

# Tuberculosis Treatment Outcome In Patients With Tb-Hiv Co-Infection In Kuala Lumpur, Malaysia

**Diana Safraa Selimin**

Universiti Kebangsaan Malaysia

**Aniza Ismail** (✉ [aniza@ppukm.ukm.edu.my](mailto:aniza@ppukm.ukm.edu.my))

UKM

**Norfazilah Ahmad**

Pusat Perubatan Universiti Kebangsaan Malaysia

**Rohani Ismail**

Kementerian Kesihatan Malaysia

**Nurul Farhana Mohd Azman**

Kementerian Kesihatan Malaysia

**Amaleena Azman**

Kementerian Kesihatan Malaysia

---

## Research article

**Keywords:** TB-HIV co-infection, determinants, treatment outcome

**Posted Date:** November 7th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.16876/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Background** Tuberculosis (TB) is a serious health threat to people living with human immunodeficiency virus (HIV). This study aimed to identify the characteristics, unsuccessful TB treatment rate and determinants of unsuccessful TB treatment outcome among patients with TB-HIV co-infection in Kuala Lumpur.

**Methods** This was a cross-sectional study. The data of all patients with TB-HIV in the federal territory of Kuala Lumpur from 2013 to 2017 were collected and reviewed. The data were retrieved from the national database (TB Information System) at the Kuala Lumpur Health Department from 1 March 2018 to 31 May 2018.

**Results** Out of 235 randomly selected patients with TB-HIV, TB treatment outcome was successful in 57.9% (cured and completed treatment) and unsuccessful in 42.1% (died, failed or defaulted treatment). Patients who did not receive DOTS (directly observed treatment, short course) (adjusted odds ratio [aOR] 21.71; 95% confidence interval [CI]: 5.36–87.94) and those who received shorter treatment duration of <6 months (aOR 34.54; 95% CI: 5.97–199.93) had higher odds for unsuccessful TB treatment outcome.

**Conclusions** Nearly half of the patients with TB-HIV had unsuccessful TB treatment outcome. Therefore, it is important to ensure that such patients receive DOTS and continuous TB treatment of >6 months. It is crucial to strengthen and widen the coverage of DOTS, especially among high-risk groups, in healthcare settings. Strict follow-up by healthcare providers is needed for patients with TB-HIV to gain treatment adherence and for better rates of successful TB treatment.

## Introduction

It is undeniable that tuberculosis (TB) and human immunodeficiency virus (HIV) co-infection poses a major public health threat worldwide(1, 2). Worldwide, it has been estimated that more than one-third of people living with HIV (PLHIV) are infected with TB(2, 3). An estimated 70.0% of PLHIV are from Sub-Saharan African countries(4). Despite the Southeast Asian Region (SEAR) experiencing 34% decreased TB incidence among PLHIV within an 11-year period until 2013, high TB-HIV disease burden was still observed in Indonesia, Myanmar, Thailand, India and Nepal(5). The prevalence of TB-HIV co-infection in Malaysia was 12.6%(6).

TB is known as the most common opportunistic infection among PLHIV; treatment management is complicated and TB is the main culprit in most HIV deaths(2, 3, 7). The World Health Organization (WHO) has reported that around 400,000 PLHIV deaths are due to TB infection(3). PLHIV have a higher risk for latent TB infection to progress to active TB. As a result of active TB, the immune system of PLHIV is suppressed further as the viral load increases and CD4 levels decrease. Managing TB-HIV co-infection presents enormous challenges to physicians(8).

In the future, concurrent TB-HIV infection will become a burden on a country's expenses, as prolonged treatment may be required as compared to countries with only TB infection(3, 9). In 2013, the Malaysian government spent about USD15 million on TB intervention and control(10).

Patients with TB-HIV without anti-retroviral therapy (ART) tend to have poorer TB outcome compared to those who are on ART(6, 11, 12). TB infection with late presentation and HIV diagnosis are further risk factors for unsuccessful TB treatment outcome among patients with TB-HIV(13-15). Other than that, patients with positive sputum culture upon TB diagnosis are at higher risk for unsuccessful TB treatment outcome(16).

The Regional Strategic Plan towards Ending TB in the SEAR 2016–2020 was implemented to achieve successful TB elimination in the region by 2035. Hence, TB and HIV programmes need to be strengthened and aimed towards successful implementation by understanding the characteristics of patients with TB-HIV with successful or unsuccessful treatment outcomes(5). However, studies, especially local studies, for determining the characteristics of such patients, including their clinical status(17), are scarce to date.

The objective of the present study was to identify the characteristics of patients with TB-HIV, describe the TB treatment outcome and identify the associated factors for unsuccessful TB treatment outcome in such patients in Kuala Lumpur, Malaysia.

