Improving indicators of tuberculosis program cascades by leveraging HIV program strategies

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Background: To improve rates of human immunodeficiency virus (HIV) case detection and treatment, the Nigerian Ministry of Defense Health Implementation Program and the US Army Medical Research Directorate-Africa/Nigeria introduced a HIV standard of care (SOC) package. Given the integration of tuberculosis (TB) and HIV programs and evolving policies, we evaluated the impact of this strategy on TB program indicators.

Methods: Routine, de-identified program data from 27 Nigerian military hospitals were analyzed. Using Wilcoxon signed-rank test, bivariate analyses were performed to compare data from 12 months before and after implementation of the SOC package.

Results: Our data showed improvements post-implementation as follows: the number of individuals receiving antiretroviral therapy (ART) screened for TB increased from 14 530 to 29 467 ($P < 0.001$); the number of individuals with presumptive TB identified increased from 803 to 1800 ($P < 0.001$); the number of ART clients bacteriologically tested for TB increased from 746 to 1717 ($P < 0.001$); and the number of ART clients treated for TB increased from 152 to 282 ($P < 0.001$). Newly registered or relapsed TB cases increased from 436 to 906 ($P < 0.001$), the number of TB cases with known HIV status increased from 437 to 837 ($P < 0.001$), the number of TB-HIV co-infected cases increased from 182 to 301 ($P = 0.006$), and the number of TB-HIV co-infected clients who started ART increased from 101 to 176 ($P = 0.003$).

Conclusion: The implementation of the updated HIV SOC package led to the improvement in key TB diagnosis and treatment indicators. When emulated, this could help improve the performance of other TB programs in countries other than Nigeria.

among HIV-infected people, accounting for 25–35% of all deaths.^{4–6}

In 2018, Nigeria completed the National AIDS Indicator and Impact Survey (NAIIS), which reported a prevalence rate of 1.4% and an HIV burden of an estimated 1.9 million individuals nationally.⁷ However, out of a population of over 180 million, only 37% of Nigerians have been tested for HIV. Nigeria is one of the 30 highest burden countries with respect to TB and TB-HIV co-infection.² It is one of the eight countries accounting for two thirds of the TB case burden in the world, with an incidence rate of 219 cases per 100 000 population.³ However, TB diagnosis and treatment rates remain poor. Globally, there is a 4.3 million-person gap between incident and notified TB cases; Nigeria, along with India and Indonesia, account for 50% of this gap.² Moreover, only 24% of all estimated TB patients in Nigeria receive treatment.^{2,3} Morbidity and mortality among HIV-TB co-infected people in Nigeria are substantial, and an estimated 57 000 HIV-positive patients die of TB each year.²

In 2015, the World Health Organization (WHO) recommended that antiretroviral therapy (ART) be started in all adults with HIV infection, regardless of the stage of disease or CD4 count.⁸ In support of the WHO recommendation for this “Test and Start” strategy, the US President’s Emergency Plan For AIDS Relief (PEPFAR) Scientific Advisory Board rolled out initiatives worldwide to scale up HIV diagnosis and treatment and to improve treatment outcomes.⁹ Critical to this strategy to improve services was the education of health care workers, particularly with regard to the benefits of immediate ART initiation upon diagnosis as HIV-positive, and an emphasis on comprehensive HIV care, including TB screening and treatment services.⁹ Individuals infected with HIV are about 20–30 times more likely to develop TB than those without. It is therefore important that PLHIV are adequately screened, diagnosed and treated for TB.¹⁰ Efforts were also made to increase the availability of health care services, and reduce barriers to treatment within communities.⁹

In 2016, PEPFAR Nigeria also introduced the use of linkage coordinators (otherwise called facility trackers or community volunteers) as part of the SOC package introduced to implement “Test and Start” in Nigeria.¹¹ One of the major roles of the linkage coordinators was to ensure that all clients who visited the hospital were tested for HIV, linked to HIV clinics if HIV-positive, and retained on treatment. These linkage coordinators contacted patients by telephone and visited their homes if they missed their appointments. The pro-

