

**TUBERCULOSIS CONTACT REMINDER
SYSTEM IN IMPROVING TUBERCULOSIS
SCREENING AND RETENTION RATE IN
PERAK: AN INTERVENTIONAL STUDY**

by

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- D. Consent form and research information sheet
- E. Tuberculosis Contact Reminder System Manual Guide
- F. *Soal Selidik Kepuasan Pengguna Sistem Elektronik (Perubatan dan Kesihatan)*
- G. Proforma form
- H. TCRS Invitation card
- I. Screening notice
- J. Reminder letter
- K. TCRS Appreciation card

LIST OF ABBREVIATIONS

Adj. OR	Adjusted odds ratio
AFB	Acid fast bacilli
AIDS	Acquired immune deficiency syndrome
aMR	Adjusted mean ratio
APPPB	Akta Pencegahan & Pengawalan Penyakit Berjangkit
ART	Antiretroviral therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CONSORT	Consolidated Standards of Reporting Trials
CVI	Content validity index
CXR	Chest x-ray
DOSM	Department of Standard Malaysia
DOTS	Directly observed treatment short course
EMR	Electronic medical record
EPTB	Extra-pulmonary tuberculosis
FVI	Face validity index
GSM	Global System for Communications
HIC	High income countries
HIV	Human immunodeficiency virus
HMB	Health belief model
I-CVI	Item content validity index
IDR	Institute Darul Ridzuan

IGRA	Interferon-Gamma Release Assays
TBIS	Tuberculosis Information System
JEPeM	Jawatankuasa Etika Penyelidikan Manusia USM
JKN	Jabatan Kesihatan Negeri
JKN(P)	Jabatan Kesihatan Negeri (Perak)
KPI	Key performance indicator
LCMI	Low and middle-income countries
LTBI	Latent tuberculosis infection
MCMC	Malaysian Communications and Multimedia Commission
MDR	Multi-drug resistance
mHealth	Mobile health
MOH	Ministry of Health
NCD	Non-communicable disease
NGT	Nominal group technique
NMRR	National Medical Research Register
OPD	Out-patient department
OR	Odds ratio
PDA	Personal digital assistance
PMT	Protection motivational theory
PMTCT	Prevention of mother-to-child transmission
PPE	Personal protective equipment
PPKP	Penolong pegawai kesihatan persekitaran
PTB	Pulmonary tuberculosis
COPD	Chronic obstructive pulmonary disease
RCT	Randomized controlled trial

RD	Risk difference
RM	Ringgit Malaysia
ROC	Receiver operating curve
RR	Relative risk
SCT	Social cognitive theory
S-CVI	Scale-level content validity index
SD	Standard deviation
SMS	Short message system
TCRS	Tuberculosis Contact Reminder System
SPSS	Statistical Package for the Social Sciences
STD	Sexually transmitted diseases
TB	Tuberculosis
TPB	Theory of planned behavior
TRA	Theory of reasoned action
TST	Tuberculin skin test
UIP	Unit Inspektorat dan Perundangan
USM	Universiti Sains Malaysia
WHO	World Health Organization
XDR	Extensively drug-resistant tuberculosis

ABSTRAK

PENGUNAAN SISTEM PERINGATAN KONTAK TUBERCULOSIS BAGI MENINGKATKAN KADAR SARINGAN TUBERKULOSIS DAN KADAR RETENSI DI PERAK: KAJIAN INTERVENSI

Latar belakang: Saringan tuberkulosis dalam kalangan kontak adalah salah satu asas kepada kejayaan dalam mengawal penyakit tuberkulosis (tibi). Kadar saringan dalam kalangan kontak di Perak, Malaysia adalah rendah dari tahap yang ditetapkan. Tempoh saringan penyakit yang panjang menjadi cabaran besar untuk mengekalkan kadar saringan dan retensi dalam kalangan kontak.

Objektif: Objektif kajian ini adalah membandingkan keberkesanan di antara sistem yang baru dibangunkan iaitu Sistem Peringatan Kontak Tuberkulosis (TCRS) berbanding sistem semasa dalam meningkatkan kadar saringan dan kadar retensi pada saringan berikutnya dalam kalangan kontak tibi, tahap kepuasan anggota dan diskriptif kos pelaksanaan.

Metodologi: Kajian ini merupakan sebuah kajian operasi, prospektif, secara selari dan pragmatik melalui percubaan kawalan rawak secara kluster di Perak dengan empat daerah yang dipilih secara rawak dan diagihkan secara peruntukan rawak bagi sama ada menerima TCRS atau sistem semasa. Data dianalisa menggunakan perisian SPSS versi 24. Analisa regresi logistik mudah dan berganda digunakan untuk menilai keberkesanan intervensi. Soal selidik kepuasan pengguna digunakan untuk menilai tahap kepuasan anggota kesihatan dan analisa deskriptif kos pelaksanaan.

