

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



LSHTM Research Online

Teixeira de Siqueira-Filha, N; Militao de Albuquerque, MF; Cunha Rodrigues, L; Legood, R; Costa Santos, A; (2018) Economic burden of HIV and TB/HIV coinfection in a middle-income country: a costing analysis alongside a pragmatic clinical trial in Brazil. Sexually transmitted infections. ISSN 1368-4973 DOI: <https://doi.org/10.1136/sextrans-2017-053277>

Downloaded from: <http://researchonline.lshtm.ac.uk/4647040/>

DOI: <https://doi.org/10.1136/sextrans-2017-053277>

Usage Guidelines:

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact researchonline@lshtm.ac.uk.

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

<https://researchonline.lshtm.ac.uk>

The economic burden of HIV and TB/HIV co-infection in a middle-income country: a costing analysis alongside a pragmatic clinical trial in Brazil

¹Noemia Siqueira-Filha PhD, ²Maria de Fatima Militao PhD, ¹Laura C Rodrigues PhD, ¹Rosa Legood PhD, ¹Andreia C Santos PhD

¹London School of Hygiene and Tropical Medicine (LSHTM), UK; ²Centro de Pesquisa Aggeu Magalhaes, Fundação Oswaldo Cruz (FIOCRUZ-PE), Brazil

Corresponding author: Noemia Teixeira de Siqueira Filha, LSHTM, 15-17, Tavistock Place, London, WC1H 9SH, United Kingdom, +44(0)2079272908, noemia.teixeira-filha@lshtm.ac.uk

Sources of support: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (470554/2013-4) and Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (APQ-0184-4.06/13). Some of the investigators received partial support from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq): Scholarship PQ-308491/2013-0 to Maria de Fatima Militao de Albuquerque; Scholarship 220144/2012-5 to Noemia Teixeira de Siqueira.

Word count: 2,939

Number of tables: 4

Conflict of interest: We declare no competing interests.

Abstract

Objective: The objective of this study is to measure the costs of people living with HIV (PLHIV) as well as active tuberculosis (TB/HIV), latent tuberculosis infection (LTBI/HIV) or without TB (HIV/AIDS).

Methods: We analysed the costs through the entire pathway of care during the pre-diagnosis and treatment periods from the Brazilian Public Health System perspective. We applied a combination of *bottom-up* and *top-down* approaches to capture and estimate direct medical and non-medical costs. We measured mean cost per patient per type of care (inpatient, outpatient and emergency care) and disease category, HIV/AIDS, HIV/AIDS death, TB/HIV, TB/HIV death and LTBI/HIV.

Results: Between March 2014 and March 2016 we recruited 239 PLHIV. During the follow-up 26 patients were diagnosed and treated for TB and five received chemoprophylaxis for LTBI. During the pre-diagnosis and treatment period, the mean total costs for HIV or AIDS and AIDS death categories were US\$1,558 and US\$2,828, respectively. The mean total costs for TB/HIV and TB/HIV death categories were US\$5,289.0 and US\$8,281, respectively. The mean total cost for the LTBI/HIV category was US\$882.

Conclusions: TB/HIV patients impose a higher economic burden on the health system than HIV/AIDS and LTBI/HIV. Patients with LTBI/HIV were the lowest cost group among all disease categories, indicating that preventive TB treatment can avoid the further costs treating active TB.

Funding: National Council of Technological and Scientific Development (CNPq) and Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE).

Clinical trial registration number: RBR-22t943

Key messages

- TB/HIV patients can cost 3.4 more than those with HIV/AIDS alone. TB/HIV death can cost almost three times more than an AIDS death.
- Patients with LTBI/HIV had lower costs than all the other disease categories.
- Results can support policy planning and direct resource allocation for the Brazilian response to the HIV epidemic
- The study could be a reference for economic evaluation for countries with similar socio-economic and epidemiological characteristics.

INTRODUCTION

The AIDS epidemic has affected 37 million people worldwide and caused 1.1 million deaths in 2015. Among these deaths, one in three was due to HIV associated tuberculosis (TB). Additionally, one-third of people living with HIV (PLHIV) presented latent tuberculosis infection (LTBI)¹. The lack of, or delays in, diagnosis and treatment of active TB can explain the high mortality rate among co-infected patients^{2,3}. The reduction of AIDS-related deaths is a milestone established by the United Nations through Sustainable Development Goal 3 (SDG 3)^{1,4} and tackling TB co-infection is a key vehicle for reducing AIDS-related deaths. The treatment of LTBI is also crucial for the reduction of TB incidence in PLHIV. Mathematical models have predicted that the scaling-up of LTBI treatment, together with the diagnosis and prompt treatment of active TB, can sharply reduce TB incidence^{5,6}.

