Current GOLD recommendations and its implementation within hospitalised COPD patients in Malta

Jonathan Gauci, Kentaro Yamagata, David Bilocca, Maria Mifsud, Stephen Montefort

Abstract:

Introduction: In 2012, GOLD revised their classification of Chronic Obstructive Pulmonary Disease patients, incorporating spirometry, symptoms and recent exacerbations.[1]

Aims and Objectives: To assess if patients admitted with an exacerbation of COPD were properly staged prior to the admission, and whether their treatment on presentation was in accordance with GOLD recommendations.

Materials and Methods: All patients admitted to Mater Dei Hospital, Malta with a COPD exacerbation during February, May and August 2013 were studied. Spirometry was considered relevant if performed within the previous two years. The mMRC score of each patient, the number of exacerbations over the previous 12 months, and patient co-morbidities were also recorded.

Results: A total of 124 patients were admitted with an exacerbation during the study period. Of the patients who were known to have COPD, only 48.5% had spirometry performed in the previous two years. Most patients admitted were in GOLD Stage 3 (34.0%), and most were classified as GOLD Group D (73.2%). A long acting bronchodilator was not prescribed in 48.8% of cases where it was indicated. An inhaled corticosteroid was not prescribed in 25.6% of cases where it was indicated, while 10.3% of patients were prescribed an inhaled corticosteroid when this was not indicated.

Conclusion: It is noted that there is a need to improve diagnosis and treatment of COPD on a local basis.

Jonathan Gauci M.D., M.R.C.P.(UK)*
Mater Dei Hospital
Msida, Malta
jonathan.gauci@gov.mt

Kentaro Yamagata M.D.
Mater Dei Hospital,
Msida, Malta

David Bilocca M.D., M.R.C.P.(UK)
Mater Dei Hospital,
Msida, Malta

Maria Mifsud M.D., M.R.C.P.(UK)
Mater Dei Hospital,
Msida, Malta

Stephen Montefort M.D., Ph.D.(S'ton.), F.R.C.P.
Mater Dei Hospital,
Msida, Malta

Corresponding author

Introduction

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) maintains that Chronic Obstructive Pulmonary Disease (COPD) is a clinical diagnosis that should be based on history-taking, the presence of symptoms and assessment of airway obstruction. GOLD recommends spirometry as the gold standard for accurate and repeatable measurement of airway obstruction, measured as the post-bronchodilator Forced Expiratory Volume in one second (FEV_1). GOLD regards a FEV_1/FVC ratio (Forced Expiratory Volume in one second / Forced Vital Capacity) of less than 0.70 as compatible with COPD.

It was previously believed that most COPD patients followed a path of disease progression in which the severity of the disease process paralleled the severity of the airflow limitation. However, more recent studies have shown that on an individual patient basis, the level of airflow limitation (FEV_1) on its own is an unreliable marker of the severity of breathlessness, exercise limitation, and health status impairment. This has led GOLD to revise its guidelines in 2011, presenting a new way of assessing COPD patients, taking into account level of patient's symptoms, severity of airflow limitation, and recent exacerbations, as well as the presence of comorbidities. The most recent GOLD update from January 2015 has retained this combined level of assessment.[1]

The first aim of our audit was to check if patients admitted to Mater Dei Hospital with an exacerbation of COPD, were staged by spirometry at any point during the previous two years. Secondly, the audit aimed to compare the treatment on admission of each patient, with that recommended by GOLD guidelines for the particular GOLD patient group in question.

Materials and Methods
Inclusion and Exclusion Criteria

All patients admitted to Mater Dei Hospital with an exacerbation of COPD during February, May and August 2013 were included in the study. Those patients who were newly diagnosed with COPD and those who were not previously residing in Malta prior to the admission, were excluded from the rest of study, because understandably no previous spirometry would be available in the Mater Dei Hospital records.

Current Level of Patient's Symptoms

The modified Medical Research Council Dyspnoea Score (mMRC) was used to assess patient symptoms. The patients were contacted and asked how they would rank themselves on the mMRC score in the month preceding the hospital admission, rather than the last few days prior to admission. This is because the GOLD guidelines being highlighted by this audit, are focused on the management of stable COPD, not the actual exacerbation.