Keputusan: Sejumlah 288 kontak tibi telah direkrut antara 12 Februari hingga 11 Mei 2018. Dua subjek di dalam kumpulan intervensi telah dikecualikan berpindah ke negeri lain dan satu meninggal dunia kerana sakit tua menyebabkan kumpulan intervensi berbaki 141 subjek manakala 144 subjek didalam kumpulan kawalan. Kadar pengambilan saringan tibi keseluruhan secara signifikan adalah lebih tinggi bagi kumpulan intervensi berbanding kawalan OR 2.48 (95% CI; 1.20, 5.12) dan Adj. OR 3.16 (95% CI; 1.26, 7.85) dengan pelarasan ciri-ciri asas. Kadar retensi terhadap saringan seterusnya adalah lebih tinggi pada kumpulan intervensi berbanding kawalan dengan OR 3.74 (95% CI; 2.25, 6.22) dan Adj. OR 2.26 (95% CI; 1.18, 4.34) dengan pelarasan ciri-ciri asas. Kesemua responden mendapati sistem ini adalah berguna (100%) dan majoriti 81.8% berpuas hati secara keseluruhan. Namun, separuh daripada responden berpendapat bahawa sistem itu telah berjaya dilaksanakan. Kos sistem peringatan ini ialah sebanyak RM 0.87 untuk pemeriksaan TB pertama dan RM 0.57 bagi pemeriksaan berikutnya. Kos tambahan sebanyak RM 1.03 sekiranya tidak hadir saringan.

Kesimpulan: Pengambilan saringan dan kadar retensi terhadap saringan tuberkulosis dalam kalangan kontak boleh dipertingkatkan secara berkesan oleh TCRS, serentak mengurangkan jumlah cicir saringan, meningkatkan kepatuhan kepada program saringan dan mengurangkan pengesanan kes cicir. TCRS berpotensi menjadi sistem sokongan baru terhadap sistem sedia ada.

Kata kunci: tuberkulosis, kontak, peringatan, saringan.

ABSTRACT

TUBERCULOSIS CONTACT REMINDER SYSTEM IN IMPROVING TUBERCULOSIS SCREENING AND RETENTION RATE IN PERAK: AN INTERVENTIONAL STUDY

Background: TB screening among contacts remains the cornerstone of successful TB control. Uptake of TB screening among contact in Perak, Malaysia was below required standard. Long duration of TB screening become great challenges to maintain the screening uptake and retention rate among TB contacts.

Objectives: The objective of this study was to compare the effectiveness between the newly developed Tuberculosis Contact Reminder System (TCRS) and current system in improving the screening uptake and retention rate in the subsequent screening among TB contacts, staffs' satisfaction and description of implementation cost.

Methodology: An operational research with prospective, parallel and pragmatic design through cluster randomized control trial was conducted in Perak by randomly selected four districts and cluster randomized into group either received TCRS or current system. Data analysis was conducted using SPSS software version 24. Simple and multiple logistic regression analysis were applied to estimate the effectiveness. User satisfaction questionnaire was used to assess the staffs' satisfaction level and descriptive analysis of cost of implementation.

Results: A total of 288 TB contacts were recruited between 12th February and 11th May 2018. Two of the subject in intervention group were excluded due to being transferred to other state and one died of old age which left the intervention group with 141 subjects in the intervention and 144 subjects in the control group. The total screening uptake was significantly higher in intervention compared to control OR 2.48 (95%CI; 1.20, 5.12) and Adj. OR 3.16 (95%CI; 1.26, 7.85) with adjusted baseline characteristic. Higher retention for subsequent TB screening was observed in the intervention group OR 3.74 (95%CI; 2.25, 6.22) and Adj. OR 2.26 (95%CI; 1.18, 4.34) with adjusted baseline. All respondents found the system was useful (100%) and the majority of respondents, 81.8% were satisfied overall. However, half of the respondents agreed that the system was successfully implemented. The cost of reminder system was RM 0.87 and RM 0.57 for first TB screening and subsequent screening respectively. Additional cost RM 1.03 were incurred in case of defaulted contact.

Conclusion: The uptake and retention toward TB screening among contacts can be effectively reinforced by TCRS, simultaneously reduced the number of defaulters, increase compliance to screening program and reduce need of defaulter tracing. TCRS may be a new promising system which can be considered in supporting existing contact TB management.

Keywords: Tuberculosis, contact, reminder, screening.

CHAPTER 1

INTRODUCTION

1.1 Tuberculosis Disease

Tuberculosis (TB) remain one of the deadliest infectious disease ranked top 10 leading causes of mortality worldwide. Statistic showed 10.4 million people fell ill from TB, which equals to 28,500 people every day. Approximately 1.8 million people died from TB including 400,000 with TB-HIV co-infection equivalent to 4,900 people dying from TB every day (WHO, 2016). TB disease caused by bacteria called *Mycobacterium tuberculosis* which transmit from person to person through air droplet when people with infectious TB disease cough or sneeze. Droplet nuclei able to stay in the room air about 5 to 30 minutes up to several hours depending on humidity and other environmental factors before inhaled by another person (Lever *et al.*, 2000; CDC, 2015). Once infected, there will be two TB related condition which is state of Latent TB infection (LTBI) or active TB disease.

Despite the cure for TB disease being discovered long ago since 1940s where millions of people treated every year, the annual incidence of TB disease decline approximately only 2% worldwide, far from the expectation of 4 to 5% per year to reach the first milestone of the End TB Strategy in year 2020 (WHO, 2018). There were two main reason in hold back from rapid decline of TB incidence despite of availability of effective treatment was first, missed or late diagnosis of TB cases particularly in high density population, crowded and poorly ventilated environment and secondly, large pool of latent TB infection which will continue to generate more

cases in the future (Lönnroth *et al.*, 2013). All these cases will constantly be transmitting the disease in the community and creating new infections in a never ending cycle (Yuen *et al.*, 2015; WHO, 2018). Combating infectious disease without stopping the disease transmission is like emptying a bathtub while the tap water is still flowing.

