

PHARMACISTS' INTERVENTIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE RELATED HOSPITAL READMISSIONS

*submitted in partial fulfilment
of the requirements of the
Degree of Doctorate in Pharmacy*

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*'What we face may look insurmountable... but what I learned is that we are
always stronger than we know.'*

Arnold Schwarzenegger

Dedicated to all COPD patients fighting insecurities and challenges

ABSTRACT

Acute worsening of respiratory symptoms is associated with accelerated disease progression, often leading to hospitalisations impacting patients' quality of life and the national healthcare system. The aim of this research was to propose a tool assisting pharmacists in identification of risk factors for COPD hospitalisations and readmissions. The objectives included the identification of risk factors contributing to exacerbation of COPD patients necessitating hospitalisation and early readmission for acute exacerbation of COPD, provision of education re-assessment for correct inhaler technique, and review of medication compliance. A data collection tool was compiled and validated by an expert panel comprising of participating respiratory consultant, respiratory resident specialist, clinical pharmacist, and community pharmacist. The study was conducted over 6 months at the acute general hospital, Mater Dei Hospital (MDH), Malta. A case-control approach was adopted consisting of 2 patient cohorts. The inpatient cohort consisted of patients admitted for COPD exacerbation under the care of the participating physician. The outpatient cohort was comprised of COPD patients reviewed at the medical outpatient clinics by the participating respiratory firm. A questionnaire-based interview was disseminated to patients who met the inclusion criteria. The questionnaire consisted of three sections. Section A dealt with general data collection incorporating patient-specific factors and COPD-specific variables, Section B consisted of an inhaler adherence assessment and Section C evaluated inhaler and nebulizer administration technique. In the study population (N=58), statistically significant differences between cohorts were observed ($p < 0.05$) for corticosteroid and antibiotic prescribing, side effects (irrespective of type of side effect), number of days per week patients required salbutamol, and where patients report to first when symptoms

worsen. An almost statistically significant difference was observed for locality of residence ($p=0.055$) and involvement of respiratory physiotherapists ($p=0.054$). Addressing device-specific inhaler technique difficulties and misconceptions, written self-management action plans for worsening symptoms, and optimisation of comorbidities management are fundamental areas to consider in enhancing transition of care when establishing a pharmaceutical care model in respiratory.

Keywords: risk factors, COPD exacerbations, pharmaceutical care plan, inhaler adherence, inhalation technique, pharmaceutical interventions

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LIST OF ABBREVIATIONS

A&E	Accident and Emergency department
ACCP	American College of Clinical Pharmacy
AECOPD	Acute Exacerbation of Chronic Obstructive Pulmonary Disease
BOLD project	Burden of Obstructive Lung Disease project
CAT™ score	COPD Assessment Test score
CDC	US Centres for Disease Control and Prevention
CHEST	American College of Chest Physicians
COPD	Chronic Obstructive Pulmonary Disease
CPAS	Clinical Patient Administration System
CTS	Canadian Thoracic Society
EFRAM	Estudi dels Factors de Risc d'Agudització de la MPOC (Risk Factors of COPD Exacerbation Study)
FREC	Faculty Research Ethics Committee
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GP	General practitioner
H/C	Healthcare centre
IBD	Inflammatory Bowel Disease
IDM	Integrated Disease Management program

IHD	Ischaemic Heart Disease
ISCO	International Standard Classification of Occupations
LABA	Long-acting Beta-2-adrenoceptor Agonist
LAMA	Long-acting Muscarinic Antagonists
MDH A&E	Mater Dei Hospital – Accident and Emergency Department
MDI	Metered Dose Inhaler
mMRC score	Modified Medical Research Council dyspnoea score
MOP1	Medical Outpatients 1
MOP3	Medical Outpatients 3
PHARM-CHF	PHARMacy-based interdisciplinary program for patients with Chronic Heart Failure
PLATINO study	Latin American Project for Research in Pulmonary Obstruction study
POYC	Pharmacy Of Your Choice scheme
QoL	Quality of life
RCT	Randomised Control Trial
SAMA	Short-acting Muscarinic Antagonists
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 THE FACETS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

This section attempts a brief overview of Chronic Obstructive Pulmonary Disease, looking at rate of morbidity and mortality, characteristics, exacerbations, and risk factors. The unmet need to provide an individualised tailor-made pharmaceutical service to patients suffering from COPD and its challenges, triggered off the idea behind this research and its setting.