## Methods

### Study population and sampling

This was a cross-sectional study involving patients with TB-HIV co-infection in Kuala Lumpur, Malaysia. The sample population was patients with TB who were notified and registered with the National Registry for TB database, i.e. the National Tuberculosis Information System (TBIS), by the Kuala Lumpur Federal Territory Health Department. Patients with TB-HIV were included via simple random sampling from the patient name list, and TBIS served as the sampling frame. Sample size was calculated based on the formula by Kish(18) and in reference to a previous local study(6). After considering 20% missing data, a minimum of 235 patients with TB-HIV was included in this study.

### Data collection

The TB records of all patients with TB-HIV in Kuala Lumpur from 2013 to 2017 were retrieved, reviewed and collected from the TBIS database at the Kuala Lumpur Federal Territory Health Department.

### *Outcome variables*

The study outcome was successful or unsuccessful TB treatment. Unsuccessful TB treatment was defined as death (for any reason during the treatment course), treatment failure (positive sputum smear at 5 months or later during treatment) or defaulted treatment (interrupted treatment for >2 consecutive months).

Successful TB treatment was defined as when a patient was cured (previously smear-positive patients that were smear-negative in the final month of treatment and at least once on a previous occasion) and had completed treatment (patient had completed treatment but did not meet the criteria to be classified either as cure or failure).

### *Independent variables*

The sociodemographic characteristics included in the study were age, sex, citizenship status, ethnicity, marital status and place of residence. Age was counted starting from the date of birth until the TB notification date. Sex was classified as male or female; citizenship status was classified as Malaysian or non-Malaysian. Ethnicity was considered race inherited from parents, e.g. Malay, Chinese, Indian or others. For place of residence, all flats and slums were considered low-cost residential areas. Apartments, condominiums, terrace houses and bungalows were considered medium- or high-cost residential areas; the place of residence of patients who were homeless or who were institutionalised, i.e. in detention centres or prisons was classified as 'others'.

The socioeconomic characteristics included in the study were formal education, employment status (employed or unemployed) and household income. Any formal education, regardless of duration, was classified as 'yes', and no formal education was classified as 'no'. Patients who were employed, including self-employment, were categorized as 'employed'; patients who did not work were categorized as 'unemployed'. Household income was considered low when it was under 3000 Malaysian ringgit (<MYR3000), and was considered high when it was  $\geq$ MYR3000.

The clinical characteristics retrieved were diabetes mellitus (DM) status, smoking status, Bacille Calmette-Guérin (BCG) scar status, ART status, TB type, TB case category, chest X-ray (CXR) presentation upon diagnosis, sputum smear upon diagnosis, sputum culture upon diagnosis, directly observed treatment, short course (DOTS) status and duration of TB treatment. For DM status, patients with underlying DM were categorized as 'yes', and those without DM were categorized as 'no'. For smoking status, smokers were classified as 'yes', and non-smokers were classified as 'no'. Patients with a BCG scar on any part of the body, as it varies by country, were categorised as 'present', and those without a BCG scar were categorised as 'absent'. Patients who received ART were categorised as 'yes', and those who did not receive ART were categorised as 'no'. TB type was divided into two categories: pulmonary and extrapulmonary. TB case categories were divided into new cases, relapse and return after default. New cases were all new TB cases notified among HIV patients, 'relapse' indicated previously successfully treated TB cases among patients with HIV but who became infected again with TB; 'return after default'

was defined as stopping TB treatment before the completion of treatment. CXR presentation upon diagnosis was categorized according to how severe the lesion appeared on the X-ray film: 'no or minimal lesion' if CXR showed no or few lesions, 'advanced lesion' if CXR showed extensive lesions or miliary appearance, and 'not performed' if CXR was not performed upon diagnosis. Sputum smear and sputum culture were both categorised as 'positive' if the first result was positive, 'negative' if the first result was negative, and 'not performed' if no sputum smear or culture were performed upon diagnosis. DOTS status was 'yes' if the patient received DOTS, and 'no' if the patient did not receive DOTS. TB treatment duration was divided into three categories: <6 months, 6–12 months and >12 months.

## Statistical analysis

Data were analysed using SPSS 22. For descriptive analysis, continuous data were reported as the mean and standard deviation (SD), as the data were distributed normally. Categorical data are reported as the frequency (*n*) and percentage (%). The association between the independent variables and outcome variable (unsuccessful TB treatment outcome) was determined using simple logistic regression (SLR). Multivariable analysis was conducted using multiple logistic regression (MLR) analysis to obtain the adjusted odds ratio (aOR) and 95% confidence interval (CI) and to control for possible confounders. The significance level was set at  $p < 0.05$ .

