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Pharmacist-led education intervention to improve pulmonary tuberculosis treatment adherence through the Health Belief Model in Malaysia: a study protocol for a randomized controlled trial

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Abstract

Pulmonary tuberculosis (TB) remains a significant global health concern, particularly in low- and middle-income countries, where treatment adherence is critical to improving patient outcomes and mitigating drug resistance. In Malaysia, challenges in adherence to TB treatment regimens continue to hinder disease control efforts. This study protocol outlines a pharmacist-led educational intervention to improve treatment adherence among pulmonary TB patients. This randomized controlled trial will enroll 206 pulmonary TB patients from public healthcare facilities in Penang, Malaysia, divided equally into intervention and control groups. The intervention group will receive tailored educational counseling sessions delivered by pharmacists at baseline and during months 2, 4, and 6, using materials developed by the World Health Organization and the Centers for Disease Control TB treatment guidelines. The control group will receive standard care. The pharmacist-led educational intervention will be structured around the Health Belief Model framework to systematically address psychological determinants of adherence. Adherence will be measured using the Medication Adherence Report Scale-5. Data will be collected at baseline and subsequent intervals to assess changes over time. The primary outcome will be to improve the treatment adherence of the pulmonary TB patients. The secondary outcomes will measure knowledge of the TB disease and health-related quality of life. This protocol describes a novel, theory-driven approach to addressing adherence barriers in TB treatment through pharmacist-led education. The study aims to contribute to the global effort to control TB and improve patient outcomes by providing evidence of the intervention's impact.

Key words: pulmonary tuberculosis, randomized control trial, treatment adherence.

Introduction

Pulmonary tuberculosis (PTB) remains a significant global health challenge, with approximately 10 million new cases and 1.5 million deaths reported annually [1]. Malaysia reported 26,781 new TB cases in 2023 (92/100,000 incidence), with suboptimal treatment success rates (84%) [2]. Despite Malaysia's progress in reducing TB incidence, the disease persists as a public health concern, exacerbated by suboptimal treatment adherence rates that contribute to prolonged infectivity, drug resistance, and increased morbidity [3]. Non-adherence to the lengthy and complex anti-TB regimen is multifactorial, often rooted in patients' misconceptions about disease severity, medication side effects, and insufficient understanding of treatment benefits [4].

The standard first-line anti-tuberculosis treatment regimen in Malaysia, as outlined in the National Tuberculosis Guidelines (Ministry of Health Malaysia, 2023), consists of a 6-month course divided into two phases. The intensive phase lasts for 2 months and involves daily administration of four drugs: isoniazid (H) at 5 mg/kg, rifampicin (R) at 10 mg/kg, pyrazinamide (Z) at 25 mg/kg, and ethambutol (E) at 15 mg/kg. This is followed by a 4-month continuation phase with daily isoniazid (5 mg/kg) and rifampicin (10 mg/kg) [5]. Traditional adherence strategies, while valuable, frequently overlook the psychosocial determinants of health behavior, underscoring the need for theory-driven interventions tailored to patients' perceptions and contexts.

The Health Belief Model (HBM) offers a robust framework to address these gaps by targeting individuals' perceptions of susceptibility, severity, benefits, and barriers to treatment [6]. The HBM has been applied in TB management across diverse settings, though with varying degrees of comprehensiveness. Several Asian studies have demonstrated partial application of HBM constructs: In India, Kulkarni et al. (2016) focused primarily on perceived susceptibility and severity in their community-based TB education program while neglecting self-efficacy components [7]. Similarly, a Vietnamese intervention by Nguyen et al. (2023) effectively addressed perceived benefits but provided limited structured approaches for overcoming barriers [8]. Pharmacists, as frontline healthcare providers, are uniquely positioned to deliver structured, patient-centered education grounded in HBM principles, leveraging their expertise in medication management and accessibility within communities [9]. To target perceived susceptibility, pharmacists use visual aids to illustrate TB transmission risks, emphasizing how non-adherence increases personal and community vulnerability [10]. For perceived severity, they explain potential complications (e.g., drug-resistant TB) through patient-tailored examples, linking these outcomes to participants' lived experiences [11]. To strengthen perceived benefits, pharmacists highlight treatment efficacy using clinic-specific success rates, demonstrating how adherence

reduces infectiousness and restores daily function. However, evidence on pharmacist-led interventions using HBM to improve PTB adherence remains limited in low- and middle-income settings, including Malaysia.

