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Expanding Access and Demand for TB/HIV Service through Integration in Low Income Country of South Sudan

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Abstract:

Tuberculosis (TB) remains the leading cause of death and morbidity among people living with HIV in developing countries, and HIV infection the most potent known risk factor associated with developing active TB. According to UNAIDS, there are currently an estimated 33.3 million people living with HIV/AIDS and, in 2009, 1.2 million people were initiated on antiretroviral therapy for the first time. TB is a major problem of public health in South Sudan. According to the WHO estimates for the year 2014: i) the prevalence of TB was 319 cases per 100,000 population, ii) 17,000 people were newly affected with TB, indicating an incidence of 146 new TB cases per 100,000 population and iii) 3,400 persons died of TB which resulted in a mortality rate of 29 deaths from TB per 100,000 population. The information system of the National TB Programme (NTP) indicates that TB notification has increased from 2,955 cases in 2008 to 8,856 in 2014. The many interactions between tuberculosis (TB) and human immunodeficiency virus (HIV) infection influence the design and implementation of programs to address the needs of patients living with or at risk for both diseases. Collaboration between national TB and HIV programs and some degree of integration of services at a local level have been advocated by the World Health Organization and other international bodies and are recognized as essential in areas where the 2 diseases are prevalent. However, in most settings, strategies to accomplish this are only beginning to reach the field where their impact will be made and the expectation of improving the outcome of both diseases realized. These are not exhaustive or prescriptive, but describe the range of options from linkage and close collaboration to fully collocated integration. The assessment of integration of TB/HIV show that programmatic, medical, staffing, resource, and scale-up challenges remain. In addition, they indicate that, although broad program principles of TB/HIV service integration are essential, program designs and components may vary by country and even within countries, as a result of differing TB and HIV disease prevalence, resources, levels of expertise, and differences in program settings (urban vs. rural and/or primary vs. district vs. specialty site). Large national programs can successfully provide rapid, uniform and widespread change and implementation but also must negotiate the subtleties of intricacies of TB/HIV interactions, which confound a uniform "one size fits all" public health approach. Conversely, smaller demonstration projects, even with successful outcomes, must grapple with issues related to generalization of findings, wider implementation, and scale up, to benefit larger populations of those in need.

Keywords: South Sudan, TB-HIV co-infection, TB-HIV integration and quality improvement

1. Introduction and Background

Tuberculosis (TB) remains the leading cause of death and morbidity among people living with HIV in developing countries, and HIV infection the most potent known risk factor associated with developing active TB. According to UNAIDS, there are currently an estimated 33.3 million people living with HIV/AIDS and, in 2009, 1.2 million people were initiated

on antiretroviral therapy for the first time. TB is a major problem of public health in South Sudan. According to the WHO estimates for the year 2014: i) the prevalence of TB was 319 cases per 100,000 population, ii) 17,000 people were newly affected with TB, indicating an incidence of 146 new TB cases per 100,000 population and iii) 3,400 persons died of TB which resulted in a mortality rate of 29 deaths from TB per 100,000 population. The information system of the National TB Programme (NTP) indicates that TB notification has increased from 2,955 cases in 2008 to 8,856 in 2014. The information system of NTP reported that among smear-positive pulmonary TB cases notified in 2014:

- 65% are males, which indicate a sex-ratio of 2 males for 1 female;
- One third of them belong to the age group 25-34 years in both gender groups;
- 85% are aged less than 45 years in both gender groups.

Among the total number of smear-positive pulmonary TB patients notified, two thirds were identified in 4 of the 10 states, namely: Central Equator State (38%), Warrap State (12%), Northern Bahr El Ghazal State (11%) and Upper Nile State (5%). The incidence of notified smear-positive pulmonary TB cases was 37 per 100,000 populations at national level in 2014. This notified incidence was significantly higher in males than in females in all the age groups except for those aged less than 15 years or more than 64 years (see graphs below). In the age group 25 to 44 years, males are approximately 2 times more likely to be notified for smear-positive pulmonary TB than females.