However, the funding available to address AIDS/HIV and TB/HIV co-infection is insufficient and might affect the potential success of SDG 3. Recent estimates indicate that US\$8.3 billion is needed annually to combat TB in low and middle-income countries. In 2015, US\$6.6 billion was invested and only 6% of this fund was allocated in TB/HIV co-infection actions⁷. Therefore, costing analyses can play a key role in supporting the achievement of the SDGs in a sustainable way, especially with the reduction in the amount of funding available to combat both epidemics in recent years. In addition, the majority of high TB/HIV burden countries face both financial and human resource constraints. Thus, cost analyses are essential to inform better allocation of resources and to support economic evaluations and budget impact studies for decision making.

The objective of this study is to estimate the costs of PLHIV with or without active or latent TB, from the symptomatic phase until the first year of treatment from the perspective of the Brazilian public health system. We thus aim to contribute to the literature on costs of interventions for the control of TB and HIV/AIDS.

METHODS

Study location

The study was conducted in the city of Recife, capital of the state of Pernambuco. We conducted the data collection in the Correia Picanco Hospital (CPH). The hospital provides care for approximately 60% of all individuals with HIV/AIDS in the state, carrying out almost 3,000 outpatient appointments a month, including emergency and inpatient care⁸.

Study population, inclusion and exclusion criteria

The cost study was conducted alongside a pragmatic clinical trial designed to evaluate the cost-effectiveness of a protocol for TB diagnosis in PLHIV. The costing study followed the trial criteria: we included newly-diagnosed HIV infected patients, aged 18 years or over. Participants who were being

treated for TB at the time of enrolment or had been treated for TB in the previous 3 months were excluded, as the trial aimed to test a protocol for TB diagnosis. We also excluded patients who were treated in the private sector and only visited the hospital to collect medicines. Further details of the clinical trial can be found in the Supplement.

Procedures

The cost study was conducted from the health system perspective, during the first two years of the trial (March/2014 to March/2016). We applied a mix of bottom-up and top-down approaches to capture and estimate the direct costs⁹⁻¹¹. We obtained drug prices from the Brazilian Ministry of Health (MoH) database¹² and test costs from health system records¹³. Staff wages, hospital productivity and values of contracts and utility bills were collected from the CPH administrative division. Further details on data collection and cost estimates are given in the Supplement and Tables S1 and S2. Costs were calculated in local currency (Real, 2015 prices) and converted to US dollars using an average exchange rate for the period of study as calculated by OANDA (R\$1= US\$0.34765)¹⁴.

Interviews with patients were conducted by trained technical nurses during pre-admission at CPH. The interviews were intended to collect data on the use of medical resources at emergency and outpatient care during the HIV pre-diagnosis period, from the onset of the disease until diagnosis. Interviewers also collected data on demographic, socio-economic characteristics and lifestyle habits of individuals. For those who were diagnosed with TB or LTBI during the two-year data collection period, we considered the TB/HIV pre-diagnosis period as the time between TB first symptoms and its diagnosis. As LTBI/HIV patients do not present TB symptoms, we considered pre-diagnosis the period between the first HIV symptoms and LTBI diagnosis.

Subsequent interviews were conducted at every patient appointment at CPH. Besides checking for TB or LTBI diagnosis, the interviewer also collected data on the use of medical resources at outpatient and emergency care and on hospitalisations at CPH and other health services sought by the patients during the treatment period. To assess the use of resources at inpatient care in both the pre-diagnosis and treatment period, we reviewed patients' medical notes at CPH and other health services. Details of the drug scheme for TB and LTBI treatment can be found in the Supplement.

Data cleaning and analysis

Questionnaires were double entered in an Excel spreadsheet. The cost estimates were produced in Excel and statistical analyses in Stata/IC 14. The main outcomes were the cost per type of care (emergency, outpatient and inpatient care) and total costs (pre-diagnosis + treatment period) per patient per category of disease (HIV or AIDS, AIDS death, TB/HIV, TB/HIV death, LTBI/HIV). The mean was reported for all cost estimates as measures of central tendency, as well as the associated standard deviation (SD).

To test difference in proportions, we used the Chi square test for categorical variables or Fisher's exact test when one or more cells had a frequency of five or less observations. For continuous variables with non-parametric distribution, we used the Wilcoxon-Mann-Whitney test. Differences in cost per category of patient were analysed using a Dunn's test with Benjamini-Hochberg adjustment for multiple comparisons. All *p*-values below 0.05 were considered statistically significant. We used the mean imputation approach to handle costing missing data; this assigns the mean cost of each item, at each level of care, to the missing value¹⁵. In order to compare our results with studies conducted in other countries, we also presented our results in International Dollars (\$) applying purchase power parity (2015 prices) (Table S5 and S6)¹⁶. Costs of the studies presented in the discussion section were updated to 2015 using USD inflation rate, estimated by the International Monetary Fund¹⁷ and converted to international dollars applying World Bank indices¹⁶.

Sensitivity analysis

A one-way sensitivity analysis was performed to assess uncertainties related to the parameters used. We varied the mean costs of TB/HIV, HIV/AIDS and LTBI/HIV per type of care by $\pm 50\%$, as we did not have information regarding the highest and lowest value for each cost item. We varied the following direct medical cost parameters at emergency, outpatient and inpatient care: drugs, tests, medical appointment, bed days, ART and TB drugs. Results are presented in tornado diagrams to demonstrate the impact of each parameter change in the total cost.

