Title Page

Impact of a clinical pharmacist intervention on medicine costs in patients with chronic obstructive pulmonary disease in India

(Running header: Medicine costs of COPD in India)

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(Accepted for publication PharmacoEconomics Open)

ABSTRACT
Background: Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality especially in lower and middle income countries (LMICs) such as India. Medicine costs are a key issue in LMICs with typically high patient co-payments. In addition, pharmacists are underutilised in LMICs including India. However, pharmacist-led educational interventions may improve the care of patients with COPD as well as reduce medicine costs. Consequently, the objective of this study was to assess the effectiveness of a pharmacist led intervention in reducing medicine costs. Methodology: We assessed the impact of a pharmacist intervention on direct medicine costs in COPD patients (medicine costs and pharmacist time) in a randomized controlled study involving an intervention and control group and conducted at a tertiary care teaching hospital in India. Results: The six-monthly cost of medicines at baseline increased with disease severity from a maximum of US$29.46 for those with mild COPD up to US$63.28 for those with very severe COPD. Substantial savings in medical costs were achieved with the pharmacist-led programme, up to a maximum of US$20.49 over six-months for very severe patients. This equates to a reduction of 30.6% in medicine costs ($P < 0.001$), reduced to 26.1% when pharmacists' time (US$3.00/ patient) is included. Conclusion: There could be a key role for pharmacists as educators in COPD patients in LMICs to improve care and reduce costs including patient co-payments.

Key points for decision makers

* Chronic obstructive pulmonary disease is the 4th leading cause of death globally. Moreover, 90% of COPD-related deaths typically occur in low and middle income countries (LMICs) including India.
* In India, medicine costs currently represent a major proportion of the total healthcare costs (approximately 38%). Consequently, there is a need to address this especially if most medicine costs are out-of-pocket
* A clinical pharmacist-led intervention reduced the costs of medicines for patients with COPD by up to 30.6% whilst improving medication adherence and health related quality of life, with savings marginally lower once the costs of pharmacy time are included
* This intervention is feasible and pragmatic and could potentially be implemented across India and in other LMICs given concerns with the paucity of physicians, availability of pharmacists and costs savings as India and other LMICs moves towards universal access

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease characterised by airflow limitation and obstruction (1, 2). COPD though is not fully reversible (unlike asthma) and is usually progressive (1). However, early diagnosis and treatment, including smoking cessation, reduces the rate of decline in lung function and is seen as beneficial (3, 4).

Interest in COPD has grown in recent years across countries including India with an estimated global prevalence of 210 million people and rising, with prevalence rates in India averaging 4.2%, ranging from 1% to 10% or higher depending on the State (2, 5-9). This is because COPD is a major cause of morbidity and mortality (2, 6, 10, 11). Currently, COPD is the fourth leading cause of death globally and likely to become the third leading cause by 2020 (4, 10, 12). 90% of COPD-related deaths typically occur in low and middle income countries (LMICs), with India and China accounting for two thirds of these (2, 13). Currently in India, chronic respiratory diseases are the third highest cause of mortality accounting for 11% of all deaths (6, 14), with COPD the greatest contributor at 8.7% of all deaths resulting in over 400,000 deaths a year (6, 8). As a result, deaths due to COPD in India are over four times higher than that seen among developed countries (10, 15). Lower socioeconomic status, including poor nutrition and childhood poverty, limited education and health literacy, as well as higher exposure to particulate matter in the air, are major causes of increased mortality due to COPD in LMICs such as India (16-21). Murthy *et al* in 2005 reported that incidence of COPD is higher in rural versus urban India, with lower socioeconomic status being one of the major factors (22).

Of the total global disability life years (DALYs) due to chronic respiratory diseases, 32.0% of these currently occur in India (6), with COPD in India currently accounting for 4·8% of total worldwide DALYs (6). COPD is also associated with considerable economic burden, which is increasing (23-27). In the US in 2010, the projected annual cost of COPD was $49.9 billion including $29.5 billion of direct medical costs (24). In China, current annual direct medical costs for COPD are US$30.30billion, direct non-medical costs are US$1.36billion and indirect costs are US$5.28billion, with hospitalisations accounting for 56.7% of total costs (25). In Korea, the estimated costs for COPD in 2018 were

approximately US$1.245 billion, with direct medical costs accounting for approximately 20% of this (23). In Germany, the annual excess cost of COPD in 2012 per patient compared with healthy subjects varied on average from €2,595 for Gold Grade 1 patients to €8,924 for Grade 4 patients for direct costs and €8,621 for GOLD Grade 1 patients rising to an average of €27,658 for Grade 4 patients for indirect costs (27). In Italy, average healthcare costs for patients with severe COPD is €6700 per patients per year, of which hospitalisations are a substantial proportion (over 60%) (28), and in Spain the average health care cost per patient per year with COPD is approximately €2000 with medicines comprising approximately 40% of costs (29, 30)

The current economic burden of COPD in India is largely unknown (8), although Patel *et al* (2014) calculated direct medical costs were up to Rs. 5876.00 (US$88.23) per patient from admission to discharge among hospitalised patients, with the costs of medicines a substantial proportion at over 5 times hospital charges (31). This is very different to the situation in higher income countries. Naveed *et al* (2016) calculated an average annual total direct cost per patient for COPD of Rs. 5000 (US$ 75.08) to 25,000 (US$ 375.38), considerably higher than the direct medical costs for asthma at Rs. 1000–20,000 (US$ 15.02–300.30) (32). A substantial proportion of these costs in India will be out-of-pocket (8, 33).

The morbidity, mortality and costs associated with COPD are enhanced if patients with COPD face both adherence and inhaler use barriers (34-38). As a result, multifactorial approaches that include comprehensive health education for COPD patients in all aspects of care should be considered (1). As mentioned, effective integrated interventions in ambulatory care, including earlier diagnosis and instigating strategies to help prevent disease progression, can reduce the rate of exacerbations, hospitalizations and the rising economic burden of COPD (39-43). In the global initiative for chronic obstructive lung disease (GOLD) report of 2018, pharmacists are considered as key health care professional collaborators assisting in the management of COPD through educational strategies (1). Pharmacists can help with medication management strategies as well as assist with addressing barriers to the use of, and adherence with, prescribed inhalers. Consequently, community pharmacists can potentially, help reduce the morbidity, mortality and costs associated with COPD and delay its progression (44-47).

This is particularly important in India given concerns with the number of physicians especially in rural areas due to a variety of issues (48-50). As a result, counselling of COPD patients in terms of prevention strategies and inhaler techniques, as well as the use of spirometry for diagnosis, is typically limited (51). This is a concern given the high levels of co-payment in India, which can have a devastating effect on families (8, 52, 53), as well as the current high burden of COPD in India (2, 6, 13). Consequently, effective strategies are need to address this. This includes the improved use of medicines to reduce subsequent co-payments (22). We and others have shown that structured pharmacist-led interventions can improve the care of patients with COPD and help reduce costs (46, 54-58). This is important with the role of non-physician healthcare professionals growing in India to compensate for the lack of physicians (59). Currently, there are over one million pharmacists in India, with a clinically oriented Doctor of Pharmacy (PharmD) program introduced in 2008 to help train pharmacists to provide patient-related care. This includes patient counselling and therapeutic interventions, which should help to improve the care of patients with chronic diseases in India (53). There is though limited data regarding the economic impact of pharmacists' involvement in the management of patients with COPD in India, especially with respect to medicine costs.

Consequently, we undertook this study to address this by evaluating the impact of clinical pharmacists' intervention on the costs of medicines for patients with COPD in a randomised trial, coupled with the costs of pharmacists' time, to provide future guidance as India moves towards providing universal health care (60). We concentrated on these two direct medical costs initially since the costs of medicines currently account for approximately 38% of total healthcare costs in India versus approximately 10% of total healthcare costs among developed countries, much of which is out-of-pocket (33, 53, 61, 62). In addition, as mentioned, costs of medicines for patients with COPD is currently appreciably higher than hospital charges (31).

