Cost-effectiveness of Pharmacist-managed Respiratory Medication Therapy Adherence Clinic (RMTAC) on Asthma Patients: A Prospective Multicentre Study

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Abstract

Introduction: Uncontrolled asthma contributes to a higher cost of management. In Malaysia, pharmacist-managed Respiratory Medication Therapy Adherence Clinic (RMTAC) was introduced to aid patient's asthma control through education and continuous monitoring.

Objective: To evaluate the cost-effectiveness of RMTAC service versus standard counselling service in improving asthma control in government health clinics setting.

Methods: A multicentre non-randomised controlled study was conducted in 16 government health clinics in Kuala Lumpur and Putrajaya. Subjects enrolled into RMTAC service were categorised as the intervention group, while subjects from clinics without RMTAC service were categorised as control group. Patients were followed up for six months to assess asthma control according to Global Initiative for Asthma (GINA) symptom control classification, inhalation technique and exacerbation frequency. The direct costs of intervention and control groups were calculated for the study duration. Cost effectiveness analysis was conducted from the perspective of healthcare provider.

Results: A total of 321 patients were recruited, with 158 in RMTAC group and 163 in control group. RMTAC significantly improved asthma control with 51.9% of subjects acquiring well-controlled status after 6-months intervention compared to 20.9% in control group ($p<0.001$). The mean improvement in GINA score was 1.91 and 0.81 in RMTAC and control group respectively ($p<0.001$). The majority of the RMTAC patients also mastered good inhalation technique (75.3%), significantly higher than control group (31.9%) ($p<0.001$). No significant difference was found in exacerbation frequency. The mean 6-month cost per patient for RMTAC and standard care were MYR166.27 and MYR120.22 respectively. The incremental cost-effectiveness ratio (ICER) of RMTAC was MYR41.86 per unit improvement in GINA score.

Conclusion: RMTAC service resulted in significant improvements in patient's asthma control and inhalation technique at a small additional cost. RMTAC service by pharmacists should therefore be expanded to more healthcare facilities in Malaysia to benefit more patients.

Keywords: pharmacists, asthma, cost-effectiveness

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Introduction

The prevalence of asthma has been increasing over the years. The global prevalence of asthma in adults is 4.5% with a large variation ranging from 0.2% in China to 21.0% in Australia (1). Meanwhile, the overall prevalence of asthma in Malaysia had increased by 50% from 4.2% in 1996 to 6.4% in 2011 (2,3). Globally, asthma represents a substantial financial burden that was mainly contributed by the cost of treatment on patients with uncontrolled asthma. For instance, the total estimated cost of asthma for the United States population was found to be $5.8 billion per year which consisted of direct expenditures of $5.1 billion and indirect expenditures of $673 million (4).

Three types of interventions were found to be able to enhance asthma management, namely education, environmental control and self-management (5). The commonest intervention program reported was asthma education, followed by self-management such as a written plan for monitoring peak-flow and symptoms (5). A study on hospital pharmacy-based asthma program in Sudan found that pharmacists interventions significantly reduced the frequency of acute asthma attacks, nocturnal asthma symptoms, the need of inhaled Beta-2 agonists, days of sickness and rate of hospitalisation (6). Another study done by Armour *et al*. on community pharmacy asthma care programme in Australia reported significant improvements in pharmacist intervention group in relation to asthma control, adherence to preventer medication, quality of life, asthma knowledge and inhaler technique (7).

In Malaysia, 60% of asthma patients have uncontrolled or partly controlled asthma (2). This contributed to a higher economic burden with the annual cost of asthma treatment increased from USD108 per patient in 2000 to USD275.65 in 2002 (8,9,10). Despite many strategies have been implemented, asthma control among Malaysians are still suboptimal (11,12). Thus, the Respiratory Medication Therapy Adherence Clinic (RMTAC) was introduced in 2004 in Ministry of Health Malaysia (MOH)'s healthcare facilities as part of pharmacists' efforts to collaborate with other healthcare professionals to effectively control patient's asthma (13). RMTAC is a structured programme in which RMTAC-accredited pharmacists provide more thorough counselling on disease, medication, adherence and inhalation technique as compared to the conventional counselling under standard pharmaceutical care. They review patient's medications, identify and provide solutions to any drug-related problems. RMTAC pharmacists also monitor patients' response more closely to ensure therapeutic goal is achieved, with a minimum of three follow-up appointments. A study by Yong *et al*. found that RMTAC has high probability of being more cost-effective than the standard care management alone (14,15,16).