Severity of the Airflow Limitation

The post-bronchodilator Forced Expiratory Volume in one second (FEV_1) was used as the measurement of airway limitation. The FEV_1 readings were considered to be valid if they were recorded at any point during the previous two years. Spirometry performed prior to this arbitrary two-year period, was considered to be old and not an accurate reflection of the patient's airflow limitation during the period immediately prior to the COPD exacerbation. Using the FEV_1 from spirometry carried out during the hospital admission (if any) was not considered appropriate since the GOLD guidelines being highlighted by this audit, are centred on the management of stable COPD, not the actual exacerbation. The FEV_1/FVC ratio of each patient was also checked, since a ratio of more than 0.70 is not compatible with COPD. Table 1 shows the GOLD classification system used.

Recent Exacerbations

The number of COPD exacerbations leading to hospitalisation in the preceding 12 months for each patient was obtained from the Mater Dei Hospital Electronic Case Summary database. Each patient was then called in order to collect data on the number of exacerbations which did not lead to hospitalisation.

Table 1: GOLD Stages

GOLD Stage 1 – post-bronchodilator $FEV_1 \geq 80\%$ predicted
GOLD Stage 2 – post-bronchodilator FEV_1 50 to 80% predicted
GOLD Stage 3 – post-bronchodilator FEV_1 30 to 50% predicted
GOLD Stage 4 – post-bronchodilator $FEV_1 < 30\%$ predicted

GOLD = Global initiative for chronic Obstructive Lung Disease,
FEV1 = Forced Expiratory Volume in one second

Presence of Co-morbidities

Patient co-morbidities were obtained from the discharge summary available on the Mater Dei Hospital Electronic Case Summary database.

Combined Assessment of COPD

Each patient was classified into a GOLD patient group by combining airflow limitation (spirometry), symptoms and recent exacerbations, as shown in Table 2.

Table 2: Combined Assessment of COPD

GOLD Group	Symptoms	Airflow Limitation	Exacerbations over past 12 months
A	mMRC 0-1	Low Risk Stage 1 or 2	Low Risk 0 or 1 not leading to hospitalisation
B	mMRC ≥2	Low Risk Stage 1 or 2	Low Risk 0 or 1 not leading to hospitalisation
C	mMRC 0-1	High Risk Stage 3 or 4	High Risk ≥2 or ≥1 leading to hospitalisation
D	mMRC ≥2	High Risk Stage 3 or 4	High Risk ≥2 or ≥1 leading to hospitalisation

GOLD = Global initiative for chronic Obstructive Lung Disease,
mMRC = modified Medical Research Council dyspnoea score

When assessing risk, the highest risk according to airflow limitation or exacerbation history should be used. For example, a patient with a mMRC score of 1 with a post-bronchodilator FEV_1 of 70% (therefore Gold Stage 2) and 2 exacerbations over the past year, was classified as Group C.

Pharmacologic Therapy for Stable COPD

The patients were asked what treatment they were taking prior to the admission, and this was compared to that recommended by GOLD. The Recommended First Choice and the Alternative Choice were considered optimal for the particular GOLD group in question (Table 3). The treatment options listed in the Other Possible Treatments section of the GOLD guidelines, were not considered optimal.

Table 3: Optimal Pharmacological Therapy

GOLD Group	Recommended First Choice	Alternative Choice
A	SAMA prn or SABA prn	LAMA or LABA or SAMA + SABA
B	LAMA or LABA	LAMA + LABA
C	ICS + LABA or LAMA	LAMA + LABA or LAMA + PDE-4 inhibitor or LABA + PDE-4 inhibitor
D	ICS + LABA and/or LAMA	ICS + LABA + LAMA or ICS + LABA + PDE-4 inhibitor or LAMA + LABA or LAMA + PDE-4 inhibitor

SAMA = short-acting anti-muscarinic agent,
SABA = short-acting beta-agonist,
LAMA = long-acting anti-muscarinic agent,
LABA = long-acting beta-agonist,
ICS = inhaled corticosteroid,
PDE-4 = phosphodiesterase type 4

Results
Patient Demographics

A total of 124 patients were admitted with a COPD exacerbation during the study period. 57 patients were admitted in February, 40 in May, and 27 in August 2013. The patient age ranged from 40 to 98 years, with a mean of 70 years and a median of 71 years. The length of admission ranged from 1 to 25 days, with a mean of 5.9 days and a median of 5 days.