1.2 Situation in Malaysia and Perak

Malaysia was categorized as intermediate TB burden country with TB incidence 79.45 per 10⁵ population. TB disease was second most common communicable disease after Dengue Fever in this country (MOH, 2017). TB death was the highest mortality rate among all communicable disease in Malaysia at 5.56 per 10⁵ population. The incidence of TB showed steadily increasing in trend since 2002 and the ministry of health recently announced that the number of cases rose by 6% and TB death increased by 15% in 2016 compared to the previous year which made TB disease as one of the re-emerging disease that requires serious attention.

The incidence of TB in Perak steadily increasing in trend since 2011 from 53.6 to 66.6 per 10⁵ population but still lower than the national TB incidence in the same year (JKNP, 2016). Unfortunately the incidence of TB death in this state was 6.2 per 10⁵ population higher than the national TB death and exceeds the performance indicator which only allows less than 5 TB mortality per 100,000 population (JKNP, 2016).

One of the common issue in management of TB disease was poor attendance of TB screening and high default rate in the screening which lead to incomplete TB screening among identified TB contact. Four years data showed that on average, the

rate TB screening uptake severely reduce in the subsequent screening from 87% who attended the first screening (at 0 month), to 10.5% in the second screening (at 3rd month), to 4.1% in the third screening (at 6th month) and only 1.3% completed until fourth screening (at 12th month). Therefore, only KPI for 1st contact screening was achieved the target more than 70%. Whereas, 4th screening was far from the target which set at more than 25% of TB contacts complete until 4th screening.

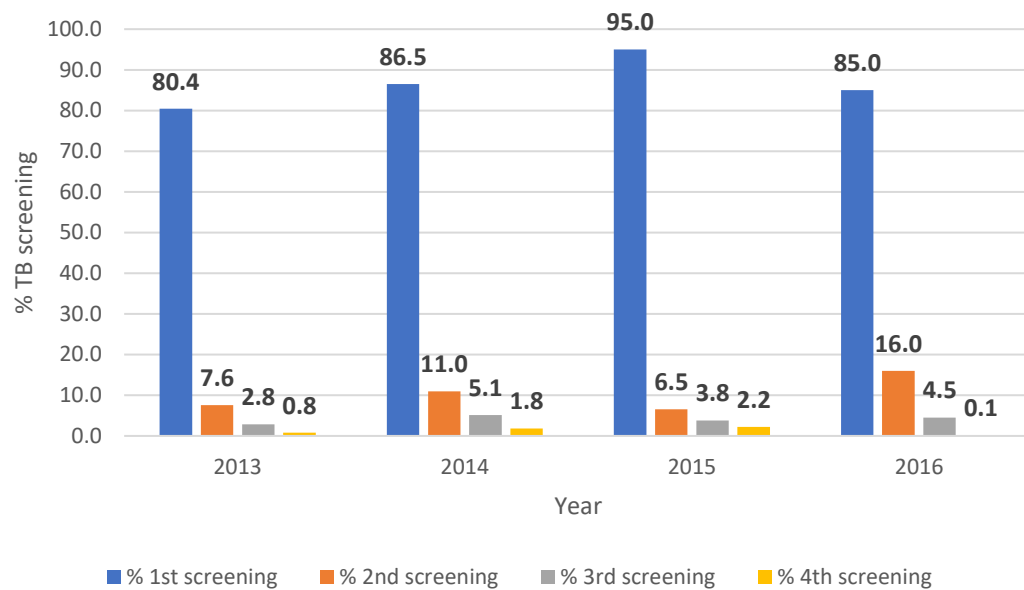


Figure 1.1: Screening uptake in Perak from 2013 to 2016 among TB contacts.

1.2.1 Latent TB infection and reactivation of TB

Prevalence of LTBI among household contacts of index cases in Malaysia was relatively high at 52.8% (Elmi *et al.*, 2014b). People with LTBI appear to be healthy until reactivation of *Mycobacterium tuberculosis* which will cause active TB disease within first two years up to seven years after exposure (Ling *et al.*, 2011). Lifetime risk of developing TB is about 5-15% or more in immunocompromised patients, people with chronic disease and younger age (Sloot *et al.*, 2014; Ai *et al.*, 2016; Campbell *et al.*, 2016). The highest risk of developing TB was at less than 6 months

and may occur earlier and have a higher chance in immunocompromised individuals and younger age group (Sloot *et al.*, 2014; Ai *et al.*, 2016).

1.2.2 Active TB and spreading of TB disease

Active TB refers to people that have been infected with *Mycobacterium tuberculosis* and manifested signs or symptoms of TB disease. It differs from LTBI which does not manifest signs or symptoms of any active disease. An active TB cases must be treated as early as possible without any delay using specific regime Direct Observed Therapy, Short Course (DOTS) (WHO, 2013b). Each person with untreated active TB disease may infects, on average 10 to 15 people every year (WHO, 2010). However, due to the long treatment and follow-up period, this may lead to reduction in compliance to standard TB management for both patient and contact. Finally, these factors resulted in an incomplete treatment, high defaulters rate, development of resistance TB and perpetuates the persistent TB transmission in the population (MOH, 2012).

1.2.3 TB contacts

TB contacts are generally defined as people who have been exposed to TB patients in close environments or casual exposure such as sharing a living or working space and casual exposure such as during a social function, congregation prayer and on public transport (WHO, 2012). There is no standard definition for TB contacts given in the guideline of management tuberculosis disease (MOH, 2012). Failure of contact tracing and screening will eventually lead to spreading of the disease in wider population due to late detection of active TB disease, prolonged duration of infectiousness and reactivation latent TB later among contacts (WHO, 2013b; Ariffin

et al., 2015). Due to the long period of dormancy in LTBI patient, periodic screening for all TB contacts is vital to curb the spreading of TB disease (WHO, 2013b). Therefore such missed cases are now recognized as one of the most important challenges facing TB control globally (WHO, 2013a).

