Assessment of Prescription Pattern Among COPD Patients in Departments of General Medicine Ward and Pulmonology in Tertiary Care Hospitals of Khammam Region

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ABSTRACT

Chronic obstructive pulmonary disease is a common preventable and treatable disease. It has been a leading cause of morbidity and mortality in industrialized and developing countries. Drug utilization research promotes the rational use of drugs and decreases adverse drug reactions in the population. The present study is aimed to analyze and evaluate the trends and patterns of prescribing drugs among COPD patients. A prospective observational study was conducted in 301 patients admitted in the general and pulmonary medicine departments over six months at a tertiary care hospital in Khammam region. Out of the 301 study population, male patients were more (81.39%). The majority of the patients were from the age group of 51-60 years (30.56%). Smoking was found to be more prominent in the study population (63.6%). Bronchodilators (46.90%) were mostly prescribed class of drugs in the management of COPD followed by Systemic Corticosteroids (20.60%), Antibiotics (19.09%) Most common co-morbidity was found to be Hypertension (19.85%). The study concludes that symptomatic treatment was given to COPD patients in the hospital. The prescribing pattern was found to be in concordance with the current GOLD guidelines in the management of COPD patients

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common lung disease in which airflow limitation is the characteristic feature (Buist et al., 2007; Gershon et al., 2011). 5 percent of the population was affected by COPD and is associated with a high death rate (CDC, 2011; GBD, 2017). In the US, it ranks 4th place by killing more than 1,20,000 people per year (Kochanek et al., 2016). Obstructive lung disease (OLD) indicates a decreased ability to inhale or exhale air out of the lungs. The airflow reduction may be due to the shrinkage of the airways (bronchospasm), a loss of airway integrity (bronchomalacia), or a loss of elasticity of air sacs (emphysema)
which lead to lowering of driving pressure (Dipiro et al., 2009). This condition requires prolonged treatment, which may cause irrationality in drug use results prior to the disease (Mia et al., 2015). As per WHO, "Chronic obstructive pulmonary disease (COPD) is a lung ailment that is characterized by a persistent blockage of airflow from the lungs. It is an under-diagnosed, life-threatening lung disease that interferes with normal breathing and is not fully reversible (WHO, 2016; Reilly, 2012).

Several studies have established that airway obstruction in COPD is due to changes affecting small airways and lung parenchyma, while the contribution of proximal airway epithelium remodeling is less clear (Hogg, 2004; Battaglia et al., 2006; Sturton et al., 2008). The reduced FEV1 (Forced expiratory volume) in COPD is due to the increased thickness of the walls and little airway conduction, and mucous reserves cause the obstruction of airways (Lapperre et al., 2007). As it is a chronic & high prevalent disease, it requires continual intervals of physicians visit and numerous hospitalizations due to acute exacerbations and needs for long term therapy. Performing a correct diagnosis in COPD is important as appropriate treatments reduce the symptoms like dyspnea, which also decreases the number of acute exacerbations and improves the quality of health, ability to exercise and life expectancy (Rennard and Vestbo, 2006). As current and former smokers have more risk to other medical conditions to which management is distinct, and without correct diagnosis & evaluation, the symptoms are not accounted for COPD. India is a large country with vast geographical, environmental, economic, racial, religious and socio-political diversities. Chronic disease incidence, prevalence and management may be affected by these factors. Both globally and in India, Chronic Respiratory Diseases are a common cause of disease burden. About 100 million people are sufferers of obstructive lung diseases (Jindal et al., 2012; Global initiative For Asthma, 2006).

There is evidence that most of the prescriptions are not in accordance with GOLD recommendations or other national guidelines resulting in high prescribing of ICS and exposing patients to more side effects (Jochmann et al., 2010; Jones et al., 2008; Lucas et al., 2008).

Prescription pattern monitoring studies (PPMS) are drug utilization study which is an aid that mainly targets on prescribing and administering of drugs. They reduce abuse or misuse of monitored drugs and promote the appropriate use of monitored drugs. Inappropriate prescribing patterns lead to failure in therapeutic effectiveness, increased exacerbation, decreased quality of life along with higher costs. In this present study, an effort was made to study prescribing patterns considering the prescribing behavior of physicians (Faheemuddin et al., 2016). The objective of this study was to assess the pattern of prescriptions among the patients admitted to tertiary care hospitals in Khammam, Telangana state, India.

