Taking tuberculosis preventive therapy implementation to national scale: the Nigerian PEPFAR Program experience

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Background: Tuberculosis (TB) preventive therapy (TPT), including isoniazid preventive therapy (IPT), has been implemented within the Nigerian human immunodeficiency virus (HIV) programme since 2014. However, drug procurement and logistic support has remained the responsibility of the National Tuberculosis and Leprosy Control Programme. The US President's Emergency Plan for AIDS Relief-Nigeria (PEPFAR Nigeria) reviewed the key bottlenecks to TPT implementation in 2016.

Method: The logistics of delivery of isoniazid (INH) were integrated with the antiretroviral (ARV) logistics management and information system (LMIS). Drug order and requisition forms at the facility level were revised to include INH, along with training on appropriate quantification and requisition of INH with ARVs. Support was provided for last mile delivery of INH directly to every implementing site, alongside ARV.

Results: We observed an increasing trend in TPT uptake between the pre-and-post intervention periods: 6% in fiscal year (FY) 2015, 7% in FY2016 and 12% in FY2017. Overall, the logistical changes in the LMIS to include INH in 2016 led to a 69% increase in TPT by the end of FY2017; this was statistically significant.

Conclusion: Addressing logistical challenges to TPT implementation will ensure that the TB and HIV programmes can tackle the increasing burden of TB infection in people living with HIV. We recommended that the provider-to-client stage of TPT implementation be driven by the HIV programme and that cross-communication between the two programmes be improved.

TUBERCULOSIS (TB) is the leading cause of death for people living with human immunodeficiency virus (PLHIV) infection. An estimated 40% of deaths in PLHIV worldwide are due to TB.¹ TB preventive therapy (TPT) reduces 5-year mortality among PLHIV by 37%, independent of antiretroviral therapy (ART).² The most common form of TPT is isoniazid (INH) preventive therapy (IPT). Although IPT has been a World Health Organization (WHO) recommendation for PLHIV and children aged <6 years exposed to persons with TB since 1993, global IPT uptake has been slow.³ Of the 34.5 million adults living with HIV, only 4.8 million (14%) have reportedly started IPT since 1993.⁴

Nigeria is ranked by WHO as one of the 30 high TB and TB-HIV co-infection burden countries in the world.⁵ Among HIV-TB co-infected people in Nigeria, 14% of TB patients are diagnosed with HIV, and 35 000 HIV-positive patients die from TB every year. TB re-

mains the most common opportunistic infection among HIV-positive people.^{6,7} The WHO recommends that all PLHIV (including pregnant women, breastfeeding women, and children living with HIV), receive at least 6 months of IPT.³ In high TB burden settings, PLHIV in whom active TB disease has been ruled out, should receive at least 36 months of IPT.⁸ PLHIV should be screened for TB with a series of four questions regarding cough, fever, weight loss, or night sweats. In the absence of these symptoms, they should be offered IPT.⁸ If PLHIV have symptoms, they should be evaluated for TB.

The National Tuberculosis and Leprosy Control Programme (NTBLCP) has adopted the 6 month course of IPT and have been implementing it following the revision of the national guidelines in 2014.⁹ Funded by the US President's Emergency Plan for AIDS Relief (PEPFAR), the procurement and supply chain management (PSM) has played a significant role in improving INH delivery of TPT implementation. It is being monitored across all PEPFAR implementing partners, with emphasis on reporting treatment completion following the introduction of the new PEPFAR indicator, TB_PREV. This indicator focuses on the proportion of eligible HIV-positive clients who are "expected to complete a 6 month course of IPT" (denominator) and those who "completed a 6 month course of IPT" (numerator).¹⁰

PEPFAR Nigeria has continuously reviewed its program implementation strategies, identifying successes, challenges and bottlenecks to program implementation in order to provide the best service to over 800 000 PLHIV in its care and treatment program in Nigeria. Healthcare workers have been trained, through continuing medical education, on the importance of IPT for PLHIV. However, uptake of IPT has remained low. As the burden of TB continues, especially among PLHIV, it is expected that IPT scale-up could make significant improvements in patient outcomes. Hence, the need for continuous policy review and introduction of new innovative strategies.