## Results

From 2013 to 2017, there were total of 690 patients with TB-HIV. Of these, 235 patients were included in the study. Patients who were transferred out, aged <18 years and with multi-drug resistance TB (MDR-TB) were excluded from the study. The mean patient age was 39.49 (SD 9.35) years. Most of the patients were Malaysians (89.8%), male (85.5%), Malay (48.9%) and lived in medium- or high-cost residences (62.1%) (Table 1).

Most of the patients had received formal education (79.6%), were unemployed (51.1%) and had low household income, i.e. <MYR3000 (88.5%) (Table 1).

The majority of patients was classified as new TB cases (84.7%); 74% were classified as pulmonary TB. Most patients did not receive ART (60.9%), were non-diabetic (96.2%), non-smokers (51.5%) and had BCG scars (90.6%). Upon diagnosis, the majority had no or minimal lesion on CXR (67.7%), 50.6% had negative sputum smear and 50.6% had negative sputum culture. Most patients were under DOTS (66%); 48.1% had 6–12 months' TB treatment. One hundred and thirty-six patients (57.9%) had successful TB treatment outcome, and 99 patients (42.1%) had unsuccessful TB treatment outcome (Table 2).

SLR showed that a few significant factors were associated with TB treatment outcome, namely citizenship status, ethnicity, formal education received, employment status, household income, BCG scar,

ART, CXR upon diagnosis, sputum culture upon diagnosis, DOTS status and TB treatment duration (Table 3).

After adjusting for other factors, the determinants for TB treatment outcome were determined using binary logistic regression. Table 4 shows the final model. Patients who did not receive DOTS had 22 times higher odds of having unsuccessful TB treatment outcome (aOR 21.71, 95% CI: 5.36–87.94,  $p \leq 0.001$ ). Patients with shorter TB treatment duration, i.e. <6 months, had 35 times higher odds of having unsuccessful TB treatment outcome (aOR 34.54, 95% CI: 5.97–199.93,  $p \leq 0.001$ ). This model had no multicollinearity and was stable (variance inflation factor [VIF] < 10), and there was no interaction problem.

## Discussion

In the present study, TB treatment outcome in patients TB-HIV was closely associated with that of a study performed in 2010 in the Klang Valley, Malaysia, that reported 53.4% successful treatment outcome and 46.6% unsuccessful treatment outcome(6). However, in the district of Kota Bharu, Malaysia, 93% of patients with TB-HIV had successful treatment outcome(19). By comparison, other studies conducted in South Africa also showed better TB treatment outcome in patients with TB-HIV(20). Therefore, these differences must be due to multifactorial aspects such as diverse outlook on sociodemographic structure and service provision settings.

Here, the determinant factors for unsuccessful TB treatment outcome were: not receiving DOTS and TB treatment duration of <6 months. Our findings are supported by other studies that reported that DOTS can improve the cure rate(7, 21). By contrast, a qualitative study showed that the rigidity of DOTS was one of the factors of treatment non-adherence by patients with TB-HIV, which led to treatment default and therefore unsuccessful treatment outcome(22).

Taking anti-TB medications for at least 6 months is another determinant factor for successful treatment of TB, which supports the present findings(23). Most patients with TB-HIV are cured with a standard 6-month treatment regimen(8). Another study comparing 6-month and 9-month treatment reported similar treatment outcomes but with significantly lower recurrence rates compared to a 6-month, thrice-weekly regimen(24). It has also been proven that a longer treatment regimen can yield a more favourable treatment outcome for patients with TB-HIV,(25) which supports our observations. Besides, low TB treatment adherence may lead to increased risk of drug resistance, treatment relapse as well as mortality. Therefore, it is important for healthcare providers to ensure that patients with TB-HIV adhere to the TB treatment regimen(22).

The present study shows that non-Malaysians had higher odds of having unsuccessful TB treatment outcome but it was not statistically significant; thus, it was not included as a determinant in this study. This is in concordance with another study performed in Malaysia(19). The small number of non-Malaysian patients with TB-HIV could have contributed to the non-significant findings of both studies. Migration is a risk factor for TB, especially for migrants from high–TB burden countries. Immigrants tend to have a higher risk for defaulting treatment, which further contributes towards unsuccessful TB treatment outcome(23). The WHO has emphasised efforts to control TB in order to assist governments worldwide in terms of policies for migrants by preventing HIV/AIDS among migrants, as they are a vulnerable group(26).

Here, lack of formal education, being unemployed and low household income were significantly associated with unsuccessful treatment outcome, compared to having received formal education, being employed and high household income. These findings are in concordance with other studies that show that people with low socioeconomic backgrounds tend to have a higher risk of poorer TB treatment outcome(22, 23). The risk of developing TB increases among people with low socioeconomic backgrounds, as they usually live in areas with poor ventilation, have poor knowledge and behavioural practices regarding the disease itself, and are malnourished, which may lead to low immunity(23).