DOTS strategy was initiated at very low scale in 2002 with 12 health facilities which provided TB diagnosis and treatment services. The NTP adopted the WHO Stop TB Strategy in 2006 which focused on the extension of basic DOTS services and the implementation of TB/HIV collaborative activities. Until 2014, TB services have been implemented in 87 TB diagnosis and treatment centres; none of the 792 PHCUs that are available across the country is ensuring any TB services. In early 2015, the NTP adopted the WHO End TB Strategy to achieve the objectives identified in the 2015-2019 NSP.

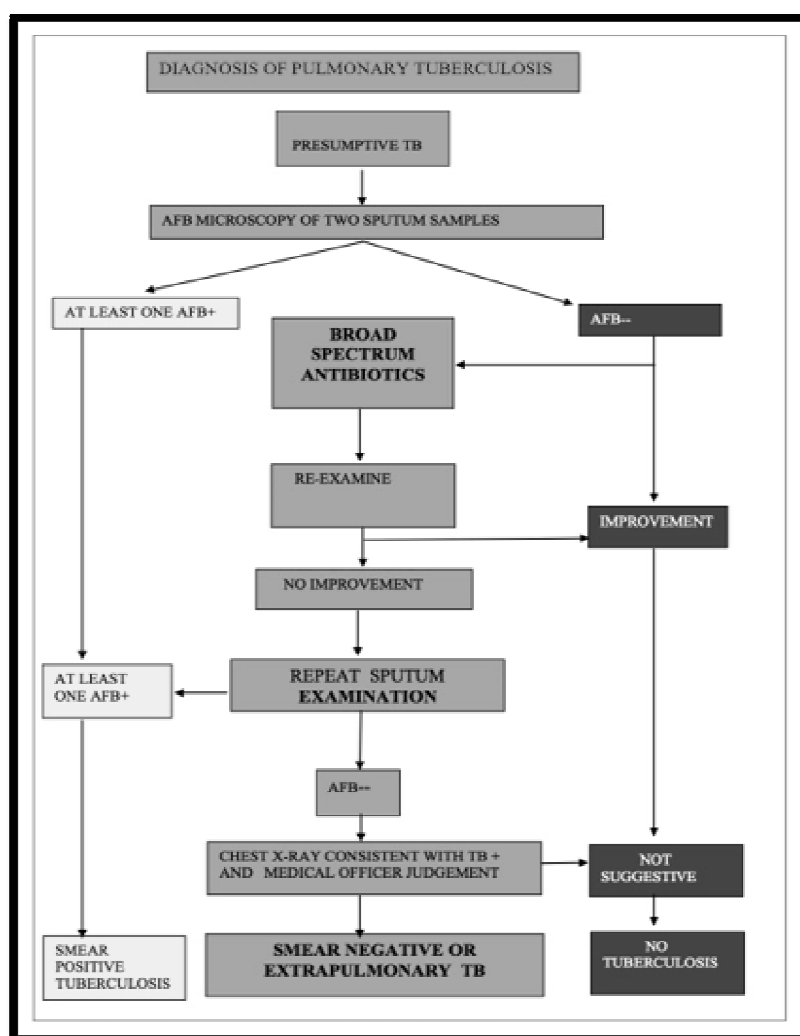


Figure 1

The profound impact that HIV and TB epidemics have had on health systems worldwide, particularly those in low-resource countries, has prompted the World Health Organization (WHO) to issue strategic guidelines for the integration of TB and HIV in 2012 in order to combat both epidemics. Unlike the traditional approach where both diseases are tackled separately by the corresponding units in departments of health, these guidelines highlight WHO's Three I's- Intensified Case Finding (ICF), Isoniazid Preventive Therapy (IPT) and TB Infection Control (IC), as well as systematic testing and

treatment of HIV in TB patients which all constitute key strategies to combat TB and HIV co-infection through an integrated delivery of these services.