2. Patients and Methods

2.1 Study Design and Subjects

The study was carried out as part of a larger study evaluating the impact of structured pharmacist-led interventions on improving medication adherence in patients with COPD and the subsequent impact on their health-related quality of life (44, 46).

An open-label randomized controlled study was conducted at Kasturba Medical College Hospital, Manipal, India, which is a tertiary care teaching hospital, over a three-year period. The study subjects were selected based on inclusion criteria (confirmed diagnosis of COPD as per GOLD guidelines) and their informed consent. Patients were randomized (by sealed envelope method) into two groups, which were the intervention group [IG] and the control group [CG], to ensure as far as possible matching between the two groups.

2.2 Sample size

Based on previous published literature (54, 55), we estimated the minimum sample size (based on measures of variation) of 100 patients in each group in order to demonstrate minimum clinical significance of 5% (power =80%). The target sample size was estimated to be 260 patients (130CG and 130 IG) taking into account a 30% potential dropout rate.

2.3 Treatment Costs

Medicine costs were collected before and after the intervention were based on the data collected from case record forms (CRF) and personal interviews. The costs of medicines included the cost of glucocorticoids, anticholinergics, antibiotics, methylxanthines and bronchodilators. This excluded any medicines that were returned and could be re-used. The cost of medicines used to treat non-respiratory conditions were also excluded as we wanted to concentrate solely on the cost medicines for COPD.

Medicine costs were collected for each patient from the billing system in the hospital. These were collated from the hospital pharmacy billing system for each patient for the three data collection time points and recorded on their CRF as total combined costs without being broken down into their respective components (different inhalers and oral medicines). In addition, during the interviews with the patients, information regarding over-the-counter (OTC) medicines and their costs were collected as well as the cost of any other medicines purchased from outside hospital to ensure all medicines costs were included. Costs were collected for the fiscal year 2012 to 2014 in Indian rupees (INR) and inflated to 2017 costs using current Indian inflation rates (63). These were subsequently converted to 2017 United States Dollars (US$) using an average exchange rate (1 USD = 66.60 INR). The costs were grouped into periods of six months for comparative purposes. This was six months prior to the documented time, i.e. 6 months before the baseline as well as the six-month period prior to 12 and 24 months. A six month period was chosen to cover possible monthly fluctuations in inhaler use.

Since the variation in the severity of COPD disease may affect the median estimated direct costs for the patient in each group, the cost difference in the median estimated costs between two groups was also assessed using the cost ranges in each group via boxplots.

The cost of the clinical pharmacy input was also calculated to provide a more complete picture of overall potential cost savings. This was based on an average monthly salary of a clinical pharmacist in India in 2017 being approximately 28000 INR (US$420), although this may vary according to their qualifications and experience (64). Typically, a clinical pharmacist in India works 8 hours per day for 25 days in a month, making 200 working hours a month. This corresponds to 140 INR (US$2)/ hour.

As mentioned, no attempt was made to look at the impact of any changes in medicine use on longer term costs including future hospitalisations due to exacerbations as the main emphasis was on the costs of medicines, the principal cost component (31), much of which will be out-of-pocket (8, 33). In addition, we had previously shown that this structured pharmacist-led intervention significantly improved medication adherence in COPD patients, which has been shown to decrease the number of emergency department visits and and the length of stay in hospitals among patients with chronic respiratory diseases (46, 65).

2.4 *Assessments*
The baseline data for each patient was collected using a custom designed and validated CRF that we have previously used and discussed (46). The collected data included demographic measures, clinical characteristics, as well as respiratory and non-respiratory medication regimen. Follow up assessments were repeated at 12 and 24 months in both the CG and IG groups.

2.5 Structured Pharmacist Intervention
Patients recruited in the IG were educated by the principal clinical pharmacist (SA). The counselling sessions (typically 15-20 minutes) and patient information leaflets (PILs) emphasised the following: (i) the importance of medication compliance, (ii) the dose and frequency of prescribed medicines, (iii) the need for smoking cessation, (iv) the need for simple exercise, (v) the proper use of prescribed inhaler devices and (vi) the need for timely monitoring by the pulmonary medicine department. There were five counselling sessions during the 2-year follow up period.

Each patient was followed up for a period of two years, and adherence was re-assessed every six months. PILs describing the above techniques had been developed, validated and supplied to patients for reinforcing the content delivered through counselling (66). Patients were further contacted by telephone each month to enhance medication adherence and timely follow up. During the follow-up, patients in the IG were further trained regarding the proper use of inhaler devices and motivated regarding the need for medication adherence.

The control patients just received normal care in the clinic without any pharmacy counselling and follow-up by the clinical pharmacy team.

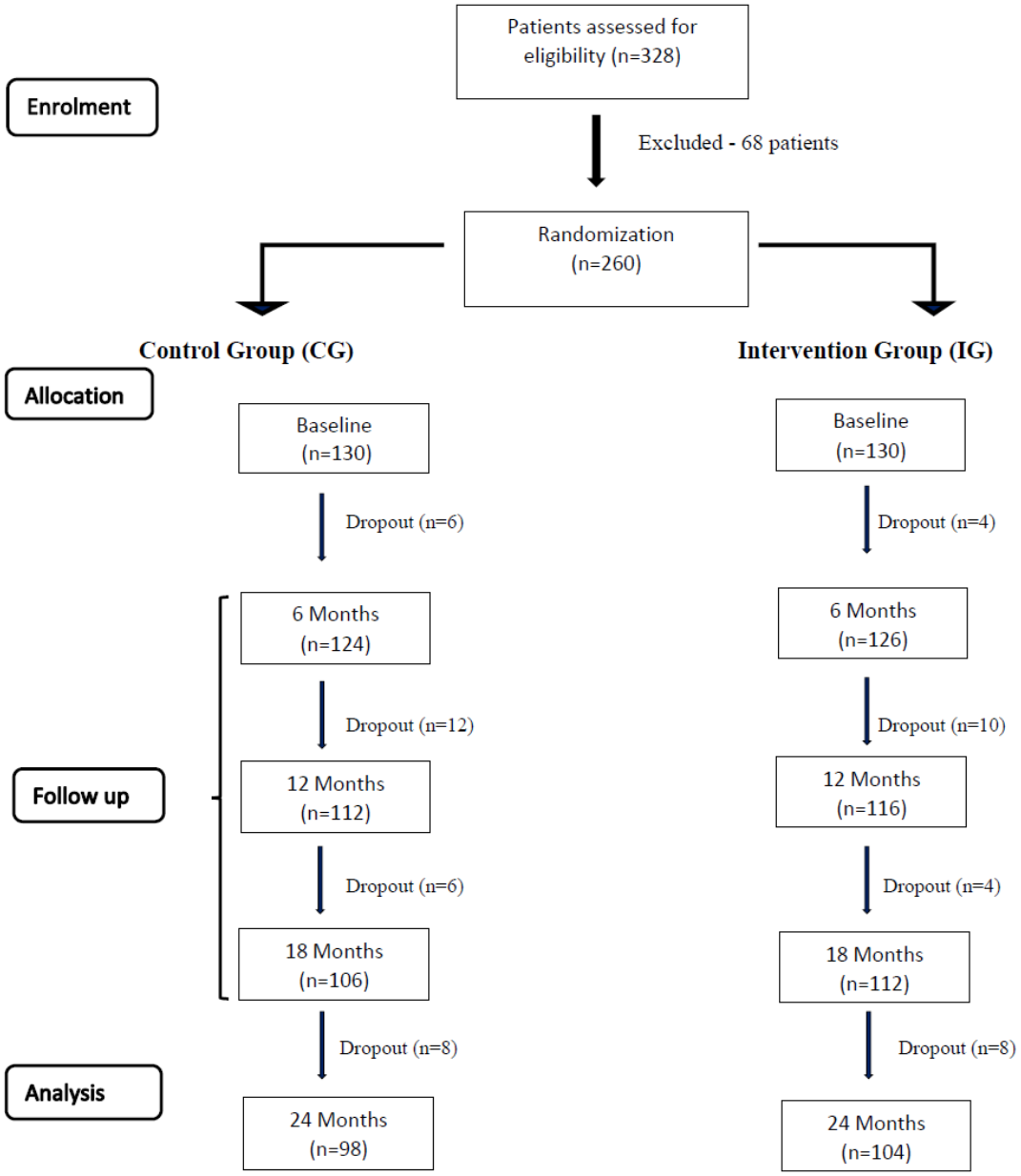
2.6 Data analysis
SPSS version 20.0 was used for statistical analyses (data screening, descriptive statistics and univariate analysis). A *P*-value of <0.05 was considered statistically significant.

