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Research Article

Treatment of COPD in one university hospital setting in Thailand: the real-life prescribing patterns and treatment expenditures

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ABSTRACT

This study aims to examine prescribing patterns of COPD medications, adherence to The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2013 guideline, and impact of the adherence on clinical and economic outcomes. A retrospective study was conducted at Ramathibodi hospital. All COPD patients receiving treatment during July 1- December 31, 2012 were identified from electronic database. Index date was determined as the first date with FEV_1 during the recruitment period. Data on treatment, cost, and clinical outcomes were reviewed for 1 year after index date. The results were included 109 patients. 84 patients (77.06%) and 25 patients (22.94%) were classified into group 1 ($FEV_1 \geq 50\%$) and group 2 ($FEV_1 < 50\%$), respectively. It was found that group 1 reported significantly lower exacerbation rate (26.19% vs 80.00%) than group 2. SABA/SAMA was the most prescribed drugs (97.61% in group 1 and 100% in group 2). Over-treated with ICS was common (63.09%) with $FEV_1 \geq 50\%$. Average annual treatment expenditure per capita was US$ 411 for group 1 and US$ 703 for group 2. No association between adherence to GOLD 2013 guidelines and clinical or economic outcomes was identified, possibly due to short duration of study. Adherence to GOLD 2013 guideline was sub-optimal. To promote the adherence to GOLD 2013 guideline, further long-term and well developed studies are clearly needed.

1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities, is recognized as an important public health concerns globally. In 2015, approximately 3.17 million deaths or approximately 5% of all death globally was caused by COPD[1]. In high-income countries, COPD was the fifth leading cause of death while it ranked the sixth leading cause of death in low and middle-income countries[2]. Furthermore, the burden from COPD was projected to increase. It was estimated that COPD will be the fourth leading causes of death by 2030[3].

COPD imposed significant economic burden. The annual direct expenditures for COPD treatment per patient in Europe and North America ranged US$ 520 in France to US$ 4,120 in the US (2002 value)[4]. According to the review, most direct costs were

incurred from hospitalizations[4]. In addition, indirect costs of COPD due to sick leaves,restricted activity day and disability day were substantial with the estimated annual indirect cost of US$ 1,521-US$ 3,348 per patient (2010 value). In the studies that assessed both direct and indirect cost, it was found that indirect costs accounted for 27%-61% of total costs[5].

Since 1997, the Global Initiative for chronic obstructive lung disease (GOLD) was established to raise awareness of COPD and to improve prevention and treatment of this disease. According to the 2009 GOLD criteria, severity of COPD patients with an $FEV_1/FVC < 0.70$ was classified based on post bronchodilator lung function into 4 groups as follows; 1. GOLD 1 (mild): $FEV_1 \geq 80\%$ predicted; 2. GOLD 2(moderate): $80\% > FEV_1 \geq 50\%$; 3. GOLD 3 (severe): $50\% > FEV_1 \geq 30\%$; and 4. GOLD 4 (very severe): $80\% > FEV_1 < 50\%$. Later in 2011, the "ABCD" assessment tool that incorporated patient reported outcome and highlighted the importance of exacerbations was proposed. In the "ABCD" assessment scheme, patients are required to undergo spirometry, either assessment of dyspnea using Modified Medical Research Council dyspnea scale (mMRC) or symptoms using COPD Assessment Test (CAT). In addition, patient's history of exacerbations was taken into account.

According to GOLD 2014, short-acting bronchodilator medication either short-acting muscarinic agonist (SAMA) or short-acting β_2-agonists (SABA) are recommended for immediate relief from symptoms while one or more long-acting including long-acting β_2-agonists (LABA) or long-acting muscarinic antagonist (LAMA) are recommended for long term maintenance therapy in patients with moderate to severe COPD. Inhaled corticosteroid (ICS) is recommended in addition to a maintenance treatment with a LABA and/or LABA+LAMA for patients with severe or very severe air flow limitations and/or 3 or more exacerbations per year[7,8]. Similar to GOLD, NICE guidelines also recommended ICS in addition to a LABA for patient with severe airflow limitation ($FEV_1 < 50\%$) and recurrence exacerbations and/or breathless[6].