Chronic Obstructive Pulmonary Disease (COPD) is classified as the fourth leading cause of death globally (Lozano et al, 2012). It is considered one of the primary causes of chronic morbidity and consequent hospitalisation (Barnes et al, 2019). In 2010, COPD mortality was eight times more common than asthma. It contributed to 3.17 million deaths in 2015¹, and it is estimated that COPD becomes the third leading cause of death by 2030 (Mathers and Loncar, 2006). In Malta COPD affects approximately 20,000 individuals² with morbidity and mortality continuously increasing. Persistent respiratory symptoms together with spirometry confirmed airflow limitation are the main characteristics of COPD. Pathophysiological changes to the airway and alveoli occur due to exposure to noxious particles and gases such as smoking or occupational inhalant exposure (GOLD, 2020). Other independent risk factors studied to-date, include male gender, ageing, low educational standard, familial and childhood history of respiratory diseases (Buist et al, 2007; Zhong et al, 2007; Hooper et al, 2012). The Chinese Epidemiology survey of COPD identified an association between occupational

¹ World Health Organisation (WHO). Chronic Obstructive Pulmonary Disease [Internet]. Geneva: WHO; 2019 [cited 2019 Jan 20]. Available from: <https://www.who.int/respiratory/copd/en/>

² TVM. More Maltese are falling ill with lung diseases [Internet]. Malta: TVM; 2018 [cited 2019 Nov 19]. Available from: <https://www.tvm.com.mt/en/news/more-maltese-are-falling-ill-with-lung-diseases-professor-montefort/>

exposure to dusts, vapours, or gas and chronic airflow obstruction (Zhong et al, 2007). This observation was not reported in the international Burden of Obstructive Lung Disease (BOLD) study (Buist et al, 2007;Hooper et al,2012) but an association between the number of years of exposure to occupational dust and chronic airflow obstruction was identified. Individuals who smoke or are exposed to passive smoking through second-hand smoking have a higher risk of developing this respiratory condition. An association between chronic airflow obstruction prevalence and mean pack-years, passive smoking, ambient and household pollution (Burnett et al, 2014; Burney et al, 2014) have been reported.

1.1.1 Exacerbations: a myriad of challenges

Exacerbation of COPD is defined as acute worsening of respiratory symptoms and is associated with accelerated disease progression, diminished health-related quality, mortality, and morbidity (Doll and Miravitlles, 2005). COPD patients experiencing frequent exacerbations (defined as two or more COPD exacerbations yearly) have been associated with worse health status, and morbidity than patients with less frequent COPD exacerbations (Seemungal et al, 1998). What leads to exacerbations of COPD? What is the impact of exacerbations on morbidity and mortality of COPD patients?

Criner et al, (2015) compares COPD exacerbation to *'what myocardial infarctions are to coronary artery disease... acute, trajectory-changing, and often deadly manifestations of a chronic disease.'* COPD exacerbations are regarded as heterogenous events within a heterogenous disease (Hurst & Wedzicha, 2009). This further underlines the need to appropriately diagnose COPD exacerbation through differentiation of relevant alternative diagnoses (GOLD, 2020). Respiratory tract infections and air pollution contribute to two-thirds of the exacerbations with one-third of the exacerbations diagnosed by exclusion (Celli et al, 2004). One Cochrane review conducted by Kruis et al, in 2013 aimed to assess the effect of integrated disease management programs (IDM) in COPD on the number of exacerbations, exercise tolerance, and health-related quality of life (QoL). Although no difference in mortality was observed between case and control arms, statistically significant differences were noted in disease specific QoL and exercise capacity. Significant reduction in hospital admissions and hospital stay were also reported. Exacerbations of COPD often lead to hospitalisations which in turn

impacts patients' quality of life and the national healthcare system (Almagro et al, 2006; Soriano and Rodríguez-Roisin, 2011).

