# Integrating tuberculosis and HIV services in rural Kenya: uptake and outcomes

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**Setting:** Seventeen rural public health facilities in Western Kenya that introduced three models of integrated care for tuberculosis (TB) and human immunodeficiency virus (HIV) patients.

**Objective:** To assess the uptake and timing of cotrimoxazole preventive therapy (CPT) and antiretroviral treatment (ART) as well as anti-tuberculosis treatment outcomes among HIV-infected TB patients before (March-October 2010) and after (March-October 2012) the introduction of integrated TB-HIV care.

**Design:** A before-and-after cohort study using programme data.

**Results:** Of 501 HIV-infected TB patients, 357 (71%) were initiated on CPT and 178 (39%) on ART in the period before the introduction of integrated TB-HIV care. Following the integration of services, respectively 316 (98%) and 196 (61%) of 323 HIV-infected individuals were initiated on CPT and on ART (P < 0.001). The median time to CPT and ART initiation dropped from 7 to 2 days and from 42 to 34 days during the pre- and post-integration phases, respectively. Overall TB success rates did not vary with integration or with type of model instituted.

**Conclusion:** Integration of TB and HIV services enhanced uptake and reduced delay in instituting CPT and ART in rural health facilities. There is a need to increase impetus in these efforts.

A n estimated 35.3 million persons worldwide were living with the human immunodeficiency virus (HIV) in 2012,<sup>1</sup> while 8.6 million people developed tuberculosis (TB),<sup>2</sup> the majority of them in sub-Saharan Africa. Kenya is one of the world's 22 high TB burden<sup>2</sup> and high HIV burden countries.<sup>1</sup>

TB-HIV co-infected patients are known to have higher mortality rates and an increased risk of recurrent TB.<sup>3–5</sup> Early antiretroviral treatment (ART) and cotrimoxazole preventive therapy (CPT) improve survival.<sup>3,4,6–10</sup> In mid-2010, the World Health Organization (WHO)<sup>11</sup> recommended that all HIV-infected TB patients, irrespective of CD4<sup>+</sup> cell count, be offered CPT and ART as early as 2 weeks and no later than 8 weeks following the initiation of anti-tuberculosis treatment. Those with severe immunosuppression (e.g., CD4<sup>+</sup> cell count <50 cells/mm<sup>3</sup>) require early ART initiation, i.e., within 2 weeks of anti-tuberculosis treatment initiation.

Despite this and other recommendations,<sup>12,13</sup> the uptake of ART among HIV-positive TB patients in Kenya was low, at 48%, in 2010.<sup>14</sup> This mirrored the

global figure of 46% for the same year.<sup>15</sup> One possible reason for this low uptake is the lack of linkage between TB and HIV services, with patients attending separate HIV and TB clinics at different locations.<sup>16,17</sup> The benefits of integration (and of the implementation of the 2010 WHO ART guidelines) have been shown to accelerate the uptake of ART and reduce delays in starting this life-saving treatment.<sup>17–26</sup> However, most of these studies have been conducted outside the realm of rural, resource-constrained public health facilities. The operational impact on treatment outcomes has also been inconsistent.<sup>27</sup>

In Western Kenya, since early 2011, the Academic Model Providing Access to Healthcare (AMPATH, Eldoret, Kenya), in collaboration with the National Tuberculosis, Leprosy and Lung Disease Unit (NTLD, Nairobi, Kenya), has been rolling out integrated models of TB and HIV care in health facilities. Depending on the resources of the individual facility, we implemented one of the following three models (Figure 1): Model 1, whereby all TB, regardless of HIV status, and all HIV patients are seen under the same roof by the same staff; Model 2, whereby HIV-infected TB and all HIV patients are seen under the same roof by the same staff (non-HIV-infected TB patients are seen by separate staff in separate building); and Model 3, a strengthened referral model, where the TB clinic is moved next to the HIV clinic while staffing remains separate.

We hypothesised that such service integration would lead to increased ART and CPT uptake in this rural, low-resource setting. We further hypothesised that the various implemented models would lead to a reduction in time to initiation of ART as well as an improvement in anti-tuberculosis treatment outcomes. We thus assessed uptake of HIV services and treatment outcomes among TB patients before and after introducing the various integration models in 17 health facilities in rural Western Kenya. For each period, and in relation to the three models, we compared 1) the uptake of and time to CPT and ART, and 2) anti-tuberculosis treatment outcomes.