2.7 Ethical clearance
Institutional ethical clearance (IEC 88/2012) was obtained prior to the study and the study was registered with the Indian clinical trial registry (CTRI/2014/08/004848).

3. Results

3.1 Patient Flow and Baseline characteristics
Of the 328 COPD patients screened during the study period, 260 were recruited. Of these, 202 patients completed the follow-up (98 in CG and 104 in IG). The reasons for dropping out, in decreasing order of events were: (a) lost to follow up (18 in CG and 11 in IG), (b) death (8 in CG vs 9 in IG), and (c) withdrawal at different stages of the study (5 in CG vs 3 in IG). Figure 1 indicates the number of patients at different stages of the study.

Figure 1: Flow chart indicating patient numbers at different stages of the study



The randomisation process ensured the CG and IG groups were matched for baseline socio-demographic and clinical characteristics (Table 1) including (a) mean age (61.1 ±8.4 vs. 60.6 ±7.9 years), (b) male gender (94.4 vs 96.9%), (c) duration of COPD (15.3±5.7 vs 14.6 ±6.6 years), (d) mean forced expiratory volume (FEV_1) % (41.9±14.7 vs 44.4±14.5), (e) average number of medicines used (7.2±2.1 vs 6.3±1.7), (f) co-morbidity rate (74% vs 69%), and (g) current smoking status (53.8% vs 56.9%). They were also matched in terms of baseline medicines (Figure 2).

As per Kuppuswamy's socioeconomic classification (67), the largest proportion of patients belonged to the upper lower category in both groups (CG = 30.5% vs IG = 29.8%). The 'smoking score' (Pack years) was estimated to be 21.7 ±12.6 in CG and 23.2 ±11.4 in IG. The largest proportion of the patients belonged to the GOLD III (severe) category (45.4 vs 47.6 %). The socio-economic status of patients was based on published classifications (18).

Table 1: Baseline characteristics of study population

Characteristics	CG	IG	P-value
Gender (Male, %)‡	94.4	96.9	0.08
Age (Mean±SD)†	61.1±8.4	60.6±7.9	0.67
Age Category‡			0.12
40-50	20	15	
50-60	32	47	
60-70	78	68	
Socioeconomic status (%)‡			0.73
Lower	35.8	37.4	
Upper lower	30.5	29.8	
Middle	23.7	20.6	
Upper middle	7.1	6.4	
Upper	2.9	5.8	
FEV_1 % predicted¶ (Mean±SD)†	41.9±14.7	44.4±14.5	0.16
Severity as per GOLD (%)‡			0.34
Mild	12.7	13.8	
Moderate	21.9	20.1	
Severe	45.4	47.6	
Very severe	20.0	18.5	
Pack years (Mean± SD) †	21.7±12.6	23.2±11.4	0.42
Smoking Status (%)‡			0.24
Ex-Smoker	43.1	46.2	
Current smoker	56.9	53.8	
Duration of COPD(Mean± SD) †	15.3±5.7	14.6±6.6	0.36
Co morbid conditions (%) ‡	74	69	0.64
No. of Medications (Mean±SD) †	7.2±2.1	6.3±1.7	0.68

NB: IG: Intervention group, CG- Control group, SD- standard deviation, FEV_1-Forced expiratory volume in one second, COPD-Chronic Obstructive Pulmonary Disease, GOLD- Global Initiative for Chronic Obstructive Lung Disease; †Data were analysed by t test; ‡Data were analysed by Chi square; ¶ FEV_1 calculated based on spirometry.

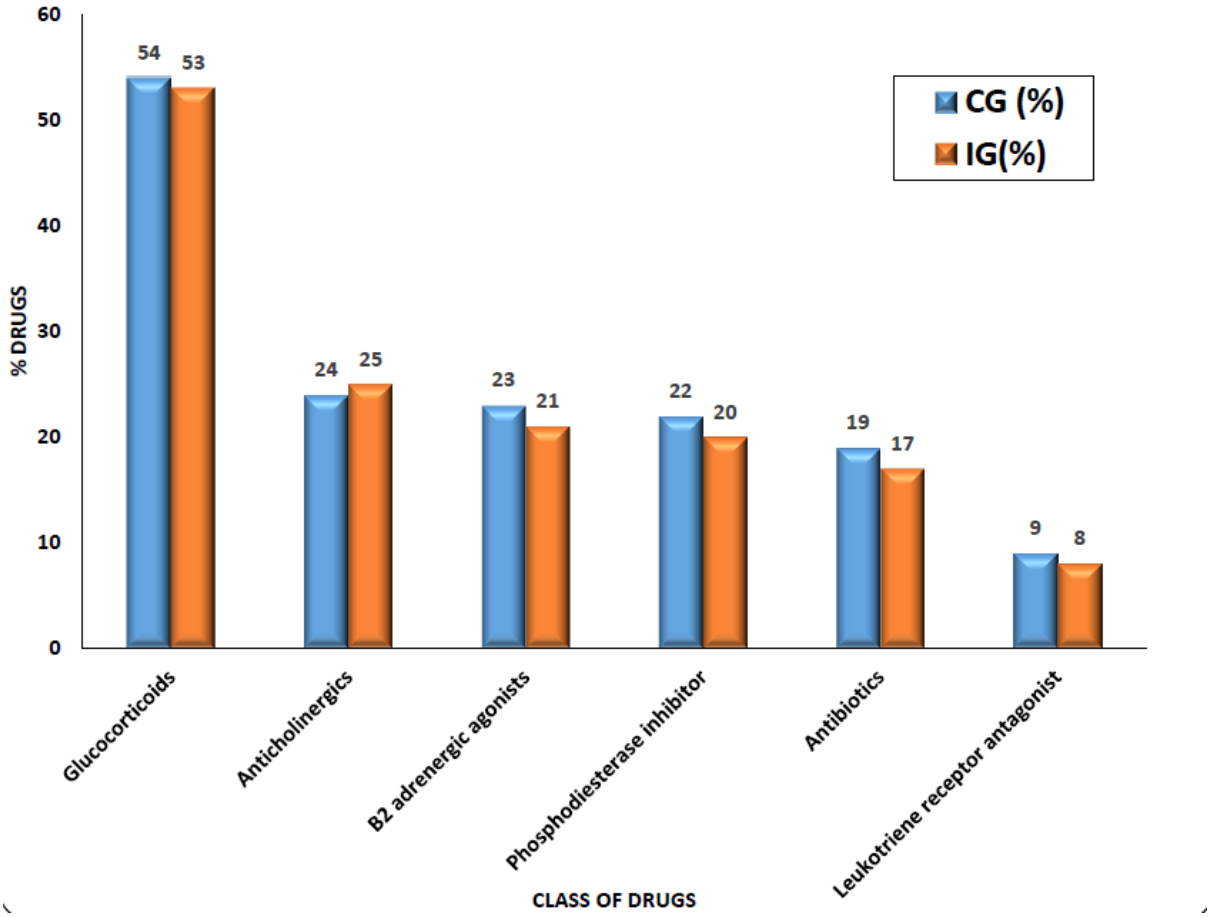
3.2 Medicine costs in COPD patients

At baseline, the average medicine costs of the enrolled patients were highly correlated with disease severity. Box 1 lists the medicines prescribed/ dispensed in both groups among the COPD patients to treat their COPD, with Figure 2 giving a further breakdown showing a similar use of the different medicine types between both groups at baseline. These were typically different inhalers (short and long acting beta 2 agonists, steroids and anticholinergics).