The Directorate of Health Information and Research in Malta has reported that there has been an increase in age and gender standardised COPD-related admission rates from 135 per 100,000 population in 2009 to over 190 admission per 100,000 population in 2012 (Grech et al, 2015). The EFRAM³ cross-sectional study assessing risk factors of COPD exacerbation conducted by Garcia-Aymerich et al, (2000) established that patients hospitalised for COPD exacerbation have a high prevalence of potentially modifiable risk factors. This included lack of influenza vaccine administration, inappropriate administration of long-term oxygen therapy (LTOT), incorrect inhaler technique and smoking. A case-control study by Garcia-Aymerich et al, (2001) inferred that history of hospitalisation and lower Forced Expiratory Volume in 1 second (FEV1) are also significant risk factors. A randomised control trial by Gadoury et al, (2005) with a two year follow up concluded that female sex, higher education, and increased walking distance were predictive of reduced hospitalisation. Hurst et al, (2010) analysed data from the ECLIPSE study examining susceptibility to exacerbation and its frequency. It was observed that one particular group of patients, irrespective of disease severity (moderate, severe, very severe) were susceptible to exacerbations and referred to in the study as the exacerbation-susceptible phenotype. This phenotype can be identified based on history of exacerbations.

³ Estudi dels Factors de Risc d'Agudització de la MPOC (Risk Factors of COPD Exacerbation Study)

Inappropriate inhaler technique and device-specific administration errors might influence drug delivery of inhaled therapy (Chrystyn et al, 2017). This been associated with higher rates of uncontrolled asthma and severe COPD exacerbations (Maricoto et al, 2015; Molimard et al, 2017). A relationship between poor inhalation techniques and the economic burden of Asthma and COPD has previously been stipulated by Lewis et al, (2016) and postulated to be one of the contributing factors to increased healthcare costs and utilisation of secondary healthcare resources in COPD by Usmani et al, (2018).

The interplay of psychological factors including depression and anxiety as determinant comorbidities of COPD exacerbation and treatment outcomes has been studied in several settings. Dahlen and Janson (2002) inferred that depression and anxiety were related to emergency treatment outcome in COPD patients and readmission rates.

1.1.2 The risk factors for re-admissions

Variability in readmission rates was observed by Bahadori et al, (2009) amongst three large urban hospitals studied. Differences in healthcare delivery between hospitals and the patient populations they cater for may explain such variability. Lusuardi et al, (2009) highlights the importance of adherence to standards of care and recommendations particularly the use of spirometry for diagnosis whereby in this observational, prospective study 40% of the patients were flagged as COPD patients without spirometry test. In Malta, Micallef et al, (2015) reviewed MDI technique of hospitalised or outpatient reviewed asthmatics and COPD patients. The need to study the relationship between hospitalisation and readmissions with gender, level of education, and occupation was put forward. Another scenario studied was the association between HIV infection and risk of AECOPD. Depp et al, (2016) conducted a longitudinal study and established that HIV-infected patients were at an increased risk of AECOPD particularly after stratification according to the CD4 cell count when compared to non-infected patients. Deficiencies documented to predispose patients to poor outcomes such as unplanned early readmissions include inadequate patient education, insufficient patient health literacy, missed or lack of scheduled follow-ups, and medication errors (Scott, 2010). A systematic review conducted by Kansagara et al, (2016) inferred that prior hospitalisation, high medication burden, comorbidities, and older age were themes associated with increased risk of rehospitalisation.