In current practice, all TB contacts were identified by health inspector during case investigation on an index TB case. Those identified contacts obligated to undergo a systematic TB screening at nearby chest clinic. The screening consisted of few follow-ups at 0 month for first screening, after 3-month intervals for second screening, followed by third screening after another 6 months interval from the previous screening and the fourth screening, which was 12 months after the third screening (MOH, 2012). The screening was held in health clinics or chest clinic in hospital. In general, chest x-ray was the first line investigation for TB screening and three sample of sputum for acid fast bacilli (AFB) test for symptomatic contact. Tuberculin skin test (TST) were given to those asymptomatic based on the clinical evaluation of their risk. There was other method of contact screening being practiced in this state such as Interferon Gamma Release Assays (IGRA) which has less false positive value and higher positive predictive value than TST (MOH, 2012). However, it is more expensive and only used in special cases or circumstances, but not in daily practices

The ratio of 1:10 was a key performance indicator or target used to enhance contact tracing for every notified index TB case currently practiced in Perak (JKNP, 2016). In every notification of a new TB case, the healthcare staff shall find at least 10 TB contact for that index case. This was to ensure that we have do our best to search for those who has been exposed to TB bacilli from index case or the potential primary case that transmitting the disease. There were 13011 to 19468 TB contacts

identified in Perak between 2013 and 2016 (TBIS, 2017). Eighty nine percent loss of follow up at the second screening and 98% did not completed the whole course of TB screening. The screening was set at very long interval between each follow-up which cause high number of defaulter among TB contact with various reason of not attending the screening. However, one of the popular reason of not attending appointment was forgot the appointments date, forgot to make an early arrangement with daily routine, working, not see it as an important thing to do especially in asymptomatic and healthy (Zailinawati *et al.*, 2006; Liew *et al.*, 2009; Abbas and Yusof, 2011; Triasih *et al.*, 2016). Thus, cause low turn up rate for contact screening. Based on the current performance rate of contact screening we have lost approximately at least range between 58 and 98 new TB cases or case contact per year since 2013 to 2016 due default TB screening. The calculation was based on the previous study by Atif *et al.* (2012) with yield of TB among contact 0.5% from screened contact. However, the actual number of missed TB cases could be more that than.

1.2.4 Act and regulation in TB disease

Enforcing legislation is one of the effective tools in public health which is widely used in NCD such as control of tobacco and alcohol and in communicable disease such as tuberculosis disease, dengue control, recently zika and ebola virus disease (Anderson *et al.*, 2009; Hershey *et al.*, 2017). Health legislation facilitate the control of TB disease by the regulation of prevention and control of communicable disease (Coker *et al.*, 2007).

There are three main strategies which are closely related to health legislation in prevention and control of TB disease such as, 1) identification and treatment of people with TB disease; 2) detection of person exposed to TB infection including the evaluation process to determine the status of TB infection or disease and providing an appropriate treatment; and 3) prevent progression of disease by testing high risk population and providing an appropriate treatment (Jeffries *et al.*, 2017). The regulatory authority has the right to detain, medically examine and conditionally release persons who were believed to have TB disease in order to prevent introduction and spreading of the disease. Similar to those who has been exposed or infected was subjected to the right of local authority to quarantine, isolate or place under surveillance for a certain duration (Jeffries *et al.*, 2017). Study showed European countries has implemented stricter legislation to combating tuberculosis through compulsory screening, examination, vaccination treatment, isolation and detention which shown to be effective (Coker *et al.*, 2007).

Tuberculosis is one of the mandatory notifiable infectious disease in Malaysia. CDC Act 1988 (Act 342) stated that all TB cases must be notified by written notification using the standard notification form within a week after diagnosis has been made. Failure to comply to such obligation will be liable to be compounded (Act 342, 1988). In section 15 subsection (1), CDC Act 1988, allow an authorized officer to order any contact of infectious disease to undergo necessary screening or examination. Legal preparedness is a critical component in the control of infectious diseases such as TB disease and many other public health threats. In the case of high non-attendance and defaulter rate, strong and coordinated method of intervention were required to support the whole system (Mukherjee *et al.*, 2016).

1.3 Telemedicine and mhealth (mobile health)

Mobile health or mHealth is growing in popularity for the past few decades. The mHealth was defined by WHO as a medical and public health practice supported by mobile devices such as mobile phone, monitoring devices, personal digital assistance (PDA) or other wireless devices (Kay *et al.*, 2011). Mobile health offers a unique solution to a specific challenge in medical environment. The revolution of mHealth intervention not only occurs in high income countries but also in low and middle income countries covering various diseases and problems such as in the management of chronic disease, glycaemic control, reducing hospitalization, coronary artery disease, weight loss reduction program, behavioural and lifestyle changes, process care, attendance rate, medication adherence in TB and HIV disease (Marcolino *et al.*, 2018). The secret of mHealth success in intervention lies in their ability to enable disease management, general wellness motivation, providing action feedback and encourage self-management (McLean *et al.*, 2016).