Several overseas studies were done to evaluate the economic effectiveness of pharmacist intervention programs in asthma management. Studies have supported that pharmacist's intervention in asthma management programs are beneficial in reducing healthcare cost (16,17,18). A study done in the United Kingdom found that pharmacists giving advice to patients via telephone call significantly lower non-adherence and medicine-related problems among studied patients. Moreover, the intervention was less costly, with 90% probability that the intervention is cost effective (17).

Economic evaluation studies in Asian region, however, are still inadequate. In view of the differences in cultural, health care systems and protocol of pharmacist's intervention programs, economic evaluation in Malaysia context is needed. Whilst there was a local economic study done by Yong *et al*. using Markov Model, the economic evaluation using real world input in Malaysia setting is still limited (16). Therefore, this study aimed to evaluate the cost-effectiveness of RMTAC service versus standard pharmaceutical service in improving patient's asthma control in Kuala Lumpur and Putrajaya public primary health care setting, from the health care provider's perspective, which is the Ministry of Health Malaysia. The findings from this study will help policy makers to advocate policy change which expand the role of pharmacists in a comprehensive asthma management program at the national level, across public and private sector.

Methods

This was a multicentre non-randomised controlled study conducted at the pharmacies of 16 government's primary health clinics under the Health Department of the Federal Territory of Kuala Lumpur and Putrajaya to assess the cost effectiveness of RMTAC. The study was done in a duration of 21 months. The study subjects were recruited between January 2017 and March 2018 and each subject was followed up for 6 months (19). This study was approved by the MOH Medical Research and Ethics Committee (MREC) and registered in the National Medical Research Register (NMRR) (NMRR-16-1388-31720).

The inclusion criteria were patients aged 18 years old and above with confirmed diagnosis of asthma by a physician, who completed six months follow-up period and received Step 2 asthma treatment (inhaled corticosteroids) or higher according to Global Initiative for Asthma (GINA) asthma management guideline.

Furthermore, patients must be able to communicate in Malay, English or Mandarin. Patients with cognitive defects or diagnosed with other comorbidities namely chronic obstructive airway disease (COAD) and congestive heart failure (CHF) were excluded. Sample size was calculated from the primary outcome measure, using the true difference in the experimental and control means of 0.57 and standard deviation 1.8, based on an alpha of 0.05 and power of 80%. Assuming 20% of dropout rate, 158 subjects were needed for each arm.

Asthma patients were identified by the doctors using patients' medical record and being recruited into this study by investigating pharmacists after assessing patients' eligibility base on the inclusion and exclusion criteria. Subjects recruited from clinics which provide RMTAC service were categorised into intervention group and received RMTAC care, while subjects from clinics without RMTAC service were in the control group and received standard pharmaceutical care which is conventional counselling. Study protocol was explained and consent was obtained from all study subjects who participated in this study. All enrolled patients were given an asthma diary for them to record the frequency of emergency visits due to asthma exacerbation. Data of intervention group patients were collected from patient's MTAC records and asthma diaries by the site RMTAC pharmacists after assessment by the doctors, while data of the control group patients were collected from patients' medical records and asthma diaries by the site pharmacists. The flow of study subjects from both groups were depicted in Figure 1.

This study used cost-effectiveness analysis to compare the cost over health outcome between RMTAC and standard pharmaceutical care (20). The cost-effectiveness analysis was conducted from the healthcare provider's perspective, which is the Ministry of Health Malaysia. The cost parameters included were direct medical costs such as personnel, medications and materials for both scheduled and unscheduled visits. The cost for laboratory and diagnostic imaging were not included because it was not part of routine investigation for asthma patients in studied clinics. Personnel involved in the asthma treatment care were family medicine specialists, medical officers, medical assistants, pharmacists, pharmacist assistants, nurses and administrative clerks. The personnel cost was calculated based on the time spent by the personnel using time-motion study, multiply by their wages. The wages per minute were determined by their average monthly salary in accordance with the New Remuneration System for The Malaysian Public Service implemented through Service Circular No.2 of 2015 (21). The six-month cost of asthma related medications of each patient was calculated based on the dispensed drug to the study subjects on every visit and follow up. The costs of pamphlets, asthma diaries and peak flow meter mouthpieces that were given to the study subjects during the six-month follow-up period were included. Unscheduled visits in this study included unplanned visits to any private or public healthcare facilities either for in-patient or out-patient utilisation. Data for costs of visits to government and semi-government healthcare facilities were adapted from published literature (10), while the costs of unscheduled visits to private facilities were based on the amount the patients paid. These data were self-reported and documented in the study subjects' asthma diaries.