South Sudan TB management guidelines and Tuberculosis Prevention Therapy among people living with HIV mandating that they be screened for TB, and recommending that those where active TB was ruled out be started on IPT. South Sudan adopted WHO'S policy on collaborative TB/HIV activities including the Three I's, early initiation of HAART and speeding up the expansion of HAART through decentralization and clinical Initiation and Management of patients on HAART.

The World Health Organization recommends that treatment of tuberculosis (TB) in HIV-infected patients should be integrated with HIV care. Little is known about the integration of tuberculosis (TB) and human immunodeficiency virus (HIV) treatment in fragility and resource limited setting of South Sudan. Tuberculosis (TB) is the leading cause of death in HIV-infected patients and HIV-infection is the most important risk factor for developing active TB. The dual epidemic of TB and HIV is cause for great concern, especially in sub-Saharan Africa where 80% of the burden of co-infection resides and health systems are already weak and overstretched. In order to fully implement these collaborative activities integration of health systems for HIV and TB service delivery should be in place, although there is a lack of consensus on how to implement this integration.

To decrease the joint burden of HIV and TB disease, the World Health Organization (WHO) formulated a strategic framework for collaborative TB/HIV activities. These activities focus on reducing the burden of TB among HIV-infected patients by the "three I's": intensified case finding, isoniazid preventative therapy and infection control. Decreasing the burden of HIV in TB patients is to be done by providing HIV counseling and testing, the use of co-trimoxazole and by introducing highly active antiretroviral therapy (HAART). Based on evidence from several randomized controlled trials showing reduced mortality, recent guidelines state that co-infected patients should be initiated on HAART as soon as possible after TB treatment initiation

South Sudan TB programme identified and quality improvement action point of outdoor integrated "One-Stop Shop" TB/HIV clinic was instituted for established quality improvement committees of TB and HIV clinics at the 40 targeted health facilities in South Sudan, to improve the TB treatment completion rate, to standardize diagnosis and care in co-infected patients and to reduce nosocomial transmission of TB. Our objective was to investigate whether integrating HIV and TB care results in improved patient management, measured by improved TB treatment outcomes (survival and treatment completion) and by prompt HAART initiation in eligible patients according the guideline.

2. Fragmented care before integration

In south Sudan TB screening and diagnosis was being done separately, systematically and was performed at the discretion of medical officers during routine HIV follow-up visits in TB and HIV clinic. After diagnosis of active TB, treatment and follow-up according to the guideline guidelines was provided at distinct clinics of TB and HIV. Directly Observed Therapy (DOT) or tracing of patients lost to follow-up was not done

Patients collected HAART at their HIV clinic during monthly HIV-doctor visits. They collected TB treatment weekly at their TB or local clinic under the DOTS program; at times, this corresponded with TB-doctor visits. Save for DOTS-collections, TB- and HIV-doctor visits were considered lengthy and inconvenient. Appointments were given by date, not exact times, mandating a 3–7 hour wait. Employed patients requested time off work, with some receiving compensation upon providing a medical note. However, most patients did not disclose HIV to employers, and accessed "vacation" or unpaid leave for HIV care.

Patients experienced logistic problems coordinating TB and HIV appointments. At the co-located site, they enjoyed the convenience of accessing dual services under one roof. However, appointments were not given within a shared timeframe mandating duplicate commutes for individual doctor visits; HCWs conceded appointments were not always made with consideration to their co-located team. Distinct queues further precluded patients from completing any one appointment in time to adhere to the other. The onus to maintain distinct days for TB and HIV appointments was even greater for patients attending non-integrated clinics. Coinciding appointments had caused at least one patient to miss an HIV appointment, delaying his commencement of HAART.

Patients described being routinely referred to other infectious disease programs, primary healthcare clinics and/or hospitals for emerging issues that their TB and HIV clinics did not manage. They expressed frustration at having to endure additional commutes and time off work to be examined by different doctors. TB- and HIV-HCWs echoed their perceived mandate to attend to strictly TB- and HIV-related issues, respectively, considering their workload and limited resources. However, they also commiserated about the difficulties experienced accessing medical information from other facilities, noting patients remained the only informative link connecting their multiple service providers.