This study protocol outlines a randomized controlled trial (RCT) to evaluate the efficacy of a pharmacist-led educational intervention, guided by the HBM, in enhancing treatment adherence among PTB patients in Malaysia. By integrating behavioral theory with pharmacists' clinical roles, the intervention aims to empower patients through personalized counseling, addressing knowledge gaps, perceived barriers, and motivational drivers. The findings will contribute to scalable, evidence-based strategies for TB control in Malaysia and similar settings while advancing the understanding of theory-informed adherence interventions in infectious disease management.

Materials and Methods

Study design

A single-blinded non-clinical randomized controlled prospective study will be carried out in this phase. A simple approach will be used, i.e., one control group and one intervention group. The included patients are diagnosed with PTB based on the National Treatment Guideline under the Directly observed therapy (DOT) strategy by the Health Ministry of Malaysia and WHO [12]. The DOT approach follows Malaysia's standardized national TB guidelines, which mandate thrice-weekly supervised medication administration for all patients. The participants will not be aware of the group assignments (single-masked). The intervention group will receive counselling after baseline data collection, while the control group will receive the usual standard DOT therapy and counselling from the nurses. Assessments will be carried out at baseline, two, four, and six months. This RCT study is registered with clinicaltrials.gov under the ID NCT06608069. The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions, and assessments is added in Figure 1.

Study setting

The study will be conducted at the respiratory clinic in Hospital Pulau Pinang, Malaysia. Penang has a significant burden of PTB cases, making it a relevant location for studying TB-related issues. Penang was selected because of the large number of PTB cases, which is more than 1,000 yearly [13].

Study participants

Individuals who have been clinically diagnosed with PTB and will be undergoing treatment during the duration of the study in the respiratory clinic, Hospital Pulau Pinang, will be involved in the study. Permission will be sought from the hospital authority to allow the researcher to collect the information from PTB patients.

Eligibility criteria

Patients who will meet the following requirements will be included in this study, 1) Patients diagnosed with PTB by sputum smear and chest X-ray and are receiving first-line anti-TB drugs. 2) TB patients who can give informed consent physically and who can abide by the provided intervention with no difficulty. 3) Patients who can commit to the entire course of the study. 4) Patients who can understand and speak the English and Malay languages. 5) Patients aged 18 years or older.

Ethical approval

The ethical study approval is obtained from the hospital and the Medical Research & Ethics Committee (MREC) under the Malaysian Ministry of Health, with reference numbers NMRR ID-22-01964-WWH (IIR) and Jawatankuasa Etika Penyelidikan Manusia USM (JEPeM) from Universiti Sains Malaysia JePEM: USM/JEPeM/PP/23120985.

Sample size calculation

Sample size estimation was calculated using the two-population means formula [14,15]. The mean adherence score for the control and intervention groups was observed from the previous literature to support the calculations [16]. The sample size was calculated based on the study's primary objective, to evaluate the impact of pharmacist intervention to improve treatment adherence;

$$n = (Z\alpha/2 + Z\beta)^2 \times 2 \times \sigma^2 / d^2$$

$Z\alpha/2$ = the critical value of the Normal distribution at $\alpha/2$ (e.g., for a confidence level of 95%, α is 0.05, and the critical value is 1.96), $Z\beta$ = the critical value of the Normal distribution at β (e.g., for a power of 80%, β is 0.2, and the critical value is 0.84), $\sigma = 0.25$ (assuming a 25% variability in adherence rates), $d = 0.10$ (10% difference between both groups). The sample size will be 98 per arm. By taking into account a 5% attrition rate, a total sample size of 98 (98 + 5 = 103) participants will be required for each group, giving a total sample size of 206 participants. A 5% attrition rate

was adopted based on a recent Malaysian TB study reporting 3-6% attrition when using active follow-up protocols [17].

