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Referral of tuberculosis symptomatic clients from private pharmacies to public sector clinics for diagnosis and treatment in Cambodia

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Abstract

Rationale, aims and objectives Cambodia is one of the 22 countries with a high burden of tuberculosis (TB). People often first seek treatment for cough and other TB symptoms through private pharmacies. The National Tuberculosis Programme trained willing private sector pharmacies to refer TB symptomatic clients to their closest public sector clinic for diagnosis and treatment. The study objective was to investigate factors associated with referral of TB symptomatic clients from pharmacies to public sector clinics in Phnom Penh, Cambodia.

Method Face-to-face structured interviews were conducted with staff from a stratified random sample of 180 private pharmacies in Phnom Penh in 2012. Trained interviewers were Khmer speakers. Logistic regression was used to compute odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with self-reported referral during the previous 3 months.

Results Fifty (29.6%) pharmacies reported that they had referred 125 clients (range 1–10) to public sector clinics during the previous 3 months. In total, 164 (96.5%) pharmacies reported that they always referred all TB symptomatic clients to DOTS (directly observed treatment, short course) clinics. More than 6-year participation in the programme (OR 5.23, 95% CI 1.93–14.18) and willingness to always continue referring (OR 12.24, 95% CI 11.61–93.10) were associated with referral of one or more clients in the previous 3 months. Referral to the client's closest clinic was negatively associated with referral (OR 0.45, 95% CI 0.23–0.99).

Conclusion Pharmacies' ongoing commitment to the Referral Programme was strongly associated with referral. Increased advocacy among the high number of non-referring pharmacies may improve programme performance. Factors negatively associated with referral may need investigation.

Introduction

Tuberculosis (TB) is a leading cause of death worldwide. An estimated 8.6 million people developed TB and 1.3 million people died from TB in 2012 [1]. Cambodia is one of the 22 countries classified as having a high burden of TB. The World Health Organization strategy known as DOTS (directly observed treatment, short course) is implemented nationwide through public sector clinics and referral hospitals. Implementation of the DOTS strategy has resulted in high treatment success rates. However, two-thirds of Cambodians have latent TB infection – acquired *Mycobacterium tuberculosis* infection held in check by the patient's immune response. This infection may activate later in the patient's lifetime to become the disease, tuberculosis. The high prevalence of latent TB contributes to the high burden of active TB. This is despite a declining overall incidence rate [2].

Most National Tuberculosis Programmes rely upon passive case detection to identify people with TB [3]. In Cambodia, the

National Center for Tuberculosis and Leprosy Control (CENAT) has implemented a public/private mix (PPM-DOTS) TB Referral Programme involving private clinics, private pharmacies and public sector clinics. As part of this programme, clients who present to private pharmacies with symptoms suggestive of TB are referred to public sector clinics for free diagnosis and DOTS treatment. In Cambodia and other low- to middle-income countries, pharmacies are often the first point of contact with the health care system for people seeking care for cough [4]. An average of 11.6% of TB cases has been detected from private provider referrals in Cambodia over the period 2005–2012 inclusive [5].

The systematic involvement of private pharmacies in TB control is progressing globally. India launched a nationwide PPM-DOTS programme to involve private pharmacies in treatment observation and referral in 2012 following earlier pilot studies. Understanding provider-related barriers and facilitators in the delivery of pharmacy-based TB care may provide important insights for policy-makers in Cambodia and other high burden countries. The objective of this study was to investigate factors associated with referral of TB symptomatic clients from pharmacies to public sector clinics in Phnom Penh, Cambodia.

Method

Study context and setting

The study evaluated the PPM-DOTS TB Referral Programme, which has been implemented in the four operational health districts of the Phnom Penh Municipal Health Department since 2005. Over 380 of 600 registered pharmacies in the city provide TB referral services. As mandated by the programme, TB symptomatic clients are referred by the pharmacy provider to one of 17 public sector DOTS clinics in each district whichever is closest or most convenient for the patient.

Prior to participating in the programme, pharmacy owners or staff attended a 3-day training workshop conducted by CENAT and its programme partners: PATH (Programme for Appropriate Technology in Health, a USAID-funded non-government organization known from 2014 as PATH) and the Pharmacists Association of Cambodia (the professional body representing pharmacy owners). Pharmacy staff were trained to identify, counsel and refer TB symptomatic clients presenting at the pharmacy. Training also included visits to DOTS clinics to meet with physicians. Owners and/or staff who completed the training were the designated TB referral service provider for their pharmacy. While registered pharmacies in Cambodia must hold a licence from a university-qualified pharmacist, it is unusual for this pharmacist, or any university-qualified pharmacist, to be in daily attendance at the pharmacy.