Ethics

The study was approved by the Fundacao Oswaldo Cruz (No 279.324) and the London School of Hygiene and Tropical Medicine (Ref: 7371) ethics committees. All patients signed a consent form. The clinical trial was registered at Brazilian Registries for Clinical Trials (RBR-22t943). We attest that we have obtained appropriate permissions and paid any required fees for use of copyright protected materials.

RESULTS

In a two-year study period, 315 PLHIV were recruited, 15 patients were excluded at the randomisation stage, 25 were transferred to another health service and 37 were considered lost to follow-up. The final sample for this study was 239 PLHIV, with 79 patients in the control arm (72 HIV or AIDS, 7 TB/HIV, none LTBI/HIV) and 160 in the intervention arm (136 HIV or AIDS, 19 TB/HIV and 5 LTBI/HIV). In total, during the follow-up period, 208 patients were treated for HIV or AIDS, 26 were diagnosed and treated for active TB/HIV co-infection and five were diagnosed and treated for LTBI/HIV (Figure S1). Tables 1, S3 and S4 show the baseline characteristics of the patients included in our analysis. In the HIV or AIDS and TB/HIV categories, most patients were male whilst most of the LTBI/HIV patients were female ($p = 0.007$). For all disease categories, most patients were in the 18-39 years age group and

most patients were literate with a minimum of four years of study (90% of the total sample). When compared with HIV or AIDS and LTBI/HIV, patients in the TB/HIV category presented higher rates of alcohol dependence ($p = 0.009$) and use of illicit drugs, crack ($p = 0.002$) and glue ($p = 0.009$).

Treatment characteristics

Patients in the TB/HIV category were seen more frequently at emergency care in both pre-diagnosis and treatment period, but frequency of use only differed from that of the HIV/AIDS category in the pre-diagnosis period ($p < 0.001$). The average length of hospitalisation during the treatment period was twice as high as that during pre-diagnosis period for both disease categories. Patients in the TB/HIV category presented lower CD4 counts (< 200 cells/ m^3) at first appointment than the other categories ($p = 0.009$). LTBI/HIV and TB/HIV co-infected patients started ART later than HIV/AIDS patients ($p = 0.003$). Also, the proportion of deaths was higher among TB/HIV patients than HIV/AIDS patients (31% vs 6%; $p = 0.001$) (Table 2).

Cost per site of care

During the pre-diagnosis period, the TB/HIV category had the highest costs at emergency, outpatient and inpatient care. The difference in the mean total costs was higher between the TB/HIV and HIV/AIDS categories: emergency care – US\$419 vs US\$ 109; outpatient care - US\$269 vs US\$64. There was no hospitalisation among LTBI/HIV patients during the pre-diagnosis period and the mean total cost was higher for the TB/HIV patients than the HIV/AIDS patients, US\$,532 and US\$1,710, respectively.

During the treatment period, the LTBI/HIV category patients did not have emergency care and only one patient was hospitalised (US\$ 549). At outpatient care, all patients presented similar costs, with the HIV/AIDS patients presenting a slightly higher mean total cost: HIV or AIDS – US\$777; TB/HIV - US\$687; LTBI/HIV – US\$609. At inpatient care, the mean total cost for TB/HIV was almost double that of the HIV/AIDS patients, US\$4,372 vs US\$2,850 (Table 3).

Costs per patient category

The category TB/HIV death presented the highest mean costs (pre-diagnosis, treatment and total) when compared with other categories. The mean total direct cost (pre-diagnosis + treatment period) of TB/HIV death was almost three times that of the mean cost of HIV or AIDS death: US\$ 8,281 vs US\$ 2,828. When compared with the LTBI/HIV category, the mean direct cost of the TB/HIV category was more than five times higher; US\$5,289 vs US\$882 (Table 4). Statistical significance in the total costs (pre-diagnosis plus treatment period) was found for HIV or AIDS vs TB/HIV ($p < 0.0001$), TB/HIV vs LTBI/HIV ($p = 0.0015$) and AIDS death vs TB/HIV death – (pre-diagnosis period only) ($p = 0.0016$). Table S7 shows the complete statistical analysis for the pre-diagnosis, treatment period and total cost.

Sensitivity analysis

During the pre-diagnosis period, the cost item ‘medical appointment’ had the highest impact on the total cost for all types of care and disease categories. During the treatment period, the cost item ‘ART’ had highest impact on outpatient care for HIV or AIDS and TB/HIV categories. Medical appointment also had the highest impact on all other types of care. Tornado diagrams are presented in Figure S2.