Box 1 - List of medicines most commonly prescribed/dispensed among the patients with COPD

Beta 2 adrenergic agonists (short and long acting inhalers)
Salbutamol, Levosalbutamol
Salmeterol
Formoterol
Anticholinergics (inhalers)
Ipratropium
Glucocorticoids
Prednisolone (oral)
Budesonide (inhaler)
Fluticasone (inhalers)
Phosphodiesterase inhibitors (oral)
Doxophylline, Theophylline
Acebrophylline

Figure 2 – Medicines prescribed in each group (CG and IG) as a percentage of total medicines prescribed (items)



Mild COPD cost the least per patient for medicine costs at baseline (CG=US$29.46 vs. IG=US$27.44. Predictably, patients with very severe COPD incurred the highest medicine costs initially (CG = US$62.00 vs IG = US$63.28) (Table 2).

The cost of medicines decreased significantly after the pharmacist intervention in the IG for all levels of severity of COPD. For patients with mild COPD, the average six-monthly medicine costs at 24 months were US$41.47 for the CG group and US$31.46 per patient for the IG. For those with very severe COPD, the medicine costs were US$66.94 for the CG group and US$46.45 per patient for those in the IG group. Overall, the structured pharmacist-led intervention saved US$10.01 per patient for medicine costs over a six-month period prior to 24 months for those with mild COPD versus US$20.49 for those patients with very severe COPD, equating to a reduction ranging from 17.1% (moderate) up to 30.6% (very severe) (Table 2).

Table 2: Medicine costs median) in COPD patients over a six-month period at baseline and prior to 24 months

Severity of COPD	Baseline (cost in US$)		24 months (cost in US$)		Medicine costs saved by a structured pharmacist-led intervention (US$ and %)	Statistical significance of the reductions at 24 months
	CG	IG	CG	IG	IG[a] (24 months)	P value (T-test)
Stage-I (Mild)	29.46	27.44	41.47	31.46	10.01 (-24.1%)	P < 0.001
Stage-II (Moderate)	35.41	38.35	42.28	35.03	7.25 (-17.1%)	P < 0.001
Stage-III (Severe)	53.69	52.00	58.24	43.00	15.24 (-26.2%)	P < 0.001
Stage-IV (Very severe)	62.00	63.28	66.94	46.45	20.49 (-30.6%)	P < 0.001

NB: CG: control group, IG: intervention group, COPD: Chronic Obstructive Pulmonary Disease, US$: US Dollar, [a] Compared to CG (24 months)

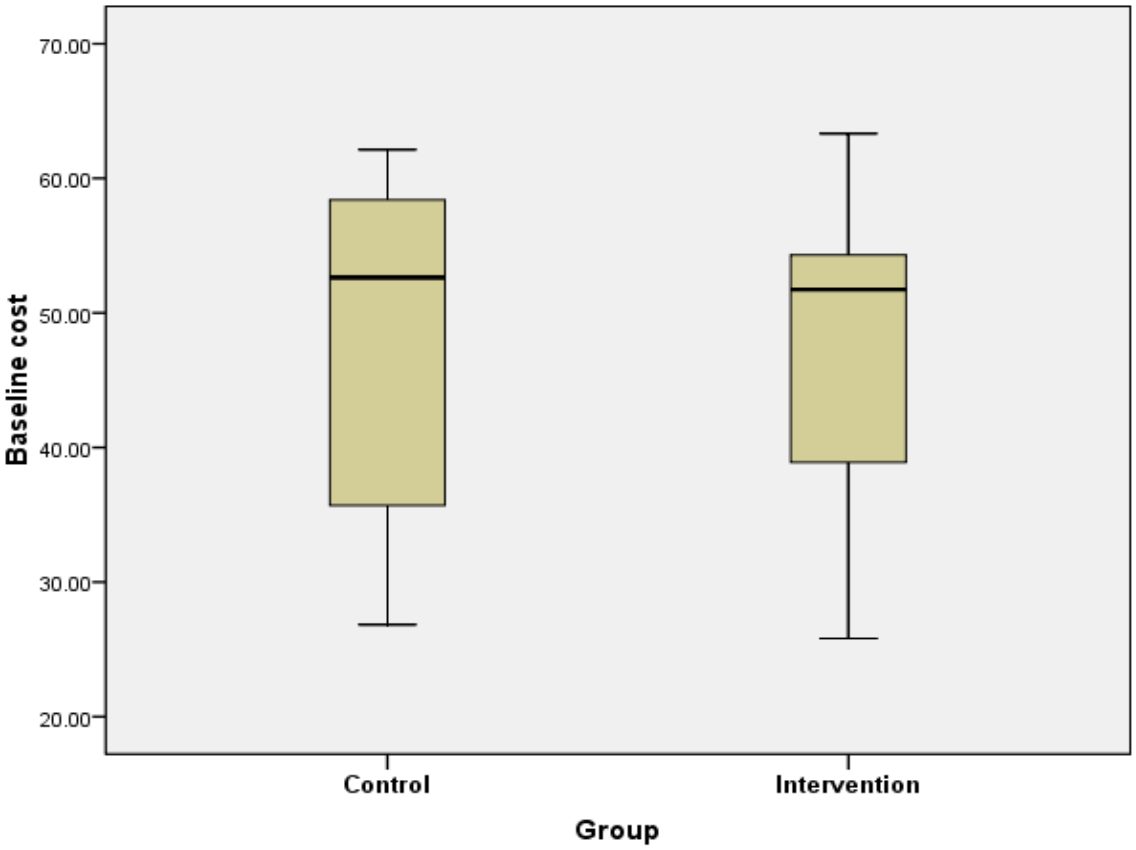
3.3 Comparative analysis of medicine costs among COPD patients

The cost differences in estimated medicines costs between the two groups were assessed by using the cost ranges in each group as shown in the boxplots.

3.3.1 Estimated median medicine costs among COPD patients at baseline

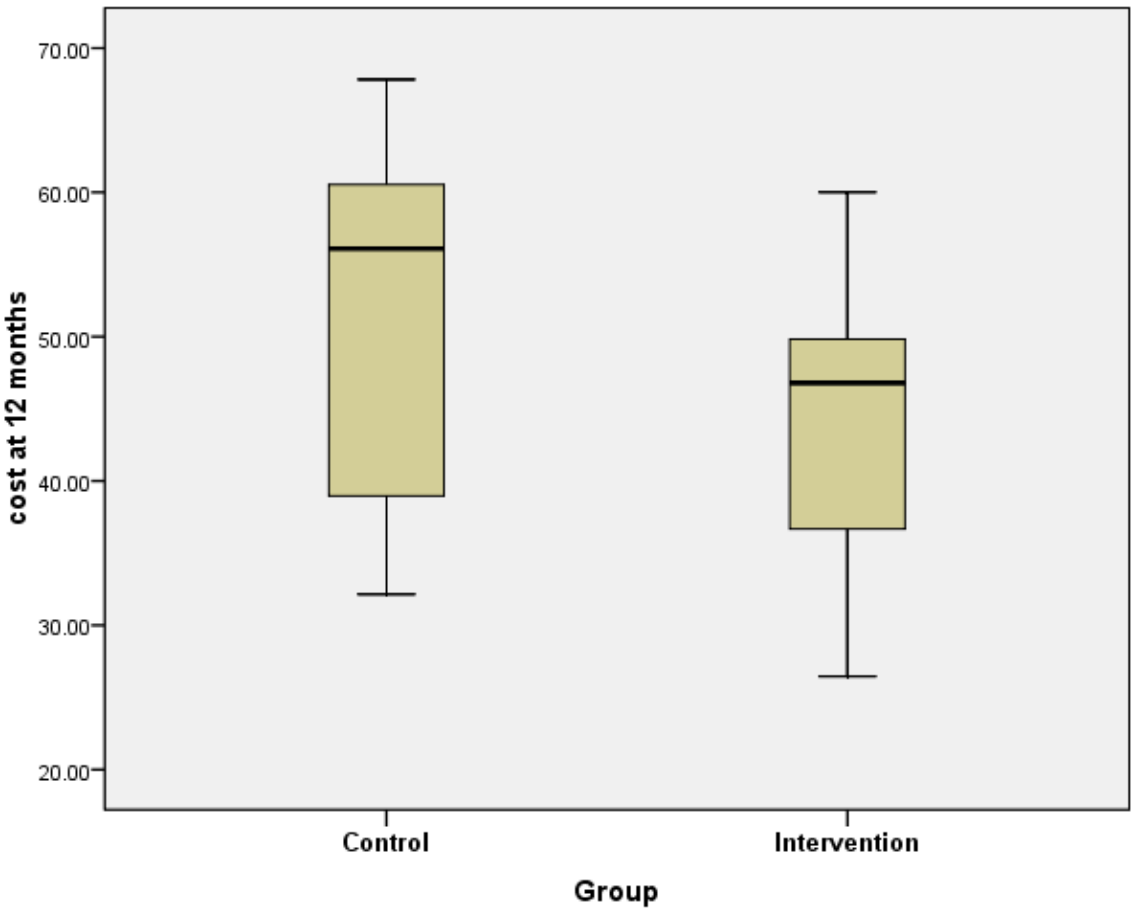
The median estimated direct medicine costs at baseline were similar between the CG and IG groups (US$52.63 vs 51.73, P = 0.916). The medicine costs ranged from a minimum of US$ 26.84 in the CG and US$25.81 in IG to a maximum of US$62.13 (CG) and US$63.33 (IG). Figure 3 shows the boxplot of the cost comparison between the CG and IG groups at baseline.