Pharmacies receive no payment or fee for providing TB referral services. Programme participation also requires compliance with government regulations prohibiting the stock and sale of anti-TB medications in the private sector. This regulation was introduced to control the incidence of multidrug-resistant TB in Cambodia.

Study design

From a list of the 380 programme pharmacies provided by the Municipal Health Department, a stratified random sample of 180 pharmacies was selected using computer-generated number sequences. Pharmacies were stratified according to their location in one of the four operational health districts – Central, North, South and West. The sample was 47% of the study population.

Data collection

Face-to-face interviews were conducted using a 23-item structured interview guide. To ensure content validity, the interview guide was based upon results from in-depth interviews with Referral Programme stakeholders and focus group discussions with pharmacy owners to ensure content validity [6,7]. Data were collected for the 3-month CENAT reporting period immediately prior to conduct of interviews to minimize recall bias. Items comprised questions related to referral statistics, self-reported referral practices, participant perceptions of the Referral Programme and demographic data. The structured interview guide was pilot-tested for face validity at 10 pharmacies in September 2012. All documents were translated from English to Khmer by an accredited translation organization and back translated by accredited interpreters and Khmer-speaking investigators. To achieve a high response rate, interviews were conducted by Khmer-speaking interviewers in preference to a postal self-administered questionnaire [8].

Two Khmer/English-speaking interviewers and a supervisor were trained at a 1-day workshop conducted by investigators prior to the pilot study. Training comprised explanation and purpose of interview terms and protocols and interview conduct. Training was conducted to ensure reliability of the interview process. Using a train-the-trainer approach, a further three Khmer-speaking interviewers were trained by the supervisor. The final team comprised two female and three male interviewers from Phnom Penh. All interviewers were familiar with the TB Referral Programme. One TB-trained owner or staff member was interviewed per pharmacy on-site during daytime business hours. All study participants provided informed consent. All interviews were conducted in Khmer. At least three interviewers were allocated per operational district. Interviews were conducted over 7 days in November 2012.

Data analysis

Data entry was double-checked by an independent research assistant for quality assurance. The data were descriptively analysed and reported using proportions, means with standard deviations (SDs) and medians. Chi-squared test or Fisher's exact test was used to compare proportions and Student's *t*-test or Mann–Whitney *U*-test to compare means or medians. Binomial logistic regression models were used to compute unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with referral. The dependent variable in each model was referral of TB symptomatic patients in the previous quarterly reporting period (yes vs. no). Linearity of independent variables was assessed. If the linearity assumptions were not met, continuous variables were categorized prior to inclusion in the logistic regression models as categorical variables. All analyses were performed using the Statistical Package for the Social Sciences (SPSS, Version 21, SPSS Inc., Chicago, IL, USA).

Ethical considerations

The study was approved by the Human Research Ethics Committee of The University of Sydney and the National Ethics Committee for Health Research Cambodia. The study was supported by the National Center for Tuberculosis and Leprosy Control and the Phnom Penh Municipal Health Department.

Results

Nine pharmacies were either closed or had re-located. The remaining 171 pharmacies approached agreed to participate in the study. TB-trained pharmacy owners and staff, the study participants, completed 170 survey forms. One participant withdrew from the interview after commencement. All participants who were interviewed were the trained and designated TB referral service provider for their pharmacy.

Demographic characteristics of pharmacy referral service providers

Participants had a median age of 42 years (range 21–72 years) and 47% were male (Table 1). Participants had completed an average 13 years (SD 3.8) of formal education and had worked at their current pharmacy for an average of 15 years (SD 7.5). Pharmacies averaged 5.6 years (SD 1.6) participation in the Referral Programme.

Referral practices at programme pharmacies

During the previous 3-month period, 50 (29.6%) pharmacies referred one or more symptomatic clients (1–10) to DOTS clinics. A total of 125 symptomatic clients were referred (Table 2). A total of 164 (96.5%) study participants stated that they always referred all TB symptomatic clients to DOTS clinics (Table 3). A total of 92 (54.1%) *always* referred the client to the DOTS clinic closest to their home, 58 (34.1%) *sometimes* did and 20 (11.8%) *never* referred to the closest DOTS clinic. Ninety-three (57.3%) participants reported taking 10 minutes or more to assess and counsel symptomatic clients. Infection control measures of any type were implemented by 157 (94%) pharmacies. Seventy (42.9%) participants reported that clients they referred were previously known to them and 96 (56.0%) participants stated that symptomatic clients returned to their pharmacies as customers following referral.