Evidences from several countries indicated that the adherence to GOLD recommendations was suboptimal[7-13]. Over-treatment especially among mild and moderate COPD was commonly observed[9-10,12]. While existing evidence indicated that the use of ICS has been associated with increased risk of pneumonia[14-15], a significant proportion of mild and moderate COPD patients being treated with ICS was reported in several studies[7,9,11]. On the other hand, under-treatment was also identified[8,11].

Besides the low adherence to GOLD guideline, the impact of adherence to such guideline on clinical outcomes of COPD and cost of treatment was limited and unclear. Previous study[10] found that there was no relationship between adherence and exacerbation while the recent study[8] identified inverse relationship between non-adherence and exacerbation. One study reported the lower cost among the adherence group compared to non-adherence group[16].

In Thailand, according to the Bureau of epidemiology, Department of disease control, prevalence of COPD was estimated at 176.77 per 100,000 populations in 2013. COPD ranked the fifth leading cause of DALY loss among Thai male in 2009[17]. Age-adjusted deaths from COPD in Thailand was estimated at 48.0 per 100,000[2]. The average cost per patient per year ranged from 6,084 baht for mild to 16,527 baht for very severe patient (2015 value, 30 baht = $1)[18]. The majority of direct costs were incurred in out-patient care[18]. Very little is known about the prescribing patterns of COPD treatment in upper-middle-income countries including Thailand. Thus, the objectives of this study were to examine the prescribing patterns and COPD treatment expenditure at one university hospital in Thailand. In addition, we aim to examine whether treatments were in line with GOLD 2013 guideline and to determine the impact of adherence to the guideline on clinical outcomes and cost of treatments.

2. METHODS

2.1. Study design and participants

This study is a retrospective study conducting at Ramathibodi hospital, a 1000-bed teaching hospital in Bangkok.

Participants

Participants were all COPD patients receiving care during July 1- December 31, 2012. Participants were identified from electronic database using International Classification of Diseases and Related Health Problem, Tenth Revision (ICD-10) codes (J44).

Table 1. COPD severity stage and recommended therapies based on GOLD 2004 recommendations.

COPD severity stage	Spirometric criteria $FEV_1/FVC < 70\%$	Recommended therapies
Group 1 (mild + moderate)	$FEV_1 \geq 50\%$	As needed SABA/ SAMA Add regular treatment with one or more LAMA/ LABA
Group 2 (severe + very severe)	$FEV_1 < 50\%$	As needed SABA/ SAMA Add regular treatment with one or more LAMA/ LABA Add ICS if repeated exacerbations

Sample and sample size calculation

The total number of COPD patients included in this study (n) was calculated using following equation: $n = Z^2_{1-\alpha/2} * P(1-P)/ M^2$[2,19]. As there was no previous data on prevalence of adherence to GOLD guideline in Thailand (P) before, then P was set at 0.5[19]. By using type 1 error (α) at 0.05 and setting margin of error (M) at 10%, the required sample size was estimated at 100. Patients were excluded if they had no information on post bronchodilator FEV_1/FVC ratio and the FEV_1 on their medical records or had incomplete medical record.

With the assumption that approximately 15% of COPD patients had information on post bronchodilator FEV_1/FVC ratio and the FEV_1 on their medical records and that the total number of COPD patients identified from electronic database during the recruitment period were approximately 1,600, 50% of all identified COPD patients (800) were randomly selected.

Then, their medical records were reviewed to determine the eligibility. Index date was determined as the first date with post bronchodilator FEV_1 during the recruitment period.

2.2. Data collection

The study was approved by the Human Research Ethics Committee of Ramathibodi hospital in 2014. For each eligible patient, data on treatment, cost, and clinical outcomes were reviewed for 1 year after index date. The following data were collected from electronic medical recording; age, gender, type of insurance, pharmacological treatments, number of outpatient visits, admission data, number of exacerbation, and number of emergency room visits. Treatment expenditure, which included charges of drug, X-ray, and other services incurred from outpatient visit emergency room visit and hospitalization, were also collected from electronic database.