Current Level of Patient's Symptoms

Fig. 1 shows the distribution of patient according to mMRC score.

Severity of the Airflow Limitation

Table 4 shows that 48 patients (38.7%) had valid spirometry, i.e. performed in the last two years. After eliminating the newly-diagnosed COPD patients and those not previously residing in Malta, only 48 patients (48.5%) were found to have valid spirometry. Of these patients, 34.0% were classified as Stage 3. Both Stage 2 and 4 comprised 27.7% of patients, while 10.6% were classified as Stage 1.

Recent Exacerbations

The mean number of exacerbations per patient over the past 12 months, was 1.2. The range was 0 to 14. 67 patients (54.0%) were classified as Low Risk, meaning they had 0 or 1 exacerbations over the past 12 months, which did not lead to hospitalisation. 57 patients (46.0%) were High Risk, having at least 2 exacerbations over the past 12 months, or at least one exacerbation which led to hospitalisation.

Presence of Co-morbidities

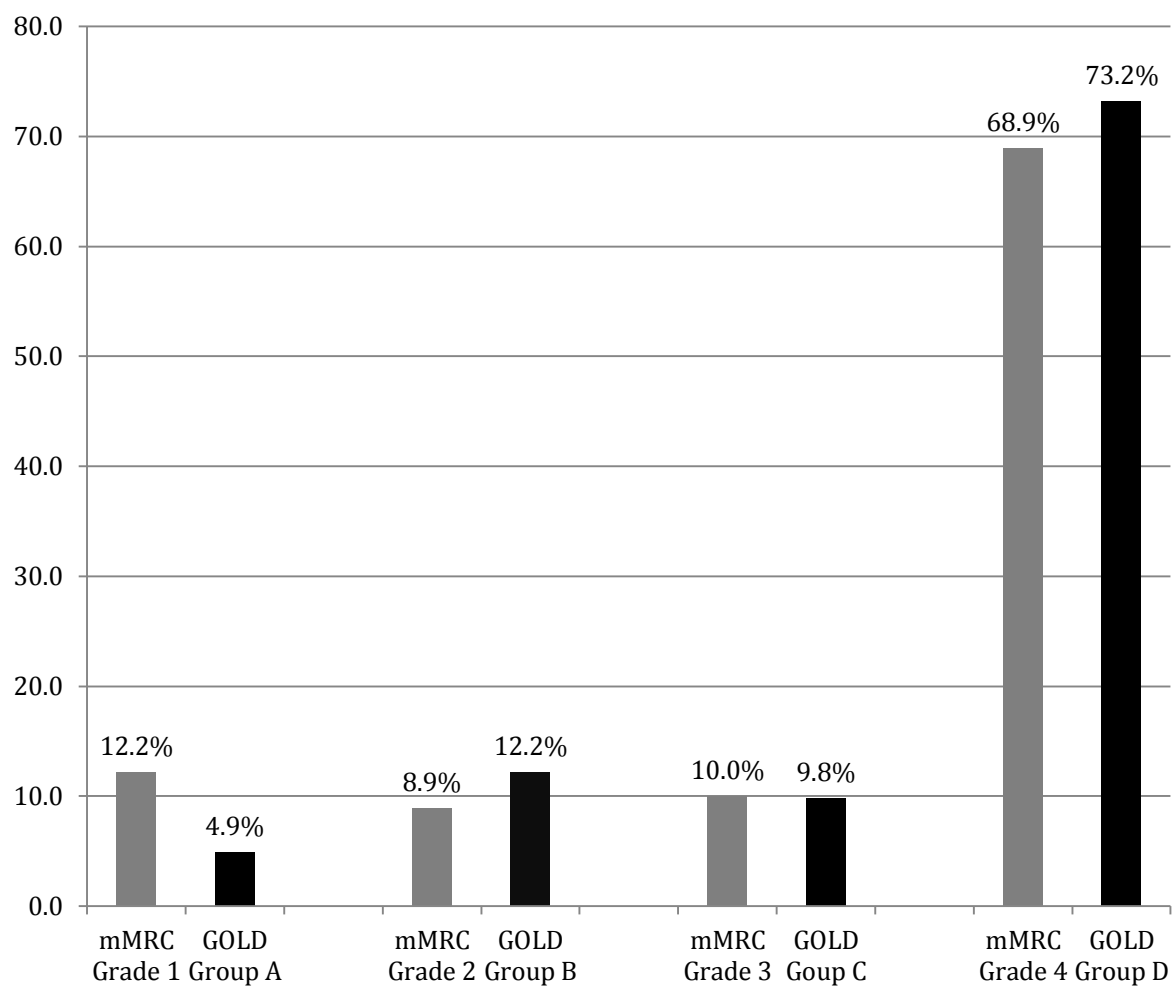COPD was found to be highly co-morbid with a number of disorders, as shown in Fig. 2.