# **METHODS**

## Study design

This was a before-and-after cohort study.

## Study setting

Kenya has a population of 44.4 million, 75% of whom reside in rural areas.<sup>28</sup> AMPATH, which supports TB-HIV care in Western Kenya, is a partnership between Moi Teaching and Referral Hospital, Moi University

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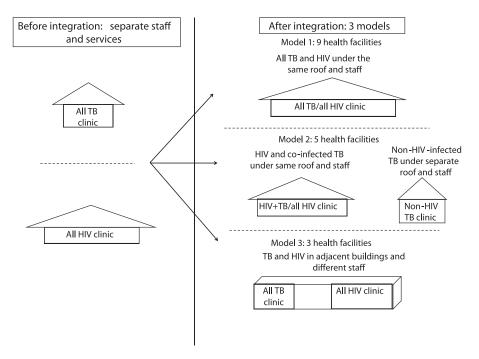
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#### **KEY WORDS**

one-stop shop; integration; TB-HIV; ART; treatment outcome

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**FIGURE 1** Three integrated TB-HIV models in 17 health facilities, Western Kenya. TB = tuberculosis; HIV = human immunodeficiency virus.

(Eldoret, Kenya), Kenya's Ministry of Health (MoH, Nairobi, Kenya) and a consortium of North American academic medical centres led by Indiana University (Bloomington, IN, USA). AMPATH offers its services to 35 main and multiple satellite clinics within MoH facilities in eight of the country's 47 counties. Seventeen of the main clinics (10 district hospitals and seven health centres) with active implementation of integrated TB-HIV activities were selected for the study (Table 1).

## HIV services for TB patients before integration

Before integration, HIV and TB care were offered in vertical systems: AMPATH provided HIV services, while the NTLD provided TB care. Formal communication and interaction between the staff of the two services were limited. In practice, co-infected TB patients received clinical care, HIV testing, CPT, ART and TB drug refills as well as follow-up appointments at two separate clinics, and separate records were maintained. Patients lost to follow-up were traced independently based on different criteria. HIV testing in both settings was performed using rapid tests according to national guidelines. Standard TB screening and diagnostic algorithms recommended by the WHO and Kenya's NTLD were being used.<sup>13,29</sup>

Before integration, ART eligibility criteria for HIV-positive TB patients depended on the availability of CD4<sup>+</sup> cell count. If this was unavailable, all HIV-positive TB patients were deemed eligible for ART; if available, those with CD4  $\leq$ 350 cells/mm<sup>3</sup> were deemed eligible.<sup>12,13</sup>

## HIV services for TB patients after integration

Integration involved the relocation of clinics under one roof or in close proximity, improved staff interaction and joint record keeping (Figure 1 and Table 1). TB clinics were moved into existing HIV clinics, as the HIV care system had better infrastructural and human resources. Most TB clinics were single-roomed and were primarily run by a single nurse (who often had other non-TB duties), with the assistance of one or two community 'cough monitors' during TB clinic days. The district TB officer would visit the TB clinic every 2-3 weeks for mentorship, clinical care and reporting purposes. HIV clinics had on average 3-5 resident physician assistants (clinical officers), several nurses and staff from other support specialties such as nutrition, social work, outreach and pharmacy. A roving medical officer and at times a physician also visited these clinics on weekly basis. A 'TB-HIV focal person' i.e., a health care worker in the facility, was appointed and incentivised to oversee the implementation of TB-HIV activities in each facility. The 2010 WHO ART guidelines on early ART among all HIV-infected TB patients<sup>11</sup> were implemented concurrently, as were feasible infection control measures (Table 1).

# Study population and definitions

We selected all consecutive TB patients registered in the TB treatment registers between the periods March– October 2010 (pre-integration) and March–October 2012 (post-integration). The intervening period—January 2011 to February 2012—was excluded, as this was a transition period with varying degrees of implementation (Table 1).