**METHODOLOGY**

**Study design and setting**

The prospective observational study was conducted for 6 months, in the inpatients of pulmonology and general medicine ward of tertiary care hospitals in Khammam region. Data was collected by using the specially designed data entry form. The following information was collected for each patient: social demographics, lifestyle, smoking history, presence of comorbidities, socio-economic class, disease severity, prescribed COPD treatments and exacerbation history.

**Subjects**

301 COPD patients with or without co-morbidity admitted to pulmonology and general medicine department during the study period.

**Inclusion Criteria**

Inclusion Criteria satisfies the COPD patients of either sex with (or) without co-morbid condition admitted in general medicine and pulmonary medicine and age 18-80 years.

**Exclusion criteria**

Patients who refuse to participate, Pediatrics, Pregnant and lactating women were excluded from the study.

**Data analysis**

This data was analyzed by using Microsoft Excel and results were presented as percentages.

**RESULTS AND DISCUSSION**

In this study, 301 subjects were included, among them, 245(81.39%) were males and 56(18.61%) were females. The mean age of patients is 52.93 years and the standard deviation was in the range of (11.17). The results were given in Table 1 and Figure 1.

Subjects are separated according to BMI were 4(1.33%) were underweight, 221(73.42%) were normal weight, 67(22.25%) were overweight, 9(2.99%) were obese class-1. The mean BMI of
Table 1: Mean and standard deviation of Age distribution in COPD patients

| Analysis variable: Age | N   | Mean   | Std Dev | Minimum | Maximum |
|------------------------|-----|--------|---------|---------|---------|
| Age                    | 301 | 52.9302326 | 11.1784815 | 19.0000000 | 82.00000 |

COPD patients is 23.85kg/m² and the standard deviation was in the range of (2.623). The results were presented in Table 2 and Table 3.

Figure 1: Age distribution of COPD patients

Among these mostly effected people were farmers, i.e., 99 (32.89%) followed by daily workers 83(27.57%), others 41(13.62%), business personalns 39(12.95%), professionals 31(10.29%), unemployed 8(2.65%). On the whole 4(1.33%) have highest earnings of 51-60K, followed by 4(1.33%) with 41-50K, 13(4.31%) with 31-40K, 22(7.30%) with 21-30K, 76(25.24%) with 11-20K, 182(60.46%) with 1-10K. Out of these, the lower class is mostly effected with 177(58.80%) subjects, while 79(26.24%) were in the middle class, 45(14.95%) were in the upper class. The results were given in Table 4.

Among these, 4(1.33%) were with a mild condition, 120(39.86%) with a moderate condition, 163(54.15%) with a severe condition, 14(4.65%) with a very severe condition. The results were presented in Table 5.

Out of these, 191(63.45%) subjects are smokers, while 110(36.54%) are non-smokers, and 113(37.5%) are alcoholics and 188(62.5%) are non-alcoholics. The results were presented in Table 6.

Among these few subjects were undergone through chest x-ray and provided with impressions of pleural effusion for 27, airway blockade for 23, hyperfiltration for 3, mucous accumulation for 10, remaining 238 hadn't undergone for chest x-ray examination. The results were presented in Table 7.

Few of the patients having different allergies like allergic to change in environment 3, to drugs 1, to cold 1, to dust 2. The results were presented in Figure 2.

Figure 2: Incidence of COPD due to allergies

Among these, the most common comorbidity was found to be Hypertension (19.85%) and less occurred comorbidity is GERD (0.36%). The results were given in Table 8.

Pattern of drug use in COPD patients

In total 301 patients Theophylline was maximum prescribed drug n=109(18.25%) followed by Ipratropium n=79(13.23%), Azithromycin n=36(6.03%), Budesonide n=51(8.54%), Albuterol n=42(7.30%), Hydrocortisone n=41(6.86%), Methyl Prednisolone n=36(6.03%), Ceftriaxone n=35(5.86%), Tiotropium n=34(5.69%), Dexamethasone n=24(4.09%), Prednisone n=22(3.68%), Fluticasone n=17(2.84%), Amoxicillin n=15(2.51%), Levofloxacin n=12(2.01%), Montelukast n=6(1%), Levoctizine n=5(0.83%), Ciprofloxacin n=4(0.67%), Formetrol n=3(0.5%), Salmetrol, Clarithromycin, Diphenhydramine were least prescribed drugs used in equal number of patients n=1(0.16%).