DM is a risk factor for developing TB. Similar to another study, the present findings show no significant difference in TB treatment outcome between patients with and without DM(19). Patients with DM tend to have poorer TB treatment outcome compared to those without DM comorbidity, as DM patients with TB can have worsened glycaemic index(27). However, patients with TB-HIV have low immunity due to the underlying HIV. On the other hand, patients with underlying HIV have higher chances of developing TB compared to patients with underlying DM(23).

The presence of a BCG scar may be a protective factor against developing TB infection. The present study suggests that patients with TB-HIV without a BCG scar have 4.2 times higher odds of having unsuccessful TB treatment outcome compared to patients with a BCG scar, but it was not significantly associated with unsuccessful TB treatment outcome. Likewise, this finding is supported by the findings of Nik Nor Ronaidi et al.(19).

Here, we found that not receiving ART was significantly associated with unsuccessful TB treatment outcome, and this is consistent with previous studies worldwide(6, 11, 12, 28, 29). However, our results contradict that of a study in India(30). A study from Iran found that patients with TB-HIV who had not been started with ART prior had a higher chance of dying earlier. Physicians had limited time to start such patients on ART due to the shorter duration of hospitalisation because they died earlier(12).

In the present study, advanced CXR presentation was not significantly associated with unsuccessful TB treatment outcome. In contrast, advanced CXR findings have been suggested as a determinant factor for unsuccessful TB treatment outcome(19). In patients with TB-HIV, up to 10–15% of such patients with proven TB may have normal CXR due to the delayed immune response(31).

Here, sputum smear upon diagnosis was not significantly associated with unsuccessful TB treatment outcome. The numbers of patients with smear-negative and smear-positive TB were almost identical in the present study, and this might explain why it was not associated with the treatment outcome. Nevertheless, this condition can also be due to the non-specific symptoms and broad-spectrum immune response among patients with TB-HIV, which may produce false negative sputum smear results among such patients(31-35). These findings were concordant with that of Nguyen et al. and Nik Nor Ronaidi et al.(16, 19). Others have however showed that positive sputum smear is significantly associated with unsuccessful TB treatment outcome(1, 29).

Here, positive sputum culture upon diagnosis was significantly associated with unsuccessful TB treatment outcome. This finding was supported by similar findings by Prado et al., Nguyen et al. and Swaminathan et al.(1, 16, 24). Patients with TB-HIV with positive sputum culture may have higher TB bacterial loads, which may thus worsen the prognosis. Sputum culture is more accurate for diagnosing TB and for determining the prognosis in patients with TB-HIV, even though their sputum smear is negative(33). This is consistent, as sputum culture is the gold standard for TB diagnosis, especially among patients with HIV, as it has higher sensitivity compared to sputum smear(31, 36).

The present study identifies the determinants of TB-HIV treatment outcome, which could guide healthcare facilities, especially those in Kuala Lumpur, to focus on those areas for better treatment outcome among patients with TB-HIV so that better treatment outcome can be achieved in the future. Other than that, the TB data were obtained from a reliable source (TBIS), which represent the population studied.

Nevertheless, this study has some limitations. Although the patients were selected randomly, they were all from the Kuala Lumpur Federal Territory Health Office registry. Hence, the outcome of this study is mainly limited to patients within the Federal Territory of Kuala Lumpur, and it is not known if it can be generalised to other states in Malaysia or to other countries. Second, as it was secondary data, it was very difficult to determine the sputum conversion rate after 2 months of treatment, as not all patients with TB-HIV have these data. Besides, the transferred-out patients excluded from the study would produce bias results because they could not be included in the study due to the inability to assess the treatment outcome, as their records were unavailable.

## Conclusions

Nearly 50% of patients with TB-HIV have unsuccessful TB treatment outcome. Crucial measures are needed to ensure that such patients receive DOTS and continuous TB treatment of >6 months. Healthcare settings are required to strengthen and widen DOTS service coverage and to prioritize DOTS, especially among the high-risk groups. Accordingly, rigorous follow-ups from healthcare professionals are needed to ensure intensified treatment adherence and better rates of successful TB treatment outcome among patients with TB-HIV.

## Declarations



## **AVAILABILITY OF DATA AND MATERIALS**

The datasets generated and analysed in this study are not publicly available due to restriction in which it contained health information that could compromise the privacy of research participants but are available from the corresponding author upon reasonable request.