Combined Assessment of COPD

Fig. 1 shows the distribution of patients according to GOLD group, with 73.2% of patients being classified as Group D.

Pharmacologic Therapy for Stable COPD

The treatment of only 14 patients (36.0%) was in accordance with the first recommended choice or the alternative choice recommended by GOLD. The remaining 64.0% of patients were not on optimal therapy. Inhaled long-acting beta-agonist (LABA) treatment is recommended for all patients in Group B to D, of which 48.8% were not receiving LABA therapy. Inhaled corticosteroid therapy (ICS) is recommended for all patients in Group C and D, of which 25.6% were not on ICS treatment. On the other hand, 10.3% of patients in Groups A and B were on ICS therapy, when this is not recommended by GOLD (Fig. 3).

Figure 1: Patient Symptoms and GOLD Group

mMRC = modified Medical Research Council dyspnoea score,
GOLD = Global initiative for chronic Obstructive Lung Disease

Table 4: Validity of Spirometry

Spirometry	Percentage
Spirometry in last 2 years	38.7%
Spirometry more than 2 years ago	11.3%
No Spirometry done since migration to MDH	29.8%
New diagnosis of COPD	16.1%
Non-Residents	4.0%

Figure 2: *Presence of Co-morbidities*
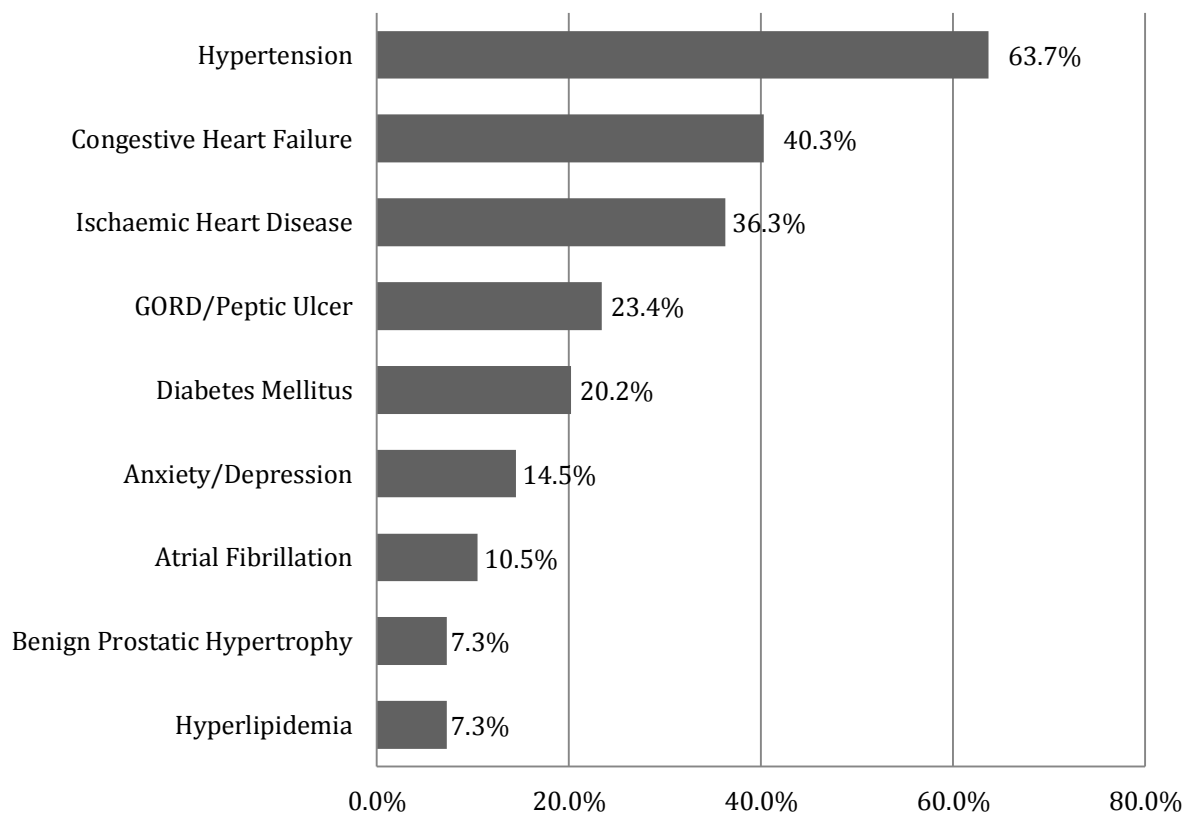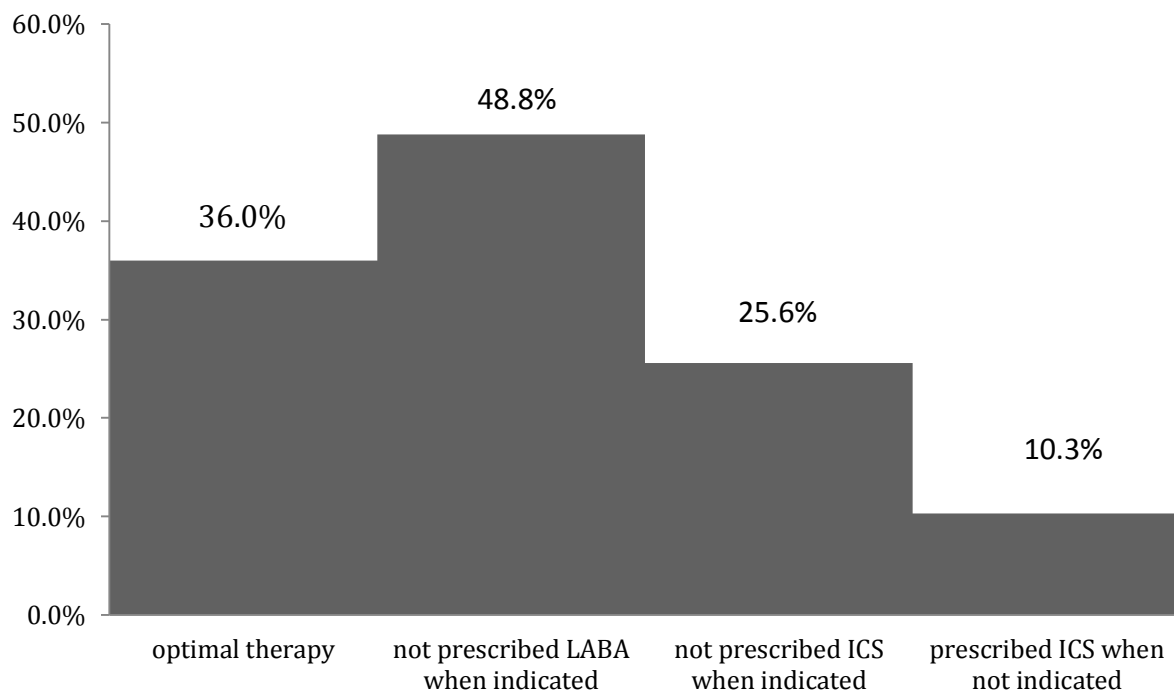

Figure 3: *Pharmacological Therapy*

LABA = long-acting beta agonist,
ICS = inhaled corticosteroid

Discussion

The results obtained from this local audit are comparable to the figures from the 2010 European COPD Audit, which was an observational multicentre study, collecting data from 15821 patients in 422 hospitals around Europe, including Mater Dei Hospital, with the aim of assessing hospital care for COPD patients.[2] The number of patients in the local study was 124, with a median age of 68, while the number of Maltese patients included in the European study was 112, with a median age of 72 years. The median length of hospital stay for an exacerbation of COPD in Malta was found to be 5 days in both studies, when compared to 8 days for Europe as a whole. The mean number of exacerbations per patient over the previous year was 1.2 in the local study, similar to the median number for Europe, which was 1.