Table 2. Characteristics of all COPD patients classified by FEV_1

Characteristics	N (%) or Mean ± SD		p-value
	Group 1 (n = 84)	Group 2 (n = 25)	
FEV_1	73.01 ± 13.34	34.95 ± 9.70	< 0.001*
Age	71.22 ± 9.70	70.54 ± 12.01	0.958
Gender			
Male	69 (82.14)	20 (80.00)	0.808
Female	15 (17.86)	5 (20.00)	
Co-morbidities			
1 co-morbidity	20 (23.80)	9 (36.00)	0.506
2 co-morbidities	27 (32.14)	7 (28.00)	
3 co-morbidities	22 (26.19)	4 (16.00)	
More than 3 Co-morbidities	15 (17.87)	5 (20.00)	
Type of health insurances			
CSMBS	40 (47.61)	14 (56.00)	0.726
UC	1 (1.19)	0	
SSS	4 (4.76)	0	
Out of pocket	39 (46.44)	11 (44.00)	

Notes: CSMBS = Civil Servant Medical Benefit Scheme, UC = Universal Coverage,
SSS = Social Security Scheme, FEV_1 = Forced Expired Volume in one second.
- Independent t-tests were conducted for age and FEV_1. Chi-square tests were conducted for the other variables.
*statistical significant difference

Table 3. Comparison of clinical outcomes and resource utilizations

Characteristics	N (%) or Mean ± SD		p-value
	Group 1 (n = 84)	Group 2 (n = 25)	
Patient with exacerbation (person)	22 (26.19)	20 (80.00)	< 0.001*
Number of exacerbations (time)	1.27 ± 0.45	2.47 ± 1.93	< 0.001*
Patients with ER visit (person)	8 (9.52)	6 (24.00)	0.085
Total number of ER visits (time)	0.11 ± 0.60	0.68 ± 1.64	0.119
Patients with hospitalization (person)	5 (5.95)	4 (16.00)	0.206
Total number of hospitalizations (time)	0.06 ± 0.21	0.28 ± 0.72	0.235
Length of stay (day)	0.51 ± 2.54	2.72 ± 10.92	0.235

Notes: ER = emergency room, IPD = inpatient department
- Mann-Whitney U tests were conducted for number of exacerbations, total number of ER visits and total number of hospitalizations. Chi-square tests were conducted for the other variables.
* statistical significant difference

2.3. Data analysis

Each eligible patient was classified into 2 groups as group 1 ($FEV_1 \geq 50\%$) and group 2 ($FEV_1 < 50\%$). Pattern of treatments was reported in terms of descriptive statistics. Patients were then classified as receiving appropriate and inappropriate (i.e. over-treated, under-treated) treatments based on GOLD recommendations, as shown in Table 1. If patients were prescribed medications that were recommended for a more severe stage than their own classification they were classified as being over-treated. On the other hand, if they were prescribed treatment based upon the severity category less severe than their own severity stage they were considered as under-treated. Comparison of clinical outcomes such as number of exacerbations, number of hospitalizations, number of ER visits, and cost was conducted by independent t-test. Mann-Whitney U test was used if data were not normally distributed. Level of significant difference was set at p-value < 0.05. Annual treatment expenditure per capita per year was also calculated for each group of patients.

3. RESULTS

Of the total 1,608 COPD patients identified from the electronic database, 804 (50%) were randomly selected. Only 109 patients who had information on post bronchodilator FEV_1/ FVC ratio and the FEV_1 and had complete medical record were included in the study. Then, 84 patients (77.1%) were classified into group 1 ($FEV_1 \geq 50\%$) while 25 patients (22.9%) were classified into group 2 ($FEV_1 < 50\%$). Characteristics of included patients were summarized in Table 2. The mean FEV_1 in group 1 was 72.5%, while that of group 2 was 34.8%. There was no significant difference between the two groups in terms of age, gender, co-morbidity and health insurance coverage.

Table 4. Comparison of patterns of COPD medications

Characteristics	N (%) or Mean ± SD		p-value
	Group 1 (n = 84)	Group 2 (n = 25)	
Number of prescribed drugs (items/person)	7.87 ± 7.14	18.16 ± 19.12	0.166
Number of patients received the following medication (person):			
SABA-SAMA (terbutaline, salbutamol, ipratropium)	82 (97.61)	25 (100.0)	0.595
LABA (indacaterol)	2 (2.38)	0 (0)	0.593
LABA (bambuterol)	3 (3.57)	1 (4.00)	0.652
LAMA (tiotropium)	26 (30.95)	14 (56.00)	0.032
Oral xanthine (theophylline)	27 (32.14)	10 (40.00)	0.461
ICS (budesonide)	2 (2.38)	0 (0)	0.436
ICS+LABA; fluticasone/ salmeterol	45 (53.57)	23 (92.00)	< 0.001*
ICS+LABA; budesonide/ formoterol	6 (7.14)	1 (4.00)	0.572