Mhealth has an extremely wide coverage with the reported GSM signal coverage cover over 85% of the world's population far beyond the reach of the electrical grid (Kay *et al.*, 2011). A survey showed that 97.5% of Malaysian have access to mobile phone in 2015. The figure was 3.3% higher compared to year 2013 (DOSM, 2017). Whereas the percentage of household access to mobile phone were almost saturated with 0.9% increase to 97.9% in 2015 (DOSM, 2017). The penetration rate in Malaysia and Perak was 144.2 and 149.2 per 100 inhabitants respectively. Perak was the fifth largest share of handphone user 8.5% in Malaysia (MCMC, 2014). Even in the study conducted in the past 6 years in east coast of peninsular Malaysia 86% of the patients owned at least a mobile phone (Lua and Neni, 2012). Wide usage

of mobile phone in this country give an opportunity to improve the uptake of TB screening among TB contacts. There were few evidences from local study showed that mobile phone was significantly effective in improving medication adherence, screening uptake and clinic attendance (Rashid *et al.*, 2013; Khonsari *et al.*, 2015; Abdulrahman *et al.*, 2017a).

People always have their mobile phone with them, which allow them to be connected at all time. Seventy six percent of our population will turn back to get their phone if they left it at home and 71.4% constantly check their handphones even when it does not ring (MCMC, 2014). Therefore, the high connectivity with their mobile gadget give a great advantage to serves as a reminder tool to alert on the appointment for TB screening and clinic follow up to TB contacts. Study showed that SMS and telephone call reminder was proven effective in improving adherence in long duration follow ups, treatment outcome and lowers the incidence of TB among HIV patient on ART in Malaysia (Abdulrahman *et al.*, 2017a). Two other local study showed similar findings where the SMS reminder through mobile phone help to reduce the non-attendance rate in chronic disease and outpatient care (Leong *et al.*, 2006; Liew *et al.*, 2009). It is possible to use similar approaches to improve adherence to appointment for TB screening among identified TB contacts in Perak.

1.5 Problem Statement

The rate of TB screening uptake and completed the entire screening until fourth TB screening was very low, especially in this state. It was much lower than the key performance indicator set for TB screening aimed at 25% of contact to complete until the fourth screening. Repeated periodic screening, long term appointment makes contacts tend to forget the date of appointment. Healthy state or asymptomatic make them less motivated to complete the screening.

Existing system relies heavily on staffs to trace thousands of missing contacts at a time lead to inefficient contact tracing procedure. Line sharing and only one call can be made at a time in many of the health setting lead to long waiting time and long work process. High competition between other more acute and severe impact case causing the priority for defaulter tracing of TB contact goes at the bottom list.

Lack of knowledge and understanding among the public on TB disease and its legal consequences based on Prevention and control of Infectious Diseases Act 1988 due to inadequate education by healthcare staffs, cause the order for contact TB screening were taken lightly.

Unscreened TB contact may not only have risk of becoming an active TB, but may also be the source of infection to index case. Delay in detecting them will let the chain of transmission of TB disease to progress further and infect other people. Therefore, it is vital to interrupt the chain of TB transmission as early as possible.

1.6 Study Rationale

Early detection and immediate treatment during contact screening is crucial to halt the transmission of disease in community, maximize chance of successful treatment outcome and prevent contact from developing severe TB due to late detection. Compliance and retention to screening is necessary to avoid missing of any potential cases especially in the first few months after diagnosis of an index case was the highest risk of TB incidence in contacts.

More efficient methods to enhance screening uptake and compliance to scheduled follow-up is now needed. TB contact reminder may save time of healthcare professionals and reduce their workload with only cheap cost intervention. Efficient management of contact able to avoid losing of potential case contact and waste of valuable resources. Timely TB screening not only prevent spreading of the disease, but also save financial and human resources such as underutilization of healthcare professional time, appointment waiting time which will later impact on overall function of health care facilities.

Due to lack of published RCT assessing reminder system on entire process of contacts screening, this study will be the first study to report the effectiveness of such reminder system for TB contacts in Malaysia. This study will be able to provide adequate evidence, causal, temporal, biologically plausible and significant association between such intervention and outcome of the study.

1.7 Research Question

1. What is the effectiveness of new developed Tuberculosis Contact Reminder System in improving uptake and retention rate of TB screening among registered TB contacts compared to the current practice?

1.8. General Objective

To evaluate the effectiveness of Tuberculosis Contact Reminder System in improving the uptake of TB screening; improving the retention rate to subsequent TB screening; level of staff's satisfaction and description of implementation cost.

1.8.1 Primary Objectives

1. To compare the uptake of first TB screening among registered contacts between Tuberculosis Contacts Reminder System and the current system.

1.8.2 Secondary Objectives

1. To compare the retention rate in the subsequent TB screening among contacts of first screening between Tuberculosis Contact Reminder System with the current system.
2. To assess staff's satisfaction and cost of implementation of TCRS.

1.9 Hypothesis

Tuberculosis Contact Reminder System is more effective in improving the uptake of TB screening; and have higher retention rate to TB screening among TB contacts compared to current system.

CHAPTER 2

LITERATURE REVIEW

2.1 Risk of active TB and LTBI in contacts

Prevalence of active TB and latent TB infection (LTBI) among TB contacts in low and middle-income countries (LMIC) was 3.1% and 51.5% respectively indicated high number of positive cases hiding among TB contacts (Fox *et al.*, 2013). Meta-analysis study showed the yield of active TB disease among TB contacts during contact tracing in LMIC was 4.9% (Morrison *et al.*, 2008). However, local study produce much lower yield 0.5% of new active TB among contacts in the study conducted in Penang General Hospital (Atif *et al.*, 2012). The large discrepancy of the prevalence estimate could be due to unmatched comparison where majority of the study in the meta-analysis was from country with high TB prevalence. And possible of suboptimal contact tracing procedure in our care and inaccurate estimation since the study was made based on the registry in study by Atif *et al.* (2012).