METHODS

Intervention

In 2016, PEPFAR Nigeria reviewed the bottlenecks to IPT implementation in its program. One of the key bottlenecks identified focused on the logistics of quantification, requisition and distribution systems of single-tablet INH 300mg (hereafter referred to as INH 300mg). The NTBLCP procures INH 300mg in a fixed-

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dose combination (FDC) tablet with other anti-TB medications for use in the treatment of TB and the single-tablet INH 100mg tablet for prophylaxis in children aged <6 years. The funding stream for INH 300mg is different from that of the INH 300mg FDC tablet. Although implemented within the National HIV Programme, IPT delivery depended on the NTBLCP for procurement, supply and distribution of INH 300mg used for TPT. This arrangement had negatively impacted the HIV programme ownership and accountability, and constituted an impediment to scaling up IPT.

To surmount this, PEPFAR Nigeria worked with the NTBLCP to revamp the logistics system. The logistic management and information system (LMIS) for INH 300mg was integrated into the antiretroviral treatment (ART) programme's LMIS and was assigned to the PEPFAR partner in charge of ART drug logistics for the HIV programme. This ensured that the HIV programme took responsibility for the supply and last mile distribution of INH 300mg for TPT implementation, while the NTBLCP continued with the central procurement. The combined requisition information, report and result form (CRIRRF) used for HIV drug commodities was updated to accommodate INH, and health facilities were required to complete the CRIRRF to obtain INH and ARV commodities. At the facility level, INH 300mg was dispensed in quantities synchronized with amounts prescribed for ARV drugs or refills. Further support was provided for last mile delivery of INH to every implementing site, alongside ARV. Health care workers were also trained in appropriate quantification, requisition and reporting systems for INH and ARV. This intervention was implemented across all PEPFAR-supported sites in the country from the beginning of fiscal year (FY) 2017 (Figure 1).

Data collection and statistical analyses

Data used for this study were retrieved from PEPFAR Nigeria's Data for Accountability, Transparency and Impact (DATIM) tool that was built on a District Health Information System (DHIS) version 2 platform (<https://www.dhis2.org/>). The data used were pooled nationwide program data from PEPFAR Nigeria-sup-

ported sites. We analysed the IPT uptake trend over a 3-year period between 2015 and 2017, hereafter denoted as FY2015, FY2016 and FY2017. FY2015 and FY2016 represented the pre-intervention phase, while FY2017 represented the post-intervention phase. We used the number of PLHIV currently receiving treatment during the reporting period, to determine the number of PLHIV eligible for IPT. We took into account PEPFAR FY2015 data for TB-HIV co-infection rate (20%) and assumed that 5% of clients would not be eligible for INH due to drug reactions or other situations precluding clients from receiving INH. In line with the national guidelines, we also took into consideration those who had taken INH in the past, but who were no longer eligible for a repeat IPT.⁹ Simple data aggregation, percentage computation and graphical representation were performed in Excel v2013 (Microsoft; Redmond, VA, USA). A trend analyses technique using linear regression was done to compare IPT uptake pre and post intervention periods.

Ethical considerations

The study was reviewed in accordance with the US Centers for Disease Control and Prevention (CDC) Office of Human Research Protection Procedures and determined to be non-research, program evaluation. This study required no direct contact with human subjects (via interview nor sample collection) and only utilized de-identified, pooled program data that formed part of the standard of care, thus no informed consent was required.