3. Creation of Integrated TB/HIV Program

Capacity building was done through TB partners formed Quality improvement committees in target facilities offering TB and HIV services. The committees identified a joint integration of TB/HIV services as an action point for improvement to improve diagnosis and care for co-infected patients at 40 TB/HIV target facilities in South Sudan and to improve infection control for both patients and clinic staff. The committee laid the groundwork for a more integrated TB/HIV service and created evidence-based standard operating procedures for diagnosis and management of TB in HIV-infected patients, a set of "cross-learning" TB/HIV clinics.

The improvement process of outdoor integrated TB/HIV clinic was set up in all 40 target facilities. In this clinic, TB suspects and patients diagnosed with TB can access care for both diseases simultaneously, by the same staff. Care was provided by a trained team of either clinical, medical or nurse based of facility capacities supported by health promoters. General HIV clinic personnel were trained to recognize common TB symptoms and to direct patients suspected to have TB to the integrated clinic for assessment. Standardized TB diagnosis, treatment initiation and follow-up were reinforced by the use of "cross-learning" TB/HIV clinic management forms. This set of six forms guides clinicians in the appropriate management of the co-infection and includes all TB program definitions and algorithms for switching or initiation of HAART in patients with active TB. These forms together with all clinical information on TB are kept in the "master" HIV clinic patient file. Through integration tracing of co-infected patients lost to follow-up was done on an approximately two-weekly from through health promoters at community level and using mobile phone where there is network. After completion of TB treatment or after exclusion of active TB, the patient is referred back to the general HIV clinic

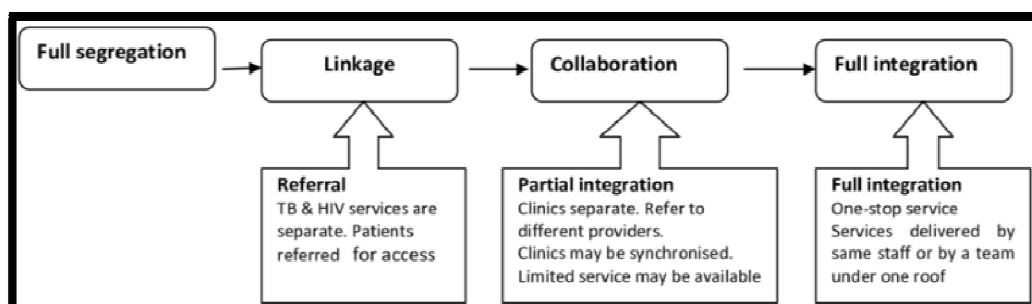


Figure 2

4. Material and Methods

4.1. Results

Integration was conceptualized and quality improvement initiative for 40 health facilities TB/HIV services for diagnostic and treatment units (DTUs). A total of 9,832 presumptive cases were identified and screened for TB, and of these 1,833 bacteriologically positive TB cases were identified, All new and relapse TB cases identified and put on treatment were 3964 cases against the donor target of 1680 giving a percentage achievement of 236%

As a result of integration treatment success rate improved to from 75% in 2017 to 79% in 2018. Of all TB cases new and relapses identified, 92% were tested for HIV and received their results. All (100%) TB/HIV co-infected clients were started on Cotrimoxazole Preventive Therapy (CTX) while 93% of the TB/HIV co-infected clients were initiated on HAART.