Risk of acquiring all types of TB is higher among contacts compared to non-contacts OR 4.5 (95% CI: 4.3, 4.8) and period of first year after exposure was the greatest annual incidence of TB disease among TB contact 4.5% (95% CI 4.3,4.8) (Morrison *et al.*, 2008). This finding were strongly supported by few other studies (Ling *et al.*, 2011; Fox *et al.*, 2013; Shah *et al.*, 2013).Therefore, screening of TB contacts need to be done periodically for certain period of time. In Malaysia, the periodic screening will be complete between one and a half up to two years (MOH, 2012). A study done in Taiwan have a higher yield of active TB during household

contact screening was 0.96% to 2.83% with the duration of screening follow-ups being 2 years in total or 6 months longer than ours (Ling *et al.*, 2011; Wang *et al.*, 2012). However, compared to local performance, the yield was higher within 1 year period of follow-ups suggests there was a room for improvement if we able to improve on retention and compliance to TB screening among our contacts (Ling *et al.*, 2011).

Most of TB contacts were identified during contact tracing procedure. Contact tracing is a systematic evaluation procedure to identify active TB or LTBI cases among contacts of known TB patients (Fox *et al.*, 2013). Based on recommendation by WHO (2013b) household contacts and other close contacts were strongly recommended to undergo systematic TB screening to identified those exposed to TB infection from index cases or in the stage of active TB disease for an early diagnosis and appropriate treatment (Kranzer *et al.*, 2013). Contact to index cases such as spouse, household members, colleague at work, friends and relatives are most likely to be infected due to prolonged exposure to causative organism from index cases (Wang *et al.*, 2012). However, the risk of infection depends on proximity of contact, duration of exposure, infectiousness of index case and susceptibility of the contact (Gounder *et al.*, 2015).

2.2 Current management for TB contact

In current practices, contact tracing procedure was based on the national CPG and state protocol of TB contact tracing (TBIS, 2002; MOH, 2012). Initially TB contacts will be identified by health inspector during case investigation of TB index cases. The list of identified contact will be send to health clinic and will be given an appointment date for TB screening.

All contacts attended the clinic appointment will be registered in clinic registry, files for TB contact will be created and TBIS-10C3 form will be filled up. All identified contacts will be ordered to attend for first TB screening within 2 weeks in nearby health facility. Subsequent screening will be at 3rd month after the previous screening, 6th month after second screening and 12th month after third screening (MOH, 2012). Each TB contact is expected to complete up to 4th screening which usually taken about one and half up to two years duration.

Chest x-ray (CXR) was the first line investigation, followed by three sample of sputum for acid fast bacilli (AFB) for symptomatic contact with normal or abnormal CXR based on clinical judgement. TST will be given to asymptomatic contact based on clinical evaluation of their risk and high risk group is strongly suggested to undergo TST (MOH, 2012).

In the case of defaulted screening, TBIS 10D form will be issued to health inspector in district health office for contact tracing. Currently there is no standard procedure to manage the defaulted contacts. Furthermore, the management of TB contact was considered very loose as the main focus was concentrated on index cases (JKNP, 2016). Large number of TB contacts was another barrier to trace the defaulter individually. Therefore, better system is needed to keep the identified contact comply with the scheduled screening and ease for healthcare worker to reach them in future.

2.3 Summary of the factors influence on uptake of TB screening

2.3.1 Personal factors

There are numerous factors that prevented contacts from attending TB screening (Roberts *et al.*, 2016). Personal factor such as forgetfulness, not aware of the appointment due to long duration of follow-up interval, occurrence of unexpected events, lack of information regarding the needs of screening, the implication and consequences of missed TB screening (Zailinawati *et al.*, 2006; Car *et al.*, 2012; Stuurman *et al.*, 2016; Nhavoto *et al.*, 2017; Sari *et al.*, 2017). Study showed, those who not received any reminder were more unaware or tend to forget the appointment date (MacLellan *et al.*, 2016).

State of asymptomatic state make people don't feel they should attend the appointment and they belief they will not develop TB in future (Zailinawati *et al.*, 2006; Triasih *et al.*, 2016). Lack of perceived susceptibility, perceived severity, high perceived barrier, limited knowledge, poor awareness and stigma holding them from attending the screening (Tornee *et al.*, 2005; Li *et al.*, 2013; Ayakaka *et al.*, 2017; Shariff *et al.*, 2017). Thus, the element education to improve on knowledge and awareness is vital in improving the contact screening.

2.3.2 Social Factors

Stigma toward TB disease hindering people from attending the screening. Stigma of TB disease are not exhaustive or mutually exclusive because it linked to many thing such as social position, minority, age and others (Craig *et al.*, 2017). Fear of disclosure and isolation consequence of information disclosure have prevented them from being cooperative, access to the screening and delayed medical attention

(MacLellan *et al.*, 2016; Craig *et al.*, 2017). Mistrust and poor relationship with healthcare staffs also one of the identified factors (Ayakaka *et al.*, 2017). Therefore, proposed intervention needs to consider privacy issues as well. Through SMS or phone call reminder we were able to provide more privacy to contact by conducting less home visits or active case finding. Education, professionalism and ethics is paramount for the handling of each case and contact.