1.1.3 Risk mitigating factors

Dang-Tan et al, (2015) reported that self-management skills in COPD contributed to risk reduction in A&E visits, integrated care was associated with a reduction in the mean number of hospital admissions, and telecommunications reduced the number of unscheduled physician visits annually. The joint evidence-based guideline for the Prevention of Acute Exacerbation of COPD Guideline (AECOPD) developed by CHEST and CTS (Criner et al, 2015) has compiled a number of recommendations for the prevention of exacerbations. Yearly influenza vaccination uptake has been associated with reduced risk of influenza-triggered severe COPD exacerbations. The 23-valent pneumococcal vaccine is not specifically recommended for the prevention of AECOPD but is suggested by WHO and CDC for all adults ≥ 65 years or adults with comorbidities that are predispose to a greater risk of pneumococcal infections. Evidence supports pulmonary rehabilitation services for patients who had an exacerbation within the last 4 weeks whereas patient education and specialist follow-up is highly recommended for patient with a recent or history of COPD exacerbations to reduce rehospitalisation. LAMAs and LABAs are the mainstay maintenance inhaled therapy, strongly recommended for the prevention of moderate and severe AECOPD, with LAMAs preferred over SAMAs for improving QoL and lung function.

1.2 PHARMACEUTICAL CARE: AN APPROACH TO ASSIST COPD PATIENTS

The American College of Clinical Pharmacy defines clinical pharmacy as a discipline based on pharmaceutical care, designed in a manner to optimize treatment modalities ensuring optimal patient outcomes (ACCP, 2008). Clinical pharmacy is the fulcrum of pharmaceutical services seeking to assist and serve patients suffering from long-term conditions as well as minor illnesses. Different approaches of pharmaceutical care service implementation have been adopted in various clinics and hospitals within various conditions. These include pharmaceutical care plans, medicines reconciliation, authorization of prescriptions within community and hospital, leadership in medicines management and contribution to education and training (Figure 1.1).

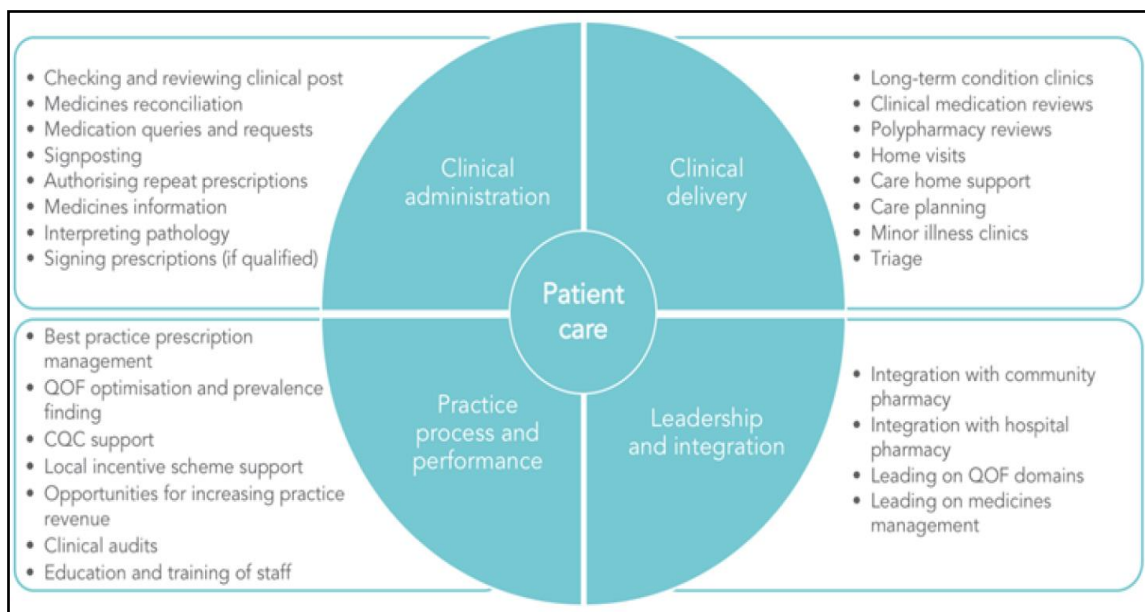


Figure 1.1: Clinical Pharmacy Service

Adopted from: Rao S, Prescott A. Clinical Pharmacists; setting up for clinical success. Guidelines in Practice [Internet]. 2018 [cited 2020 Feb 23]. Available from: <https://www.guidelinesinpractice.co.uk/home/clinical-pharmacists-setting-up-for-success/454289.article/>.