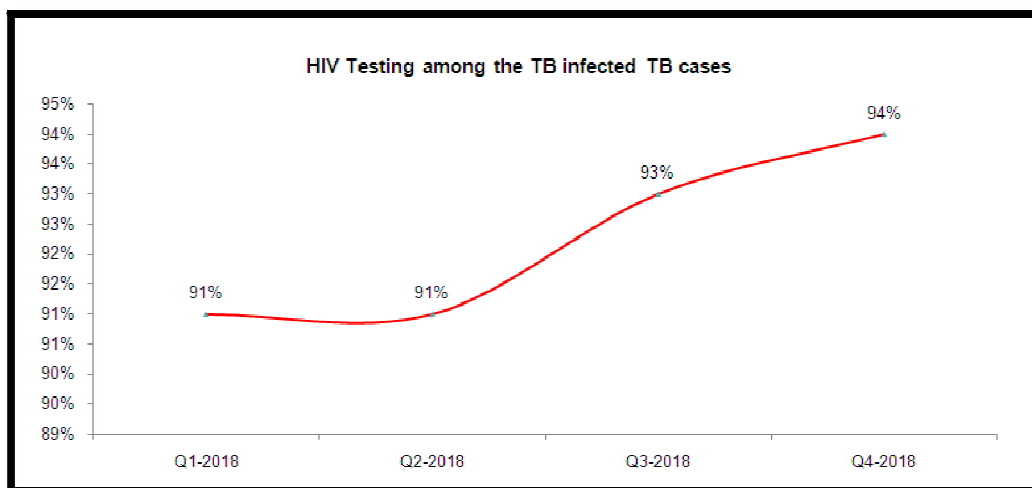


Figure 3

TB/HIV Integration has improved Case management with identification of 15 MDR TB cases and 14 initiated on second line treatment while 12 are active on second line treatment. Two patients died and one was a lost to follow up Implementation if integrated TB/HIV improved the tracking availability of TB commodities and joint integrated Support Supervision with other implementing partners supporting primary health care services. The facilities maintained a satisfactory above 95% timely order submission rates. There was stable availability of Anti TB medicines but need to strengthen redistribution mechanism to resolve shortage and avoid waste and drug expiry.

	Q1-2018	Q2-2018	Q3-2018	Q4-2018
TB Suspects	1126	3286	2462	2958
Total TB cases	452	1641	1093	1047
Bacteriologically confirmed TB	247	661	494	431
Number of notified cases of all forms of TB - bacteriologically confirmed plus clinically diagnosed, new and relapses	432	1562	987	983
Percentage of TB cases, all forms, bacteriologically confirmed plus clinically diagnosed, successfully treated (cured plus treatment completed) among all new TB cases registered for treatment during a specified period	79%	81%	77%	79%