Under evaluation of different classes of drugs used in the therapy we found that Systemic Corticosteroids 123(20.60%) were frequently used followed by Antibiotics 114(19.09%), Anticholinergics 113(18.92%), MethyIxanthines 109(18.25%), Inhaled Corticosteroids 68(11.39%) followed by Bronchodilators 58(9.71%), Leukotriene receptor antagonist were least used only in 6(1%) of patients.

The results were presented in Table 9.

Along with monotherapy, some are prescribed with combination therapies. A total of 11 different combinations are used in the whole study. The most frequently used combination is Amoxicillin+Clavulunicacid in 18(31.58%) of patients. Secondly, Ipratropium bromide+Salbutamol used in 8(14.03%) patients followed by Levalbuterol sul-
### Table 2: BMI in COPD patients

| Body Mass Index     | Males        | Females      | Total        |
|---------------------|--------------|--------------|--------------|
| Underweight         | 4 (1.63%)    | 0 (0%)       | 4 (1.33%)    |
| Normal weight       | 176 (71.8%)  | 45 (80.36%)  | 221 (73.42%) |
| Overweight          | 56 (22.9%)   | 11 (19.64%)  | 67 (22.25%)  |
| Obesity class-I     | 9 (3.67%)    | 0 (0%)       | 9 (2.99%)    |
| Total               | 245          | 56           | 301          |

### Table 3: Mean and standard deviation of BMI in COPD patients

| Analysis of variable: BMI | Mean  | Std Dev | Minimum | Maximum |
|---------------------------|-------|---------|---------|---------|
| N                         | 301   | 23.852392 | 2.628399 | 18.090000 | 34.400000 |

### Table 4: Occupational, financial, economic status, along with disease condition among COPD patients

| Variable                        | Male Percentage | Female Percentage |
|---------------------------------|-----------------|-------------------|
| Occupation                      |                 |                   |
| Professional                    | 10.61           | 8.93              |
| Business                        | 14.29           | 7.14              |
| Farmer                          | 35.91           | 19.64             |
| Daily worker                    | 29.4            | 19.4              |
| Others                          | 8.16            | 37.5              |
| Unemployed                      | 1.63            | 7.15              |
| Total                           | 245             | 56                |
| Income                          |                 |                   |
| 1-10K                           | 56.73           | 76.79             |
| 11-20K                          | 27.34           | 16.09             |
| 21-30K                          | 8.58            | 1.78              |
| 31-40K                          | 4.89            | 1.78              |
| 41-50K                          | 1.23            | 1.78              |
| 51-60K                          | 1.23            | 1.78              |
| Total                           | 245             | 56                |
| Socio-economic class            |                 |                   |
| Upper class                     | 15.9            | 10.7              |
| Middle class                    | 27.3            | 21.5              |
| Lower class                     | 56.8            | 67.8              |
| Total                           | 245             | 56                |

### Table 5: Severity of COPD in patients

| FEV 1    | Male Percentage | Female Percentage |
|----------|-----------------|-------------------|
| <80% (Mild) | 1               | 3.5               |
| 50-80% (Moderate) | 102             | 32.1              |
| 30-50% (Severe) | 131             | 57.1              |
| <30% (Very severe) | 10              | 7.1               |
| Total    | 245             | 100               |
Table 6: Classification of alcoholics in COPD patients

| Smokers classification | No. of patients | Percentage |
|------------------------|----------------|------------|
| Heavy smokers          | 12             | 3.9        |
| Light smokers          | 70             | 23.2       |
| Current smokers        | 99             | 32.8       |
| Former smoker          | 10             | 3.3        |
| Non-smoker             | 110            | 36.5       |
| Alcoholics             | 113            | 37.5       |
| Non-Alcoholics         | 188            | 62.5       |

Table 7: Diagnosis tests in patients

| Chest X-ray Impression         | No. of patients |
|--------------------------------|-----------------|
| Pleural effusion               | 27              |
| Airway blockade                | 23              |
| Hyperfiltration                | 3               |
| Mucous accumulation            | 10              |