DISCUSSION

TB/HIV patients cost 3.4 times more than those with HIV/AIDS and those who died due to TB/HIV co-infection cost almost three times more than those who died due to AIDS. In the meantime, patients with LTBI/HIV presented the lowest cost among all disease categories, indicating the treatment of patients at the latent phase can be cheaper than the active phase. The highest cost for TB/HIV was mainly due to inpatient care. Our findings reinforce the hypothesis that TB/HIV patients have more complications during treatment and, therefore, are hospitalised more frequently and treated with more expensive drugs¹⁸. Indeed, in our study, the cost of drugs and tests at inpatient care was higher for TB/HIV than HIV or AIDS. Another study carried out in Sudan found greater costs of hospitalisation among TB/HIV co-infection than TB/HIV negative patients. Nevertheless, the updated costs of hospitalisation in international dollars (2015) found in the Sudanese study were lower than the costs found in our study: \$2,847 vs \$6,801. The mean treatment cost of TB/HIV category was also lower compared with our study: \$1,568 vs \$ 6,341¹⁹.

Other studies carried out in low- and middle-income countries reported similar or lower costs compared with our study. In Burundi, the mean annual cost to treat HIV/AIDS patients was \$3,223 vs \$ 2,032 in Brazil²⁰. In Thailand the mean costs to treat TB/HIV patients was \$1,535 vs \$6,341 in Brazil²¹. In China, TB was the most expensive opportunistic infection in PLHIV after Cytomegalovirus infection, \$647 and \$3,189, respectively²². In South Africa, the cost of hospitalised TB/HIV patients was \$3,925. In the same study, the treatment of other common diseases in PLHIV presented higher costs, such as endocrine and metabolic disease (\$5,260) and gastrointestinal disease (\$4,889)²³. Another South African study reported hospitalisation costs of TB/HIV patients varying from \$2,541 to \$4,885 according to type of TB, ART status and ward (adult and paediatric)²⁴.

In contrast to ART, the cost of TB drugs was lower at outpatient care. Furthermore, in Brazil, TB drug costs in HIV patients were lower than in other low and middle-income countries: \$36 vs \$50 in Burundi; \$338 in China and \$397 in Thailand²⁰⁻²². In Sudan, the cost of TB drugs in PLHIV varied from \$113 to \$380 according to TB outcome and TB drug scheme¹⁹.

The higher cost of TB/HIV can be explained by the higher proportion of patients presenting with CD4 counts below 200 cells/m³, which indicates that co-infected patients are arriving at the health service at a more advanced stage of HIV infection for the first appointment. Another hypothesis is the delay in

TB diagnosis and treatment, which can cause a deterioration in the patient's health and, consequently, increase treatment costs. Also, analysing the lifestyle of TB/HIV patients, we perceive higher rates of lifestyle vulnerability, such as drug and alcohol dependency. All these aspects can be linked to rising costs and worse outcomes, such as higher mortality and hospitalisation rates, within TB/HIV patients. UNAIDS states that the achievement of the Fast-Track Target prevention and treatment tools could decrease the number of HIV-related deaths, including TB deaths in HIV patients, by 81% up to 2030²⁵.

In our study, only five out of 213 HIV/AIDS patients received IPT to prevent TB. During the study period, the hospital faced a shortfall in the provision of TST reagent and IPT was based only on the history of contact with TB patients and a medical practitioner's decision as to whether treatment was offered. Our estimates showed that the mean cost to treat LTBI/HIV was much cheaper than the treatment of TB/HIV (US\$882 vs US\$5,289). The treatment is strongly recommended by WHO to prevent TB in PLHIV and should be provided to those who are unlikely to have TB, regardless of TST readings^{26,27}. Thus, the scaling-up of IPT for all PLHIV should be adopted to prevent deaths and save costs related to treatment of TB/HIV co-infection.

The trial design raises some limitations to our study, in spite of advantages that it also brings, such as reduction in potential bias due to the randomisation, practicality of the data collection, and collection of costing data and outcomes at patient-level²⁸. In our study, the gene Xpert test, which is not routinely implemented in the hospital, was used in patients from the intervention arm. However, it was applied at outpatient care and only nine TB suspect patients were able to perform the test due to lack of sputum. Thus, this cost does not seem to influence the final cost of the disease in outpatient care. Furthermore, we cannot generalise our results to countries where costs are likely to be different; thus, our results have a low external validity. The artificial environment created by a trial (patient tracing, for instance) is also another issue to be considered when extrapolating our data, although the pragmatic design is likely to reduce the limitations created by this artificial environment²⁸. Another limitation relates to the price of laboratory tests collected from the Brazilian MoH database. These values represent amounts paid to providers to partially cover their laboratory costs, and do not represent the full costs of the tests. In our sensitivity analysis, these costs did not present an important impact on the cost estimates by disease categories. The small sample size, especially for TB/HIV and LTBI/HIV patients could also be a limitation for the generalisability of our results.

Successful experience of TB/HIV control in another Latin American country, Peru, was evaluated. The Community-Based Accompaniment with Supervised Antiretroviral (CASA) was a cost-saving intervention and decreased the rate of death from 30% to 9%²⁹. In Brazil, the strengthening of collaborative TB/HIV activities, early and accurate TB diagnosis, IPT and other policies addressing vulnerable populations can save further costs for the public health system and can contribute to the achievement of SDG and UNAIDS Fast-Track goals in a sustainable and consolidated way.