Table 1

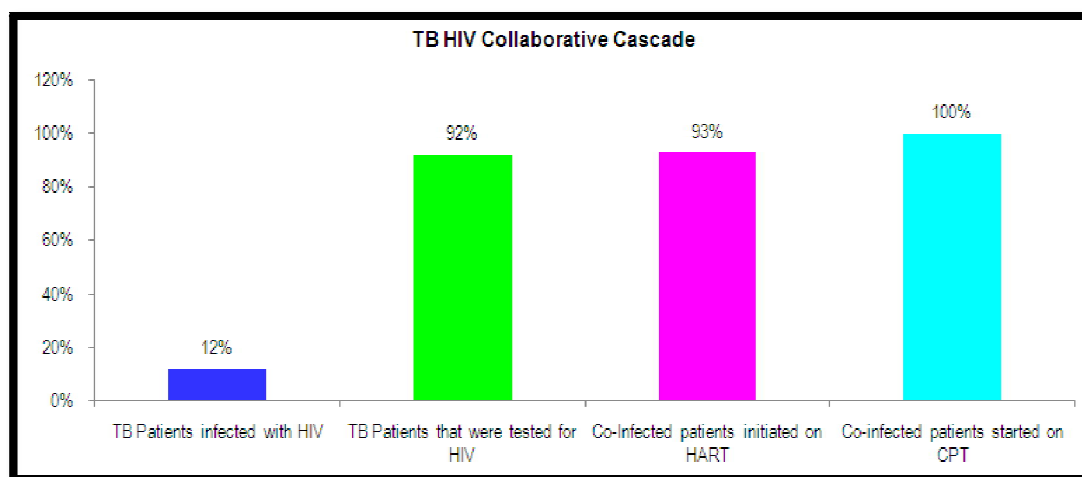


Figure 4

	Target	Q1-2018	Q2-2018	Q3-2018	Q4-2018
Percentage of laboratories showing adequate performance in external quality assurance for smear microscopy among the total number of laboratories that undertake smear microscopy during the reporting period	100%	85%	90%	100%	100%
Percentage of TB patients who had an HIV test result recorded in the TB register	85%	91%	91%	93%	94%
Percentage of HIV-positive registered TB patients given anti-retroviral therapy during TB treatment	85%	96%	96%	90%	89%
Percentage of previously treated TB patients receiving DST (bacteriologically positive cases only)	95%	89%	89%	100%	93%
Number of TB cases with rifampicin-resistant (RR-TB) and/or MDR-TB notified	2	2	2	5	4
Number of cases with drug resistant TB (RR-TB and/or MDR-TB) that began second-line treatment	2	4	2	5	3
Percentage of HMIS or other routine reporting units submitting timely reports according to national guidelines	100%	63%	63%	87%	83%

Table 2

To meet the ambitious UNAIDS 90-90-90 targets for HIV testing, HAART initiation, and virologic suppression, as well as improving HIV-TB integration in practice, significant scaling up of case-finding strategies (for both TB and HIV) outside of traditional facility-based testing and robust linkage to care are necessary. As shown in this study integrated TB-HIV is a novel strategy to increase mechanism for improved testing coverage, linkage to care, and TB-HIV integration. The full potential of TB/HIV integration delivered interventions on the trajectory of both TB and HIV epidemics may only be fully realized by including comprehensive prevention as part of integrated service delivery.

4.2. Study Design

The study design was an open-label cluster randomized controlled trial. Monitoring performance of 40 quality improvement intervention clinics distributed in 7 states within South Sudan as randomized case facilities while control

groups are either facilities offering full segregation and linkage for TB and HIV patients. The cases who are the intervention group of 40 facilities integrated TB/HIV service delivery is based on (provision of standard government guidance with active enhancement of TB-HIV care integration through a quality improvement approach)

4.3. Sampling Procedure

The study sampling procedure and methodology is purposive targeting 40 intervention health facilities designed as pilot centres of excellence through monitoring implementation of continuous quality improvement initiative of TB/HIV integration for improved health outcome and enhance quality TB prevention care and control service

4.4. Target Population

We analyzed programme report and assessed the service flow in target 40 public health facilities in the high TB/HIV prevalence in 7 States covered by TB programmes which include Torit State, Kapoeta State, Jubek State, Greater Upper Nile States, Wau State, Northern Leitch State, and Lol State in South Sudan for the period January –December 2018

4.5. Data Management

Assessment of the success of the quality improvement initiatives was done through programmatic monitoring and reporting of the adherence to guidance and supervision reports. Quality assurance measurement was done through simplified functionality and service readiness and availability tool which collected qualitative and quantitative data from the intervention sites and analyzed thematically for this study.

4.6. Study Limitation

We conducted the functionality assessment only in health facilities offering TB/HIV service because of the high incidence and prevalence our results might therefore not be representative of health facilities with lower TB/HIV prevalence and health facilities not yet integrated. The study used service rapid service readiness and availability assessment only included a few facilities in each state, thus limiting the generalizability of our results. Our small sample size reduced the power of the study, and may have concealed statistically significant differences in our study population. A larger sample size could have shown an association between factors such as facility type and location of HAART provision, and facility type and method of initiation and management of HAART. We sought to maximize external validity through purposive sampling and by selecting sites based on the targeted intervention on TB/HIV Integration. Further, all selected facilities are public health facilities offering TB/HIV services to public. Our results might not be representative of TB/HIV integration in private sector health facilities.

4.7. Ethical Consideration

All data collected from routine project implementation with expressed and implied permission in contractual agreement, and project document. Assurance provided for sole use of this study and sharing experience. All qualitative and quantitative data from this study were either in the public domain or shared in fully anonymized format. Approval and authority to undertake the study was/will be sought from Ethics Review Committee of the South Sudan Ministry of Health (Apr 2018).