Table 8: Comorbidities in COPD patients

| Comorbidities                  | Males           | Females          | Total            |
|--------------------------------|-----------------|------------------|-----------------|
| Type 2 diabetes                | 37(19.4%)       | 7(8.53%)         | 44(16.27%)      |
| Asthma                         | 10(5.26%)       | 5(6.09%)         | 15(5.51%)       |
| Hypertension                   | 49(25.9%)       | 5(6.09%)         | 54(19.85%)      |
| Gastritis                      | 1(0.53%)        | 2(2.43%)         | 3(1.01%)        |
| Corpulmonale                   | 8(4.2%)         | 2(2.43%)         | 10(3.67%)       |
| Anxiety                        | 3(1.57%)        | 1(1.22%)         | 4(1.47%)        |
| Emphysema                      | 7(3.68%)        | 2(2.43%)         | 9(3.30%)        |
| Edema                          | 5(2.63%)        | 1(1.22%)         | 6(2.20%)        |
| Tonsilitis                     | 0(0%)           | 1(1.22%)         | 1(0.36%)        |
| Bacterial Pneumonia            | 5(2.63%)        | 3(3.66%)         | 8(2.94%)        |
| Gastroesophageal reflux disease| 0(0%)           | 1(1.22%)         | 1(0.36%)        |
| Depression                     | 4(2.1%)         | 0(0%)            | 4(1.47%)        |
| Hypothyroidism                 | 2(1.05%)        | 2(2.43%)         | 4(1.47%)        |
| Gallstones                     | 5(2.63%)        | 2(2.43%)         | 7(2.53%)        |
| Cardiovascular disease         | 26(13.68%)      | 12(14.63%)       | 38(13.97%)      |
| Hyperlipidemia                 | 3(1.57%)        | 9(10.97%)        | 12(4.41%)       |
| Osteoarthritis                 | 8(4.21%)        | 10(12.19%)       | 18(6.61%)       |
| Thrombocytopenia               | 1(0.52%)        | 3(3.66%)         | 4(1.47%)        |
| Thromboembolism                | 1(0.52%)        | 4(4.88%)         | 5(1.83%)        |
| Insomnia                       | 3(1.58%)        | 7(8.53%)         | 10(3.67%)       |
| Lumbar Spondylitis             | 10(5.26%)       | 1(1.28%)         | 11(4.04%)       |
| Obesity                        | 2(1.08%)        | 2(2.46%)         | 4(1.47%)        |
| Total                          | 190             | 82               | 272             |

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Table 9: Medication prescribed in COPD patients

| Category                        | Drugs          | No. of patients | Percentage |
|---------------------------------|----------------|----------------|------------|
| Bronchodilators                 |                |                |            |
| Short-acting beta-2 agonists    | Albuterol      | 42             | 7.30       |
|                                 | Levalbuterol   | 12             | 2.01       |
| Long-acting beta-2 agonists     | Salmeterol     | 1              | 0.16       |
|                                 | Formoterol     | 3              | 0.5        |
| Inhaled corticosteroids         | Fluticasone    | 17             | 2.84       |
|                                 | Budesonide     | 51             | 8.54       |
| Anti- Cholinergics              | Ipratropium    | 79             | 13.23      |
|                                 | Tiotropium     | 34             | 5.69       |
| Methyl Xanthines                | Theophylline   | 109            | 18.25      |
| Anti- Histamines                | Diphenhydramine| 1              | 0.16       |
|                                 | Levocetirizine | 5              | 0.83       |
| Leucotriene receptor antagonist | Montelukast    | 6              | 1          |
| Systemic Corticosteroids        | Dexamethasone  | 24             | 4.09       |
|                                 | Prednisone     | 22             | 3.68       |
|                                 | Hydrocortisone | 41             | 6.86       |
|                                 | Methyl Prednisolone | 36       | 6.03       |
| Antibiotics                     | Azithromycin   | 59             | 9.88       |
|                                 | Ceftriaxone    | 35             | 5.86       |
|                                 | Ciprofloxacin  | 4              | 0.67       |
|                                 | Amoxicillin    | 15             | 2.51       |
|                                 | Clarithromycin | 1              | 0.16       |
| Total                           |                | 597            | 100        |

phate+Ipratropium bromide in 6(10.53%) patients 
other combinations used an equal number of 
patients. The results were presented in Figure 3.