## **ACKNOWLEDGEMENTS**

The authors would like to express their special gratitude to the Director General, The Ministry of Health Malaysia, and the Federal Territory of Kuala Lumpur Health Department Director for granting permission to publish this paper and for the opportunity to conduct this research within their facilities using their valuable database management support. The authors would also like to thank the Medical Research & Ethics Committee, Ministry of Health Malaysia (MREC) (NMRR-18-872-40791) and the Universiti Kebangsaan Malaysia Medical Centre Research Ethics Board (UKMMC REC) (UKM PPI/111/8/JEP-2019-017) for approving this study.

## **ETHICAL APPROVAL**

This study was conducted in compliance with the ethical principles and approval by MREC (NMRR-18-872-40791) and with ethics permission from UKMMC REC (UKM PPI/111/8/JEP-2019-017).

## **FUNDING**

None.

## **AUTHORS' CONTRIBUTIONS**

DSS and AI designed the study and wrote the article. RI helped in the design of the study and provided the data, DSS, NFMA, and AA analysed the TB data. NA and AI supervised the study, reviewed and edited the article. All of the authors read and approved the final manuscript.

## **COMPETING INTERESTS**

None declared.

## References

1. Prado TNd, Rajan JV, Miranda AE, Dias EdS, Cosme LB, Possuelo LG, et al. Clinical and epidemiological characteristics associated with unfavorable tuberculosis treatment outcomes in TB-HIV co-infected patients in Brazil: a hierarchical polytomous analysis. *Brazilian Journal of Infectious Diseases*. 2017;21(2):162-70.
2. Tiberi S, Carvalho ACC, Sulis G, Vaghela D, Rendon A, Mello FCdQ, et al. The cursed duet today: tuberculosis and HIV-coinfection. *La Presse médicale*. 2017;46(2):e23-e39.
3. World Health Organization. WHO Global Tuberculosis Report 2016. . 2016:214.
4. Ansa GA, Sifa JS. Tuberculosis and HIV integration in sub-Saharan Africa. *Asian Pacific Journal of Tropical Disease*. 2015;5(11):841-9.
5. World Health Organization. Ending TB in the South-East Asia Region: Broad Strategic Plan 2016 - 2020. 2016.
6. Ismail I, Bulgiba A. Determinants of unsuccessful tuberculosis treatment outcomes in Malaysian HIV-infected patients. *Preventive medicine*. 2013;57:S27-S30.
7. Singhal S, Jaiswa P. Presentation of tuberculosis in TB-HIV co-infection patients and the treatment outcome with directly observed short course therapy. *Asian Pacific Journal of Tropical Biomedicine*. 2011;1(2):S266-S7.
8. Medical Development Division Ministry of Health Malaysia. Guidelines for the management of adult HIV infection with antiretroviral therapy 2011. 1-98 p.
9. de Siqueira Filha N, Legood R, Rodrigues L, Santos A. The economic burden of tuberculosis and latent tuberculosis in people living with HIV in Brazil: a cost study from the patient perspective. *Public health*. 2018;158:31-6.
10. World Health Organization. Regional Framework for Action on Implementation of the End TB Strategy in the Western Pacific, 2016–2020. 2016
11. Belayneh M, Giday K, Lemma H. Treatment outcome of human immunodeficiency virus and tuberculosis co-infected patients in public hospitals of eastern and southern zone of Tigray region, Ethiopia. *The Brazilian Journal of Infectious Diseases*. 2015;19(1):47-51.
12. Tabarsi P, Chitsaz E, Moradi A, Baghaei P, Marjani M, Mansouri D. Treatment outcome and mortality: Their predictors among HIV/TB co-infected patients from Iran. *International journal of mycobacteriology*. 2012;1(2):82-6.
13. Gebremariam G, Asmamaw G, Hussen M, Hailemariam MZ, Asegu D, Astatkie A, et al. Impact of HIV status on treatment outcome of tuberculosis patients registered at Arsi Negele Health Center, Southern Ethiopia: a six year retrospective study. *PloS one*. 2016;11(4):e0153239.
14. Ifebunandu NA, Ukwaja KN, Obi SN. Treatment outcome of HIV-associated tuberculosis in a resource-poor setting. *Tropical doctor*. 2012;42(2):74-6.