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KEY WORDS

tuberculosis; human immunodeficiency virus; PLHIV

Since the start of the global human immunodeficiency virus (HIV) epidemic in 1981, 76 million people have been infected with HIV, 37 million people are currently living with the disease and 35 million people have died from acquired immune-deficiency syndrome (AIDS) related illnesses.¹ There are 1.8 million new infections and 1 million AIDS-related deaths annually.¹ Despite these staggering numbers, tuberculosis (TB) has overtaken HIV and now ranks alongside it as the leading cause of death worldwide.² In 2017, there were 10 million incident cases of TB worldwide, 9% of which were among people living with HIV (PLHIV).³ In the same year alone, TB contributed to 1.6 million deaths, 300 000 of which were among HIV-positive people.³ TB is the leading killer

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TABLE TB diagnostic and treatment cascade indicators

TB diagnostic cascade indicators	TB treatment cascade indicators
Number of PLHIV clinically screened for TB, identified using the WHO-recommended symptom screen, i.e., cough of >2 weeks, fever, night sweats and weight loss (TB_Screen)	Number of new or relapsed TB cases (TB_Cases)
Number of PLHIV who screen positive with at least one of the above symptoms (TB_Presumptives)	Number of new or relapsed TB cases with documented HIV status (TB_STAT)
Number of PLHIV who had a specimen sent for bacteriological diagnosis of TB based on AFB smear or Xpert testing (TB_Evaluated)	Number of new or relapsed TB cases who tested positive for HIV (TB_STAT POS)
Number of PLHIV with confirmed bacteriological diagnosis of TB (TB_detected and treated)	Number of new or relapsed TB cases with documented HIV-positive status who are on ART during the TB treatment period (TB_ART)

TB = tuberculosis; PLHIV = people living with HIV; WHO = World Health Organization; HIV = human immunodeficiency virus; AFB = acid-fast bacilli; ART = antiretroviral therapy.

gram further implemented the symptomatic screening of all PLHIV for TB at every clinical visit (i.e., provider-initiated symptom screening for TB). Within health facilities, the job responsibilities of the linkage coordinators were extended to tracking and linking all PLHIV with presumptive TB to TB diagnostic services, and also to link diagnosed TB patients for HIV testing and treatment services. This was done to both reduce comorbidity and bridge the gap between HIV and TB treatment service delivery points. Before this period, the HIV program did not engage linkage coordinators and provider-initiated symptom screening for TB was non-existent. Also, the HIV and TB programs ran parallel activities, with no active or intentional collaboration.

Although this SOC package does not exclusively focus on TB, it was anticipated that the improvement of the health systems in order to meet the goals set forth to increase HIV diagnosis and treatment, as well as increasing health care workers' knowledge of HIV co-infections (chief among them being TB), would also have collateral benefit of improving TB diagnosis and treatment.

The present program evaluation critically analyzed specific, routinely collected, PEPFAR-dictated TB-HIV program indicators during the period before (pre-) and after (post-) implementation of the new HIV program SOC package initiated in 2016, and examined programmatic diagnostic and treatment strategies to better understand how programmatic changes affect the TB-HIV co-epidemics in Nigeria.

METHODS

Sample size

We analyzed program data from 27 comprehensive HIV treatment sites under the Care and Treatment Program of the Nigerian Ministry of Defense Health Implementation Program (NMODHIP) and US Army Medical Research Directorate-Africa/Nigeria (USAMRD-A/N). Between 20 000 and 25 000 PLHIV were screened for TB annually at these sites and of these, approximately 500–1000 proceeded with further TB diagnostic work-up, which routinely included clinical evaluation, sputum evaluation using acid-fast bacilli (AFB) smear and Xpert® MTB/RIF testing (Cepheid, Sunnyvale, CA, USA). Overall, approximately 500 patients are treated for TB per year at these sites. There are 14 GeneXpert machines installed at these sites: 13 of them were installed before the implementation of the SOC package initiative, while one machine was installed during the period of implementation of this SOC package. All sites were equipped to provide for AFB microscopy.