5. Discussion

5.1. Policy Changes

Whilst changes in criteria for site readiness and the development of nurse-based models for HAART delivery are welcomed, these fail to address the complexity of increasing access to HAART within an overburdened and fragile health system. Although less stringent, criteria for site readiness may still be used at district or facility level to delay HAART rollout. Policies and regulations to transform HIV treatment from a doctor-led to a nurse-led programme need to be amended. These include clarification of regulations related to task shifting, standardization of dispensing practices for HAART and TB drugs, formalization of guidelines on indirect supervision of pharmacist assistants by pharmacists, supervision of phlebotomy by staff nurses and registration of trained lay health workers for fingerpick HIV testing. Guidelines for donor organisations stipulating the integration of vertical programmes into general PHC service delivery must be developed and not-for-profit organisations monitored to ensure they address the comprehensive health needs of patients. Practices promoting the exceptionalization of HIV, for example confidentiality, at the cost of integration should be changed. Instead, privacy in service settings and in all communication should ensure rights of all patients.

5.2. Health System Reforms

For Programme synergies each step in the treatment journey from work-up, diagnosis, treatment to community-based care is an opportunity for integration. Provider-initiated HIV testing should be offered at all health facilities, and at least all antenatal patients or those diagnosed with TB with unknown status should be offered an HIV test. HIV testing capacity is under-utilized with many counselors testing 10–20 clients a week (Harrison 2009). Counselors could see many more patients, reduce time spent on pretest counseling and emphasize post-test follow-up and enroll patients into care. Post-test follow-up should provide support, transmission prevention and condom provision. TB clinics are a logical place for HIV testing if HIV status is unknown, education about HIV, its prevention and condom provision. Similarly, HIV case management is an obvious place for TB case finding, educating patients about TB risk and signs. Integration and increased

vigilance will increase case finding of TB and HIV in both high-risk groups. The provision of point-of-care CD4 cell count testing to assess HAART eligibility should be prioritized in TB clinics. This would reduce delays and the risk of mortality and TB disease in HIV-positive patients (Lawn et al. 2009). Preparation for HAART, including the social, clinical and laboratory work-up of clients, could be carried out in TB clinics.

5.3. Integration of TB into HIV Services

HAART can unmask TB and there is a high risk of TB in patients with low CD4 counts. Up to a quarter of patients commencing HAART has positive TB sputum cultures and 11% on HAART develop TB during their first year on treatment (Lawn et al. 2009). Patients with a CD4 count >500 cells/ μ l are twice as much at risk of TB as HIV negative patients from the same community, and patients with a CD4 count 500 cells/ μ l. Two recent studies suggest that given the high prevalence of HIV and tuberculosis, screening for TB in HIV-positive patients is insufficient and sputum microscopy and culture should be performed before HAART initiation, regardless of symptoms (Bassett et al. 2010; Lawn et al. 2010). HAART should never be delayed in an eligible co-infected patient. A recent study on randomized control trial demonstrated high mortality among patients when HAART was initiated at the end of TB treatment, compared with initiation during TB treatment (Abdool Karim et al. 2010). These guidelines recommend HAART initiation 2–8 weeks after starting TB treatment (University of Cape Town Lung Institute 2009). To promote adherence, HAART regimens can be adapted to a daily dose administered simultaneously with TB drugs and efavirenz based regimens used to minimize drug–drug interactions (Gandhi et al. 2009).

Facility-based DOTs is promoted in some parts of South Sudan to improve adherence, and patients with active TB attend health facilities daily for medication. This practice should be reconsidered to promote patient autonomy and reduce the risk of nosocomial TB transmission. Chronic patients returning monthly to PHC facilities for treatment spend hours in waiting areas, to be seen by clinicians or at the pharmacy for their medication. Integrated TB and HIV services with simultaneous treatment for both conditions waiting once to be seen by a clinician and once in the pharmacy queue will limit the opportunities of nosocomial transmission.