Figure 3: Boxplot of medicine cost comparisons between the intervention and control groups at baseline (Median (IQR)



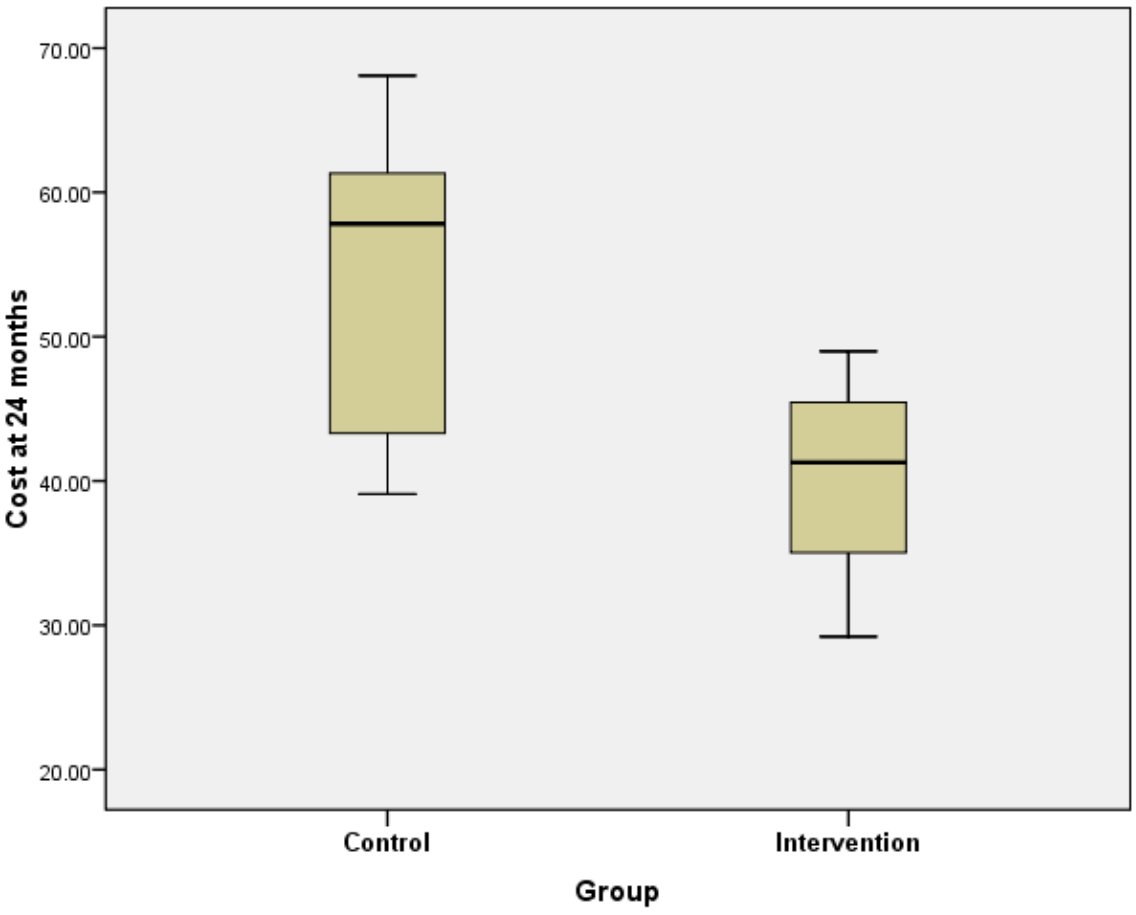
3.3.2 Estimated median medicine costs (USD) among COPD patients at 12 months
The median estimated medicine cost at 12 months were significantly higher for the CG than the IG (US$56.09 vs US$46.79, P < 0.001). The medicine costs ranged from a minimum of US$32.15 in the CG and US$ 26.45 in the IG to a maximum of US$ 67.82 (CG) and US$ 60.01 (IG). Figure 4 shows the boxplot of cost comparisons between the CG and IG groups at 12 months.

Figure 4: Boxplot of medicine cost comparison between the intervention and control groups at 12 months (median (IQR)



3.3.3 Estimated median medicine cost (US$) of COPD patients at 24 months
The median estimated medicine costs at 24 months were significantly higher for the CG than the IG group (US$ 57.82 vs US$ 41.29, P < 0.001). The medicine costs ranged from a minimum of US$ 39.09 in the CG and US$ 29.21 in the IG group to a maximum of US$68.09 (CG) and US$48.98 (IG). Overall, median medicine costs were reduced by 28.6% in the IG vs CG groups. Figure 5 shows the boxplot of cost comparisons between the CG and IG at 24 months.

Figure 5: Boxplot of medicine cost comparison between the intervention and control groups at 24 months (median (IQR)



3.4 Costs of clinical pharmacist time

The time for counselling of each COPD patient was found to be 20 minutes on average during the 5 sessions of counselling per patient during the study period. Consequently, the estimated average counselling time for each patient was 1 hour 40 minutes (over the two years). This equates to 200 INR (US$3) per COPD patient. The inclusion of these costs reduces potential savings; however, they are still substantial (Table 3).

Table 3 – Potential direct medicine cost savings from the pharmacist intervention programme

Severity of COPD	Median medicine cost saved by structured pharmacist-led intervention (US$) (Table 2)	Pharmacist costs (US$)	Overall savings (US$)	Overall % cost reduction from CG costs (Table 2)
Stage-I (Mild)	10.01	3.00	7.01	-16.9%
Stage-II (Moderate)	7.25	3.00	4.25	-10.1%
Stage-III (Severe)	15.24	3.00	12.24	-21.0%
Stage-IV (Very severe)	20.49	3.00	17.49	- 26.1%

NB: CG: control group, IG: intervention group, COPD: Chronic Obstructive Pulmonary Disease, US$: US Dollars

4. Discussion

To the best of our knowledge, we believe this is the first randomised controlled study from India to evaluate the impact of a pharmacist-led intervention on the cost of medicines to treat patients with

their COPD. The savings can be substantial, reducing six-monthly medicine costs among those with very severe COPD by US$20.49 to US$46.45, i.e. by 30.6% (Table 2), with lower savings with milder COPD. These savings are still high at US$17.49 (a reduction of 26.1%) when factoring in clinical pharmacy time (Table 3), with the percentage reduction at 30.6% for those with very severe disease if we had evaluated medicine costs over twelve rather than six months. The findings that the costs of medicines increase with disease severity is expected, similar to those of Hilleman and others (27, 31, 68). These savings in medicines costs are important given the extent of co-payments for medicines for patients with COPD in India as well as in other LMICs (8, 33, 52, 53). In India, most COPD patients are from rural areas; consequently, the cost of therapy remains a high burden for patients and their families. Affordability of medicines is a key issue in LMICs with their costs accounting for up to 70% of total healthcare costs, most of which will be out-of-pocket and potentially catastrophic for patients and their families if family members become ill (52, 69).

