. (Female, age 49 years, facility-based model)

3) Disclosing IPT treatment supported completion: almost all participants (94.9%) told someone they were taking IPT, with most (84.0%) reporting they disclosed to a family member. Those who disclosed reported how it supported their adherence through medication reminders and being able to take their medicines openly. One participant relayed that,

My wife became my treatment supporter; she encouraged and reminded me on a daily basis to take my pills. (Male, age 42 years, facility-based model)

There were no significant differences in disclosure between the two IPT delivery models ($P > 0.05$). Most (71.3%) reported no difference in how their clinician explained IPT to them compared to how they explain other medicines. All participants who received IPT via the community-based model completed their IPT in 6 months, as did almost all (96.6%) in the facility-based model. Most participants (80.0%) reported not missing any of their IPT pills.

DISCUSSION

The present study identified the critical factors that led to a high IPT treatment completion rate among a cohort of PLWH who self-selected their IPT delivery model that was coordinated with their ART refills. To our knowledge, ours is the first study to offer IPT delivery choices to PLWH; this indicates that having choices may contribute positively to treatment adherence. While most participants chose facility-based delivery (the likely

health system default option), they reported value in having a choice of IPT delivery options, rather than being assigned to one. Offering patients choices in their care, whenever possible, can engage patients in their care by empowering them as active participants. Shared decision-making and negotiated treatments that accommodate patient goals and preferences has led to improved adherence and clinical outcomes in patients with chronic diseases such as asthma and diabetes.^{10,11} Historically, TB care has been focused on administering therapy under more program-centered, rather than patient-centered, measures to ensure adherence, such as directly observed therapy (DOT), which has been criticized for not being a patient-centered approach.¹² This approach to TB care has thus been brought under scrutiny,¹³ and in recent years evolved from one of treatment enforcement or patient policing to one of patient support and accompaniment.^{14,15} Some models have also allowed patients to choose their DOT supervisor and location, with improved outcomes noted among those at high risk for non-completion (e.g., retreatment patients).¹⁶

In our model, patients were able to choose the most convenient delivery location for their routine and recurring follow-up care and medication refills. Participants highlighted factors such as facility proximity, transportation issues, family and work routines or schedules as significant in making their choice for facility- or community-based care. To note, the majority of participants chose the facility-based model. As discussed previously, this preference suggests a selection for health care efficiency and desire to maintain existing routines for medical care and/or fear of HIV status disclosure to neighbors through care delivered in the community.⁵ Furthermore, participants may have had less experience, and were therefore less comfortable, with community-based treatment since it is a newer practice in Eswatini.⁵ Our current findings, which reveal participants' positive perceptions of their respective health facilities and the services they offer, suggest a trust and favorable inclination that may have also influenced decisions to continue care at their current facility.

While the vast majority in both delivery model cohorts reported that being offered a choice of delivery helped them complete their IPT, this was more pronounced among those who

chose community-based care. This finding suggests that having a choice mattered more to those seeking specialized or personalized care. Being able to choose the model of one's ongoing care is an approach consistent with a newly recommended people-centered model of TB care that is holistic, individualized, empowering and respectful, and encourages informed decision-making and self-determination.¹⁷ Also, more community-based than facility-based care participants felt that they received special treatment from clinic staff compared to other patients not on IPT, further suggesting an appreciation of their unique, individually delivered IPT services.

In addition to indicating that having a choice in their care delivery mattered, most participants also said it was important that their IPT was linked to their ART pick-up. This suggests that integrated care combining IPT and ART delivery can play a critical role in IPT completion. For most, IPT fit easily into their daily routine of taking ART, making IPT completion easier. Integration of TB and HIV care has been shown to be helpful in a variety of settings and was the only intervention that tended towards favorable IPT treatment completion in our previous systematic review.¹⁸ A review of HIV and TB care delivery found that siloed or vertical programming was less effective and efficient than integrated care.¹⁹ Recent studies of IPT treatment adherence cite the need for thoughtful and integrated TB-HIV care delivery solutions.²⁰ Our findings elucidating the benefits of easier access, efficiency and less perceived stigmatization (discussed below) are also in line with the current WHO recommendation for integrating TB and HIV services.²¹

Participants were exceptionally knowledgeable about the benefits of IPT and valued the knowledge they received from the nurses, which enabled them to alert friends and family to the dangers of TB. They also remarked that the way this education was delivered increased their trust in the competence of the healthcare workers and may have increased their acceptance and acquisition of the TB educational information.

A higher than expected number of participants disclosed being in a TB study and taking IPT to family members and friends which they found offered opportunities for support and medication reminders. Of note, we only inquired about disclosure regarding undergoing IPT. While receiving IPT may suggest co-infection with HIV, we did not collect HIV disclosure information specifically. However, several participants shared that they had already disclosed their HIV status to the same family members or friends. Disclosing health information suggests the presence of strong social networks, which researchers have shown increased disclosure among PLWH.²² Furthermore, a meta-analysis by Smith et al. found a positive, heterogeneous correlation between disclosure and social support, suggesting that when individuals share their status with friends, family, and others, they have a better chance of adhering to their treatment.²³ This finding is consistent with our results and with the concept of intersectional stigma (stigma stemming from the dynamic interaction of multiple social statuses or identities), confirming the importance of interpersonal factors and their association between disclosure and adherence to treatment.²⁴ New data also demonstrate the important role that social science plays in understanding the complex impact that TB has on patients and their families.^{25,26} While a recent study emphasized this point specifically in relation to multi-drug-resistant TB among children,²⁷ the same complicating factors of stigma, household relationships, and notions of disclosure and choice are relevant in our patient population. Given the benefits that disclosure to friends and family members seemed to

have on IPT completion in both our study cohort and as described in the literature, appropriate disclosure should be encouraged.