One hundred and forty-four (84.7%) participants stated they would *always* provide referral services; 25 (14.7%) reported they would *sometimes* refer in the future; and 1 participant stated he/she would not continue providing referral services. Over 159 (93.5%) participants were satisfied with implementation support services provided by the Municipal Health Department; with 141 (83.9%) participants believing that further training may increase referral numbers. Seventy-one (41.8%) participants believed that pharmacies should receive a financial incentive when providing referral services.

Factors associated with referring and non-referring pharmacy-based providers

Participation in the programme for 6 years vs. less than 6 years (OR 5.23, 95% CI 1.93–14.18) and willingness to *always* continue providing referral services (OR 12.24, 95% CI 1.61–93.10) were associated with referral (Table 4). During the previous 3-month period, those who *sometimes* referred clients to their closest clinic were less likely to refer compared with those who *always* referred

Table 1 Characteristics of referring and non-referring participants (n = 170)

Characteristic	Referred *n* (%)	Did not refer *n* (%)	Total *n* (%)
Age, years – median (range)	47 (21–72)	41 (21–70)*	42 (21–72)
Gender, male – *n* (%)	26 (54.2)	53 (43.8)	79 (46.7)
Formal education, years – mean (SD)	12.9 (3.4)	13.6 (3.9)	13.4 (3.8)
Employment at present pharmacy, years – mean (SD)	15.4 (7.6)	13.9 (7.5)	14.8 (7.5)
Participation in Referral Programme, years – mean (SD)	6.3 (1.1)	5.3 (1.7)*	5.6 (1.6)
Completion of TB Referral Programme training – *n* (%)	48 (100)	121 (100)	169 (100)†

*P-value < 0.05. P-values were calculated using Pearson's chi-squared test or Fisher's exact test for categorical variables and t-test or Mann–Whitney U-test for continuous variables.
†Missing data for one pharmacy.
SD, standard deviation; TB, tuberculosis.

Table 2 Referral data by operational health district (previous 3-month period)

Operational district	Pharmacies surveyed *n* (%)	Pharmacies referring ≥ 1 person(s) *n* (%)	Persons referred *n* (%)	Referral rate per pharmacy
Central	38 (22.5)	10 (20.0)	27 (21.6)	2.7
North	43 (25.5)	13 (26.0)	48 (38.4)	3.7
South	44 (26.0)	11 (22.0)	29 (23.2)	2.6
West	44 (26.0)	16 (32.0)	21 (16.8)	1.3
Total	169* (100)	50 (100.0)	125 (100.0)	2.5

*Missing data for one pharmacy.

Table 3 Self-reported attitudes and practices of referring and non-referring participants (n = 170)

Factor	Referred *n* (%)	Did not refer *n* (%)	Total *n* (%)
Operational district			
Central	9 (18.8)	29 (24.0)	38 (22.2)
North	13 (27.1)	30 (24.8)	45 (26.3)
South	10 (20.8)	34 (28.1)	44 (25.7)
West	16 (33.3)	28 (23.1)	44 (25.7)
All clients always referred to public sector clinics	48 (100)	115 (95.0)	164 (96.5)
All clients referred to their closest public sector clinic			
Always	31 (64.6)	60 (49.6)	92 (54.1)
Sometimes	11 (22.9)	47 (38.8)	58 (34.1)
Never	6 (12.5)	14 (11.6)	20 (11.8)
Time to assess symptomatic persons ≥10 minutes	30 (62.5)	63 (55.3)	93 (57.1)
Referred clients previously known to participant	22 (45.8)	47 (41.2)	70 (42.9)
Referred clients return to pharmacy as customers	31 (64.6)	62 (53.0)	93 (56.0)
Infection control measures implemented at pharmacy	46 (95.8)	110 (93.2)	157 (94.0)
Satisfaction with Municipal Health Department support	46 (95.8)	112 (92.6)	159 (93.5)
Desire for additional training to increase rates of referral	43 (89.6)	97 (81.5)	141 (83.9)
Desire for financial incentive to be paid to referral pharmacies	24 (50.0)	47 (38.8)	71 (41.8)
Willingness to continue providing referral services			
Always	47 (97.9)	96 (79.3)*	144 (84.7)
Sometimes	1 (2.1)	24 (19.8)	25 (14.7)
Never	0 (0)	1 (0.8)	1 (0.6)

* P-value < 0.05. P-values calculated using Pearson's chi-squared test or a Fisher's exact test.