Patients on ART at the time of anti-tuberculosis treatment initiation were excluded from the analysis of uptake of HIV services but were considered in the TB outcomes analysis (Figure 2). 'On ART' or 'on CPT' was defined as those whose HIV medical records indi-

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Preparatory stage	
Planning centrally and regionally teams	for the onsite (at facility) meetings, involving both regional NTLD and AMPATH TB-HIV directors and management
Attendees included:	
5, , 5	nal NTLD directors, AMPATH's TB-HIV directors
	districts' TB in-charge, laboratory in-charge, HIV care in-charge
	in-charge, laboratory in-charge, AMPATH in-charge, TB personnel, HIV personnel
	nal NTLD head and AMPATH TB-HIV in-charge
Carry out other support supervis	es (the whys, whats and whos), assess current situations in the facility, set objectives and timelines for implementatio ion for TB-HIV
Implementation stage	
5	of health care workers (nurses, clinicians, pharmacists, records staff, etc.) on TB-HIV
Appointing TB-HIV focal person	(nurse or physician assistant)
(Re)alignment of resources:	
Rooms (for clinical care and ot	
Filing systems and record keep Pharmacy services (CPT, ART, 7	-
Communication platforms	
TB-HIV clinical care and consu	Itations
HIV testing	
Synchronised follow-up appoir	ntments
Personnel for nutrition services	s, social support services, adherence and disclosure counselling, outreach and patient tracing
Key infection control practices	(see below)
Regular feedback platforms at th	e facility level led by the TB-HIV focal person
Monitoring stage	
	arious in-charges and TB-HIV focal person
	training and mentorship on TB-HIV of staff by the HIV and TB heads
At the district level by the district Regional support by the regional	t TB, HIV and laboratory chiefs I NTP heads and AMPATH TB-HIV in-charge
0 11 7 0	nstituted after the introduction of integrated TB-HIV care in the 17 health facilities:
Separate clinic days for TB (co-in	
Careful selection of TB/TB-HIV co	onsultation rooms to allow:
Maximum cross-ventilation	
Patient flow circuit minimising	interaction with routine HIV patients
5	ige in the main patient waiting bays
5 5	initiation of anti-tuberculosis treatment by:
5 1	time to <48 h in all the facilities
5 1 1	g with HIV at every clinical encounter
-	therapy to all eligible HIV-positive patients person' i.e. a physician assistant (clinical officer) or a nurse in each of the facilities to oversee implementation of
TB-HIV activities.	person', i.e., a physician assistant (clinical officer) or a nurse in each of the facilities to oversee implementation of
	pdeficiency virus: NTLD = National TB. Leprosy and Lung Disease Unit: AMPATH = Academic Model Providing Access to Healthcare: CF

TB = tuberculosis; HIV = human immunodeficiency virus; NTLD = National TB, Leprosy and Lung Disease Unit; AMPATH = Academic Model Providing Access to Healthcare; CPT = cotrimoxazole preventive therapy; ART = antiretroviral therapy.

cated that they had initiated these medications. Standard definitions of TB outcomes were followed,<sup>30,31</sup> as recorded in the TB registers. Treatment success was defined as cured or treatment completed, and these end points were aggregated.

# Data and analysis

Data extraction was performed with pre-designed forms in early 2013 by the TB-HIV focal persons. These were then double-entered into EpiData software, version 3.1 (EpiData Association, Odense, Denmark) by two data entry clerks and cross-checked for errors.

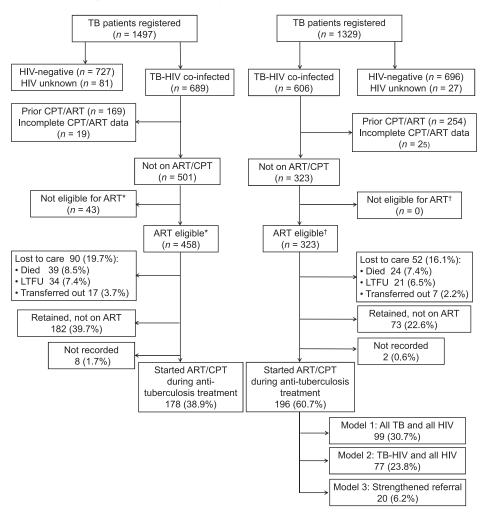
Analysis was performed using EpiData Analysis software, version 2.2.2.180. We described and compared baseline characteristics, the proportion initiating ART and outcomes using  $\chi^2$  or Fish-

er's exact test for categorical variables and the *t*-test for continuous variables. For patients initiating ART, we also calculated the median time and interquartile range (in days) from anti-tuberculosis treatment initiation pre- and post-integration and stratified by model of integration. Relative risks (RRs) were used to measure the strength of associations. Level of confidence was set at 95%.