Data collection

Program data were pooled from the District Health Information System, version 2 (DHIS-2; <https://www.dhis2.org/>), which is the

repository for the program data. De-identified and aggregated data are entered at the facility level into the DHIS-2 system from the registers by site providers (with facility-level access clearance), while program managers (with program-level access clearance) can view and collate data from all the facilities. Data quality is assured by quarterly facility visits for validation with the registers. The period of data collection covers the 12-month period before the implementation of the SOC package (pre-implementation: April 2015–March 2016) and the 12-month period after implementation of the SOC package (post-implementation: April 2016–March 2017). The TB program indicators collected were divided into two categories: those from the TB diagnostic cascade and those from the TB treatment cascade (Table).

A relapsed TB case was defined as a person who had previously been treated for TB, had been declared cured or had completed treatment at the end of their most recent course of treatment, and was re-diagnosed with a recurrent episode of TB.¹¹

Data analyses

The performance of TB indicators in the pre-SOC package era was compared to their performance in the post-SOC package era. Due to the non-parametric metrics used to compare the two study periods, we used Wilcoxon signed-rank test, as the data from different facilities would not fit a normal distribution curve well; two-tailed *P* value (*P* < 0.05) was used as a measure of statistical significance. Percentage computation was used to highlight performance improvements. Group bar charts with dot plots in Excel v2013 (Microsoft; Redmond, WA, USA) was used for graphical representation of data.

Ethics statement

The study was approved by the National Health Research Ethics Committee, Abuja, Nigeria, and the Walter Reed Army Institute of Research Institutional Review Board (Silver Spring, MD, USA). As the study did not require direct contact with human subjects (neither via interview nor sample collection), and only de-identified, routinely collected and aggregated SOC program data were used, informed consent was not required.

RESULTS

Effect of implementing standard-of-care HIV package on TB diagnostic cascade

The TB diagnostic cascade is based on the clinical needs of PLHIV in care, who receive clinical screening (TB_Screen) for symptoms of TB (prolonged cough duration of >2 weeks, night sweat, fever and weight loss).¹² Those who responded affirmatively to any of the screening questions were designated as presumptive cases

FIGURE 1 Number of patients in the TB diagnostic cascade both before (pre-) and after (post-) implementation of the revised standard of care package. The percentage improvement represents performance changes between the two study periods. PLHIV = people living with human immunodeficiency virus; TB = tuberculosis.

(TB_Presumptive) and were subsequently evaluated bacteriologically for TB (TB_Evaluated). After the evaluation, those who tested positive for TB were treated (TB_Detected and Treated) according to the Nigerian national TB guidelines.¹² The data (Figure 1) show improved performance of TB diagnostic indicators between pre- and post-SOC package implementation with an increase in numbers as follows: TB_Screen: from 14 530 to 29 467 (203%, $P < 0.001$); TB_Presumptive: from 803 to 1 800 (224%, $P < 0.001$); TB_Evaluated: from 746 to 1 717 (230%, $P < 0.001$); and TB_Detected and Treated: from 152 to 282 (186%, $P < 0.001$).

Effect of implementing standard-of-care HIV package on TB treatment cascade

The TB treatment cascade indicators are program indicators emanating from the clinics implementing the DOTS strategy. As part of the effort to integrate TB and HIV programs, HIV testing ser-

vices (HTS) are incorporated into TB program services at the study sites. As the cascade flows, patients diagnosed with TB (TB_cases) are required to know their HIV status or be tested for HIV (TB_STAT); HIV-positive patients (TB_STAT POS) are started on ART (TB_ART). The data (Figure 2) show increments in the following TB treatment cascade indicators on implementing the SOC package: TB_cases: from 436 to 906 (208%, $P < 0.001$); TB_STAT: from 427 to 847 (198%, $P < 0.001$); TB_STAT POS: from 182 to 301 (165%, $P = 0.0058$); and TB_ART: from 101 to 176 (174%, $P = 0.0032$).