RESULTS

In FY2015 the number of PLHIV currently receiving treatment was 592 842, 444 632 of whom were eligible for IPT, and 25 416 commenced IPT. In FY2016 700 262 PLHIV were receiving treatment, 499 781 of whom were eligible for IPT and 36 084 commenced IPT. However, in FY2017, with the introduction of the new logistic system, 772 510 PLHIV were receiving treatment, 517 883 of whom were eligible for IPT and 61 161 commenced IPT. The percentage of IPT uptake was computed to show IPT uptake of 6%, 7% and 12% for

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FIGURE 1 INH distribution system, pre- and post-intervention, Nigeria, FY2016. *Chemonics, PEPFAR-funded unified logistic partner. INH = isoniazid; FY = fiscal year; GDF = Global Drug Facility; GF = Global Fund; NTP = National TB Programme; ARV = antiretroviral; HIV = human immunodeficiency virus; TB = tuberculosis; PEPFAR = President's Emergency Plan for AIDS Relief.

FIGURE 2 Trends in IPT uptake among eligible PLHIV, Nigeria, 2015–2017. PLHIV = people living with human immunodeficiency virus; ART = antiretroviral therapy; FY = fiscal year; IPT = isoniazid preventive therapy; TB = tuberculosis.

FY2015, FY2016 and FY2017 respectively (Figure 2). This translates to a 69% increase in IPT uptake following the program intervention. The trend analyses show a positive slope, which indicates an increasing trend in IPT uptake; the test of proportion indicated that the difference in pre-and-post intervention IPT uptake was significant ($P < 0.001$).

DISCUSSION

Uninterrupted supply of INH is a pre-requisite for effective TPT implementation. With the increasing number of PLHIV enrolled in HIV care and treatment, INH supply chains need to expand and be sustained to ensure availability for eligible PLHIV needing INH for TPT. Designing an effective and sustainable supply chain system for drugs and other commodities is important, but can be complex.¹¹ To ensure an efficiently run distribution system, systems must be put in place for the procurement, storage, and efficient transport of INH and other commodities. Furthermore, the reduction of theft and fraud and provision of information for forecasting needs requires good management of a simple but well-designed information system in place.¹¹

In Nigeria, TB drugs, including INH for TPT are procured by the NTBLCP through grants from the Global Fund for AIDS, Tuberculosis and Malaria (GFATM). TPT implementation within the PEPFAR program had depended on the NTBLCP for INH procurement, supplies and distribution. INH, a key drug in TB treatment, was routinely procured by the NTBLCP for use in TB treatment and INH prophylaxis in children aged <6 years. However, to meet TPT needs for INH 300mg, PEPFAR Nigeria's partners relied on an ad hoc arrangement with the NTBLCP and in most cases their needs were not met.

Key challenges to program implementation, such as unreliable provision of INH due to logistic inefficiencies, can significantly improve uptake when addressed.¹² Addressing logistics and other challenges to TPT implementation can ensure that programs are equipped to tackle the increasing burden of TB infection in the PLHIV population. The combination of HIV and latent TB increases the lifetime risk of active TB development to 50–70%, as against 10% in individuals who are not infected with HIV.¹³ It is therefore imperative that programs continuously make efforts to curb preventable deaths of PLHIV due to TB by increasing access to INH to eligible PLHIV population.

Our study had some limitations. Following the alignment of the INH 300mg LMIS with that of ARV, and the improved logistic management system, other activities were concurrently implemented across supported facilities to address other provider- and patient-related gaps in implementation. Awareness creation for TPT, provision of tools and continued supportive supervision were also implemented; this may have also contributed to the improved uptake. Also, we focused on having improved number of clients started on IPT and an improved system of INH delivery to the sites, hence, there was little focus on IPT completion rates, which was an objective of the IPT scale-up. However, the new system informed improved program monitoring and prioritization of TPT implementation within the program.

With approximately 12% TPT coverage out of the 90% target set by the Office of the Global AIDS Coordinator at the end of FY2017, a gap still exists that needs to be covered. However, significant improvement in TPT uptake was made following the implementation of an intervention that solely addressed the key logistic bottleneck. Other key challenges to TPT scale up that will continue to be addressed and prioritized by PEPFAR Nigeria are continuous on-site mentorship, awareness creation, and client education on the benefits of INH to improve demand and completion rates.