The main limitation of this study is that we enrolled only those who completed IPT and did not include those who did not complete IPT. The study therefore lacked a comparison cohort. This approach was necessary as the number of non-completers who could be located was too small to be included in any powered analysis. Furthermore, their reasons for non-completion were previously described and were unrelated to the interventions of interest.⁵ The surveyed patients also preferentially used the public health system, with fewer than 10% using private clinics and smaller numbers frequenting other types of healers. This population may thus have been predisposed to adherent behavior and have greater trust in their providers and the care offered at their chosen facility. Finally, because this was a retrospective study, there may have been recall bias that affected participants' responses.

In conclusion, IPT initiation and completion has been a challenge in Eswatini, as in other countries. Clearly in this setting, linking ART and IPT delivery enhances completion of IPT. Patients should be offered a choice of IPT delivery and enabled to disclose their status in order to accommodate each patient's circumstances and facilitate IPT completion. Healthcare worker education regarding IPT enables effective transfer of relevant information to patients and sensitizes their families to the value of IPT and risks of untreated TB. These factors should be prioritized when designing IPT delivery services in Eswatini and similar high TB-HIV burden settings.

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Contexte : Cinq structures de prise en charge du virus de l’immunodéficience humaine (VIH) au Swaziland (Eswatini).

OBJECTIF : Identifier les facteurs cruciaux qui ont permis aux personnes vivant avec le VIH d’achever avec succès un traitement préventif de 6 mois par isoniazide (TPI) fourni par une sélection de systèmes de fourniture en structures de santé ou en communautés, en coordination avec un renouvellement du traitement antirétroviral (TAR).

Schéma : Etude rétrospective transversale à méthodes mixtes.

Résultats : Entre juin et octobre 2017, nous avons interviewé 150 participants qui avaient achevé le TPI au cours de l’année précédente. Quatorze participants ne se souvenaient pas avoir pu choisir et ont été exclus de l’analyse. Sur les 136 participants restants, 56,6% ont été des femmes, 64,7% ont choisi des soins basés en structure de santé et l’âge médian a été de 42,5 ans. La majorité des participants

ont déclaré qu’avoir le choix avait été important pour l’achèvement du traitement (87,7%) et que lier le TPI et le renouvellement du TAR facilitait la prise du TPI (98,5%). Les participants ont acquis des connaissances relatives aux bénéfices du TPI et ont apprécié l’éducation reçue de leurs prestataires de soins. Les participants ont également rapporté un taux élevé de divulgation du TPI (95%) à leurs amis et à leurs familles.

Conclusion : Offrir aux patients le choix du mode de fourniture du TPI, lier le TPI avec le renouvellement du TAR, mettre l’accent sur l’éducation du patient et l’engagement avec les travailleurs de santé et soutenir la divulgation du TPI sont des facteurs cruciaux favorisant l’achèvement du TPI. Ces interventions devraient être étendues à tout le Swaziland et dans des contextes similaires durement frappés par la tuberculose et l’infection par le VIH.

Marco De Referencia: Cinco establecimientos de atención de la infección por el virus de la inmunodeficiencia humana (VIH) en Eswatini.

Objetivo: Reconocer en las personas con infección por el VIH los principales factores que favorecen la compleción satisfactoria del tratamiento preventivo con isoniazida (TPI) de 6 meses, al ofrecer la opción de suministro institucional o comunitario, coordinado con las reposiciones del tratamiento antirretroviral (TAR).

Método: Fue este un estudio transversal retrospectivo.

Resultados: Entre junio y octubre del 2017 se entrevistaron 150 participantes que habían completado el TPI en el año anterior. Catorce de ellos no recordaron que se les hubiese ofrecido una opción de suministro y se excluyeron del análisis. De los 136 restantes, el 56,6% era de sexo femenino, 64,7% había escogido el suministro institucional y la mediana de la edad era 42,5 años. La mayoría de los participantes afirmó que el hecho de tener la

posibilidad de escoger el tipo de suministro había sido importante para completar el tratamiento (87,7%) y que coordinar el TPI con la reposición del TAR facilitaba la ingestión del TPI (98,5%). Los participantes conocían los beneficios del TPI y apreciaban la educación que habían recibido de sus prestadores de atención de salud. También refirieron una tasa alta de revelación del TPI a los amigos y los miembros de la familia (95%).

Conclusión: Los factores primordiales que facilitan la compleción del TPI son el hecho de ofrecer a los pacientes una opción para el suministro del TPI, la coordinación del TPI con la reposición del TAR, el hincapié en la educación de los pacientes, la comunicación con los profesionales de salud y el apoyo a la revelación de estar recibiendo el TPI. Sería importante incorporar estas intervenciones en la atención en toda la provincia de Eswatini y en otros entornos con carga de morbilidad alta por tuberculosis e infección por el VIH.