Notes: SABA = short-acting $beta_2$ agonist, LABA = long-acting $beta_2$ agonist, SAMA = short-acting muscarinic agonist, LAMA = long-acting muscarinic agonist, ICS = inhaled corticosteroid
- Chi-square tests were conducted for all variables except number of prescribed drugs, where Mann-Whitney U test was conducted.
* statistical significant difference

Table 5. Comparison of appropriateness of COPD treatment

Characteristics	N (%)		p-value
	Group 1 (n = 84)	Group 2 (n = 25)	
Appropriate	24 (28.60)	24 (96.00)	< 0.001*
Over-treated [a]	58 (69.00)	0 (0)	
Under-treated [b]	2 (2.40)	1 (4.00)	

[a] For Group 1: over-treated = ICS or ICS+LABA were prescribed.
[b] For Group 1: under-treated = no prescribed medication.
For group 2: under-treated = SABA, SAMA, LABA (single)
- Chi-square test were conducted to compare for appropriateness of medications.
* statistical significant difference

Clinical outcomes

Clinical outcomes and resource utilizations were shown in Table 3. COPD patients in group 1 reported significantly lower exacerbation rate (26.19%) than patients in group 2 (80.00%). The mean frequency of exacerbation in past year was also lower in group 1 (1.27 VS 2.47). None of them were death during the study period. In terms of resource utilizations, there was no significant difference between group 1 and group 2 in terms of number of patients visiting to ER as well as number of ER visit, as shown in Table 3.

Prescribing patterns

Details on medication treatments of the patients were displayed in Table 4. Average number of drug items prescribed among patients with poor lung function (group 2) was higher than that of patients with well-preserved lung function (group 1) approximately two times. However, significant difference was not observed. In terms of prescribing patterns, SABA-SAMA were prescribed in 97.61% of group 1 and 100.00% of group 2. ICS+LABA combinations (fluticasone/ salmeterol and budesonide/ formoterol) were prescribed in 60.71% of group 1 and 96.00% of group 2 patients. LABA (indacaterol and bambuterol) was prescribed in 5.95%, and 4.00% of group 1 and group 2, respectively. LAMA was prescribed in 30.95% and 56.00% in group 1 and group 2, respectively. When comparing between group 1 and group 2, it was found that LAMA and ICS+ LABA (fluticasone/ salmeterol) were significantly prescribed in group 2 more than group 1.

When focused on comparison of appropriateness of COPD medications based on GOLD 2013 guideline in Table 5, for group 1 patients, 28.60% of patients receive appropriate treatment while approximately 69.00% and 2.40% were considered over-treated and under-treated, respectively. On the other hand, 96.00% of patients with post bronchodilator FEV_1< 50% (group 2) received appropriate while 4.00% (n =1) were under-treated.

Economic outcomes

As shown in Table 6, for group 1 patients, average annual treatment expenditure per capita was US$ 411. Drug was the major part of the total expenditures (71.23%). It was found that cost incurred in OPD was the highest (90.74%).

Table 6. Comparison of treatment expenditures

Characteristics	Treatment expenditures (US Dollar)										
	Group 1 (n = 84)					Group 2 (n = 25)					p-value
	Drug	X-ray	Others	Total	%	Drug	X-ray	Others	Total	%	
Department											
Emergency	82	97	80	259	0.74%	108	374	335	815	4.64%	NA
Outpatient	24,010	4,290	2,997	31,297	90.74%	13,668	637	704	15,008	85.41%	NA
Inpatient	477	269	2,185	2,931	8.52%	493	651	1,022	2,166	9.95%	NA
Total cost	24,569	4,656	5,262	34,487	100%	14,269	1,662	2,061	17,989	100%	NA
% of total cost	71.23%	14.84%	13.93%	100%	NA	81.16%	7.28%	11.56%	100%	NA	NA
Annual cost per patient (Mean ± SD)	293 ± 42	55 ± 39	63 ± 22	411 ± 391		571 ± 92	50 ± 35	83 ± 17	703 ± 624		
Annual cost per patient (Median)	293	55	63	411	NA	561	65	81	707	NA	0.156

Notes: all costs were converted from Thai baht (THB) to US Dollars (2013 value, 32 THB = $1). We presented only US Dollar in cost because of international unit in the world. Mann-Whitney U test was conducted to compare median cost per patient between group 1 and group 2.