This figure captures the essence of a pharmaceutical service provision targeting patient needs. Such a service is built on an integrated system of human resources including pharmacists operating at different sections and levels assisted by pharmaceutical technologists/technicians within an interdisciplinary and multidisciplinary scenario involving other professionals such as clinicians, nurses, physiotherapists, and social workers.

Makowsky et al, (2009) attempted to delineate how pharmacy can contribute to healthcare teams in maximising patient safety through enhanced evidence-based drug therapy decision-making and focusing on continuity of care between different healthcare sectors. Clinical pharmacists can contribute significantly towards improved patient care. This has been long established in literature. In 2015, NHS England launched the pilot program 'Clinical Pharmacists in General practice Pilot' with the intention of extending pharmaceutical services to general practitioner surgeries. An NHS England funded report by the School of Pharmacy at the University of Nottingham in collaboration with University of Queensland, Australia analysed the implementation of this pilot in engaging clinical pharmacists in general practice and primary care multidisciplinary teams. Clinical Pharmacists were involved particularly in medication reviews which incorporated patient education, medication adherence assessments, and deprescribing. Pharmacy contributions significantly improved patient appointment capacity, saved GP hours, provided better outcomes and quality of life for patients with chronic conditions. It was concluded that the pilot study also contributed to a reduction in opioid use, prescribing errors, and patient readmission post discharge (Mann et al, 2018). In a recent study carried out by Ronan et al, (2020), the authors investigated the impact of pharmacist-led medication reviews in relation to cost avoidance, possible clinical harm, and the perception of nursing staff of the pharmacist's role within a 192-bed university teaching hospital. Medication omissions, medication history taking, and duplication of therapy were the most common interventions encountered. The study concluded that the pharmacist-led medication reviews for inpatients were cost effective with nursing staff expressing the need to

have pharmacists deployed to offer care at ward level where pharmacists can be pivotal in ensuring patient safety and improving quality of care.

A meta-analysis of randomised controlled trials conducted by Ospina et al., (2017) reviewed different studies that analysed discharge care bundles for content, effect on readmissions and improvement in quality of life (QOL). A discharge care bundle was defined as a structured, set of evidence-based interventions offered upon discharge with the aim of improving patient outcomes through provision of consistent and standardised practice. The most common intervention topics presented were:

- patient demonstration of adequate inhaler technique
- patient education on self-management
- tailored self-management plans
- review and/or referral for pulmonary rehabilitation
- agree on outpatient follow-ups
- referral to smoking cessation programs.

These pharmaceutical interventions upon discharge were associated with reduced readmission rates in COPD but no improvement in mortality or QOL. Scott (2010) documents that multicomponent interventions were possibly more effective than single-component interventions in reducing readmissions, encompassing timely interventions at pre- and post-discharge settings. Taking heart failure as a preset example, Peter et al, (2015) investigated possible ways and means of reducing 30-day readmission rate of heart failure patients. The workgroup established that appropriate communication strategies, identification of patient's health literacy, and implementation of the teach-back method were effective, easy, and inexpensive discharge interventions that contributed to a 12% reduction in readmission rates and

shorter hospital stay for subsequent admissions. A randomised trial conducted by Jack et al, (2009) reviewed interventions intended to reduce utilization of hospital resources using all-cause 30-day readmission as the primary outcome measure within a general urban academic medical centre. The implemented discharge service in the Re-Engineered Discharge (RED) project that reduced readmission by 30% included the following components:

- educate patients on diagnosis and treatment through the teach-back method
- schedule follow-up appointments and post-discharge monitoring
- propose, confirm, and present a written action plan
- ensure concordance with clinical guidelines
- follow-up phone calls 2-3 days post-discharge to reinforce discharge plan and provide problem-solving patient advice.