Three health outcomes were measured in this study. The primary outcome was asthma control, which was assessed based on the GINA symptom scoring tool (22). GINA symptom scores classify a patient's asthma symptom control into 3 categories, in which score 0 is controlled, score 1 to 2 as partly controlled and 3 to 4 as uncontrolled. In the analysis, we grouped the subjects into well-controlled (0-2 score) and uncontrolled asthma (3-4 score). The secondary outcomes were inhalation technique and frequency of unscheduled visit. Inhalation technique was assessed and scored were given based on the six-point checklist in RMTAC protocol (13). The frequency of unscheduled visit was obtained from the subject's diary. Data included were date of visit, type of healthcare facility visited, treatment received and costs.

For economic analysis, the incremental cost-effectiveness ratio (ICER) of RMTAC over standard care were estimated. The primary outcome was used in the cost-effectiveness analysis. The total costs were the sum of direct medical costs and costs of unscheduled visit. The ICER was defined as the additional cost of RMTAC to improve GINA scores by one unit when compared to standard care. ICER was calculated by dividing the differences in costs between RMTAC and standard care with the differences in their mean improvement in GINA scores. One-way sensitivity analysis was conducted to ascertain the robustness of the cost-effectiveness analysis. The base case parameters, namely the costs and outcomes RMTAC and standard care, were varied by 25% in the one-way sensitivity analysis to test the sensitivity of ICER towards the changes in these parameters.

Statistical analysis were completed using IBM SPSS Statistics for Windows, version 25. Statistical significance was set at *p* value less than 0.05. Means and standard deviations (SD) were calculated for the

continuous variables; whereas frequencies (n) and percentages (%) were calculated for the categorical variables. A comparison of the continuous variables between two groups was accomplished using independent t test; while categorical variables were analysed using Chi-square test or Fisher's exact test.

Results

In this study, 203 study subjects and 178 study subjects were recruited into RMTAC group and standard care group respectively. In the RMTAC group, 158 study subjects completed the study with a completion rate of 77.8%, while 163 study subjects in the standard care group completed the study with a completion rate of 91.6% (Figure 1). The baseline sociodemographic characteristics of the study subjects were summarised in Table 1.

Most of the study subjects were Malay and female with mean age of 45 to 46 years old. At baseline, there were no statistically significant differences between RMTAC group and standard care group except smoking status. In the RMTAC group, only 1.3% of study subjects were smokers and 19% of study subjects were passive smokers. Standard care group had a significantly higher percentage of smokers (6.7%) and passive smokers (38.7%). Majority of study subjects (79.7%) in the RMTAC group were free from smoke whereas only half of the study subjects (50.3%) in the standard care group were free from smoke.

The baseline clinical characteristics of the study subjects were summarised in Table 2. Both study arms had similar baseline clinical characteristics except baseline asthma control. At baseline, standard care group had a significantly higher percentage of study subjects with uncontrolled asthma (95.1%) as compared to RMTAC group (94.3%) (p=0.002).