By investing 200 INR (US$3) per COPD patient in pharmacist-led interventions, approximately US$7 to US$18 can be saved in medicine costs in mild and very severe disease respectively (Table 3), greater if we had evaluated medicine costs over twelve rather than six months. Encouragingly, care appears not be compromised with these savings. If anything, care appears to be improved with this pharmacist-led intervention, with the findings from other parts of this research project showing improved adherence to medicines as well as improved HRQOL in patients with COPD following the intervention(44, 46). This is encouraging given the extent of COPD in India and its current impact on morbidity, mortality and costs (5, 6, 8, 10, 15, 31).

Our study corroborates previous reports that demonstrate the value of pharmacist-driven patient educational activities among patients with COPD, reinforcing that medication adherence and inhaler technique are very important issues to discuss at every follow up visit with patients to improve their care and help reduce overall costs (47, 54, 55, 70). In agreement with our study results (Table 2), other authors have also demonstrated that the introduction of self-management plans in COPD patients have economic benefits (57, 71). Pharmacist led self-management plans can also minimize or help prevent medicine related problems, avoiding unnecessary hospital admissions in patients with COPD (47). From previous studies (29, 44-47, 65), it is clear that adherence to medication in patients with COPD leads to improved disease control, reducing drug dosages and frequency, the use of emergency medicines and hospitalisations. This ultimately reduces costs including medicine costs. In contrast, poorly controlled COPD, which is typically associated with failure to use inhaled medications correctly, was estimated to increase costs in patients with COPD in Italy by at least €9 billion per year, with the costs falling substantially with appropriate inhaler and other care (28, 72). This is not surprising as adherence to inhaler therapy is typically low in routine care (73-75). As a result in the GOLD guidelines (1), COPD management is described as 10% medication and 90% education, with only 17% of patients achieving perfect medication adherence without assistance (76). Consequently, we believe based on our findings and those of others, there is a potential role for pharmacists to educate patients about importance of medication adherence to manage their COPD when dispensing the different inhalers and other prescribed medicines to treat their disease. This in turn will help to stabilize their disease, and decrease overall medicines costs as well as overall costs (including pharmacists' costs). This is particularly important in LMICs with their high patient co-payments and current burden of COPD.

This should be of help to key stakeholder groups in India with pharmacists currently a major healthcare work force, with over 1 million in practice in India (53). Pharmacists are ideally placed in the healthcare system as they act as a link between patients and physicians, and are often the first healthcare professional that patients in LMICs approach with health-related problems (77). They can also help review the quality of prescribing including prescribing against agreed national guidance, which is currently being under-utilised in India (78-81). In addition, pharmacists can help address concerns with generics to reduce co-payments (82) as well as help limit tobacco smoking to reduce COPD (83-86) alongside other policies to reduce smoking. Other initiatives include increasing the cost of cigarettes and through greater enforcement of legislation prohibiting smoking in public places (22). Consequently, we believe that our study endorses expanding pharmacists' role as an economically viable strategy in India as well as improving patient care, and we will be monitoring this in the future. This may apply to other LMICs especially those where there is currently high morbidity, mortality and costs due to COPD.

We are aware of a number of limitations with this study. The major one being that this study was conducted in only one centre in India, which could affect the generalisation of study findings to other institutions. However, we believe that in view of the robustness of the study design and the fact that pharmacy counselling skills are easily transferable, our findings are valid and provide future direction to others. We are also aware we focused only on medicine costs in this study. In addition, we did not break down the medicine costs into the different drug components (different inhalers and oral treatments). However, as mentioned, previous studies in India have shown that medicine costs are a substantial part of overall costs of treating patients with COPD with typically low salaries unlike high-income countries. Medicine costs can account for over 70% of total healthcare costs in LMICs, and in India much of this will be out-of-pocket putting considerable strain on families where family members become ill especially those in rural areas. Consequently, initiatives to reduce medicine costs whilst improving the care of patients with COPD should be welcomed.

5. Conclusion:

In conclusion, we believe our study demonstrates a potentially pivotal role of pharmacist in reducing the direct medicine cost in COPD patients through a structured educational intervention. These savings can be achieved with minimal costs in terms of pharmacists' time. Consequently, we believe our findings will be of interest to the authorities in India and other LMICs with high morbidity, mortality and costs due to COPD.

Compliance with ethical standards

Institutional ethical clearance (IEC 88/2012) was obtained prior to the study and the study was registered with the Indian clinical trial registry (CTRI/2014/08/004848). Patients gave their informed consent prior to enrolment and patient confidentiality was maintained throughout the study in accordance with clinical trial practices.

Data Availability Statement
Further data will be available on request.

Authors' contribution
SAb, MKU, MKM, SAl, AAAlr and AAAlf developed the concept for the study. SAb, MKU, and AAAlr undertook data collection and initial analysis with further input from MKM, SAl, APM, and BBG. SAb, MKU, AAAlr and BBG undertook the initial draft manuscript with all authors subsequently contributing to further drafts. All authors approved the final manuscript.

Acknowledgements
We are grateful to Manipal College of Pharmaceutical Sciences, Kasturba Hospital, Manipal, and Manipal Academy of Higher Education, India for their support during the study.

Conflict of Interest
The authors (Suhaj Abdulsalim, Mazhuvancherry Kesavan Unnikrishnan, Mohan K Manu, Saud Alsahali, Alian A. Alrasheedy, Antony P Martin, Brian Godman, and Abubakr A Alfadl) declare that they have no conflicts of interest.

Funding
There was no external funding for this study.

References

1. GOLD. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2018 Report. Available at URL: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf.
2. Rajkumar P, Pattabi K, Vadivoo S, Bhome A, Brashier B, Bhattacharya P, et al. A cross-sectional study on prevalence of chronic obstructive pulmonary disease (COPD) in India: rationale and methods. BMJ open. 2017;7(5):e015211.
3. Csikesz NG, Gartman EJ. New developments in the assessment of COPD: early diagnosis is key. International journal of chronic obstructive pulmonary disease. 2014;9:277-86.