Continuity of care between different healthcare settings has been considered essential to avoid and reduce as much as possible hospital admissions whilst facilitating discharge from hospital setting to the community setting (Bisognano et al, 2009). Transitional care interventions deemed effective by Kansagara et al, (2016) in minimising readmission rates were generally more comprehensive, adaptive to patient's needs, and cover different aspects of transitional care. Ensuring appropriate and timely transitional care interventions increased patient satisfaction, decreased A&E visits, readmissions, and contributed to more efficient use of secondary healthcare resources (Brown, 2018). The research tries to tackle pharmaceutical service from a different proactive approach by providing pharmacists an approach to pre-empt COPD exacerbations where possible.

1.3 RESEARCH SETTING

The acute general teaching hospital, Mater Dei Hospital which is the main public hospital of the Maltese islands provided the research setting. The hospital offers inpatient and outpatient services in addition to specialised clinics including respiratory clinics. Patients requiring hospitalisation are very often admitted through the Accident and Emergency route. These patients are triaged accordingly under the care of admitting teams. If a patient has been admitted for a chronic condition exacerbation, the admitted team liaises with the patient's caring specialist and subsequently the patient is transferred under the care of the specialist consultant for further review as inpatients. Once a patient is deemed fit for discharge, junior doctors prepare a discharge letter. The hospital pharmacy supplies a 3-day discharge supply of medication, and patient is discharged from hospital. Collection of long-term medications occurs through the pharmacy of your choice scheme within the community setting. Outpatient follow-up reviews are conducted in designated consultation rooms by specialist consultants and their assistants. Patients hospitalised for COPD exacerbation, are usually reviewed 6 weeks post-discharge as part of the recommended follow-up strategies by GOLD.

1.4 RESEARCH RATIONALE

A key component in the management of COPD is prevention of exacerbations (GOLD, 2020). Previous studies conducted in Malta evaluate adherence to GOLD recommendations as compared to European hospitals (Gauci et al, 2015). There is less emphasis locally on understanding factors responsible for increased risk of exacerbations necessitating hospitalisation. COPD exacerbations are not only of significant detriment to the patient but consume a considerable portion of healthcare expenditure. The Centre for Disease Control and Prevention estimate that by 2020 COPD expenditure will increase to \$49 billion.⁴ The European Respiratory Society reported that the annual cost of respiratory disease in the EU zone amounts to over €380 billion of which €48 billion can be attributed to COPD related healthcare and lost productivity costs.⁵ One local study conducted by Spiteri et al., (2018) identified that on average every hospitalisation due to COPD exacerbation costs the local healthcare system approximately €1,500. The rationale of this research is formulated on an attempt to identify variables contributing towards exacerbation of COPD which lead to hospitalisation whilst highlighting the contribution of the pharmaceutical service provision. The rationale of the research was triggered through a discussion of the researcher and the lead respiratory clinician during an experiential placement undertaken as part of the researcher's doctoral studies.

⁴ Centre for Disease Control and Prevention (CDC). Chronic Obstructive Pulmonary Disease [Internet]. Atlanta: CDC; 2018 [cited 2020 Jan 5]. Available from URL: <https://www.cdc.gov/copd/infographics/copd-costs.html>

⁵ European Respiratory Society (ERS). European Lung White Book. In: The economic burden of lung disease [Internet]. Sheffield: ERS; 2020 [cited 2020 Jan 16]. Available from URL: <https://www.erswhitebook.org/chapters/the-economic-burden-of-lung-disease/>

1.5 RESEARCH QUESTION

What factors contribute to hospitalisation and early readmission of COPD patients experiencing an exacerbation? What contributions can the pharmacy profession provide towards chronic respiratory conditions such as COPD in reducing readmission rates?

1.6 AIM

The aim of this research is to develop and validate a tool which could assist pharmacists in different care settings to identify issues relating to COPD hospitalisations and readmissions.

The objectives were to:

- i. identify risk factors associated with hospitalisation and early readmission rates secondary to COPD exacerbations.
- ii. provide an assessment of inhaler technique and use.
- iii. review medication compliance in terms of COPD medications.