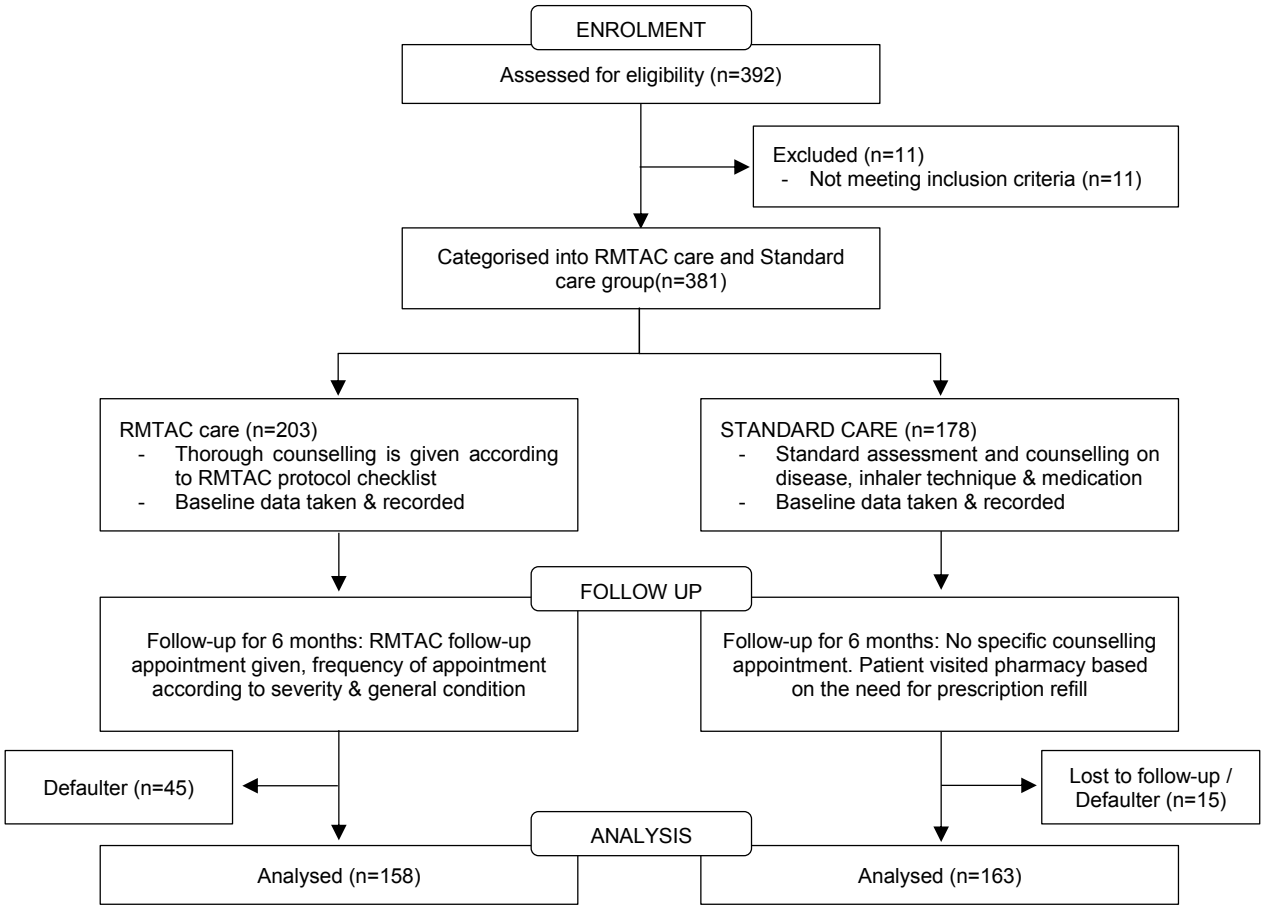

Figure 1: Flow of study subjects in the study

Table 1: Baseline sociodemographic characteristics of the study subjects (n=321)

Characteristics	RMTAC, n=158	Standard Care, n=163	*p*-value
Age at recruitment, year, mean ± SD	45 ± 15.4	46 ± 14.0	0.551 [a]
Gender, n (%)			0.631 [b]
Male	38 (24.1)	43 (26.4)	
Female	120 (75.9)	120 (73.6)	
Race, n (%)			**0.039** [c]
Malay	106 (67.1)	119 (73.0)	
Chinese	22 (13.9)	8 (4.9)	
Indian	26 (16.5)	33 (20.3)	
Others	4 (2.5)	3 (1.8)	
Occupation, n (%)			0.984 [c]
Government employee	34 (21.5)	30 (18.4)	
Private employee	40 (25.3)	45 (27.6)	
Self-employed	13 (8.2)	16 (9.8)	
Unemployed	10 (6.3)	8 (4.9)	
Housewife	45 (28.5)	49 (30.0)	
Student	7 (4.4)	6 (3.7)	
Government pensioner	5 (3.2)	4 (2.5)	
Private retiree	4 (2.6)	5 (3.1)	
Education level, n (%)			0.750 [c]
None	3 (1.9)	1 (0.6)	
Primary	26 (16.5)	27 (16.6)	
Secondary	76 (48.1)	75 (46.0)	
Tertiary	53 (33.5)	60 (36.8)	
Monthly household income category, n (%)			0.623 [c]
< RM 8000	157 (99.4)	160 (98.2)	
≥ RM 8000	1 (0.6)	3 (1.8)	
BMI category, n (%)			0.423 [b]
Not obese (BMI < 30)	115 (72.8)	112 (68.7)	
Obese (BMI ≥ 30)	43 (27.2)	51 (31.3)	
Smoking status, n (%)			**<0.001** [c]
Smoker	2 (1.3)	11 (6.7)	
Smoker and passive smoker	0	7 (4.3)	
Passive smoker	30 (19.0)	63 (38.7)	
Free from smoke	126 (79.7)	82 (50.3)	