Among 301 patients Sulfonylurea was prescribed to 49(14.04%) subjects , Anti-fibrinolytics to 8(2.29%) , Diuretics to 91(26.07%), Beta-blockers to 26(7.45%) , Histamine-2 blockers to 69(19.77%), PPI’s to 23(6.59%) , NSAIDS to 33(9.45%) , Anti-pyretics to 16(4.58%) , Opiate analgesics to 2(0.57%) , Multi-vitamin to 2(0.57%) , Laxatives to 10(2.86%), Statins to 14(4.01%) , Anti-depressants, 
Hormones, Anti-coagulants were prescribed in equal number in 2(0.57%) patients. The results were given in Figure 4.

In this study, about 27(25%) subjects were 
affected with Vomiting, 22(20.37%) with Dizziness, 
17(15.78%) with Abdominal discomfort, 
11(10.18%) with GI disturbances,9(8.33%) with 
Constipation, 7(6.48%) with Diarrhea, equal no. Of 
patients, 5(4.62%) affected with Dry mouth, Fatigue. 
Chest pain and Insomnia 1(0.92%) occurred in the 
same number of patients. The frequency of side 
effects was reported in Figure 5.

Based on the data of the present study, COPD was 
most common among males rather than females as 
most of the men smoke. The highest number of 
COPD patients were from the age group of 41-50 
years. People of age group 41-63 years are more 
prone to COPD. It is a condition where its symp-
toms take years to get developed. It mostly occurs in 
elderly patients as they frequently expose to smoke.

The most common comorbid condition in our study is 
HTN (19.85%), followed by DM-2(16.27%), Cor-
pulmonale (13.9%). The highest number of patients 
is under normal weight. The mean BMI of patients 
is 23.85kg/m². COPD also causes weight loss and 
nutritional abnormalities. About (32.89%) patients 
are farmers who affected with COPD as farmers 
exposed to pesticides & insecticides and noxious 
gases, which may cause allergic reactions.

Almost (60.46%) subjects earn only 1-10K. They use 
tobacco, which containing a higher amount of nicotine like beedi, gutka, which easily leads to the COPD condition. In this study (58.80%), patients belonging 
to the lower class, who may be daily workers and labors, due to the lack of knowledge of the disease 
they get exposed to noxious particles.
Among 301 patients, 63 subjects underwent through chest x-ray as it doesn’t give exact results when compared to spirometry. As spirometry is the mandatory test for COPD, every individual performed spirometry. Among these (53%) are in stage-III of COPD, the majority of them are males who are current and former smokers. On the whole, alcoholics are of (37.5%). About 3 subjects are allergic to change in environment, as seasonal changes like cold conditions may also worsen the disease condition.

The maximum prescribed drug is Theophylline (18.25%), followed by Ipratropium (13.23%), which causes bronchodilation and plays a vital role in symptomatic relief. Inhaled corticosteroids Budesonide (8.54%) are third commonly prescribed, which are in accordance with GOLD guidelines and which are used to reduce the frequency of exacerbations. Systemic corticosteroids like Hydrocortisone (6.86%) are mostly prescribed, followed by Dexamethasone & Prednisone. These are in accordance with the GOLD guidelines, as they decrease the recovery time and hospital stay and improves lung function.
Figure 5: Drug-induced side effects reported in the study

Short-acting beta-2 agonists Albuterol (7.3%) was prescribed in accordance with the GOLD guidelines, which quickly relieves the symptoms of patients. Other LABA's Formeterol (0.5%), Salmeterol (0.16%) are prescribed. Leukotriene antagonist Montelukast was prescribed to (1%) of the study group by considering the financial status of individuals.

The most commonly used Fixed-dose combinations are Amoxicillin+Clavulunic acid (31.58%), as there is a chance of occurrence of other respiratory infections followed by Ipratropium+Salbutamol (LABA+SABA) (14.03%) which causes increased bronchodilation and removes blockage of airways and ICS+LABA in (10.24%) of a study group.

CONCLUSIONS

In this study, it was found that predominantly males are affected with COPD compared to females. The majority of the drugs are prescribed in accordance with the GOLD guidelines. As a prescription containing more than 6 drugs, decreasing of drugs may help in reducing adverse drug reactions and drug interactions. In this study, the major risk factor of the disease is smoking, so patients should be counseled to quit smoking and also encouraged to use masks to prevent inhaling of noxious particles. In this study, no patient was undergone for vaccination, so it should be made available to the patients as per GOLD recommendations.