15. Yone EWP, Kuaban C, Kengne AP. HIV testing, HIV status and outcomes of treatment for tuberculosis in a major diagnosis and treatment centre in Yaounde, Cameroon: a retrospective cohort study. *BMC infectious diseases*. 2012;12(1):190.
16. Nguyen DT, Jenkins HE, Graviss EA. Prognostic score to predict mortality during TB treatment in TB/HIV co-infected patients. *PloS one*. 2018;13(4):e0196022.
17. Wejse C, Patsche CB, Kühle A, Bamba F, Mendes M, Lemvik G, et al. Impact of HIV-1, HIV-2, and HIV-1+ 2 dual infection on the outcome of tuberculosis. *International journal of infectious diseases*. 2015;32:128-34.
18. Kish L. *Survey sampling*, John Wiley and sons, NY.". 1965.
19. NM NNR, Mohd N, Sharina D. Factors associated with unsuccessful treatment outcome of pulmonary tuberculosis in Kota Bharu, Kelantan. *Malaysian Journal of Public Health Medicine*. 2011;11(1):6-15.
20. Jacobson KB, Moll AP, Friedland GH, Shenoi SV. Successful tuberculosis treatment outcomes among HIV/TB coinfectd patients down-referred from a district hospital to primary health clinics in rural South Africa. *PloS one*. 2015;10(5):e0127024.
21. Joseph MR, Thomas RA, Nair S, Balakrishnan S, Jayasankar S. Directly observed treatment short course for tuberculosis. What happens to them in the long term? *Indian Journal of Tuberculosis*. 2015;62(1):29-35.
22. Gebremariam MK, Bjune GA, Frich JC. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. *BMC public health*. 2010;10(1):651.
23. Duarte R, Lönnroth K, Carvalho C, Lima F, Carvalho A, Munoz-Torrico M, et al. Tuberculosis, social determinants and co-morbidities (including HIV). *Pulmonology*. 2018;24(2):115-9.
24. Swaminathan S, Narendran G, Venkatesan P, Iliayas S, Santhanakrishnan R, Menon PA, et al. Efficacy of a 6-month versus 9-month intermittent treatment regimen in HIV-infected patients with tuberculosis: a randomized clinical trial. *American journal of respiratory and critical care medicine*. 2010;181(7):743-51.
25. Padmapriyadarsini C, Narendran G, Swaminathan S. Diagnosis & treatment of tuberculosis in HIV co-infected patients. *The Indian journal of medical research*. 2011;134(6):850.
26. Organization WH. *Tuberculosis control in migrant populations: guiding principles and proposed actions*. Manila: WHO Regional Office for the Western Pacific; 2016.
27. World Health Organization. *Global Report on Diabetes*. 2016.
28. Nagu TJ, Aboud S, Mwiru R, Matee MI, Rao M, Fawzi WW, et al. Tuberculosis associated mortality in a prospective cohort in Sub Saharan Africa: Association with HIV and antiretroviral therapy. *International Journal of Infectious Diseases*. 2017;56:39-44.
29. Sileshi B, Deyessa N, Girma B, Melese M, Suarez P. Predictors of mortality among TB-HIV Co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study. *BMC infectious diseases*. 2013;13(1):297.

30. Ambadekar N, Zodpey S, Soni R, Lanjewar S. Treatment outcome and its attributes in TB-HIV co-infected patients registered under revised national TB control program: a retrospective cohort analysis. *Public health*. 2015;129(6):783-9.
31. Ministry of Health Malaysia, Academy of Medicine Malaysia, Malaysian Thoracic Society. Management of Tuberculosis - Clinical Practice Guidelines (3rd Edition)2012.
32. Badie B, Mostaan M, Izadi M, Alijani M, Rasoolinejad M. Comparing radiological features of pulmonary tuberculosis with and without HIV infection. *Journal of AIDS and Clinical Research*. 2012;3(10).
33. Cain KP, McCarthy KD, Heilig CM, Monkongdee P, Tasaneeyapan T, Kanara N, et al. An algorithm for tuberculosis screening and diagnosis in people with HIV. *New England Journal of Medicine*. 2010;362(8):707-16.
34. Montales MT, Beebe A, Chaudhury A, Patil N. Mycobacterium tuberculosis infection in a HIV-positive patient. *Respiratory medicine case reports*. 2015;16:160-2.
35. Walker NF, Meintjes G, Wilkinson RJ. HIV-1 and the immune response to TB. *Future virology*. 2013;8(1):57-80.
36. World Health Organization. Systematic screening for active tuberculosis: Principles and recommendations. Geneva: WHO Press; 2013.

## Tables

Table 1. Characteristics of patients with TB-HIV co-infection ( $n = 235$ ).

<i>Sociodemographic characteristics</i>	
Age (years)	<i>n</i> (%)
18–39	120 (51.1)
40–59	110 (46.8)
≥60	5 (2.1)
Sex	
Male	201 (85.5)
Female	34 (14.5)
Citizenship	
Malaysian	211 (89.8)
Non-Malaysian	24 (10.2)
Ethnicity	
Malay	115 (48.9)
Chinese	61 (26)
Indian	26 (11.1)
Others	33 (14)
Place of residence	
Low-cost	64 (27.2)
Medium-/high-cost	146 (62.1)
Others (homeless/institutional)	25 (10.6)
<i>Socioeconomic characteristics</i>	
Formal education	
Yes	187 (79.6)
No	48 (20.4)
Employment status	
Employed	115 (48.9)
Unemployed	120 (51.1)
Household income (MYR)	
Low (<MYR3000)	208 (88.5)
High (≥MYR3000)	27 (11.5)

Table 2. Clinical characteristics of patients with TB-HIV co-infection ( $n = 235$ ).