In conclusion, TB/HIV patients impose a higher economic burden on the public health system than HIV or AIDS and LTBI/HIV patients in all pathways of care. Further studies should address the costs of scaling-up of IPT. It is important that other studies addressing the budget impact of social protection programmes for TB/HIV patients and costs of intensive TB case finding algorithms and more accurate TB diagnosis among HIV patients are carried out in the Brazilian context.

Contributors

The study was designed by NTSF, MFPMA and ACS. NTSF was responsible for data collection, analysis and writing the manuscript. ACS, LR, RL and MFPMA reviewed the manuscript.

Acknowledgments

We thank all participants who consented to take part in this study. The direction of CPH, Dr. Ângela Karine Queiroz e Silva, who authorised and supported the implementation of the study. The field work team who performed the data collection: Adriana Barros, Marcela Santos, Perla Serejo, Marina Siqueira, Livia Vasconcelos, Joilson Gonzaga and Erivelton Martins. Dr. Luciana Siqueira, who classified all drugs and tests. We also thank the Institute for Health Technology Assessment (IATS) for the support with travel expenses and scholarships for the field work team.

"The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in STI and any other BMJPGJ products and sub-licences such use and exploit all subsidiary rights, as set out in our licence <http://group.bmj.com/products/journals/instructions-for-authors/licence-forms>".

Table 1. Socio-economic, demographic and lifestyle characteristics of the study population

Variable	Total (N=239)		HIV or AIDS (N=208)		TB/HIV (N=26)		LTBI/HIV (N=5)		P- value ¹
	N	%	N	%	N	%	N	%	
<i>Socio-economic</i>									
<i>Gender</i>									
Female	64	27	57	27	3	12	4	80	0.007
Male	175	73	151	73	23	88	1	20	
<i>Age</i>									
18-28	81	34	72	35	8	31	1	20	0.906
29-39	75	31	63	30	10	38	2	40	
40-50	60	25	53	25	6	23	1	20	
≥51	23	10	20	10	2	8	1	20	
<i>Literate</i>²									
Yes	216	90	190	91	21	81	5	100	0.212
No	23	10	18	9	6	19	0	0	
<i>Income</i>³									
No income	38	16	35	17	3	12	0	0	0.265
< Minimum wage	81	34	65	31	13	50	3	60	
≥ Minimum wage	120	50	108	52	10	38	2	40	
<i>Lifestyle habits</i>									
<i>Smoking</i>									
Current	58	24	52	25	6	23	0	0	0.034
Never	137	57	122	59	10	38	5	100	
Former	44	18	34	16	10	38	0	0	
<i>Alcohol</i>⁴									
Low risk	146	61	134	64	9	35	3	60	0.009
Hazardous drinking	48	20	41	20	5	19	2	40	
Harmful drinking	18	7	14	7	4	15	0	0	
Alcohol dependence	27	11	19	9	8	31	0	0	
<i>Illicit drug use – last year</i>									
<i>Cannabis</i>									
Yes	20	8	16	8	3	11	1	20	0.458
No	217	91	190	91	23	88	4	80	
<i>Cocaine</i>									
Yes	10	4	6	3	3	12	1	20	0.074
No	228	95	201	97	23	88	4	80	
<i>Glue</i>									
Yes	2	1	0	0	2	8	0	0	0.025
No	236	99	207	99	24	92	5	100	
<i>Crack</i>									
Yes	8	3	4	2	4	15	0	0	0.039
No	228	95	201	97	22	85	5	100	

¹ Fisher's exact. After exclusion of LTBI/HIV patients from the analysis, only the variables smoking ($p = 0.028$), alcohol ($p = 0.002$), glue ($p = 0.012$) and crack ($p = 0.009$) remain statistically significant.

² Minimum of four years of study (mec.gov.br)

³ Brazilian minimum wage, 2015 = US\$ 251.7 per month

⁴ As defined by the WHO: The Alcohol Use Disorders Identification Test (AUDIT), 2011

Table 2. Characteristics of treatment and health outcomes for patients treated at the Correia Picanco Hospital, Recife/Brazil