Table 7. Comparison of clinical outcomes, resource utilizations, and total expenditures per capita between patients receiving appropriate treatment and inappropriate treatment among group 1 patients

Characteristics	N (%) or Mean ± SD		p-value
	Appropriate treatment (n = 24)	Not appropriate treatment (n = 61)	
Patient with exacerbation	7 (29.20)	15 (25.00)	0.785
Number of exacerbations	0.33 ± 0.57	0.37 ± 0.71	0.906
FEV_1	77.03 ± 12.99	72.15 ± 12.24	0.469
Patients with ER visit	2 (8.30)	6 (10.00)	0.588
Number of ER visits	0.17 ± 0.34	0.25 ± 0.95	0.860
Patients with IPD visit	1 (4.20)	4 (6.70)	0.662
Number of IPD visits	0.04 ± 0.20	0.07 ± 0.25	0.942
Length of stay (day)	0.42 ± 2.04	0.55 ± 2.65	0.942
Annual cost per capita (US Dollar)	302	330	0.277

Notes: all costs were converted from Thai baht (THB) to US Dollars (2013 value, 32 THB = $1) and compared in Median.
- Mann-Whitney U tests were conducted for number of exacerbations, FEV_1, number of ER visits, number of IPD visits, length of stay, annual cost per capita. Chi-square tests were conducted for the other variables.

For group 2 patients, average annual treatment expenditure per capita was US$ 703. Similar to group 1 patients, drug was the major part of the total expenditure and cost incurred in OPD was the highest.

Impact of adherence to GOLD 2013 guideline

When considered patients in group 1, as shown in Table 7, there was no significant difference between patients with appropriate treatment and inappropriate treatment in terms of clinical outcomes, resource utilizations (i.e. proportions of patients reported having exacerbation, number of exacerbations, proportion of patients reported having ER visit, number of ER visits, proportion of patient reported have been hospitalized, number of hospitalizations, and length of stay), and annual expenditure per capita. On the other hand, almost all of patients in group 2 (96.00%) received appropriate treatment. Therefore, comparison of clinical outcomes between patients with appropriate treatment and inappropriate treatment was not conducted.

4. DISCUSSION

Due to the lack of information on mMRC and CAT, we categorized patients only from FEV_1. In our study, however, more than half of COPD did not completely undergo spirometry and were excluded from the study, so we classified patients into only 2 groups as having $FEV_1 \geq 50\%$ (group 1) and $FEV_1 < 50\%$ (group 2). Although our criterion was slightly different than GOLD, we confirmed that COPD patients in group 2 reported significantly higher exacerbation than group 1. This confirmed that, in case of limited data on mMRC and CAT, FEV_1 alone was an acceptable criteria to classify COPD severity.

When looking at treatment patterns, SABA-SAMA was the most prescribed drugs (97.61% in group 1 and 100.00% in group 2). ICS+LABA was the second most prescribed drug and was prescribed to 60.71% of patients with post bronchodilator $FEV_1 \geq 50\%$. Our findings were similar to those of previous studies[9-12]. Jochmann et al found that ICS+LABA regimen was the most prescribed drug (60% of all patients). Price et al found that ICS+LABA and ICS+LABA+LAMA were the most frequently used treatments in well-preserved lung function (49.9% in group A & 46.6% in group B). Gunen et al found LABA+LAMA+ICS regimen was noted in 62% of mild to moderate lung function.

In line with many previous studies which found that adherence to treatment guideline is suboptimal ranking from 19%[8] to 60%[12] and that overuse of ICS among patient with mild and moderate COPD was common[7-9,11-12], we found that only 44% of COPD patients received appropriate treatment (28.60% for group 1 and 96.00% for group 2). In our study, over-treated with ICS was high (69.00%) among patients with mild and moderate COPD (group 1). As patients with mild and moderate COPD had lower risk of exacerbation, over treatment medications with ICS were not appropriate and might be associated with pneumonia[14-15]. However, we did not collect data about adverse effects of ICS overuse in terms of pneumonia in this study.