2.3.3 Sociodemographic factor

Meta-analysis of observational studies showed that being male is protective factors from delayed treatment OR 0.85 (95%CI: 0.78, 0.92) due to higher suspicion during investigation, better financial capability and less stigma compared to women (Li *et al.*, 2013; Cai *et al.*, 2015). However, above finding is contradicted with local study where male sex is the independent predictor for non-attendance OR 2.04 (95% CI: 1.3, 3.2) probably due to unique help-seeking behaviour in men which tend to delay or avoid help (Zailinawati *et al.*, 2006). Unemployment, low-income level and low education level were consistently identified as factors that prevented them from timely treatment and screening for TB, OR 1.18 (95%CI: 1.07, 1.30), OR 1.23 (95%CI: 1.02, 1.49) and OR 2.14 (95% CI: 1.03, 4.47) respectively (Finnie *et al.*, 2011; Li *et al.*, 2013; Cai *et al.*, 2015). Therefore, TB contacts should be aware that TB screening and TB treatment is free in this country. Long travel time to healthcare setting and living in rural areas was associated with patient and healthcare provider delay for TB care OR 1.39 (95% CI: 1.08, 1.78) especially in difficult geographical area and challenging terrain (Brasil and Braga, 2008; Finnie *et al.*, 2011; Li *et al.*, 2013; Cai *et al.*, 2015). Live in rural areas have higher risk of patient delays OR 1.79 (95%CI: 1.62, 1.98) (Li *et al.*, 2013).

2.3.4 Health system factors.

Repeated visit, repeated screening, long waiting time, long period of screening, invasive screening and negative experience during visit will reduce the acceptability to attend the follow-up (Leong *et al.*, 2006; Triasih *et al.*, 2016; Aniza *et al.*, 2017). Lack of explanation emphasize by healthcare staffs to patients on important information such as risk of TB disease due to time limitation and their own knowledge limitation about the disease itself (Li *et al.*, 2013; Toczek *et al.*, 2013; Triasih *et al.*, 2016). Other factors include long time consumption for contact tracing of large number of defaulter, lack of a dedicated team, facilities and prioritization lead to poor quality of care and monitoring among TB contacts (Caylà and Orcau, 2011; Li *et al.*, 2013; Toczek *et al.*, 2013; Szkwarko *et al.*, 2017). Thus, an efficient monitoring system, which involves training of staff and universal health services is needed to improve in TB contact management. Lack of NTP prioritization, lack of tool such as guidelines, proper documentation of contacts, poor monitoring and limited resources lead to poor contact management and retention to TB care (Szkwarko *et al.*, 2017). Lack of facilities for screening and diagnostic such as X-ray machine and sputum AFB in primary care is one of the identified factors for diagnostic delay in Asia (Li *et al.*, 2013).

2.3.5 Factors enhance screening uptake

There were few different strategies that were identified to promote adherence to clinic attendance such as reminder systems, education and counselling, material incentives and enablers, staffs motivation and supervision and peer assistance (Liu *et al.*, 2014). Also, short distance to clinic perceived susceptibility, good relationship between TB patients and healthcare provider and presence of social support for TB

contacts to attend screening (Tornee *et al.*, 2005; Shariff *et al.*, 2017). Incentive programs such as financial support reimbursement for transport and nutrition show that they can be effective in improving TB program. Meta-analysis showed lower default rate 9.7% (95% CI: 7.5, 11.8) compare to 15% (95% CI: 12.5, 17.7) in studies that did not provide and incentives (Toczek *et al.*, 2013). Systematic review of 12 studies showed that there is no clear benefit in giving incentives and enabler in improving long term adherence to TB treatment (RR1.04). However large effect was seen in monetary form of incentives RR 14.53 and in certain subpopulation such as recently release prisoners, drug users and homeless people (Lutge *et al.*, 2015). Less effective in delayed incentives than immediately given incentives.

2.4 Clinical condition of TB contact and its index case

Presence of TB symptoms not necessarily improve on the attendance rate and early screening. Studies showed symptomatic TB patients, seeking treatment from traditional healer and cause delayed treatment especially among rural resident and lower education groups (Finnie *et al.*, 2011; Li *et al.*, 2013). However, presence of TB symptoms such as haemoptysis is a consistently associated with patients delay as protective factor with OR 0.64 (95%CI: 0.40, 1.00) (Cai *et al.*, 2015). Contact with history of prolonged cough 72.5% has significantly higher rate to be screened compared to those without prolonged cough 9.3% (Thanh *et al.*, 2014). Majority 66.2% index TB were aware that household contact with symptoms of TB should go for TB screening. However only 6.2% aware that children less than five years should go for screening (Thanh *et al.*, 2014). Therefore, presence of TB symptoms among household contact might increase the uptake of TB screening but less among children.

In certain condition of TB disease of index cases, more serious attention will be paid by healthcare staff such as, index with smear and culture positive, laryngeal TB and pulmonary TB which have higher risk of infecting others RR 3.09 (95% CI: 1.31, 7.27) (Ling *et al.*, 2011; MOH, 2012; WHO, 2012; WHO, 2013b). Thus, contact tracing was more intense with stricter monitoring which helps in improving compliance and attendance. For example, contact of MDR-TB also will have longer duration of follow-up at least 2 years compared to usual TB contact (MOH, 2012). Therefore, contact of smear positive index, MDR TB and certain type of TB such as pulmonary TB or laryngeal TB were always given extra focus and stricter monitoring by healthcare staffs which later might influence on the attendance for TB screening among identified contacts.