Variables	HIV or Aids (N =208)		TB/HIV (N = 26)		LTBI/HIV (N = 5)		P- value ³
	N	%	N	%	N	%	
Emergency care							
<i>Pre-diagnosis period¹</i>							
Yes	86	41	21	81	-	-	<0.001
No	122	59	5	19	-	-	
<i>Treatment period²</i>							
Yes	112	59	19	73	-	-	0.060
No	96	41	7	27	-	-	
Hospitalisation							
<i>Pre-diagnosis period</i>							
Yes	19	8	11	42	-	-	<0.001
No	189	92	15	58	-	-	
<i>Treatment period</i>							
Yes	39	19	20	77	1	20	<0.001
No	169	81	6	33	4	80	
Length of hospitalisation							
<i>Pre-diagnosis period</i>							
Days	12.4	12.2	18.3	14.2	-	-	0.140
<i>Treatment period</i>							
Days	18.8	17.0	28.0	22.4	-	-	0.240
CD4 count (1st appointment)							
>500	53	25	2	8	2	40	0.009
200-499	55	26	5	19	1	20	
<200	85	41	16	62	0	0	
Not informed	15	7	3	12	2	40	
First ART scheme (1st year)							
TDF+3TC+EFZ	128	61	13	50	2	40	0.010
AZT+3TC+EFZ	18	9	8	31	1	20	
Others	40	19	2	8	0	0	
Did not start ART	22	11	3	11	2	40	
Average days of ART - 1st year							
Mean	249	87.0	181	102.8	160	56.6	0.003
Outcome							
Cure or end of follow-up	195	94	18	69	5	100	0.001
Death	13	6	8	31	0	0	

¹ Pre-diagnosis period: onset of TB or HIV symptoms until TB, LTBI or HIV/AIDS diagnosis

² Treatment period: one year of treatment or death before one year for HIV or AIDS, complete TB (six to nine months) or LTBI (six months) treatment or death before end of treatment

³ Fisher's exact

⁴ Chi square

⁵ Two-sample Wilcoxon rank-sum (Mann-Whitney) test

Table 3. Mean direct medical costs (US\$) per cost category for pre-diagnosis and treatment from the public health system perspective, Correia Picanco Hospital, Recife/Brazil

Cost item	<i>HIV or AIDS</i>				<i>TB/HIV</i>				<i>LTBI/HIV</i>			
	N	Pre-diagnosis Mean (SD)	N	Treatment Mean (SD)	N	Pre-diagnosis Mean (SD)	N	Treatment Mean (SD)	N	Pre-diagnosis Mean (SD)	N	Treatment Mean (SD)
<i>Emergency care</i>	86		112		21		19					
Drugs		1.2 (4.0)		2.0 (4.3)		45.3 (193.1)		78.9 (234.8)		-		-
Tests		5.7 (15.0)		8.2 (14.1)		22.4 (30.1)		8.2 (11.6)		-		-
Medical appointment		87.6 (47.5)		110.4 (89.8)		299.6 (355.8)		489.9 (1,114.7)		-		-
<i>Total direct medical</i>		94.5 (53.3)		120.6 (95.0)		367.4 (540.6)		574.1 (1,334.0)		-		-
Overhead		15.0 (8.2)		18.8 (15.4)		51.4 (59.6)		83.4 (185.8)		-		-
<i>Total direct medical and non-medical</i>		109.5 (61.2)		139.4 (109.8)		418.8 (586.9)		657.4 (1,439.9)		-		-
<i>Outpatient care</i>	150				26		26		5		5	
Drugs		0.1 (0.5)		15.4 (52.8)		1.7 (3.1)		45.3 (50.3)		2.3 (4.8)		7.9 (5.0)
ART		-		467.7 (276.4)		70.9 (142.0)		261.6 (205.4)		7.4 (16.5)		140.9 (185.5)
TB drugs		-		-		-		23.0 (17.0)		-		4.9 (0.0)
Tests		7.8 (12.3)		61.9 (38.2)		65.0 (83.7)		45.2 (53.8)		65.5 (23.6)		65.7 (56.3)
Medical appointment		47.0 (32.8)		195.1 (119.1)		110.8 (71.3)		262.7 (155.0)		73.7 (55.0)		328.1 (207.0)
<i>Total direct medical</i>		54.8 (38.8)		740.2 (357.5)		248.5 (218.4)		637.9 (389.0)		148.8 (48.2)		547.5 (394.0)
Overhead		8.8 (6.2)		36.7 (22.4)		20.8 (13.2)		49.4 (28.6)		13.9 (9.3)		61.7 (34.8)
<i>Total direct medical and non-medical</i>		63.7 (44.7)		776.9 (369.9)		269.3 (220.4)		687.3 (406.3)		162.7 (49.9)		609.3 (383.4)
<i>Inpatient care</i>	19		38		11		20		0		1	
Drugs		111.4 (161.6)		407.9 (549.2)		172.0 (172.5)		754.7 (874.7)		-		15.3
ART		-		18.6 (37.9)		12.7 (23.7)		29.1 (36.9)		-		0.0
TB drugs		-		-		-		3.9 (4.1)		-		0.0
Tests		119.7 (109.9)		177.0 (184.9)		170.3 (165.1)		237.7 (201.7)		-		175.6
Bed day		479.9 (446.9)		733.2 (617.2)		706.5 (576.1)		1,092.4 (990.8)		-		117.0
<i>Total direct medical</i>		710.9 (633.4)		1,336.8 (1,265.3)		1,061.5 (870.1)		2,117.7 (1,795.1)		-		307.9
Overhead		999.1 (930.0)		1,513.0 (1,367.0)		1,471.0 (1,143.7)		2,254.0 (1,926.6)		-		241.5
<i>Total direct medical and non-medical</i>		1,710.1 (1,547.2)		2,849.8 (2,562.6)		2,532.5 (1,971.3)		4,371.7 (3,652.7)		-		549.5