## **Ethics** approval

Ethics approval was received from the Moi University-MTRH Institutional Research and Ethics Committee and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. Permission for the study was also obtained from Kenya's NTLD. The need for informed consent was waived for this retrospective study. Before integration (March–October 2010)

After integration (March-October 2012)



**FIGURE 2** Flow chart of TB patients registered in 17 health facilities, Western Kenya, before and after the introduction of integrated TB-HIV care services. Model 1: all TB (regardless of HIV status) and all HIV patients are seen under the same roof by the same staff. Model 2: HIV-infected TB and all HIV patients are seen under the same roof by same staff (non-HIV-infected TB patients are seen by separate staff in a separate building). Model 3: strengthened referral model where the TB clinic is moved next to the HIV clinic while staffing remain separate. \*Pre-integration (2010): TB-HIV patient eligible for ART if CD4 is not available or  $\leq$ 350 cells/µl. †Post-integration (2012): all TB-HIV patients eligible for ART irrespective of CD4 cell count. TB = tuberculosis; HIV = human immunodeficiency virus; CPT = cotrimoxazole preventive therapy; ART = antiretroviral treatment; LTFU = loss to follow-up.

# RESULTS

## Characteristics of the study population

Of the 2826 TB patients registered during the study periods (Figure 1), 689 (48.7%) co-infected individuals were identified pre-integration and 606 (46.5%) post-integration. HIV testing rates were respectively 94.6% and 98.0% (RR 1.04, 95% confidence interval [CI] 1.02–1.05, P < 0.001). Of the HIV-infected, respectively 501 (74.8%) and 323 (55.6%) were CPT- and ART-naïve pre- and post-integration and were evaluated for CPT and ART uptake. The baseline characteristics of the

CPT- and ART-naïve HIV-co-infected TB patients were similar, except in WHO staging and previous enrolment into HIV care (Table 2).

## Uptake of CPT and ART

Table 3 shows the uptake of CPT and ART pre- and post-integration. After integration, CPT uptake significantly increased by 26.5% to reach 97.8% (RR 1.37, 95%CI 1.30–1.46, P < 0.001), while ART increased by 21.8% to reach 60.7% (RR 1.56, 95%CI 1.35–1.80, P < 0.001).

Although Model 2, where only co-infected TB patients were integrated with HIV-positives, resulted in the highest ART uptake 
 TABLE 2
 Baseline characteristics of CPT- and ART-naïve TB-HIV co-infected patients before and after introducing integrated TB-HIV care services in 17 health facilities in Western Kenya

Characteristic	Before* ( <i>n</i> = 501) <i>n</i> (%)	After <sup>†</sup> ( <i>n</i> = 323) <i>n</i> (%)	<i>P</i> value
Sex			
Male	250 (50)	161 (50)	0.99
Female	251 (50)	162 (50)	0.99
Age, years, median [IQR]	35 [28–43]	34 [28–43]	0.49
BMI, kg/m <sup>2</sup> , median [IQR] <sup>‡</sup>	18 [17–20]	18 [17–20]	0.86
Children and data missing for those aged ≥15 years	131	31	0.00
Marital status	151	51	
Married	140 (47)	128 (48)	0.94§
Single	42 (14)	40 (15)	0.245
Divorced/separated	66 (22)	56 (21)	
Widowed	47 (16)	40 (15)	
Data missing	206	59	
Time taken to travel the distance between home and HIV clinic	200	57	
<30 min	121 (42)	98 (37)	0.36§
30–60 min	88 (31)	88 (34)	0100
1–2 h	50 (17)	56 (21)	
>2 h	29 (10)	20 (8)	
Data missing	213	61	
TB classification	2.0		
Smear-positive PTB	149 (30)	99 (31)	0.62§
Smear-negative PTB	194 (39)	115 (36)	
Extra-pulmonary TB	108 (22)	69 (21)	
Data missing/smear not performed PTB	50 (10)	40 (12)	
TB treatment category			
New TB	447 (89)	294 (91)	0.40
Retreatment TB	54 (11)	29 (9)	
WHO clinical stage			
Stage 3	200 (65)	194 (72)	0.049
Stage 4	109 (35)	74 (28)	
Data missing	192	55	
CD4+ cell count at start of anti-tuberculosis treatment, cells/mm <sup>3</sup> , median [IQR]	132 [47–278]	116 [49–298]	0.92
≤50	61 (26)	64 (27)	0.84
>50	174 (74)	175 (73)	
Data missing	266	84	
Enrolled in HIV care before TB diagnosis			
Yes	200 (40)	174 (54)	< 0.0001
No	300 (60)	149 (46)	

\*March–October 2010.