Abbreviations

COPD = Chronic obstructive pulmonary disease,
GOLD = Global Initiative for Chronic Obstructive Lung Disease,
BMI = Body mass index

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REFERENCES

Battaglia, S., Mauad, T., Schadewijk, A. M. V., Vignola, A. M., Rabe, K. F., Bellia, V., Hiemstra, P. S. 2006. Differential distribution of inflammatory cells in large and small airways in smokers. *Journal of Clinical Pathology*, 60(8):907–911. P. S.

Buist, A. S., Mcburnie, M. A., Vollmer, W. M., Gillespie, S., Burney, P., Mannino, D. M., Nizankowska-Mogilnicka, E. 2007. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study. *The Lancet*, 370(9589):61377–61381.

CDC 2011. Chronic obstructive pulmonary disease among adults– the United States. *Centers for Disease Control and Prevention*, 61(46):938–943.

Dipiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G., Posey, L. M., Streetman, D.-A. D. 2009. Book Review: Pharmacotherapy: A Pathophysiologic Approach. *Annals of Pharmacotherapy*, 43(2):395–395. 7th Edition.
Faheemuddin, M. D., Ramaiah, B., Kiran, S. S., Kumari, B. S., Vijayalaxmi, M. 2016. Evaluation of Medication Adherence in COPD Patients and their Drug Utilization Pattern. *I Med Pub*, 3(17):1–9.

GBD 2017. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study. *GBD Chronic Respiratory Disease Collaborators*, 5(9):691–706.

Gershon, A. S., Warner, L., Cascagnette, P., Victor, J. C., To, T. 2011. The lifetime risk of developing the chronic obstructive pulmonary disease: a longitudinal population study. *The Lancet*, 378(9795):60990–60992.

Global Initiative for Asthma 2006. Global Strategy for Asthma Management and Prevention. Revised in 2006.

Hogg, J. 2004. Peripheral lung remodeling in asthma and chronic obstructive pulmonary disease. *Eur Respir J*, 24(6):893–897.

Jindal, S. K., Aggarwal, A. N., Gupta, D., Agarwal, R., Kumar, R., Kaur, T., Shah, B. 2012. Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis in adults (INSEARCH). *The International Journal of Tuberculosis and Lung Disease*, 16(9):1270–1277.

Jochmann, A., Neubauer, F., Miedinger, D., Schafroth, S., Tamm, M., L. J. 2010. General practitioner’s adherence to the COPD GOLD guidelines: baseline data of the Swiss COPD Cohort Study. *Swiss Medical Weekly*, 140:w13053.

Jones, R. C., Dickson-Spillmann, M., Mather, M. J., Marks, D., Shackell, B. S. 2008. Accuracy of diagnostic registers and management of chronic obstructive pulmonary disease: the Devon primary care audit. *Respiratory Research*, 9(1):62.

Kochanek, K. D., Murphy, S., Xu, J., A. E. 2016. Mortality in the United States. *NCHS Data Brief*, 293(1-8).

Lapperre, T. S., Willems, L. N. A., Timens, W., Rabe, K. F., Hiemstra, P. S., Postma, D. S., Sterk, P. J. 2007. Small Airways Dysfunction and Neutrophilic Inflammation in Bronchial Biopsies and BAL in COPD. *Chest*, 131(1):53–59.

Lucas, A., Smeenk, F., Smeele, I., Schayck, C. V. 2008. Overtreatment with inhaled corticosteroids and diagnostic problems in primary care patients, an exploratory study. *Family Practice*, 25(2):86–91.

Mia, N., Camilla, B., Charlotte, S. U. 2015. Clinical characteristics of the asthma–COPD overlap syndrome — a systematic review. *International Journal of Chronic Obstructive Pulmonary Disease*, 10:1443.

Reilly, J. J. 2012. Chronic Obstructive Pulmonary Disease. 18th Edition. In *Harrisons Principles of Internal Medicine.*, pages 2151–2160, New York. McGraw-Hill.

Rennard, S. I., Vestbo, J. 2006. COPD: the dangerous underestimate of 15%. *The Lancet*, 367(9518):1216–1219.

Sturton, G., Persson, C., Barnes, P. J. 2008. Small airways: an important but neglected target in the treatment of obstructive airway diseases. *Trends in Pharmacological Sciences*, 29(7):340–345.

WHO 2016. Chronic obstructive pulmonary disease (COPD). *World Health Organisation*. 