There are several reasons for overuse of ICS in mild and moderate COPD. First, it might be due to the unfamiliar with the treatment guidelines and the concern of physicians regarding the exacerbation. Previous study[7] found that previous exacerbation was a strong predictor associated with prescribed ICS or ICS combination in mild to moderate lung function

patients. Furthermore, the other possible reason was related to the health insurance issue. In Thailand, all ICS or ICS combination were listed in essential drug list and then can be reimbursed. On the other hand, only some LABA can be reimbursed. While the price of LAMA was higher than those of ICS or ICS+LABA, LAMA was not in the essential drug list and cannot be reimbursed by the public insurance scheme. These above issues can help explaining why LAMA and LABA were less frequently used than ICS and ICS combination among mild and moderate COPD patients.

Among COPD patients with well–preserved lung functions (group 1), clinical outcomes and resource utilizations between patients receiving appropriate medications and inappropriate medications was not found to be significantly different. Our findings were in accordant with the result of previous study[10] which found no statistically significant difference between adherence and non-adherence groups in term of exacerbation year but in contrasted with recent study[8] that found inverse relationship between under-treated and exacerbation. The possible reason of non-significant impact of adherence to guideline found in our study and previous study[10] was probably due to the short duration of study.

In terms of treatment expenditures, in contrast to previous study[16] we found no significant difference between patients receiving appropriate and inappropriate treatment. This probably due to the fact that our duration of study was too short (1 year) so no significant difference in terms of clinical outcome was identified and that most inappropriate treatment in our study was overuse of ICS, which is not expensive. In contrast to other previous studies[20-22], all conducted in western countries, which found that inpatients hospitalization was the largest proportion of the overall direct cost, we found that drug expenditures incurred in outpatient department accounted for the largest part of total expenditures.

In our study, average annual treatment expenditure per capita was US$ 411 for group 1 and US$ 703 for group 2. Nevertheless, it should be noted that these figures were tend to be under-estimated as the expenditure was calculated from electronic database from Ramathibodi hospital only. It might be the case that patients had ER visits or had been hospitalized at other hospitals or purchased other COPD drugs from the drugstores. In addition, indirect cost such as caregiver cost, cost of absenteeism was not included. Thus, the true annual cost of COPD treatments may be higher than reported in this study.

There are some limitations of this study that should be acknowledged. First, due to retrospective design using electronic database, some clinical and medical histories of a patient might be missing or inaccurate due to miscoding. Nevertheless, there are many advantages of using electronic database. For example, the use of database consumed less resources in terms of cost and time, providing the opportunity for routine monitoring of drug treatment. Recently, many pharmacoepidemiology studies were conducted using hospital database[23-26]. Other limitation was that the number of eligible patients were limited as pulmonary lung function test with spirometry in COPD was not routine investigated in real-practice in many upper-middle- income countries including Thailand. As the result, many patients were excluded from the study. Another limitation was that follow up period symptoms of patient after index date was too short time (1 year). Long-term study (> 1.5 years) should be further conducted to examine the impact of overuse of ICS[27-30]. It should also be noted that our study was conducted in only one hospital with limited number of patients especially those with $FEV_1 <$ 50, therefore, generalizability of our findings should be made with caution.

As the number of studies examining impact of adherence to GOLD guideline on clinical outcomes and treatment expenditures are limited and also inconclusive, to promote the adherence to GOLD 2013 guideline, further long-term and with larger number of patients from several hospitals are clearly needed. In addition, the dosage of treatment should also be taken into account in the analysis.

5. CONCLUSIONS

Our study indicated that adherence to GOLD 2013 guideline was sub-optimal. Adherence to GOLD 2013 guideline was higher in severe group (group 2) than in mild and moderate group (group 1). Over-treated with ICS was common (63.09%) among patients with $FEV_1 \geq 50\%$. On the other hand, appropriate-treated was found almost 100% in severe group. SABA-SAMA was the most prescribed medicine in both groups. Nevertheless, no association between adherence to GOLD 2013 guidelines and clinical or economic outcomes was found among COPD patients.

Medication expenditures was the highest cost of total hospital expenditures in both groups. Majority of cost was incurred in outpatient service. Although the annual expenditure per capita was found to be higher in group 2 (US$ 703) than group 1 (US$ 411), no statistically significant difference was found. Nevertheless, due to the small sample size and short follow up duration, it was premature to conclude that adherence to GOLD guideline had no impact on clinical outcomes and economic outcomes. To promote the adherence to GOLD 2013 guideline, further long term studies conducted in large number COPD patients on the impact of adherence to GOLD guideline on clinical, economic, and humanistic outcomes are clearly needed.

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