4. Welte T, Vogelmeier C, Papi A. COPD: early diagnosis and treatment to slow disease progression. International journal of clinical practice. 2015;69(3):336-49.
5. Jindal SK, Aggarwal AN, Gupta D, Agarwal R, Kumar R, Kaur T, et al. Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH). The international journal of tuberculosis and lung disease. 2012;16(9):1270-7.
6. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990-2016. The Lancet Global health. 2018;6(12):e1363-e74.
7. Lopez-Campos JL, Tan W, Soriano JB. Global burden of COPD. Respirology. 2016;21(1):14-23.
8. Hossain MM, Sultana A, Purohit N. Burden of Chronic Obstructive Pulmonary Disease in India: Status, Practices and Prevention. Int J Pul & Res Sci. 2018; 2(5): 555599. Available at URL: https://juniperpublishers.com/ijoprs/pdf/IJOPRS.MS.ID.555599.pdf.
9. Landis SH, Muellerova H, Mannino DM, Menezes AM, Han MK, van der Molen T, et al. Continuing to Confront COPD International Patient Survey: methods, COPD prevalence, and disease burden in 2012-2013. Int J Chron Obstruct Pulmon Dis. 2014;9:597-611.
10. Stephen P, Mahalakshmy T, Manju R, Laksham KB, Subramani S, Panda K, et al. High Prevalence of Chronic Respiratory Symptoms among Autorickshaw Drivers of Urban Puducherry, South India. Indian journal of occupational and environmental medicine. 2018;22(1):40-4.
11. Jones PW, Brusselle G, Dal Negro RW, Ferrerd M, Kardose P, Levyf ML, et al. Health-related quality of life in patients by COPD severity within primary care in Europe. Respir Med. 2011;105.
12. WHO. Global Health Observatory (GHO) data. Mortality and global health estimates. 2016. Available at URL: http://who.int/gho/mortality_burden_disease/en/.
13. Salvi SS, Manap R, Beasley R. Understanding the true burden of COPD: the epidemiological challenges. Prim Care Respir J. 2012;21(3):249-51.
14. WHO. Countries India. 2016. Available at URL: https://www.who.int/nmh/countries/ind_en.pdf?ua=1.
15. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J. 2006;27(2):397-412.
16. Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: results from the Copenhagen City Heart Study. Eur Respir J. 1999;13(5):1109-14.
17. Grigsby M, Siddharthan T, Chowdhury MA, Siddiquee A, Rubinstein A, Sobrino E, et al. Socioeconomic status and COPD among low- and middle-income countries. Int J Chron Obstruct Pulmon Dis. 2016;11:2497-507.
18. Lange P, Marott JL, Vestbo J, Ingebrigtsen TS, Nordestgaard BG. Socioeconomic status and prognosis of COPD in Denmark. Copd. 2014;11(4):431-7.
19. Lawlor DA, Ebrahim S, Davey Smith G. Association between self-reported childhood socioeconomic position and adult lung function: findings from the British Women's Heart and Health Study. Thorax. 2004;59(3):199-203.
20. Sehgal IS, Dhooria S, Agarwal R. Chronic obstructive pulmonary disease and malnutrition in developing countries. Current opinion in pulmonary medicine. 2017;23(2):139-48.
21. Ture DA, Demirci H, Sengoren Dikis O. The relationship between health literacy and disease specific costs in subjects with chronic obstructive pulmonary disease (COPD). The aging male. 2018:1-7.
22. Murthy KJ and Sastry JG. Economic burden of chronic obstructive pulmonary disease. National Commission on Macroeconomics and Health background papers – Burden of disease in India. 2005; 268-288. Available from: http://www.who.int/macrohealth/action/NCMH_Burden%20of%20disease_(29%20Sep%202005).pdf
23. Kim C, Kim Y, Yang DW, Rhee CK, Kim SK, Hwang YI, et al. Direct and Indirect Costs of Chronic Obstructive Pulmonary Disease in Korea. Tuberc Respir Dis. 2019;82(1):27-34
24. Mannino DM, Higuchi K, Yu TC, Zhou H, Li Y, Tian H, et al. Economic Burden of COPD in the Presence of Comorbidities. Chest. 2015;148(1):138-50.
25. Chen X, Wang N, Chen Y, Xiao T, Fu C, Xu B. Costs of chronic obstructive pulmonary disease in urban areas of China: a cross-sectional study in four cities. International journal of chronic obstructive pulmonary disease. 2016;11:2625-32.
26. Lewis A, Torvinen S, Dekhuijzen PN, Chrystyn H, Watson AT, Blackney M, et al. The economic burden of asthma and chronic obstructive pulmonary disease and the impact of poor inhalation technique with commonly prescribed dry powder inhalers in three European countries. BMC health services research. 2016;16:251.

27. Wacker ME, Jorres RA, Schulz H, Heinrich J, Karrasch S, Karch A, et al. Direct and indirect costs of COPD and its comorbidities: Results from the German COSYCONET study. Respir Med. 2016;111:39-46.
28. Dal Negro RW, Bonadiman L, Turco P, Tognella S, Iannazzo S. Costs of illness analysis in Italian patients with chronic obstructive pulmonary disease (COPD): an update. ClinicoEconomics and outcomes research. 2015;7:153-9.
29. Darbà J, Ramírez G, García-Rivero JL, Mayoralas S, Pascual JF, Vargas D, et al. Estimating the economic consequences of an increased medication adherence due to a potential improvement in the inhaler technique with Spiromax(®) compared with Turbuhaler(®) in patients with moderate-to-severe chronic obstructive pulmonary disease in Spain. ClinicoEconomics and Outcomes Research. 2017;9:127-37.
30. de Miguel Diez J, Carrasco Garrido P, Garcia Carballo M, Gil de Miguel A, Rejas Gutierrez J, Bellon Cano JM, et al. Determinants and predictors of the cost of COPD in primary care: a Spanish perspective. Int J Chron Obstruct Pulmon Dis. 2008;3(4):701-12.
31. Patel KD, Lalwani T, Shah K. Economic Burden in Direct Cost of Chronic Obstructive Pulmonary Disease at a Tertiary Care Teaching Hospital: A Prospective Observational Cohort Study. Indian Journal of Pharmacy Practice. 2014; 7 (3): 61-8.
32. Naveed A, Ali SA, Parveen A, Yousuf S, Ahmed A, Hashmi MA, Gigani Y. Prescription patterns and cost of illness in asthma and chronic obstructive pulmonary disease patients. Int J Acad Med 2016;2:173-8. Available from URL: http://www.ijam-web.org/text.asp?2016/2/2/173/196874.
33. Ministry of Health and family welfare, Government of India. National Health Accounts Estimates for India 2014-2015. October 2017. Available at https://mohfw.gov.in/sites/default/files/National%20Health%20Accounts%20Estimates%20Report%202014-15.pdf.
34. Lavorini F, Magnan A, Dubus JC, Voshaar T, Corbetta L, Broeders M, et al. Effect of incorrect use of dry powder inhalers on management of patients with asthma and COPD. Respir Med. 2008;102(4):593-604.
35. Chrystyn H, van der Palen J, Sharma R, Barnes N, Delafont B, Mahajan A, et al. Device errors in asthma and COPD: systematic literature review and meta-analysis. NPJ primary care respiratory medicine. 2017;27(1):22.
36. Sanchis J, Gich I, Pedersen S. Systematic Review of Errors in Inhaler Use: Has Patient Technique Improved Over Time? Chest. 2016;150(2):394-406.
37. Price D, Keininger DL, Viswanad B, Gasser M, Walda S, Gutzwiller FS. Factors associated with appropriate inhaler use in patients with COPD - lessons from the REAL survey. Int J Chron Obstruct Pulmon Dis. 2018;13:695-702.
38. Sulaiman I, Cushen B, Greene G, Seheult J, Seow D, Rawat F, et al. Objective Assessment of Adherence to Inhalers by Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2017;195(10):1333-43.
39. Vestbo J, Anderson JA, Calverley PMA, Celli B, Ferguson GT, Jenkins C, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. Thorax. 2009;64.
40. Carron T, Bridevaux PO, Lorvall K, Parmentier R, Moix JB, Beytrison V, et al. Feasibility, acceptability and effectiveness of integrated care for COPD patients: a mixed methods evaluation of a pilot community-based programme. Swiss medical weekly. 2017;147:w14567.
41. Kruis AL, Smidt N, Assendelft WJ, Gussekloo J, Boland MR, Rutten-van Molken M, et al. Integrated disease management interventions for patients with chronic obstructive pulmonary disease. The Cochrane database of systematic reviews. 2013(10):Cd009437.
42. Halpern MT, Stanford RH, Borker R. The burden of COPD in the U.S.A.: results from the Confronting COPD survey. Respir Med. 2003;97 Suppl C:S81-9.
43. Britton M. The burden of COPD in the U.K.: results from the Confronting COPD survey. Respir Med. 2003;97 Suppl C:S71-9.
44. Suhaj A, Manu MK, Unnikrishnan MK, Vijayanarayana K, Mallikarjuna Rao C. Effectiveness of clinical pharmacist intervention on health-related quality of life in chronic obstructive pulmonary disorder patients - a randomized controlled study. Journal of clinical pharmacy and therapeutics. 2016;41(1):78-83.
45. Faheemuddin MD, Ramaiah B, Kiran SS, Kumari BS, Vijayalaxmi M. Evaluation of Medication Adherence in COPD Patients and their Drug Utilisation Pattern. Chron Obstruct Pulmon Dis. 2016. 1: 17.
46. Abdulsalim S, Unnikrishnan MK, Manu MK, Alrasheedy AA, Godman B, Morisky DE. Structured pharmacist-led intervention programme to improve medication adherence in COPD