Abbreviation: BMI – body mass index; SD – standard deviation
[a] Independent samples t-test
[b] Chi-square test
[c] Fisher's exact test

Table 2: Baseline clinical characteristics of the study subjects (n=321)

Characteristics	RMTAC, n=158	Standard Care, n=163	*p*-value
Medication profile, n (%)			0.646 [a]
Reliever + ICS	140 (88.6)	147 (90.2)	
Reliever + ICS + LABA	18 (11.4)	16 (9.8)	
Asthma control (GINA category), n (%)			**0.002** [a]
Well-controlled	9 (5.7)	8 (4.9)	
Uncontrolled	149 (94.3)	155 (95.1)	
GINA score, mean ± SD	2.91 ± 1.133	2.56 ± 1.134	**0.006** [b]
Duration of asthma, year, mean ± SD	18 ± 14	18 ± 12	0.928 [b]
Inhalation technique, n (%)			0.159 [a]
Good	42 (26.6)	29 (17.8)	
Poor	116 (73.4)	134 (82.2)	

Abbreviation: ICS – inhaled corticosteroids; LABA – long-acting beta agonist; SD – standard deviation
[a] Chi-square test
[b] Independent samples t-test

At the end of six-month follow up, both RMTAC group and standard care group demonstrated improvement in asthma control as evaluated by GINA symptom classification and inhalation technique. The outcome measures after six-month were summarised in Table 3. RMTAC group indicated 46.2% increment in well-controlled study subjects from 5.7% at baseline to 51.9% after six months. Standard care group demonstrated 16% increment in well-controlled study subjects from 4.9% at point of recruitment to 20.9% after six-month interval. In terms of mean GINA score, RMTAC group showed greater improvement compared to standard care group, which is from 2.91 at baseline to 0.99 after 6 months, with a mean improvement in GINA score of 1.91.

As for the measurement of inhalation technique, the RMTAC group showed 48.7% increment in study subjects with good inhalation technique from 26.6% at baseline to 75.3% after 6-month interval. Standard care group showed 14.1% increment of study subjects with good inhalation technique from 17.8% at baseline to 31.9%. Overall, RMTAC group showed significantly better asthma control and inhalation technique as compared to standard care group. However, there was no significant difference between the two groups in terms of frequency of exacerbation which is measured by frequency of unscheduled visit.

The total cost of asthma management per patient for the period of 6 months are presented in Table 4. The mean direct medical cost per patient (including personnel, medications and materials) was MYR 150.18 for RMTAC and MYR 110.37 for standard care. When the costs of unscheduled visits were included, the total cost was MYR 166.27 for RMTAC and MYR 120.22 for standard care. Figure 2 showed the cost for each component in both groups. The highest portion of costs were contributed by medications, followed by personnel, unscheduled visit and materials.

RMTAC demonstrated improved asthma control, but incurred more cost compared to the standard care. The ICER of RMTAC versus standard care was MYR 41.86 per improvement of GINA score by 1 unit (Table 5). The one-way sensitivity analysis was presented in Table 6 and Figure 3.