Table 4 Factors associated with referral

Factor	OR	95% CI
Age (≥50 years vs. <50 years)	1.99	0.99–3.99
Gender (male)	1.52	0.77–2.97
Formal education (≥13 years vs. <13 years)	0.60	0.31–1.19
Employment at present pharmacy (≥15 years vs. <15 years)	1.35	0.69–2.65
Participation in Referral Programme (6 years vs. <6 years)	5.23	1.93–14.18
Operational district		
Central	Ref	
North	1.40	0.52–3.76
South	0.95	0.34–2.65
West	1.84	0.70–4.85
All clients referred to their closest public sector clinic		
Always	Ref	
Sometimes	0.45	0.21–0.99
Never	0.83	0.29–2.37
Time to assess symptomatic persons (≥10 minutes vs. <10 minutes)	1.35	0.68–2.69
Referred clients previously known to participant	1.21	0.61–2.38
Referred clients return to pharmacy as customers	1.62	0.81–3.24
Infection control measures implemented at pharmacy	1.67	0.34–8.18
Satisfaction with Municipal Health Department support	1.85	0.38–8.89
Desire for additional training to increase rates of referral	1.95	0.69–5.49
Desire for financial incentive to be paid to referral pharmacies	1.57	0.80–3.09
Willing to continue providing referral services		
Always vs. Sometimes/Never	12.24	1.61–93.10

CI, confidence interval; OR, odds ratio.

to the closest clinic (OR 0.45, 95% CI 0.21–0.99). Age, gender, education and employment at present pharmacy were not associated with referral. Similarly, financial incentive, additional training and satisfaction with programme support were not associated with referral.

Discussion

To our knowledge, this was the first study in Cambodia to investigate the number of Referral Programme pharmacies actively referring symptomatic clients over a 3-month period and the factors associated with their decision to refer or not to refer. Understanding the barriers and facilitators to referral of TB symptomatic clients may provide important insights for policy-makers in Cambodia and other high burden countries.

A finding of the study was the low number of programme pharmacies reporting they had referred TB symptomatic clients in the previous 3 months. If data from the 3-month study period were indicative of previous referral data collection periods, the lack of referral activity among high numbers of programme pharmacies may be contributing to declining case detection rates in Cambodia – a trend also reported globally [1]. As many Cambodians visit a pharmacy for symptomatic relief of cough, pharmacies may have missed opportunities for referral. Participants believed that further training could raise awareness and lead to increased rates of referral. Discussion of referral data between pharmacies and TB units in the operational health districts may also reinforce the importance of timely referral of clients to diagnostic facilities. Encouraging referral pharmacies with long-term experience to share their knowledge and practices with non-referring pharmacies may improve the motivation and confidence to refer [9].

Pharmacy location was not associated with referral. Neither were socio-demographic characteristics of participants associated with likelihood to refer. These results may reflect the socio-demographic conditions in Phnom Penh where neither age, gender nor education-related factors appear to be significant barriers for other than the most vulnerable groups accessing health care facilities nor those providing health care services [10–12].

The number of years participating in the programme was a significant predictor of referral. The high level of satisfaction with programme support services received from the Municipal Health Department in Phnom Penh may have contributed to provider willingness to continue participating in the programme. The high response rate in the study may also indicate a high level of commitment to the programme and participants' desire to contribute their views on programme performance [7]. The fear of TB transmission in the pharmacy was a major concern of participants in an earlier study [7]. However, study data showed that infection control strategies were in place in the majority of pharmacies and infection control was not associated with referral. Programme support services included regular meetings for participants to discuss issues such as infection control and to address implementation problems generally. These services may be a particular strength of the programme with confidence-building effect for participants. Studies in PPM-DOTS implementation show that adoption of multi-faceted support strategies to complement training is motivational and contributes to long-term participation in inter-sectoral interventions [13]. Pharmacy-based PPM interventions, which rely solely upon single-component strategies, for example, training only, have been shown to have short-term effect [14,15]. The framework, or mix, of supporting strategies in CENAT's Referral Programme would appear to have the confidence of pharmacy-based participants for the long-term.