Table 4. Total mean cost (US\$) for pre-diagnosis and treatment periods from the health system perspective, Correia Picanco Hospital, Recife/Brazil

Status	N	Pre-diagnosis	Treatment	Total
		Mean (SD)	Mean (SD)	Mean (SD)
HIV or AIDS				
Drugs	195	11.3 (60.3)	76.3 (277.3)	87.6 (286.0)
Tests		19.3 (50.6)	91.9 (104.4)	11.3 (118.1)
ART		-	492.0 (266.7)	492.0 (266.7)
Medical appointment/bed day		114.4 (200.7)	373.5 (422.1)	487.9 (471.1)
Overhead		107.3 (413.3)	273.3 (800.8)	379.5 (899.4)
Total		252.4 (697.3)	1,306.0 (1,549.5)	1,558.4 (1,713.7)
AIDS death				
Drugs	13	1.5 (3.5)	344.2 (339.4)	345.8 (340.2)
Tests		12.8 (33.4)	215.2 (133.1)	228.0 (143.7)
ART		-	159.3 (236.7)	159.3 (236.7)
Medical appointment/bed day		106.6 (106.9)	730.4 (465.9)	837.0 (526.3)
Overhead		52.8 (125.4)	1,205.5 (857.7)	1,258.3 (963.1)
Total		173.8 (231.0)	2,654.7 (1,648.6)	2,828.4 (1,833.9)
TB/HIV				
Drugs	18	84.0 (238.2)	478.8 (625.5)	562.8 (834.2)
Tests		131.7 (137.9)	209.7 (182.8)	341.4 (243.0)
ART		81.3 (163.0)	354.7 (171.5)	436.0 (209.8)
TB drugs		-	33.0 (12.7)	33.0 (12.7)
Medical appointment/bed day		531.6 (488.2)	1,478.0 (1,398.2)	2,009.6 (1,767.9)
Overhead		384.6 (555.4)	1,521.7 (1,733.5)	1,906.3 (1,864.0)
Total		1,213.2 (1,189.0)	4,075.8 (3,558.2)	5,289.0 (4,190.2)
TB/HIV death				
Drugs	8	172.1 (202.9)	1,442.2 (1,123.3)	1,316.4 (1,049.5)
Tests		208.1 (183.5)	289.0 (244.0)	497.1 (203.7)
ART		65.1 (61.4)	125.1 (177.4)	190.2 (205.6)
TB drugs		-	10.1 (11.8)	10.1 (11.8)
Medical appointment/bed day		921.7 (727.0)	1,415.8 (1,144.0)	2,337.5 (821.7)
Overhead		1,359.9 (1,466.7)	2,569.9 (2,297.2)	3,929.8 (1,693.8)
Total		2,727.0 (2,523.8)	5,554.1 (4,591.2)	8,281.0 (3,466.9)
LTBI/HIV				
Drugs	5	2.3 (4.3)	10.9 (10.5)	13.2 (10.1)
Tests		65.5 (21.1)	100.8 (117.2)	166.4 (108.7)
ART		7.4 (14.8)	140.9 (165.9)	148.3 (168.5)
TB drugs		-	4.9 (-)	4.9 (-)
Medical appointment/bed day		73.7 (49.2)	351.6 (207.5)	425.2 (233.3)
Overhead		13.9 (9.3)	110.0 (114.5)	123.9 (122.7)
Total		162.7 (49.9)	719.2 (565.7)	881.9 (613.1)