Table 3: Outcome measures after 6-month interval (n=321)

Characteristics	RMTAC, n=158	Standard Care, n=163	*p*-value
Asthma control (GINA category), n (%)			**<0.001** [a]
Well-controlled	82 (51.9)	34 (20.9)	
Uncontrolled (n, %)	76 (48.1)	129 (79.1)	
GINA score, mean ± SD	0.99 ± 1.254	1.75 ± 1.224	**<0.001** [b]
Improvement in GINA scores, mean ± SD	1.91 ± 1.473	0.81 ± 1.092	**<0.001** [b]
Inhalation technique, n (%)			
Good	119 (75.3)	52 (31.9)	**<0.001** [a]
Poor	39 (24.7)	111 (68.1)	
Frequency of unscheduled visits, mean ± SD	1 ± 1	1 ± 1	0.452 [b]

Abbreviation: ICS – inhaled corticosteroids; LABA – long-acting beta agonist; SD – standard deviation
[a] Chi-square test
[b] Independent samples t-test

Table 4: Health care costs of asthma management per patient for a period of 6 months

Cost Parameters	RMTAC, MYR*	Standard Care, MYR*	*p*-value
A. Direct Medical Costs	150.18 ± 118.02	110.37 ± 79.45	**<0.001**
Personnel	60.00 ± 25.73	46.65 ± 29.66	**<0.001**
Medication	85.33 ± 106.11	62.28 ± 61.23	**0.018**
Materials	4.81 ± 1.23	1.13 ± 0.39	**<0.001**
B. Cost of Unscheduled Visit	16.09 ± 36.76	9.85 ± 29.26	0.094
Total Costs, A+B	166.27 ± 126.50	120.22 ± 83.70	**<0.001**