DISCUSSION

The HIV SOC package implementation was expected to increase the number of persons diagnosed with HIV, as well as to improve the quality of care, but as our data show, there was also a correla-

FIGURE 2 Number of patients in the TB treatment cascade both before (pre-) and after (post-) implementation of the revised standard of care package. The percentage improvement represents performance changes between the two study periods. TB = tuberculosis; HIV = human immunodeficiency virus; ART = antiretroviral therapy.

tional increase in the number of persons diagnosed and treated for TB. This supports the underlying rationale for the WHO's policy recommendation for TB and HIV program collaboration,¹³ as both programs are linked due to their epidemiological interdependencies. However, it is important to also note the possible effects of some TB program-specific changes or innovations that were ongoing concurrently with the implementation of the revised HIV SOC package. Some of these TB program-specific implementation changes include, but are not limited to, increased advocacy and roll out of Xpert testing (as the first-line TB diagnostic tool in the country), which has a higher sensitivity in diagnosing *Mycobacterium tuberculosis* than the AFB microscopy from sputum samples. On the other hand, as 13 out of the 14 GeneXpert machines at our program sites had already been installed and were functional before the advent of the HIV SOC package initiative, the addition of one GeneXpert machine during the intervention phase seem unlikely to have strongly contributed to the improvements observed in TB diagnosis. Study limitations, especially in data analyses, prevented quantification and statistical elimination of the effects of confounders such as these, but facility-level quarterly/semi-annual data validation, which forms part of the program deliverables ensured integrity of our reported data. However, a key point is that the new SOC included active screening of PLHIV by healthcare workers in the form of provider-initiated TB symptom screening, which was rarely implemented prior to the intervention period, as only patients with TB-like symptoms were further evaluated (passive screening). Provider-initiated symptom screening for TB has been shown to have a higher positive predictive and lower negative predictive values for TB diagnosis in HIV-positive individuals.¹⁴ The involvement of linkage coordinators may also have contributed to the improvements in indicators, although none of these activities could be directly said to have caused these effects alone, but in synergism. This is evident in our data, which show that the number of PLHIV screened for TB increased from 14530 to 29467 (Figure 1); this could be attributed to provider-initiated symptom screening for TB. The increase in the number of new/relapsed TB cases with known HIV status from 427 to 847 could be attributed to the activities of the linkage coordinators, who also work to bridge the HIV testing gap among TB patients, thus improving HIV case identification in this group, with subsequent linkage to ART (Figure 2). We therefore believe that the improvements seen in the TB diagnostic and treatment cascades indicators may have been a consequence of the activities implemented under the HIV SOC package. For efficient management of funds, the HIV laboratory and pharmaceutical logistics systems were integrated to accommodate TB program activities and the distribution of TB treatment drugs, diagnostic reagents and other consumables, as this further ensured closer collaboration.

In addition to their work in HIV, the trackers or linkage coordinators were also trained and deployed to perform the role of peer educators for TB, since they belong to the communities they serve and therefore understand the behaviors, beliefs, terrain and local languages. The use of community volunteers as peer educators for TB had led to improved knowledge and attitude among community members about TB in a peri-urban population in Nigeria,¹⁵ similar to the results of the strategy used to enhance TB case detection and treatment in Philippines.¹⁶ Nigeria has an estimated 407 000 TB cases per year, but only 104 900 cases per year are cur-

rently notified, as of 2017.¹⁷ If the gap in TB notification is to be bridged in Nigeria, the role of trackers in TB education and treatment linkages cannot be over-emphasized. However, the sustainability of the trackers' engagement is threatened by constantly shrinking program funds. To combat this challenge, combining the resources of two programs (HIV and TB) can benefit both programs, as shown by our data, which indicate correlational improvements in TB diagnosis by taking advantage of existing HIV infrastructure and strategy. Such leveraging of the activities, strategy and infrastructure of the HIV program could therefore positively impact the TB program within supported facilities. We also strongly believe that such leverage and coordination, when emulated, can be used to improve other programs in Nigeria and other countries, and achieve 'End TB Strategy' goals by 2035. Also, this could encourage governments at different levels, private donors and non-governmental organizations to provide more funding to support TB case identification, treatment and prevention, especially among vulnerable populations.