	<i>n</i> (%)
DM	
Yes	9 (3.8)
No	226 (96.2)
Smoking status	
Yes	114 (48.5)
No	121 (51.5)
BCG scar	
Present	213 (90.6)
Absent	22 (9.4)
ART	
Yes	92 (39.1)
No	143 (60.9)
Type of TB	
Pulmonary	174 (74)
Extrapulmonary	61 (26)
TB case category	
New case	199 (84.7)
Relapse	25 (10.6)
Return after default	11 (4.7)
CXR presentation upon diagnosis	
No/minimal lesion	159 (67.7)
Advanced	70 (29.8)
Not performed	6 (2.6)
Sputum smear upon diagnosis	
Positive	93 (39.6)
Negative	119 (50.6)
Not performed	23 (9.8)
Sputum culture upon diagnosis	
Positive	93 (39.6)
Negative	119 (50.6)
Not performed	23 (9.8)
DOTS status	
Yes	155 (66)
No	80 (34)
Duration of TB treatment (months)	
<6	103 (43.8)
6-12	113 (48.1)
≥12	19 (8.1)
TB treatment outcome	
Cured	47 (20)
Completed treatment	89 (37.9)
Died	72 (30.6)
Failure	22 (9.4)
Defaulted treatment	5 (2.1)

Table 3. SLR identification of factors associated with unsuccessful TB treatment outcome in patients with TB-HIV in Kuala Lumpur

Variable	SLR				$\chi^2$ (df) <sup>a</sup>	<i>p</i> -value
	Unsuccessful outcome	Successful outcome	Unadjusted OR	(95% CI)		
	<i>n</i> (%)	<i>n</i> (%)				
<b>A. Sociodemographic characteristics</b>						
Age (years)					1.34 (2)	0.511
18–39	47 (39.2)	73 (60.8)	1			
40–59	49 (44.5)	61 (55.5)	1.25	(0.74, 2.11)	0.68 (1) <sup>b</sup>	0.409
≥60	3 (60)	2 (40)	2.33	(0.38, 14.47)	0.82 (1) <sup>b</sup>	0.364
Sex						
Male	82 (40.8)	119 (59.2)	0.69	(0.33, 1.43)	1.00 (1)	0.317
Female	17 (50)	17 (50)	1			
Citizenship						
Non-Malaysian	17 (70.8)	7 (29.2)	3.821	(1.52, 9.61)	9.00 (1)	0.003*
Malaysian	82 (38.9)	129 (61.1)	1			
Ethnicity						
					11.67 (3)	0.009*
Malay	44 (38.3)	71 (61.7)	0.31	(0.14, 0.70)	7.93 (1) <sup>b</sup>	0.005*
Chinese	20 (32.8)	41 (67.2)	0.24	(0.10, 0.60)	9.45 (1) <sup>b</sup>	0.002*
Indian	13 (50)	13 (50)	0.50	(0.17, 1.44)	1.66 (1) <sup>b</sup>	0.198
Others	22 (66.7)	11 (33.3)	1			0.813
Place of residence						
					0.41 (2)	
Others (homeless/institutional)	12 (48)	13 (52)	1.32	(0.57, 3.10)	0.42 (1) <sup>b</sup>	0.519
Low-cost	27 (42.2)	37 (57.8)	1.05	(0.58, 1.90)	0.02 (1) <sup>b</sup>	0.882
Medium-/high-cost	60 (41.1)	86 (58.9)	1			
<b>B. Socioeconomic characteristics</b>						
Formal education						
No	31 (64.6)	17 (87.5)	3.19	(1.65, 6.19)	12.38 (1)	<0.001*
Yes	68 (36.4)	119 (63.6)	1			
Employment status						