Abbreviation: MYR – Malaysian Ringgit
* Data presented as mean ± SD

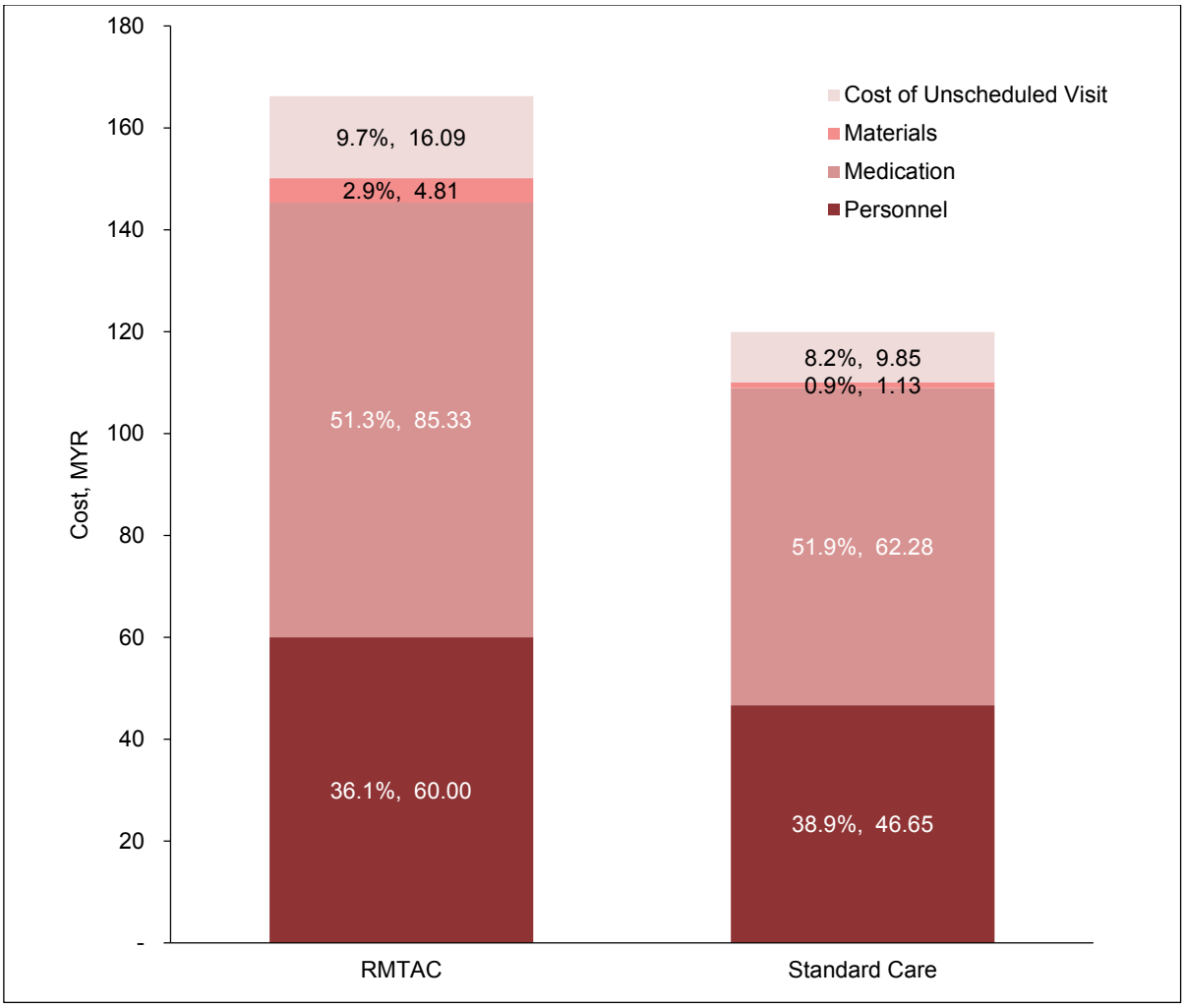

Figure 2: Cost components of asthma management for RMTAC and Standard Care Group

Table 5: Cost-effectiveness analysis of RMTAC versus standard care

	RMTAC	Standard Care	Difference
Cost per patient, MYR	166.27	120.22	46.05
Mean improvement in GINA score	1.91	0.81	1.10
ICER			MYR 41.86 *

Abbreviation: MYR – Malaysian Ringgit; ICER – incremental cost-effectiveness ratio
* ICER for RMTAC versus standard care was MYR41.86 per unit improvement in GINA score

Table 6: One-way sensitivity analysis of cost-effectiveness of RMTAC vs standard care

Varied Parameter	Varied Percentage − 25%	Varied Percentage + 25%
	ICER (MYR per unit improvement in GINA score)	
Cost of Standard care	69.19	14.54
Cost of RMTAC	4.08	79.65
Effectiveness of Standard care	35.36	51.31
Effectiveness of RMTAC	73.98	29.19

Abbreviation: MYR – Malaysian Ringgit; ICER – incremental cost-effectiveness ratio

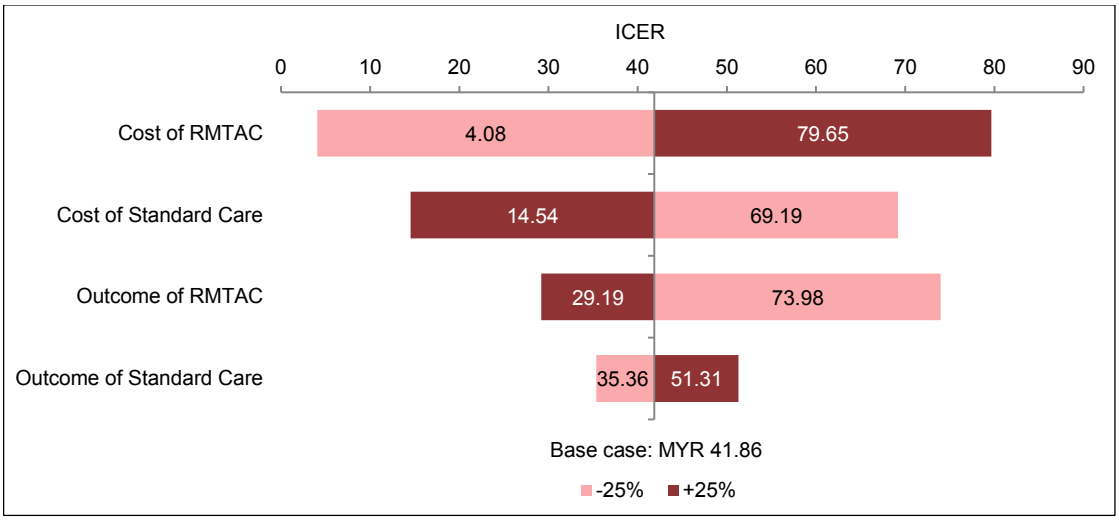

Figure 3: Tornado diagram showing the changes in ICERs (MYR per 1 unit improvement in GINA score) of RMTAC vs standard care in response to variation in input parameters

Discussion

This study was one of the first in Malaysia to assess cost-effectiveness of RMTAC using real world input instead of estimation models. In this study, RMTAC which is a pharmacist-managed asthma clinic was found to improve patients' asthma control and inhalation technique compared to standard pharmaceutical care. The result was similar to a few published studies that showed comprehensive education by pharmacists improved patients' knowledge on disease, inhaler technique skills and adherence; subsequently improve asthma control and quality of life (23,24). A study by Oh *et al*. in Malaysia also found that pharmacists' involvement in RMTAC had shown an overall improvement in asthma clinical outcomes (25).