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Contexte : Pour améliorer les taux de détection et de traitement des cas de virus de l'immunodéficience humaine (VIH), le programme a introduit un ensemble de normes de soins (SOC) relatives au VIH. Etant donné l'intégration des programmes tuberculose (TB) et VIH et l'évolution des politiques, nous avons évalué l'impact de cette stratégie sur les indicateurs du programme TB.

Méthode : Les données de programme de routine, rendues anonymes, des hôpitaux militaires du Nigeria ont été analysées. Les analyses bivariées basées sur le test de Wilcoxon signed-rank ont comparé les données des 12 mois précédant et suivant la mise en œuvre du paquet SOC.

Résultats : Nos données ont mis en évidence des améliorations avant et après la mise en œuvre: les clients recevant un traitement

antirétroviral (TAR) dépistés pour la TB ont augmenté de 14 530 à 29 467 ($P < 0,001$) ; les TB présumées identifiées ont augmenté de 803 à 1800 ($P < 0,001$) ; les clients TAR ayant eu un test bactériologique de TB sont passés de 746 à 1717 ($P < 0,001$) ; et les clients TAR traités pour TB ont augmenté de 152 à 282 ($P < 0,001$). Les cas de TB nouveaux ou en rechute sont passés de 436 à 906 ($P < 0,001$). Les cas de TB dont le statut VIH était connu se sont accrus de 437 à 837 ($P < 0,001$), les cas de coinfection TB-VIH sont passés de 182 à 301 ($P = 0,006$) et les clients TB-VIH qui ont mis en route le TAR ont augmenté de 101 à 176 ($P = 0,003$).

Conclusion : La mise en œuvre du paquet SOC VIH, mis à jour, a amélioré les indicateurs clés du diagnostic et du traitement de la TB. Son adoption pourrait améliorer d'autres programmes TB au-delà du Nigeria.

Marco de referencia: Con el propósito de mejorar las tasas de detección y el tratamiento de los casos de infección por el virus de la inmunodeficiencia humana (VIH), el programa introdujo un conjunto de normas asistenciales (SOC) para la infección por el VIH. Teniendo en cuenta la integración de los programas de tuberculosis (TB) y VIH y la evolución de las políticas, se evaluó el impacto de esta estrategia sobre los indicadores del programa contra la TB.

Método: Se analizaron los datos corrientes anónimos del programa, provenientes de 27 hospitales militares de Nigeria. Mediante análisis bivariantes y la prueba del orden con signo de Wilcoxon se compararon los datos de 12 meses antes y 12 meses después de la introducción del SOC.

Resultados: Los datos mostraron progresos después de la introducción, a saber: los usuarios que recibían tratamiento

antirretroviral (TAR) que tuvieron tamizaje de la TB aumentaron de 14 530 a 29 467 ($P < 0,001$); los casos detectados con diagnóstico presuntivo de TB aumentaron de 803 a 1800 ($P < 0,001$); los usuarios del TAR con estudio bacteriológico de la TB aumentaron de 746 a 1717 ($P < 0,001$); y los usuarios del TAR tratados por TB aumentaron de 152 a 282 ($P < 0,001$). Los registros de casos nuevos o recaídas de TB aumentaron de 436 a 906 ($P < 0,001$); los casos de TB con situación conocida frente al VIH aumentaron de 437 a 837 ($P < 0,001$), los casos de coinfección por TB y el VIH aumentaron de 182 a 301 ($P = 0,006$); y los pacientes coinfectados por la TB y el VIH que iniciaron TAR aumentaron de 101 a 176 ($P = 0,003$).

Conclusión: La introducción del SOC VIH actualizado por el mejoró los principales indicadores del diagnóstico y el tratamiento de la TB. Esta iniciativa podría mejorar otros programas de TB por fuera de Nigeria.