patients: A randomized controlled study. Research in social & administrative pharmacy. 2018;14(10):909-14.
47. Bourbeau J, Julien M, Maltais F, Rouleau M, Beaupre A, Begin R, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. Archives of internal medicine. 2003;163(5):585-91.
48. Ghose D. India suffering critical shortage of doctors: NMC Bill may finally give rural poor access to affordable healthcare. 2018. Available at URL: https://www.firstpost.com/india/india-suffering-critical-shortage-of-doctors-nmc-bill-may-finally-give-rural-poor-access-to-affordable-healthcare-4285483.html.
49. Singh D, Bose A. Tackling doctors' shortage. The Pioneer 2018. Available at URL: https://www.dailypioneer.com/2018/columnists/tackling-doctors-shortage.html.
50. Kumar R. The leadership crisis of medical profession in India: ongoing impact on the health system. Journal of family medicine and primary care. 2015;4(2):159-61.
51. Ladhani S. COPD – an Indian perspective. J Lung Pulm Respir Res. 2016;3(1):24–25. .
52. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 2009;373(9659):240-9.
53. Abdulsalim S, Unnikrishnan MK, Manu MK, Alrasheedy AA, Godman B, Morisky DE. Authors' response to the comments to "Structured pharmacist-led intervention programme to improve medication adherence in COPD patients: A randomized controlled study". Research in social & administrative pharmacy. 2018;14(4):402-3.
54. Khdour MR, Kidney JC, Smyth BM, McElnay JC. Clinical pharmacy-led disease and medicine management programme for patients with COPD. British journal of clinical pharmacology. 2009;68(4):588-98
55. Jarab AS, Alqudah SG, Khdour M, Shamssain M, Mukattash TL. Impact of pharmaceutical care on health outcomes in patients with COPD. International journal of clinical pharmacy. 2012;34(1):53-62
56. Gallefoss F, Bakke PS. How does patient education and self-management among asthmatics and patients with chronic obstructive pulmonary disease affect medication? Am J Respir Crit Care Med. 1999;160(6):2000-5
57. Gallefoss F. The effects of patient education in COPD in a 1-year follow-up randomised, controlled trial. Patient education and counseling. 2004;52(3):259-66.
58. Suhaj A, Unnikrishnan MK, Mohan MK, Kunhikkatta V, Rao CM. PRS2: Effectiveness of Clinical Pharmacist Intervention on Direct Medical Cost in Chronic Obstructive Pulmonary Disorder Patients - A Randomized Controlled Study. Value in Health. 2016. 19: A807 – A918.
59. Sharma A, Ladd E, Unnikrishnan MK. Healthcare Inequity and Physician Scarcity Empowering Non-Physician Healthcare. Economic and political weekly, 2013; 48 (13):112-117
60. Garg S. Universal health coverage in India: Newer innovations and the role of public health. Indian J Public Health. 2018;62:167-70. Available from: http://www.ijph.in/text.asp?2018/62/3/167/241090.
61. Godman B, Oortwijn W, de Waure C, Mosca I, Puggina A, Specchia ML et al. Links between Pharmaceutical R&D Models and Access to Affordable Medicines. A Study for the ENVI COMMITTEE. Available at URL: http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587321/IPOL_STU(2016)587321_EN.pdf
62. OECD. Health at a Glance 2017. Available at URL: https://www.oecd-ilibrary.org/docserver/health_glance-2017-en.pdf?expires=1531413926&id=id&accname=guest&checksum=656327F799B10217DD2D80F463DAB8732017.
63. Triami Media BV. Historic Inflation - CPI inflation year pages [Internet]. inflation.eu. 2017. Available from: URL www.inflation.eu.
64. Payscale. Average Clinical Pharmacist Salary. Available at URL: https://www.payscale.com/research/IN/Job=Clinical_Pharmacist/Salary.
65. Balkrishnan R, Christensen DB. Inhaled corticosteroid use and associated outcomes in elderly patients with moderate to severe chronic pulmonary disease. Clinical therapeutics. 2000;22(4):452-69.
66. Suhaj A, Mohan MK, Mohapatra A, et al. Development and Readability Assessment of Patient Information Leaflets for Chronic Obstructive Pulmonary Disease. Asian J. Pharm. Hea. Sci 2015; 5:1237-1241.

67. Ravi Kumar BP, Dudala SR, Rao AR. Kuppuswamy's socio-economic status scale – a revision of economic parameter for 2012. International Journal of Research and Development of Health, 2013:1(1); 2-4.
68. Hilleman DE, Dewan N, Malesker M, Friedman M. Pharmacoeconomic evaluation of COPD. Chest. 2000;118(5):1278-85.
69. Ofori-Asenso R, Agyeman AA. Irrational Use of Medicines—A Summary of Key Concepts. Pharmacy 2016;4, 35.
70. Wright D, Twigg M, Barton G, Thornley T, Kerr C. An evaluation of a multi-site community pharmacy-based chronic obstructive pulmonary disease support service. The International journal of pharmacy practice. 2015;23(1):36-43.
71. Bourbeau J, Bartlett SJ. Patient adherence in COPD. Thorax. 2008;63(9):831-8.
72. Dal Negro RW, Tognella S, Tosatto R, Dionisi M, Turco P, Donner CF. Costs of chronic obstructive pulmonary disease (COPD) in Italy: the SIRIO study (social impact of respiratory integrated outcomes). Respir Med. 2008;102(1):92-101.
73. Charles MS, Blanchette CM, Silver H, Lavallee D, Dalal AA, Mapel D. Adherence to controller therapy for chronic obstructive pulmonary disease: a review. Current medical research and opinion. 2010;26(10):2421-9.
74. Cramer JA, Bradley-Kennedy C, Scalera A. Treatment persistence and compliance with medications for chronic obstructive pulmonary disease. Canadian respiratory journal. 2007;14(1):25-9.
75. Bender BG, Pedan A, Varasteh LT. Adherence and persistence with fluticasone propionate/salmeterol combination therapy. The Journal of allergy and clinical immunology. 2006;118(4):899-904.
76. Brown P, Bluml BM, Kritzler R, Petryna M, Polley CM, Tietze KJ, et al. White paper on expanding the role of pharmacists in chronic obstructive pulmonary disease. JOURNAL OF THE AMERICAN PHARMACISTS ASSOCIATION. 2011;51(2):203-11.
77. Bojanic L, Markovic-Pekovic V, Skrbic R, Stojakovic N, Ethermanovic M, Bojanic J, et al. Recent Initiatives in the Republic of Srpska to Enhance Appropriate Use of Antibiotics in Ambulatory Care; Their Influence and Implications. Frontiers in pharmacology. 2018;9:442.
78. Mohan MK, Vineetha R. Medical insurance: promoting unethical practices? Indian journal of medical ethics. 2011;8(4):261.
79. Gustafsson LL, Wettermark B, Godman B, Andersen-Karlsson E, Bergman U, Hasselstrom J, et al. The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. Basic & clinical pharmacology & toxicology. 2011;108(4):224-33.
80. Meyer JC, Schellack N, Stokes J, Lancaster R, Zeeman H, Defty D, et al. Ongoing Initiatives to Improve the Quality and Efficiency of Medicine Use within the Public Healthcare System in South Africa; A Preliminary Study. Frontiers in pharmacology. 2017;8:751.
81. Niaz Q, Godman B, Massele A, Campbell S, Kurdi A, Kagoya HR, et al. Validity of World Health Organisation prescribing indicators in Namibia's primary healthcare: findings and implications. International journal for quality in health care. 2019;31(5):338-45
82. Cameron A, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. Switching from originator brand medicines to generic equivalents in selected developing countries: how much could be saved? Value in health. 2012;15(5):664-73.
83. Alrasheedy AA, Hassali MA, Wong ZY, Saleem F. Pharmacist-managed medication therapy adherence clinics: The Malaysian experience. Research in social & administrative pharmacy. 2017;13(4):885-6.
84. Cheng HM, Liu WC, Chua G, Liew CF, Li W, Choo W, et al. Impact of a pharmacy-led smoking cessation clinic in a dermatology centre. Singapore Med J. 2019;60(1):31-33
85. Bock BC, Hudmon KS, Christian J, Graham AL, Bock FR. A tailored intervention to support pharmacy-based counseling for smoking cessation. Nicotine & tobacco research . 2010;12(3):217-25.
86. Twigg MJ, Wright DJ. Community pharmacy COPD services: what do researchers and policy makers need to know? Integrated pharmacy research & practice. 2017;6:53-9.