In conclusion, a strategic change in the INH logistic system led to a significant increase in IPT uptake among eligible PLHIV. Although INH was mainly procured by the NTBLCP, it is recommended that the provider-to-client stage of TPT implementation should be driven by the HIV programme for improved performance. There is also the need to improve cross-communication between the HIV and the TB programmes to correctly quantify the TPT needs of clients receiving care through the HIV programme delivery units.

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Contexte: L'expansion du traitement préventif par isoniazide (TPI), est restée lente au cours des dernières années au Nigeria. Le TPI est mis en œuvre au sein du programme VIH mais l'approvisionnement en médicaments et le soutien logistique ont été la responsabilité du programme TB pendant des années. Ceci a eu un impact sur l'appropriation et l'obligation de rendre des comptes du programme et est resté un frein à l'expansion du TPI dans le pays.

Méthode: Le plan d'urgence du Président des Etats-Unis pour la lutte contre le Sida (PEPFAR-Nigeria) a revu les principales entraves à la mise en œuvre du TPI en 2016 et a intégré la logistique de l'isoniazide (INH) à la gestion de la logistique des antirétroviraux (ARV) et au système d'information (LMIS). Les formulaires de commande de médicaments et de réquisition au niveau des

structures ont été révisés afin d'inclure l'INH à la formation sur les dosages appropriés et la réquisition de l'INH avec les ARV. Un soutien a été fourni pour la distribution la plus éloignée de l'INH directement dans chaque site de mise en œuvre parallèlement à celle des ARV.

Résultats: La modification du LMIS pour l'INH en 2016 a abouti à une augmentation de 69% de l'achèvement du TPI à la fin de la période de rapport de 2017, montrant une modification statistiquement significative du profil de la couverture du TPI entre les périodes avant et après l'intervention.

Conclusion: Un changement stratégique du système logistique de l'INH a abouti à une augmentation significative de la couverture du TPI parmi les personnes infectées par le VIH qui sont éligibles.

Marco de referencia: La ampliación de escala del tratamiento preventivo con isoniazida ha sido lenta durante los últimos años en Nigeria. El tratamiento preventivo de la tuberculosis (TPT) se aplica en el marco del programa contra la infección por el virus de la inmunodeficiencia humana (VIH), pero el suministro de medicamentos y el apoyo logístico ha permanecido a cargo del programa contra la tuberculosis (TB), lo cual tiene consecuencias sobre la apropiación y la rendición de cuentas y constituye un obstáculo a la expansión del TPT en el país.

Método: En el Plan de Emergencia del Presidente (de los Estados Unidos) para el Alivio del Sida en Nigeria (PEPFAR-Nigeria) se analizaron las principales barreras a la ejecución del TPT en el 2016 y se integró la organización de la distribución de la isoniazida (INH) en los sistemas de gestión de información logística (LMIS) de los

antirretrovíricos (ARV). Se modificaron los formularios de pedido y de solicitud de pedido en los establecimientos a fin de incluir la INH y se impartió capacitación sobre la cuantificación y los pedidos de INH con los ARV. Se respaldó la distribución de la INH con los ARV hasta el final del trayecto, directamente a cada centro que ejecutaba el tratamiento.

Resultados: Con la modificación en el 2016 de los LMIS para incluir la INH, se logró un aumento de 69% de la completación del TPT al final del período de notificación del 2017, con una evolución significativa de la aceptación del TPT entre el período anterior a la intervención y el período posterior a la misma.

Conclusión: Una modificación estratégica en el sistema de distribución de la INH dio lugar a un aumento considerable de la aceptación del TPI en las personas infectadas por el VIH que cumplían los criterios para recibir el tratamiento.