Sampling method

Participants will be selected using a sequential sampling method. Sequential random sampling is ideal as it promotes unbiased participant selection, supports the validity of the results, and ensures that the sample is representative of the population [18]. Clinic nurses will identify potential participants during routine TB registration, verifying inclusion/exclusion criteria (e.g., confirmed PTB diagnosis, age 18 years). This allows the intervention's outcomes, such as improved treatment adherence or patient knowledge, to be more accurately attributed to the intervention itself and generalizable to broader settings.

Validation of the HBM questionnaire

To rigorously assess HBM constructs, we will employ a validated 20-item HBM questionnaire adapted from previous TB adherence studies [11,19-21]. The instrument measures five subscales: Perceived Susceptibility (3 items, e.g., "How likely do you think you are to develop drug-resistant TB if you miss doses?"), Perceived Severity (4 items, e.g., "How serious would drug-resistant TB be for your daily life?"), Perceived Benefits (4 items, e.g., "How much do you believe treatment will restore your health?"), Perceived Barriers (5 items, e.g., "How often do side effects make you consider stopping treatment?"), and Self-Efficacy (4 items, e.g., "How confident are you in taking medications on time?"). Each subscale uses a 5-point Likert scale (1 = "Strongly disagree" to 5 = "Strongly agree"), with higher scores indicating stronger beliefs. The questionnaire was translated into Malay following WHO guidelines (forward-backward translation) and validated, demonstrating good internal consistency (Cronbach's $\alpha = 0.78–0.86$ across subscales) and test-retest reliability (ICC = 0.81–0.89).

Data collection

All the recruited patients will be well informed that the data in the form of information will only be required from them. The data from the patients will be collected initially at the baseline, then at the 2nd month, 4th month, and the 6th month. PTB treatment typically spans 6 months.

Stigma mitigation and participation

To address the potential impact of TB-related stigma on participation and ensure robust confidentiality protections, we will implement a comprehensive protocol. For stigma mitigation, all study procedures will be designed with discretion in mind - recruitment and counselling sessions will occur in private clinic rooms separate from general TB wards, and study materials will use neutral labelling without explicit TB terminology to avoid unintended disclosure. Our research team, including pharmacists and nurses, will communicate non-judgmentally. For confidentiality protection, we will employ rigorous data handling procedures where all identifiable participant information is immediately replaced with coded IDs upon collection, with the master key stored securely in a password-protected file accessible only to the principal investigator.

Intervention

The educational intervention will be provided to patients via a structured pharmacist-led counselling program aimed at improving treatment adherence, treatment outcomes, TB knowledge, and health-related quality of life. The educational material for the intervention is taken from the validated developed global and national TB guidelines, including the WHO TB guidelines, the Centers for Disease Control and Prevention (CDC) guidelines, and the Ministry of Health (MOH), Malaysia guidelines [22,23]. The content validation is done by three academic researchers, experts in infectious diseases, and two doctors in the hospital. Face validation will also be done to ensure the clarity of the content and understanding of the patients.

During the initial sessions, patients will be introduced to the basics of PTB, the treatment process, and the expected outcomes. In follow-up sessions, the pharmacist will reinforce key messages, address any difficulties patients are experiencing, and provide additional support to ensure adherence. Each counselling session will include time for patients to ask questions and express concerns, allowing the pharmacist to address any misunderstandings and empower patients to take an active role in managing their health. This interactive approach will foster a strong patient-pharmacist relationship, which is crucial in overcoming psychological barriers such as fear or stigma associated with PTB. The intervention will be carefully documented to track patient progress and ensure consistency across all participants.

The pharmacist-led educational intervention comprises four structured, one-on-one counseling sessions delivered at baseline, 2, 4, and 6 months. The baseline session (Session 1) focuses on three key HBM constructs: (1) Perceived Susceptibility/Severity, where patients learn about PTB

transmission, disease progression, and risks of non-adherence (e.g., drug resistance); (2) Perceived Benefits, emphasizing treatment efficacy and long-term health outcomes; and (3) Self-Efficacy, where pharmacists teach practical strategies (e.g., pill organizers) to overcome adherence barriers. Follow-up sessions (Sessions 2–4) reinforce HBM principles by addressing Cues to Action (e.g., SMS alerts, family support) and dynamically problem-solving emerging Perceived Barriers (e.g., side effects, stigma, financial constraints) through role-playing or motivational interviewing. Each session lasts 30 minutes and is supported by WHO/CDC-approved materials (e.g., visual aids, pamphlets) to ensure consistency and patient comprehension.