Rationalization and standardization of monitoring and evaluation systems for TB and HIV services for high patient volumes is a priority. A limited number of critical indicators including ones to monitor integration need to be identified and registers designed accordingly. Systems tailored for different settings could minimize the collection of large volumes of routine data. This can be supplemented by sentinel surveillance to provide in-depth information and could incorporate laboratory-derived data to generate indicators such as the percentage of HIV-infected patients with positive TB sputa or viral load suppression.

TB / HIV co-management needs to be incorporated in both TB and HIV training programmes and would address poor provider knowledge enhancing service integration. The PALSA plus programme piloted in one province improved nurse-based TB and HIV services (Fairall et al. 2005). This will be rolled out nationally and should be accompanied by guidelines detailing the responsibilities of and interface between different cadres of HCWs to ensure that nurses feel supported and empowered regarding clinical decision-making. However, ongoing supportive supervision is essential to ensure the quality of care (Doherty et al. 2009).

A facility-based evaluation tool that assesses TB, HIV and STI services, programme performance and integration has been developed for both urban and rural areas and is used regularly in the Western Cape to supplement routine data (Scott et al. 2010).

5.4. Community-Level Support

The current community-level care DOT infrastructure should be adapted and strengthened to support HAART patients and treatment literacy for TB and HIV prior to and during treatment. Community-level workers should be trained to provide adherence support and adverse reaction monitoring. Workers who previously looked after either patients with TB or patients with HIV should look after both, work under the same conditions, for the same organisation and be similarly remunerated.

6. Conclusion

A large and compelling clinical evidence base has shown that integrated TB and HIV services leads to reduction in human immunodeficiency virus (HIV)- and tuberculosis (TB)-associated mortality and morbidity. Despite official policies and guidelines recommending TB and HIV care integration, its poor implementation has resulted in TB and HIV remaining the commonest causes of death in several countries in sub-Saharan Africa, including South Sudan.

Integration of TB and HIV care has led to improved TB treatment outcomes and earlier, prioritized HAART initiation. This supports rollout of a fully integrated TB/HIV service delivery model throughout high-prevalence TB and HIV settings

Our study demonstrated important progress is being made towards integration of TB and HIV services 40 targeted health facilities in South Sudan, where nearly all facilities offered routine TB screening to people living with HIV infection, and routine HIV Counseling and Testing to TB patients. However, uptake of other essential services, such as HAART and IPT, needs to be improved, as less than half of eligible people living with HIV were initiated on IPT, and only a small proportion of newly registered TB patients newly diagnosed as HIV-infected in February 2011 were initiated on HAART. Addressing those gaps is a priority and future interventions should build on existing efforts to support current national policies of routine TB screening of all HIV patients, initiation of all eligible HIV-infected patients on IPT and early HAART initiation of eligible TB patients irrespective of CD4 T-cell count.

7. Recommendation

This study has the potential to address the gap between the establishment of TB-HIV care integration policies and guidelines and their implementation in the provision of integrated care in State, PHCC and PHCUs clinics. If successful, an evidence-based intervention comprising change ideas, tools, and approaches for quality improvement could inform the future rapid scale up, implementation, and sustainability of improved TB-HIV integration in South Sudan and across sub-Saharan Africa and other resource-constrained settings.

Stakeholders should work together to facilitate provision of and access to integrated services, preferably at the same time and in the same location. They should also work to ensure a seamless continuum of care between the relevant services, within the prison system, and between prisons, other centres of detention and the community. When it is not feasible to provide all services in a single location, systems should be established and strengthened for proactive and supportive linkage.

8. Author Contribution

1st Author Created study design and wrote the study protocol 2nd and 3rd Author helped to document reviews and quality assurance of the study including data collection and reviewed and contributed to manuscript Author 4th and 5th provided inputs in data analysis methods, conceived and designed the experiments wrote the paper

9. Acknowledgement

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