There were significant differences in baseline clinical characteristics between the intervention and control groups. This is because our study was a non-randomised controlled study and one of the RMTAC referral criteria is patient with poor asthma control. Thus, most of the study subjects from the RMTAC group had higher baseline GINA mean score (2.91) compared to the standard care group (2.56).

Overall, RMTAC incurred a significantly higher cost than standard care. A big component of the costs were contributed by medications in both groups, but the medication cost was significantly higher for RMTAC patients. This could be due to active involvement of RMTAC pharmacists in optimising patients' asthma treatment as according to the asthma guideline. Similar findings were seen in a study by Perez *et al*., where higher cost of care in asthma clinics was due to the cost of medications (26). As RMTAC pharmacists spent more time with patients during RMTAC consultation and counselling, this contributed to significantly higher personnel cost for RMTAC care. However, no significant difference was found in the frequency and cost of unscheduled visits. This may be due to the self-reporting of unscheduled visits and thus subjected to study subjects' recall bias.

Our results showed that RMTAC improved patients' asthma control but was costlier. The incremental cost-effectiveness ratio (ICER) was MYR41.86 to improve GINA score by one unit. Nevertheless, it is common to have a positive cost-effectiveness ratio in healthcare settings as better outcomes may come at higher costs. The willingness-to-pay threshold for health care intervention in Malaysia was estimated by Lim *et al*. to be between MYR19,929 to MYR28,470 per quality-adjusted life year (QALY) (27), but there is no threshold set specifically for asthma control. If compared against this threshold, the ICER of RMTAC was far below the threshold and thus RMTAC could possibly be cost-effective. The one-way sensitivity analysis showed that although the estimated ICER of RMTAC was sensitive to changes in the cost and effectiveness of both RMTAC and standard care, the ICERs were still below the cost-effectiveness threshold suggested by Lim *et al*. (27) even if the cost of RMTAC increased by 25 percent.

Our study only followed up subjects for a period of six months, which is different in real life whereby patients will be under RMTAC follow up for a longer period until they have reached the desired asthma outcome for discharge. Therefore, RMTAC may eventually save cost in the long run if well-controlled asthma

patients have less exacerbation, less need to step up treatment and reduce absenteeism from work. This is supported by a study done by Perez *et al*. and Abdelhamid *et al*. which found a significant reduction in the frequency of acute attacks, use of inhaled beta-agonist and days of sickness after pharmacist's intervention in asthma management (6,26). A systematic review by Yong *et al*. concluded that the most cost-effective enhanced asthma management is a mixture of education and self-management (5). Another study done by Yong *et al*. using Markov cohort model also suggested that the implementation of RMTAC in Malaysia has high probability of being more cost-effective than the usual care management (14). As our study had shown that RMTAC significantly improve patients' asthma control and inhalation technique, it could possibly reduce the economic burden of asthma in long term. This is supported by previous studies which showed that annual medical resources utilisation for poorly controlled asthma is 2.5 to 3.5 folds of well-controlled asthmatic patients (28,29). Therefore, considering the benefits that RMTAC could potentially bring to patients, and the possibility of reducing the economic burden to our healthcare system, it is recommended to invest and expand the current RMTAC service to more health care facilities in Malaysia.

There are some limitations with this study. Firstly, data on unscheduled visits were obtained based on the assumption that study subjects accurately recorded the visits and admission in asthma diaries, thus subjected to recall bias. Secondly, study subjects were recruited into RMTAC and standard care groups from various clinics without randomisation and therefore there may be confounding factors that can interfere with the results. Thirdly, RMTAC group has more patients with higher mean GINA score at baseline compared to standard care, and this could affect the degree of effectiveness observed in RMTAC group. Follow-up period for this study was only 6 months, which may not be able to reflect the true effectiveness, frequency of unscheduled visits and the costs of treatment. Therefore, a randomised controlled study with longer follow-up period is recommended in the future.

Conclusion

Pharmacist-managed RMTAC service helps to improve patients' asthma control and inhalation technique at a small additional cost. Thus, it is recommended that the Ministry of Health should consider these findings and expand RMTAC service to more government facilities to improve the health outcome of asthma patients.

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Conflict of Interest Statement

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