References

1. UNAIDS. Prevention Gap Report. Geneva, Switzerland; 2016.
2. Foulds J, O'Brien R. New tools for the diagnosis of tuberculosis: the perspective of developing countries. *Int J Tuberc Lung Dis* [Internet]. 1998;49(SUPPL. 1):17–20. Available from: <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L27197079>
3. Dawson R, Masuka P, Edwards DJ, Bateman ED, Bekker LG, Wood R, et al. Chest radiograph reading and recording system: evaluation for tuberculosis screening in patients with advanced HIV. *Int J Tuberc Lung Dis* [Internet]. 2010;14(1):52–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20003695> <http://www.ingentaconnect.com/content/iuatld/ijtld/2010/00000014/00000001/art00009?token=00451360be77e442f20672148763f442e495b4624407b687627502b333e3568263c2b%5Cnhttp://www.ingentaconnect.com/content/iuatld/i>
4. United Nations. The Sustainable Development Goals [Internet]. New York, USA; 2015. Available from: <http://www.theguardian.com/global-development/ng-interactive/2015/jan/19/sustainable-development-goals-changing-world-17-steps-interactive>
5. Dye C, Glaziou P, Floyd K, Raviglione M. Prospects for Tuberculosis Elimination. *Annu Rev Public Health* [Internet]. 2013;34(1):271–86. Available from: <http://www.annualreviews.org/doi/10.1146/annurev-publhealth-031912-114431>
6. WHO. The End TB Strategy. Vol. 53. 2015. 1689-1699 p.
7. World Health Organization. Global tuberculosis report 2015. Vol. 1. Geneva, Switzerland; 2015.
8. SES-PE. Secretaria Estadual de Saude, Hospital Correia Picanço [Internet]. [cited 2016 Oct 10]. Available from: <http://portal.saude.pe.gov.br/unidades-de-saude-e-servicos/secretaria-executiva-de-atencao-saude/hospital-correia-picanco>
9. UNAIDS. Costing Guidelines for HIV Prevention. UNAIDS, editor. October. Geneva: Joint United Nations Programme on HIV/AIDS; 2000. 123 p.
10. World Health Organization. The tool to estimate patients' costs. 2008;1–83. Available from: [http://www.stoptb.org/wg/dots_expansion/tbandpoverty/assets/documents/Tool to estimate Patients' Costs.pdf](http://www.stoptb.org/wg/dots_expansion/tbandpoverty/assets/documents/Tool%20to%20estimate%20Patients'%20Costs.pdf)
11. Ministerio da Saude do Brasil. Diretrizes metodologicas: diretriz de avaliação econômica. 2nd ed. Ministério da Saúde do Brasil; Secretaria de Ciência Tecnologia e Insumos Estratégicos; Departamento de Ciência e Tecnologia, editors. Brasília; 2014.
12. Ministério da Saúde do Brasil. Banco de Precos em Saude. 2014.
13. DATASUS. Sistema de Gerenciamento da tabela de procedimentos, Medicamentos e OPM do SUS.
14. OANDA. Historical exchange rates. 2016 [Internet]. [cited 2016 Aug 1]. Available from: <https://www.oanda.com/fx-for-business/historical-rates>
15. Faria R, Gomes M, Epstein D, White IR. A Guide to Handling Missing Data in Cost-Effectiveness Analysis Conducted Within Randomised Controlled Trials. *Pharmacoeconomics*. 2014;32(12):1157–70.

16. The World Bank. World Development Indicators: Exchange rates and prices [Internet]. 2017 [cited 2016 Nov 1]. Available from: <http://wdi.worldbank.org/table/4.16>
17. International Monetary Fund. International monetary fund, data and statistics. 2016.
18. Colebunders R, Bastian I. A review of the diagnosis and treatment of smear-negative pulmonary tuberculosis. *Int J Tuberc Lung Dis*. 2000;4(2):97–107.
19. El-Sony AI. The cost to health services of human immunodeficiency virus (HIV) co-infection among tuberculosis patients in Sudan. *Health Policy (New York)*. 2006;75(3):272–9.
20. Renaud A, Basenya O, de Borman N, Greindl I, Meyer-Rath G. The cost effectiveness of integrated care for people living with HIV including antiretroviral treatment in a primary health care centre in Bujumbura, Burundi. *AIDS Care [Internet]*. 2009;21(11):1388–94. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20024715>
21. Kamolratanakul P, Hiransuthikul N, Singhadong N, Kasetjaroen Y, Akksilp S, Lertmaharit S. Cost Analysis of Different Types of Tuberculosis. *Southeast Asian J Trop Med Public Heal*. 2002;33(2):321–30.
22. Zhou F, Kominski GF, Qian H-Z, Wang J, Duan S, Guo Z, et al. Expenditures for the care of HIV-infected patients in rural areas in China's antiretroviral therapy programs. *BMC Med [Internet]*. 2011;9(1):6. Available from: <http://www.biomedcentral.com/1741-7015/9/6>
23. Long LC, Fox MP, Sauls C, Evans D, Sanne I, Rosen SB. The high cost of HIV-positive inpatient care at an urban hospital in Johannesburg, South Africa. *PLoS One*. 2016;11(2):1–12.
24. Thomas LS, Manning A, Holmes CB, Naidoo S, van der Linde F, Gray GE, et al. Comparative costs of inpatient care for HIV-infected and uninfected children and adults in Soweto, South Africa. *J Acquir Immune Defic Syndr*. 2007;46(4):410–6.
25. UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Geneva, Switzerland; 2014.
26. World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource- constrained settings. WHO, editor. Geneva: WHO; 2011.
27. World Health Organization. WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. *World Heal Organ Doc*. 2012;WHO/HTM/TB:1–34.
28. O'Sullivan AK, Thompson D, Drummond MF. Collection of health-economic data alongside clinical trials: Is there a future for piggyback evaluations? *Value Heal [Internet]*. 2005;8(1):67–79. Available from: <http://dx.doi.org/10.1111/j.1524-4733.2005.03065.x>
29. Cerda R, Muñoz M, Zeladita J, Wong M, Sebastian JL, Bonilla C, et al. Health care utilization and costs of a support program for patients living with the human immunodeficiency virus and tuberculosis in Peru. 2011;15(April 2010):363–8.