<sup>†</sup>March–October 2012.

<sup>‡</sup>BMI only measured in those aged  $\geq$ 15 years.

§Trend P value.

CPT = cotrimoxazole preventive therapy; ART = antiretroviral therapy; TB = tuberculosis; HIV = human immunodeficiency virus; IQR = interquartile range; BMI = body mass index; PTB = pulmonary tuberculosis; WHO = World Health Organization.

(65.8%), the differences were not statistically significant, even after adjusting for level of health facility (health centre vs. district hospital) (crude P = 0.24, adjusted P = 0.14).

## Timing of CPT and ART initiation

Post integration, the median time to CPT initiation dropped significantly from 7 to 2 days, with a similar reduction in time to ART initiation, from 42 to 34 days (Table 3). Model 2 resulted in a non-significantly earlier initiation of ART.

Post-integration, significant numbers of patients who started ART did so within 8 weeks (68% of 196 vs. 57% of 178 patients

pre-integration). There was no significant reduction in time to ART among those with CD4  $\leq$ 50 cells/mm<sup>3</sup>.

# Anti-tuberculosis treatment outcomes

There were no differences pre- and post-integration in overall registered TB patients in terms of sex, age, body mass index, TB type and anti-tuberculosis treatment category (data not shown).

Overall anti-tuberculosis treatment outcomes according to HIV status and ART initiation are shown in Table 4. There were no differences in the treatment success rates of HIV-positive TB patients on ART and HIV-negative patients pre- and post-integration.

**TABLE 3** CPT and ART uptake and timing among CPT- and ART-naïve TB-HIV co-infected patients before and after introducing integrated

 TB-HIV care services in 17 health facilities in Western Kenya

	Before* ( <i>n</i> = 501) <i>n</i> (%)	After† (n = 323) n (%)	RR (95%CI)	P value
Started CPT during anti-tuberculosis treatment	357 (71.3)	316 (97.8)	1.37 (1.30–1.46)	< 0.001
ART eligible, <i>n</i>	458‡	323‡		
Started ART during anti-tuberculosis treatment	178 (38.9)	196 (60.7)	1.56 (1.35–1.80)	< 0.001
Model 1: All TB and HIV under same roof	_	99/167 (59.3)		1.0
Model 2: Co-infected and HIV under same roof	_	77/117 (65.8)		0.26
Model 3: Strengthened referral (adjacent buildings)	_	20/39 (51.3)		0.36
Time to CPT initiation, days, median [IQR]§	7 [0–40]	2 [0–19]		0.0022
Time to ART initiation, days, median [IQR] <sup>¶</sup>	42 [27–82]	34 [19–68]		0.0028
Model 1: All TB and HIV under same roof	_	35 [20–64]		1.0
Model 2: Co-infected and HIV under same roof	_	29 [16–69]		0.69
Model 3: Strengthened referral [adjacent buildings]	_	40 [15–75]		0.39
Proportion starting ART within:				
0–2 weeks	26 (15)	41 (21)		0.11
2–4 weeks	36 (20)	43 (22)		0.69
4–8 weeks	40 (22)	49 (25)		0.57
>8 weeks	76 (43)	63 (32)		0.035
Starting ART within 2 weeks if CD4 ≤50 cells/mm <sup>3</sup>	12 (25)	17 (33)		0.36

\*March-October 2010.

<sup>†</sup>March–October 2012.

\*Before integration, TB-HIV patients with no CD4 cell counts and those with CD4  $\leq$  350 cells/mm<sup>3</sup> (if available) were eligible for ART. After integration, all TB-HIV patients were eligible for ART.

§Among those who initiated CPT.

<sup>¶</sup>Among those who initiated ART.

CPT = cotrimoxazole preventive therapy; ART = antiretroviral therapy; TB = tuberculosis; HIV = human immunodeficiency virus; RR = relative risk; CI = confidence interval; IQR = interquartile range.