Intervention fidelity

To ensure fidelity to the pharmacist-led HBM intervention, we will implement a comprehensive monitoring system combining structured protocols and quality checks. Pharmacists will follow standardized checklists during each counselling session to systematically address all HBM domains, with timing markers to ensure consistent content delivery. Additionally, the principal investigator will conduct in-person observations of 5% of sessions to evaluate real-time protocol implementation. Pharmacists will receive extensive pre-study training including 8 hours of role-playing with standardized patients and will have to demonstrate competency before participating, followed by monthly refresher workshops to address challenges and maintain intervention consistency.

Intervention group

In addition to their regular treatment, all patients in the intervention group will receive individualized patient care from a pharmacist. The educational module will remind the participants about TB medication adherence and provide recommendations for managing poor medication adherence. Direct patient monitoring, lifestyle modification education, and counselling are among the services that will be provided by the pharmacist.

Control group

The control group members will receive the same routine standard treatment care, DOTS, by the TB clinic nurse but no educational intervention during the study. DOT is a strategy used in the management of PTB to ensure that patients adhere to their treatment regimens [24]. In DOT, healthcare providers, community health workers, or trained individuals directly observe and monitor patients as they take their TB medication, ensuring that each dose is taken as prescribed.

Outcome measures

The primary outcome of this study is to improve treatment adherence among pulmonary tuberculosis patients, as measured by the validated Medication Adherence Report Scale-5 (MARS-5) questionnaire, which is available in both English and Malay versions [25]. The MARS-5 assessee specific non-adherence behaviors: forgetting to take medication, altering prescribed dosages, prematurely stopping treatment, omitting doses, and intentionally reducing medication intake. The MARS-5 score ranges from 5 to 25, with higher scores reflecting greater self-reported adherence. One item evaluates unintentional non-adherence, while four items evaluate intentional non-adherence [26]. Additionally, pharmacy refill records will be evaluated to verify medicine collection.

The secondary outcome will be to measure the pulmonary tuberculosis disease knowledge. The data will be collected through a pre-validated Malay and English language version of the TB knowledge, attitude, practice, and stigma (KAPS) questionnaire, after permission from the author [27]. The questionnaire encompassed three subdomains: general understanding of TB (11 items), symptoms (9 items), and prevention (5 items). Responses will be recorded as '1' for correct answers and '0' for incorrect answers or uncertainty. The highest possible score for knowledge was 25.

Another secondary outcome is a measurement of Health-Related Quality of Life. The EQ-5D instruments have been developed by the EuroQol Research Foundation to describe the patient-reported quality of life in a wide range of diseases [28]. The EQ-5D 3L comprises two major parts. Part one is further divided into three domains, which are Usual Activities, Pain /Discomfort, and Anxiety / Depression. For the evaluation of each domain, there are three response levels which include no problems, moderate problems, and severe problems. Part two of the EQ-5D 3L belongs to the EQ-VAS score, which is a vertical visual analogue scale with the labelled endpoints 'the best health respondent can imagine' and 'the worst health that respondent can imagine.

The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions, and assessments is added in Figure 1.

Statistical analysis

This data analysis will be done using SPSS version 29. For descriptive statistics, continuous data were expressed as mean ± standard deviation (SD), whereas categorical data will be presented as numbers and percentages, i.e., n (%). For the comparison of categorical data between groups, the chi-square test will be used to compare the differences between the two groups. As for continuous

data, an independent sample t-test will be used. For the primary and secondary interests of analysis, multivariable regression model analysis will be employed to adjust for confounding factors in the statistical effect. A value of $p < 0.05$ was considered statistically significant [29,30]. Proactive measures (e.g., monthly patient reminders, flexible visit windows, and backup data collection via phone) will minimize missing data. All missing data, imputation methods, and assumptions will be reported per CONSORT guidelines.

Results

Upon trial completion, results will be reported by CONSORT guidelines. Participant flow will be illustrated via a CONSORT diagram, detailing enrollment, allocation, follow-up, and analysis. Baseline sociodemographic and clinical characteristics (e.g., age, gender, baseline HBM scores, TB severity) will be compared between intervention and control groups to confirm randomization efficacy.