Our present audit found that 48.5% of patients admitted with a COPD exacerbation had spirometry in the last 2 years. This was almost identical to the figure reported in the European audit for Malta - 48.2% - though this figure included any previous spirometry, not only that performed in the previous 2 years. The mean European figure was 59.6%, meaning that Malta was more than 10% below the mean. While our own figures for stratification of severity are very similar to the 2010 total European figures, they were however quite different from the 2010 Maltese figures (Table 5).

Table 5: Comparison of COPD Severity Stratification Data

GOLD Stage	Gauci et al. (2013) Malta	European COPD Audit (2010) Europe	European COPD Audit (2010) Malta
Stage 1	10.6%	15.3%	46.3%
Stage 2	27.7%	23.3%	5.6%
Stage 3	34.0%	39.3%	24.1%
Stage 4	27.7%	22.1%	24.1%

Inadequate staging of COPD patients in Malta is primarily due to a lack of spirometry requests. There are several possible reasons for this. A 2013 qualitative study in Chicago concluded that the most common explanation behind primary care physicians not requesting spirometry, was that spirometry was deemed not necessary to make a clinical diagnosis of COPD.[3] GOLD maintains that spirometry is required for the diagnosis of COPD, and states that primary care physicians are in an ideal position to be able to detect COPD in its early stages and perform spirometry to confirm the diagnosis.[1]

Research has shown that the primary benefit of spirometry is to identify those symptomatic patients who might benefit from pharmacological therapy in order to decrease frequency of exacerbations. However, monitoring with spirometry to guide additional therapy or to initiate interventions in patients without bothersome respiratory symptoms does not appear to be beneficial.[4]

The local audit found that underprescription of inhaled LABA was common in Malta. The European study showed a very wide variation in the percentage of COPD patients who were receiving a LABA prior to admission, ranging from 0.6% to 45.9%.[2] The mean value for Europe was 9.3%, and the value quoted for Malta was 12.5%, meaning that LABAs are also underprescribed in several other European countries. Our audit also described inappropriate prescription of ICS in mild COPD and underprescription in severe COPD. The European study looked at the percentage of COPD patients who were receiving ICS, and gave a mean value of 12.4% for Europe, and a value of 54.5% for Malta. Malta was in fact the country where ICS were most prescribed, by almost 20%.

One possible reason for suboptimal pharmacological treatment is the lack of clear evidence that optimization of therapy improves outcomes in COPD. The 2015 systematic literature review carried out by Wilt *et al*. concluded that pharmacological interventions reduced the relative risk of exacerbations by 20 to 25%, and reduced hospitalisations by 4 to 7%, while mortality was not significantly different.[4] The review concluded that the primary benefit of pharmacological intervention is to reduce exacerbations in patients with troublesome respiratory symptoms and severe to very severe airflow obstruction ($FEV_1 < 50\%$ predicted).

Another possible explanation behind underprescription is the fear of side-effects. LABA therapy could have been purposely avoided in patients with cardiac co-morbidities, because beta-agonists are associated with an increased risk in these patients. Au *et al*. described a dose-response relationship of increased hospitalisation and death due to heart failure in patients with congestive heart failure who received increasing

amounts of beta-agonist.[5] On the other hand, there appeared to be no association between the use of inhaled beta-agonists and the risk of developing congestive heart failure. Studies specifically investigating the cardiovascular safety of LABAs have shown that both formoterol and salmeterol have a good cardiovascular safety profile[6]. GOLD also maintains that there is no evidence that COPD should be treated differently in the presence of IHD or CHF, but recommends avoidance of high doses of beta-agonists in unstable angina, as well as closer monitoring for patients with CHF.[1]