**TABLE 4** Overall TB programme outcomes according to HIV and ART initiation status of patients before and after introducing integrated

 TB-HIV care services in 17 health facilities in Western Kenya

	HIV– n (%)	HIV+/ART+ n (%)	P 1 value*	HIV+/ART– n (%)	P 2 value <sup>†</sup>	P 3 value‡	HIV unknown n (%)	P 4 value§
Before	727	347		313		81		
Success (cured+treatment completed)	578 (79.5)	277 (79.8)	0.90	208 (66.5)	<0.001	<0.001	40 (49.4)	<0.001
Died	25 (3.4)	24 (6.9)	0.01	39 (12.5)	< 0.001	0.016	5 (6.2)	0.35
Failure	6 (0.8)	0	0.56	1 (0.3)	0.36	0.45	0	>0.99
Lost to follow-up	64 (8.8)	25 (7.2)	0.37	39 (12.5)	0.07	0.023	23 (28.4)	< 0.001
Transferred out	42 (5.8)	15 (4.3)	0.32	18 (5.8)	0.99	0.40	9 (11.1)	0.06
Not recorded	12 (1.7)	6 (1.7)	0.93	8 (2.6)	0.33	0.46	4 (4.9)	0.13
After#	696	450		128			27	
Success	518 (74.4)	333 (74.0)	0.87	71 (55.5)	< 0.001	< 0.001	15 (55.6)	0.029
Died	28 (4.0)	47 (10.4)	< 0.001	25 (19.5)	< 0.001	0.006	5 (18.5)	0.011
Failure	8 (1.1)	5 (1.1)	0.95	0	0.51	0.55	0	0.6
Lost to follow-up	58 (8.3)	29 (6.4)	0.24	22 (17.2)	0.0019	< 0.001	3 (11.1)	0.80
Transferred out	66 (9.5)	33 (7.3)	0.21	8 (6.3)	0.24	0.67	4 (14.8)	0.52
Not recorded	18 (2.6)	3 (0.7)	0.018	2 (1.6)	0.75	0.61	0	0.99

\*HIV+ patients on ART during anti-tuberculosis treatment compared with HIV-negative patients.

<sup>†</sup>HIV+ patients not on ART during anti-tuberculosis treatment compared with HIV-negative patients.

\*HIV+ patients not on ART during anti-tuberculosis treatment compared with HIV+ patients on ART during treatment.

§Patients with HIV status unknown compared with HIV-negative patients.

<sup>¶</sup>March–October 2010.

#March–October 2012.

TB = tuberculosis; HIV = human immunodeficiency virus; ART = antiretroviral treatment; - = negative; + = positive.

	Before† n (%)	After‡ n (%)	P value
All TB patients, <i>n</i>	1497	1329	
Treatment success	1124 (75.1)	957 (72.0)	0.06
All TB and HIV under same roof	_	407/584 (69.7)	1.0
Co-infected and HIV under same roof	_	397/537 (73.9)	0.1
Strengthened referral (adjacent buildings)	_	153/208 (73.6)	0.3
HIV-negative TB patients, n	1497	1329	
Treatment success	578 (79.5)	518 (74.4)	0.02
All TB and HIV under same roof	_	176/245 (71.8)	1.0
Co-infected and HIV under same roof	_	236/309 (76.4)	0.2
Strengthened referral (adjacent buildings)	_	106/142 (74.6)	0.5
All HIV-co-infected TB patients, n	689	606	
Treatment success	506 (73.4)	424 (70.0)	0.2
All TB and HIV under same roof	_	227/329 (69.0)	1.0
Co-infected and HIV under same roof	_	156/218 (71.6)	0.5
Strengthened referral (adjacent buildings)	_	41/59 (69.5)	0.9
HIV+/ART+ TB patients, n	347	450	
Treatment success	277 (79.8)	333 (74.0)	0.05
All TB and HIV under same roof	_	184/248 (74.2)	1.0
Co-infected and HIV under same roof	_	121/164 (73.8)	0.9
Strengthened referral (adjacent buildings)	_	28/38 (73.7)	0.9
HIV+/ART– TB patients, n	313	128	
Treatment success	208 (66.5)	71 (55.5)	0.03
All TB and HIV under same roof	_	32/68 (47.1)	1.0
Co-infected and HIV under same roof	_	27/41 (65.9)	0.06
Strengthened referral (adjacent buildings)	—	12 (63.2)	0.2

 TABLE 5
 TB treatment success\* among patients before and after introducing integrated TB-HIV care services

 in 17 health facilities in Western Kenya

\*The sum of cured and treatment completed.