Unemployed	60 (50)	60 (50)	1.95	(1.15, 3.30)	6.27 (1)	0.012*
Employed	39 (33.9)	76 (66.1)	1			
Household income						
Low	93 (44.7)	115 (55.3)	2.83	(1.10, 7.30)	5.31 (1)	0.021*
High	6 (22.2)	21 (77.8)	1			
<b>C. Clinical characteristics</b>						
DM						
Yes	3 (33.3)	6 (66.7)	0.68	(0.17, 2.78)	0.30 (1)	0.581
No	96 (42.5)	130 (57.5)	1			
Smoking status						
Yes	49 (43)	65 (57)	1.07	(0.64, 1.80)	0.07 (1)	0.797
No	50 (41.3)	71 (58.7)	1			
BCG scar						
Absent	16 (72.7)	6 (27.3)	4.18	(1.57, 11.11)	9.32 (1)	0.002*
Present	83 (39)	130 (61)	1			
ART						
Yes	30 (32.6)	62 (67.4)	1.93	(1.12, 3.33)	5.69 (1)	0.017*
No	69 (48.3)	74 (51.7)	1			
Type of TB						
Pulmonary	73 (42)	101 (58)	0.97	(0.54, 1.76)	0.01 (1)	0.927
Extrapulmonary	26 (42.6)	35 (57.4)	1			
TB case category					0.19 (2)	0.910
Relapse	11 (44)	14 (56)	1.08	(0.47, 2.49)	0.03 (1) <sup>b</sup>	1.076
Return after default	4 (36.4)	7 (63.6)	0.78	(0.22, 2.76)	0.15 (1) <sup>b</sup>	0.782
New case	84 (42.2)	115 (57.8)	1			
CXR presentation upon diagnosis					7.75 (2)	0.021
Not performed	5 (83.3)	1 (16.7)	1.70	(0.96, 2.99)	3.31 (1) <sup>b</sup>	0.069
Advanced	35 (50)	35 (50)	8.48	(0.97, 74.30)	3.72 (1) <sup>b</sup>	0.054
No/minimal lesion	59 (37.1)	100 (62.9)	1			



Sputum smear upon diagnosis					0.12 (2)	0.944
Positive	40 (43)	53 (57)	1.04	(0.60, 1.80)	0.02 (1) <sup>b</sup>	0.884
Not performed	9 (39.1)	14 (60.9)	0.89	(0.36, 2.21)	0.07 (1) <sup>b</sup>	0.797
Negative	50 (42)	69 (58)	1			
Sputum culture upon diagnosis					15.14 (2)	0.001
Positive	14 (73.7)	5 (26.3)	5.54	(1.89, 16.26)	9.73 (1) <sup>b</sup>	0.002*
Not performed	35 (52.2)	32 (47.8)	2.17	(1.20, 3.90)	6.64 (1) <sup>b</sup>	0.010*
Negative	50 (33.6)	99 (66.4)	1			
DOTS status						
No	71 (88.8)	9 (11.3)	35.78	(15.99, 80.05)	117.22 (1)	<0.001*
Yes	28 (18.1)	127 (81.9)	1			
					206.98 (2)	<0.001*
Duration of TB treatment (months)						
<6	93 (90.3)	10 (9.7)	79.05	(15.90, 393.03)	28.52 (1) <sup>b</sup>	<0.001*
6-12	4 (3.5)	109 (96.5)	0.31	(0.05, 1.84)	1.66 (1) <sup>b</sup>	0.198
≥12	2 (10.5)	17 (89.5)	1			

<sup>a</sup> Likelihood ratio (LR) test.

<sup>b</sup> Wald test.

\* Significant at  $p < 0.05$ .

Table 4. Significant determinant factors of TB treatment outcomes in patients with TB-HIV in Kuala Lumpur, the final model ( $n = 235$ ).

Characteristic	SLR					MLR		
	Unadjusted OR	(95% CI)	$\chi^2$ (df) <sup>a</sup>	$p$ -value	aOR <sup>c</sup>	(95% CI)	$\chi^2$ (df) <sup>a</sup>	$p$ -value
DOTS status								
No	35.78	(15.99, 80.05)	117.221 (1)	<0.001*	21.71	(5.36, 87.94)	24.52 (1)	<0.001*
Yes	1	-	-	-	1	-	-	-
Duration of TB treatment (months)								
			206.98 (2)	<0.001*				
<6	79.05	(15.90, 393.03)	28.52 (1) <sup>b</sup>	<0.001*	34.54	(5.97, 199.93)	15.63 (1) <sup>b</sup>	<0.001*
6-12	0.31	(0.05, 1.84)	1.66 (1) <sup>b</sup>	0.198	0.19	(0.03, 1.38)	2.72 (1) <sup>b</sup>	0.099
≥12	1	-	-	-	1	-	-	-

<sup>a</sup> Likelihood ratio (LR) test.

<sup>b</sup> Wald test.

<sup>c</sup> Adjusted for citizenship status, ethnicity, formal education, employment status, household income, BCG scar, ART, CXR upon diagnosis, sputum culture upon diagnosis, DOTS status and duration of TB treatment using the forward LR method.

\*  $p < 0.05$ .

There was no multicollinearity ( $VIF < 10$ ) and no interaction problem.

1 = reference.