Referring symptomatic clients to their closest or most convenient clinic aims to minimize transport costs for clients and facilitate their timely arrival at the clinic for diagnosis. This is a protocol of the PPM-DOTS Referral Programme. Studies show that delayed diagnosis contributes to poor treatment outcomes for patients when eventually diagnosed. It also contributes to ongoing TB transmission in the community [11,16]. Although *always* referring clients to the closest clinic was a referral decision chosen by over half of the participants; importantly, likelihood to refer was negatively associated with pharmacies that only *sometimes* referred clients to their nearest clinic. Pharmacy decisions relating to choice of referral clinic may be influenced by reluctance to refer long-standing clients to some DOTS clinics. This was a finding of an earlier study [7]. Not all DOTS clinics were perceived to provide quality, patient-friendly services. Pharmacies may have been reluctant to expose their clients to perceived unsatisfactory services [7,10]. Perceptions of poor and inadequate public sector services among health-seekers and referrers have been shown to contribute to delayed diagnosis in other high burden countries [17,18]. While referring clients to their closest or most convenient clinic may have been a disincentive to referral for some pharmacies, other pharmacies may have referred clients to a preferred clinic. This study did not investigate choice of preferred clinic by either the patient or the pharmacy. The matter of clinic selection, however, may provide insight into the low number of pharmacies actively referring during the 3-month study period. Cambodian research shows that there is low utilization of public sector health facilities and suggests that building public sector capacity may improve health care access and services [10]. In the meantime, however, perceptions in the marketplace may be difficult to shift, leading to adverse outcomes for patients and public health.

Although the time taken to assess symptoms and counsel clients was not associated with referral, its relevance to the referral process has been reported by pharmacy-based referrers as challenging [7]. It was encouraging that over half the pharmacies in this study reported consultations of 10 minutes or more during the referral process. An average pharmacist/patient interaction has been reported at less than 2 minutes [19]. As the quality of provider/patient TB counselling can positively influence patient behaviour during referral, ongoing skills training may assist pharmacy-based referrers to improve outcomes from the time spent in counselling patients [20]. In Cambodian pharmacies with busy counters, a purpose-designed 10-minute consultation protocol may assist clients and referrers. In addition, recent studies in Cambodia highlighted increased TB incidence among identifiable population subgroups [21,22]. Using the latest evidence from national TB prevalence surveys during programme training may assist pharmacy-based referrers in the sometimes difficult challenge of referring symptomatic clients.

Participants' willingness to continue providing referral services was a positive predictor of referral and may contribute to programme sustainability. The reasons underlying this association, however, may be complex. Over half of the pharmacies interviewed did not desire a provider fee for service. Given also that income cannot be earned from the sale of anti-TB medications,

participants' current and future involvement in the Referral Programme may be motivated by factors other than short-term financial reward. Other factors may include altruism, status, acquiring knowledge, market competitiveness and the commercial advantage in maintaining long-term customer relationships [7]. The results showed that over half of referred clients returned to pharmacies as customers. Evidence from PPM interventions in other high TB burden countries has also shown the fine balance required in designing interventions to accommodate both public and private sector agendas and aspirations. This remains the long-term challenge for any PPM intervention [23–25].

Strengths and limitations

Particular strengths of this study included the stratified random sample of pharmacies by location to ensure representativeness of the sample and the high response rate thus minimizing any selection and participation bias. The recall period was selected to minimize recall bias.

Limitations of this study included collection of referral data that are related to the previous 3-month reporting period only. Referral practices and rates of referral in previous reporting periods of this 6-year Referral Programme were not investigated; therefore, study results may not be indicative of overall programme performance since 2005. Translation of documents from English to Khmer and back translation were undertaken by accredited translators to ensure accuracy. However, there are inherent challenges and limitations associated with conducting studies across language and cultural boundaries. Due to the relatively small sample size, we were not able to perform multivariate analysis. However, there were few statistically significant differences between pharmacists that did and did not refer. Restricting data collection to Phnom Penh may limit generalization of results to rural areas of Cambodia and other high burden countries.

Conclusion

The study provided insight into day-to-day realities for pharmacies implementing public/private mix interventions in TB control. The commitment of pharmacies to the Referral Programme and their willingness to continue programme participation were positive factors associated with referral and may contribute to programme sustainability. However, the requirement to refer symptomatic clients to their nearest DOTS clinic was a significant disincentive for pharmacies to refer and may have contributed to the low number of pharmacies referring during the 3-month study period. Given pharmacies are well utilized for treatment of perceived minor ailments including cough, they provide an easily accessible entry point for TB symptomatic clients on the cough-to-cure pathway. Moreover, as TB diagnosis and treatment is confined to the public sector, any disincentives to refer need to be investigated by the National Tuberculosis Programme. Optimizing patient and public health outcomes from this Referral Programme is imperative for TB control in high incidence Cambodia.

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