Presence of comorbidity such as HIV disease lead to higher suspicion for TB among contacts as one third of HIV positive are infected with TB. Higher risk of TB mortality OR 2.6 (95% CI: 1.6, 4.1) and Isoniazid prophylaxis therapy (IPT) for PLHIV will cause closer monitoring among contacts with HIV comorbidity indirectly improve the adherence to TB management (MOH, 2012). Presence of comorbidities, positive sputum smear (AFB), TB clinical manifestation or type are among the factors related to defaulted treatment being investigated in the meta-analysis study (Brasil and Braga, 2008; Stuurman *et al.*, 2016).

2.5 Reminder system in healthcare services

Reminder system has been used in healthcare services for several decades. In context of healthcare services, reminder system is a form of policy which commonly implemented to improve on clinic attendance, medication adherence and compliance (Liu *et al.*, 2014; Chaudhuri *et al.*, 2017). It works through variety of mechanism such

as phone call, SMS, letters, postcards and email. Reminder system has been previously applied to intervene disease such as HIV, cancer screening, immunization uptake and outpatient clinic attendance but not among TB contacts (Leong *et al.*, 2006; Fortuna *et al.*, 2014; Harvey *et al.*, 2015; Abdulrahman *et al.*, 2017a; Aniza *et al.*, 2017). Study showed it was effective in improving medication adherence, lowering the defaulter rate (Liu *et al.*, 2014; McLean *et al.*, 2016; Abdulrahman *et al.*, 2017a). To our knowledge, there was lack of published studies on reminder system conducted specifically among TB contacts or specific for proper contact screening for TB disease except few studies investigated on contact return for Tuberculin Skin Test (TST) reading only (Liu *et al.*, 2014; Chaudhuri *et al.*, 2017). Although there was abundant of intervention using various type of reminder has been published, the effect of reminder system on TB contact was expected to be different since the population of TB contacts might come from different sociodemographic background, motivation levels, perceived severity of the disease and priority level by healthcare provider.

2.6 Previous reminder system of other diseases in Malaysia

SMS and phone reminder are form of telemedicine that gives automated reminder or manually conducted reminder to patients. Such intervention has been applied to intervene disease such as HIV, outpatient clinic attendance, children vaccination and health promotion (Leong *et al.*, 2006; Abbas and Yusof, 2011; Abdulrahman *et al.*, 2017a; Aniza *et al.*, 2017). None of the local published studies was conducted among TB contact or TB patients.

Recent study conducted by Abdulrahman *et al.* (2017a) in tertiary hospital in Sungai Buloh using weekly SMS, phone call and counselling to improve medication adherence among HIV patients. The result showed that such intervention was

effective in improving medication adherence (92.2% vs. 54.6%), lowering the defaulter rate (14% vs. 35.5%) and give excellent HIV clinical outcome. In context of long duration follow up, its improved 15.5% of the mean adherence for six months follow up. However, pre-ART testing with vitamin training in this study could introduce selection bias and may cause overestimation of the findings and generalizability of the intervention effect in general population. Pre-ART vitamin training could have selected patient with higher motivation and committed to treatment rather than selection by random. The real effect also is expected to be lower than what it was since the sample was homogenous and effect of social desirability bias in self-report outcome. We expected smaller effect size in the subject of TB contact due to wider variation of sociodemographic, motivation, different perceived severity of the disease and priority level by healthcare provider.

Study conducted in Kuala Lumpur and Petaling Jaya showed SMS reminder efficiently worked among elderly from 55 to 70 years old subjects in improving frequency of exercise (Müller *et al.*, 2016). This study showed that use of SMS reminder was not limited to young age group but also an acceptable method among older people. SMS were regard as one of the pushing factor to action. However, frequent SMS and long intervention with the same intensity were not giving any significant result (Müller *et al.*, 2016). Probably exposed to frequent intervention lead to less satisfaction (Aniza *et al.*, 2017).

A descriptive study on the use of SMS in reminding parent on vaccination schedule of their children showed high acceptability of such system among study subjects with 45.2% regard as very useful and 54.8% as useful. In that study, majority of the subjects 71.1%, which either always or sometimes forget their child's

appointment showed that reminder system may play significant role in clinic attendance and easily accepted by public (Abbas and Yusof, 2011).

A clinical trial conducted in two primary clinics assessing the effect of SMS reminder and phone call reminder in reducing non-attendance in chronic disease follow up. Both type of phone call and SMS reminder were significantly effective with the effect size of 9.3% and 7.4% respectively. In this study phone call reminder produce slightly non-attendance rate than SMS reminder but the difference was not statistically significant which shows that both may have similar effectiveness. However, SMS was regard as having an advantage over phone call reminder as it is faster and cheaper. More than 20% of the subject in phone call reminder were unable to be reached by phone call in first attempt (Liew *et al.*, 2009).

Earlier study by Leong *et al.* (2006) on reminder was conducted in seven primary care clinics in area of Kuala Lumpur and Kota Bharu. The three arms randomized controlled trials showed both SMS and phone call reminder were significantly effective in improving the clinic attendance rate than usual care with OR 1.59 (95% CI: 1.17, 2.17) and OR 1.55 (95% CI: 1.14, 2.11) respectively. This study yielded a slightly higher effect size of 10.9% and 11.5% respectively than the study by Liew *et al.* (2009). Although there were no statistically significant difference between the two method, phone call reminder in this study also achieved slightly higher effectiveness than SMS which was similar to previous study (Liew *et al.*, 2009). However, this study was conducted among OPD patients covering chronic diseases, immunization and other preventive care which may exert different effectiveness in TB contact.