<sup>†</sup>March–October 2010.

\*March–October 2012.

TB = tuberculosis; HIV = human immunodeficiency virus; + = positive; ART = antiretroviral treatment; - = negative.

Compared to HIV-negative patients, mortality was significantly higher among HIV-co-infected patients on ART, and highest among those not on ART. Treatment success was lower and loss to follow-up (LTFU) higher among HIV-positive patients not on ART and among those with unknown HIV status. Treatment success, mortality and LTFU were significantly higher among those with CD4  $\leq$ 200 cells/mm<sup>3</sup> than in those with CD4 >200 cells/mm<sup>3</sup> (data not shown).

Table 5 compares treatment success during the pre- and post-integration periods and between the various models post-integration. Overall TB success rates (among all TB patients) did not differ. The slightly better treatment success in Model 2 compared to the other models did not reach statistical significance. Other treatment outcomes did not differ statistically (data not shown).

# **DISCUSSION**

This is the first Kenyan study to assess the effect of an integrated TB-HIV care package across a large rural region characterised by high HIV prevalence and TB mortality. The integration of HIV and TB services was feasible and led to increased uptake of CPT and ART. Delays in CPT and ART initiation were also reduced following integration.

Although the provision of ART to HIV-infected patients during anti-tuberculosis treatment improved their treatment success to equal those of HIV-negative patients, this did not translate into an overall improvement in treatment success for the NTLD. This may be attributed to a significant number of patients not initiating ART during the 'optimal window': one third did not initiate ART at all; of those who initiated ART, one third did so after 8 weeks, while two thirds of those with CD4  $\leq$ 50 cells/mm<sup>3</sup> did so after 2 weeks. Mortality was also still higher among HIV-positives, even if they underwent CPT and ART. Programmes should thus continue aiming for earlier diagnosis of both TB and HIV, as well as higher and earlier ART initiation. In addition, other causes of mortality among HIV-positives should be identified and managed.

The three integration models described here suggest that there may be differential outcomes in uptake and timing of ART initiation and treatment success. Although not statistically significant, Model 2, where care of HIV-infected TB was integrated with that of HIV, had better results than Model 1, which integrated all TB and all HIV patients into a single clinic. Whether there is a critical 'provider-to-patient' ratio that is optimal for providing 'best care' may be a factor.<sup>32</sup> Further research on workload and cost-efficiency of integration models is required.

The strengths of this study are that it involved several primary facilities, all within the rural public sector where the majority of Kenyans live;<sup>28</sup> it is thus a reflection of a 'real world' setting. In addition, missing information in key fields was minimal. Finally, both the implementation and study involved the NTLD and a consortium of North-South collaboration (AMPATH). The Kenyan MoH was actively engaged from conception, and emphasis was laid on use of local resources, favouring national ownership and

sustainability. A limitation of this study is that it does not report on the patients' immunological outcome post implementation or their virological status in general. The before-and-after nature of the study, and in particular the long interval between evaluations (2 years) may also have introduced temporal trends that are unadjusted for.<sup>22</sup>

This experience has a number of notable patient-level advantages. First, apart from the positive impact on survival both during and after anti-tuberculosis treatment, integration may help in overcoming LTFU-related challenges during the referral process, the burden of increased travel costs and the time spent in clinics.<sup>17,32</sup> Second, the 'two diseases, one patient, one clinic, one appointment, one health worker' approach avoids patient juggling and increases the knowledge and expertise of health workers in managing both diseases, particularly with regard to drug toxicities and interactions. Third, integrated counselling, social support and patient tracing interventions mutually reinforce each other rather than competing for scarce resources, making the whole service more efficient.<sup>22</sup> Fourth, from a health systems perspective, integration averts duplication of logistic and administrative services. Finally, this may serve as an example for integration in other areas of the health system such as ART in maternal and neonatal child health or integration of non-communicable diseases into HIV/acquired immune-deficiency syndrome care.33

A number of issues merit discussion. First, although integration increased ART uptake, one third of all eligible TB patients still did not start ART. Although this may have been influenced by our early assessment in the integration period and staff workload issues, definitive research is needed to determine the causes of the continued delays. Second, the median time to ART initiation after integration was about 1 month, falling well within current WHO recommendations of an 8-week window period.<sup>11</sup> However, the CAMELIA (Cambodian Early versus Late Introduction of Antiretroviral Drugs) trial demonstrated that a 2-week window for ART initiation reduced mortality by 34% compared to starting ART at 8 weeks.<sup>8</sup> Early ART initiation among TB patients is vital, and time to ART initiation should become a universal quality programme indicator.