Inhaled corticosteroids are being inadvertently prescribed in patients with mild COPD, possibly because of them being wrongly diagnosed as asthmatics. Although the role of Asthma & COPD Overlap Syndrome (ACOS) is becoming more evident, we must consider tailing off ICS gradually in mild to moderate COPD patients (Groups A and B). On the other hand, GOLD recommends adding ICS to our more severe COPD pts (Groups C and D) as this has been shown to decrease hospitalisation and exacerbations in these patients.[1] Because of increasing concern about the long-term safety of ICS use in COPD patients, the WISDOM study has evaluated the need for ICS use in severe COPD, via stepwise withdrawal of ICS in COPD patients in Stage 3 and 4 on dual bronchodilation (ICS+LABA).[7]

Limitations of the Study

Those patients who were not contactable for the purpose of enquiring about patient symptoms, were excluded from the rest of the analysis. This included those patients who were deceased, who were probably more likely to be patients from Group D, meaning that the sickest patients may have been excluded from the study.

Spirometry was considered valid if performed during the previous two years. Patients who were classified as Stage 4 on spirometry more than two years previously, may purposely not have had repeat spirometry booked since there is little or no gain from restaging a patient who is already known to be end-stage in a progressive disorder such as COPD, meaning that once again, the sickest patients may have been excluded from the study.

Recommendations for Malta

The audit concludes that the staging of COPD patients in Malta should be improved. There is a need for increased awareness about the role of spirometry in the diagnosis and staging of COPD. This is especially important in those patients with bothersome respiratory symptoms since the primary benefit of spirometry is to identify those symptomatic patients who might benefit from pharmacological therapy in order to decrease frequency of exacerbations.

Increased access to spirometry in Malta would facilitate the staging of COPD. The introduction of spirometers at Health Centres would be beneficial since primary care physicians are in an ideal position to be able to detect COPD in its early stages and perform spirometry to confirm the diagnosis.

The audit emphasizes the importance of classifying COPD patients into GOLD Group A to D, based on spirometry, symptoms and recent exacerbations. There is a need for increased awareness among doctors working in Malta about the updated GOLD guidelines. This would then allow Maltese patients to be offered the optimal pharmacological therapy in accordance with the GOLD recommendations for each GOLD patient group. This is particularly beneficial in reducing exacerbations in patients with troublesome respiratory symptoms and severe to very severe airflow obstruction ($FEV_1 < 50\%$ predicted), thereby reducing the burden of medical admissions to Mater Dei Hospital.

References
1. Global Initiative for Chronic Obstructive Lung Disease [Internet]. Global strategy for the diagnosis, management and prevention of chronic pulmonary disease; 2015 [cited 2015 Feb 21]. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2015.pdf.
2. European Respiratory Society [Internet]. An international comparison of COPD care in Europe - Results of the First European COPD Audit; 2012 [cited 2014 Oct 1]. Available from: http://www.ciberes.org/audipoc/docs/CD%20ERS%20COPD%20Audit/ERS%20COPD%20Audit%20Report%20National.pdf
3. Joo MJ, Sharp LK, Au DH, Lee TA, Fitzgibbon ML. Use of spirometry in the diagnosis of COPD: A qualitative study in primary care. COPD 2013 Aug;10(4):444-9.
4. Wilt TJ, Niewoehner D, Kim C, Kane RL, Linabery A, Tacklind J, et al. Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease (COPD). Summary, Evidence Report/Technology Assessment No. 121. Agency for Healthcare Research and Quality; 2005 Sep. AHRQ Publication No. 05-E017-2.
5. Au DH, Udris EM, Fan VS, Curtis JR, McDonell MB, Fihn SD. Risk of mortality and heart failure exacerbations associated with inhaled beta-adrenoceptor agonists among patients with known left ventricular systolic dysfunction. Chest 2003 Jun;123(6):1964-9.
6. Tashkin DP, Fabbri LM. Long-acting beta-agonists in the management of chronic obstructive pulmonary disease: current and future agents. Respiratory Research 2010 Oct;11:149.
7. Magnussen H, Watz H, Kirsten A, Decramer M, Dahl R, Calverley P, et al. Stepwise withdrawal of inhaled corticosteroids in COPD patients receiving dual bronchodilation: WISDOM study design and rationale. Respiratory Medicine 2014 Apr;108(4):593-9.