We anticipate that participants receiving the pharmacist-led HBM intervention will demonstrate significantly higher treatment adherence rates (primary outcome) compared to the standard DOT group, with a projected absolute difference of 15% in the proportion achieving 80% dose adherence. This will be analyzed through intention-to-treat principles using multilevel logistic regression adjusted for baseline covariates (age, comorbidities, urban/rural residence), reporting both adjusted odds ratios and number needed to treat (NNT) with 95% confidence intervals. For secondary outcomes, we expect meaningful improvements in HBM constructs - particularly in perceived barriers (estimated Cohen's d = 0.4) and self-efficacy (d = 0.35) - analyzed via linear mixed-effects models accounting for repeated measures. Subgroup analyses will explore intervention effects across key demographics. To evaluate the intervention's scalability across diverse settings and populations, we will conduct pre-specified subgroup analyses comparing: (1) urban versus rural participants (categorized by residential postal codes), given documented disparities in healthcare access; (2) younger versus older patients, as age may influence adherence barriers (e.g., work demands vs. comorbidities); and (3) high-risk (baseline MARS-5 15) versus lower-risk (>15) patients, to assess tailored efficacy.

Discussion

This trial will provide critical evidence on the effectiveness of a pharmacist-led educational intervention grounded in the Health Belief Model (HBM) to improve adherence to pulmonary tuberculosis (PTB) treatment in Malaysia. If successful, the findings will underscore the value of

integrating behavioral theory into pharmacist-delivered care, particularly in addressing modifiable determinants of non-adherence such as perceived barriers (e.g., medication side effects) and low self-efficacy. Conversely, null results may highlight contextual challenges unique to Malaysia, such as stigma or structural barriers to care, which future interventions should prioritize.

The study's theoretical contribution lies in its explicit linkage of HBM constructs to TB adherence behaviors, offering insights into which psychological drivers (e.g., perceived severity of drug resistance) most strongly influence patient motivation. By focusing on pharmacists—a widely accessible yet underutilized resource in Malaysia's TB response—this trial may catalyze policy shifts toward task-shifting in adherence support, aligning with WHO recommendations for multidisciplinary TB care.

While the RCT design strengthens internal validity, limitations such as reliance on self-reported adherence and the short follow-up period (6 months) may affect generalizability. However, the use of multiple adherence metrics (e.g., Pharmacy record fill, MARS 5 scores) and intention-to-treat analysis will mitigate bias. To minimize the performance bias both groups will receive identical baseline assessments and follow-up schedules. Future research should explore the intervention's long-term impact on relapse rates and evaluate cost-effectiveness to inform scalability.

Ultimately, this trial has the potential to advance Malaysia's TB elimination agenda by demonstrating a scalable, theory-driven strategy to improve adherence, reduce transmission, and curb drug resistance—a model that could be adapted for other LMICs facing similar challenges.

Conclusions

This study will provide robust evidence on the effectiveness of a pharmacist-led, Health HBM-based educational intervention in improving treatment adherence among (PTB patients in Malaysia. By integrating behavioral theory with pharmacists' clinical expertise, the intervention addresses critical psychosocial barriers to adherence while maintaining the proven benefits of directly observed therapy (DOT).

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	STUDY PERIOD					
	Enrolment	**Allocation**	**Baseline**	**2 months**	**4 months**	**6 months**
TIMEPOINT**	***-t_1***	**0**				
ENROLMENT:	X					
Eligibility screen	X					
Informed consent	X					
[List other procedures]	X					
Allocation		X				
INTERVENTIONS:						
[Intervention group]						
[Educational intervention based on HBM to improve PTB adherence]			←	—	→	
			X	X		
[Control group]						
[No educational intervention based on HBM to improve PTB adherence]			←	—	→	
ASSESSMENTS:						
[TB Adherence by MARS-5 scale]			X	X	X	X
[TB-Knowledge questionnaire]			X	X	X	X
[Health Belief Model questionnaire]			X X	X X	X	X

Figure 1. SPIRIT schedule of enrolment, interventions, and assessments.