Third, integration at a clinic level requires specific pragmatic issues to be addressed, such as infection control, infrastructure space, patient flow, staff constraints, training and supervision, drug availability and other commodity management, and clinical challenges. TB infection control is of particular concern if TB patients are brought into HIV clinics with susceptible pools of individuals.<sup>34,35</sup> We adapted this by introducing several easily achievable measures (Table 1). Transferring the HIV care of co-infected TB patients to TB clinics is another way of alleviating this challenge; however, this was not implemented due to the limited availability of resources for TB.

In conclusion, integration of TB and HIV services enhanced uptake and reduced delays in instituting CPT and ART in rural health facilities. There is now a need to increase impetus in these efforts, close the remaining gaps in uptake and enhance population-level impact.

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**Contexte :** Dix-sept structures de santé publique rurales dans l'ouest du Kenya qui ont introduit trois modèles de prise en charge intégrée de la tuberculose (TB) et du virus de l'immunodéficience humaine (VIH).

**Objectif**: Evaluer l'utilisation et le moment du traitement préventif par cotrimoxazole (CPT) et du traitement antirétroviral (ART) ainsi que les résultats du traitement de la TB chez des patients tuberculeux infectés par le VIH pendant une période avant (mars–octobre 2010) et après (mars–octobre 2012) l'introduction de la prise en charge intégrée TB-VIH.

Schéma : Etude de cohorte avant/après basée sur les données des programmes.

Marco de referencia: Diecisiete centros públicos rurales de atención sanitaria en Kenia occidental, donde se introdujeron tres modelos de atención integrada de la tuberculosis (TB) y la infección por el virus de la inmunodeficiencia humana (VIH).

**Objetivo:** Evaluar la aceptación del tratamiento preventivo con cotrimoxazol (CPT) y el tratamiento antirretrovírico (ART) y su coordinación cronológica, además de examinar los desenlaces del tratamiento antituberculoso en los pacientes coinfectados por el VIH y la TB durante una fase anterior a la introducción de la estrategia de atención integrada (de marzo a octubre del 2010) y una fase posterior a la misma (de marzo a octubre del 2012).

**Métodos:** Se llevó a cabo un estudio de cohortes anteriores y posteriores a la introducción de la atención integrada a partir de los datos del programa.

**Résultats** : Sur 501 patients tuberculeux VIH positifs, 357 (71%) ont débuté le CPT et 178 (39%) l'ART pendant la période précédant l'introduction du traitement intégré TB-VIH. Après l'intégration des services, sur 323 patients infectés par le VIH, 316 (98%) ont reçu le CPT et 196 (61%) l'ART (P < 0,001). Le délai médian de mise en œuvre du CPT et de l'ART est passé de 7 à 3 jours et de 42 à 34 jours respectivement dans les phases pré- et post-intégration. Le taux global de succès du traitement de la TB n'a pas varié avec l'intégration ni avec le type de modèle mis en œuvre.

**Conclusions :** L'intégration des services de TB et de VIH a accru le recours au CPT et à l'ART et réduit le délai de mise en route dans les structures de santé rurales. Il est nécessaire d'accélérer ces efforts.

**Resultados:** De los 501 pacientes tuberculosos coinfectados por el VIH, 357 iniciaron el CPT (71%) y 178 el ART (39%) durante la fase anterior a la introducción de la atención integrada. Después de la integración de los servicios de la TB y el VIH, de los 323 pacientes infectados por el VIH, 316 iniciaron el CPT (98%) y 196 el ART (61%; P < 0,001). La mediana del lapso hasta la iniciación del CPT disminuyó de 7 días en la fase previa a la integración a 2 días en la fase posterior a la misma y el lapso hasta la iniciación del ART disminuyó de 42 a 34 días. La tasa global de éxito del tratamiento antituberculoso no se modificó con la integración de los servicios ni con el tipo de modelo introducido.

**Conclusión:** La integración de los servicios de atención de la TB y la infección por el VIH reforzó la aceptación del CPT y el ART en los centros sanitarios de una zona rural. En la actualidad es preciso reforzar los impulsos dirigidos a estas iniciativas.

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