CHAPTER 2

METHODOLOGY

2.1 A COLLABORATIVE APPROACH TO RESEARCH DESIGN

This research started off with a collaborative identification of an unmet need and the possibility of a pharmacist's contribution to improve the service being provided by the clinicians. This collaboration was the stem of the research and continued throughout the study design. The research design and methodology were discussed and devised in collaboration with the lead respiratory consultant in Mater Dei Hospital who was also the participating consultant in this research.

2.2 RESEARCH DESIGN

A case-control study design was deemed adequate to identify differences if any between COPD patients hospitalised due to an exacerbation identified as the case (inpatient) cohort versus COPD patients not hospitalised during the previous year represented as the control (outpatient) cohort. The general acute hospital, Mater Dei Hospital (MDH) was identified as an appropriate institution for the evaluation of such risk factors in the local scenario. The methodology undertaken was further categorised into 4 Phases (Figure 2.1). Prior to initiation of the research, ethics approval was sought and granted by the Faculty Research Ethics Committee (Appendix I).

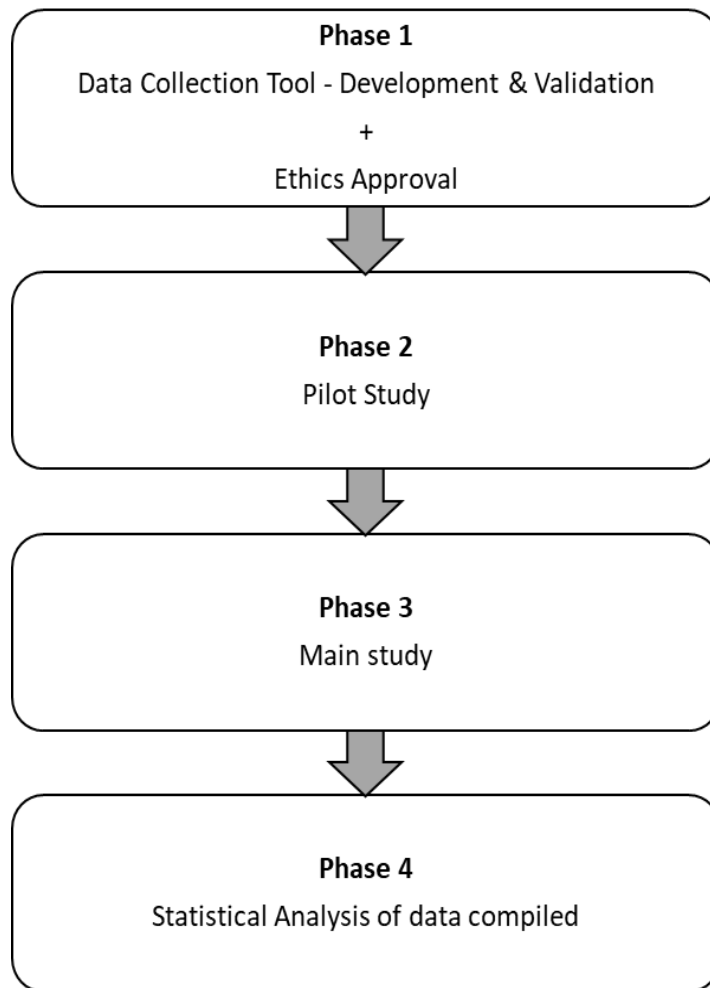


Figure 2.1: Study strategy

Phase 1 focused on the compilation of an evidence-based data collection tool specifically developed and validated for this research. The tool aimed at identifying potential factors contributing to hospitalisation of COPD patients experiencing an exacerbation. The identification of risk factors could assist pharmacists when devising pharmaceutical care plans. Other preliminary work involved attending a short training program to assist in smoking cessation. *Phase 2* constituted the pilot study focusing on the first ten patient recruited between inpatient and outpatient cohort. The scope was to test feasibility and applicability of the compiled tool, appropriateness of recruitment strategies and identify potential modifications required to improve data collection. *Phase 3 summarised* the main study capturing the study findings which were statistically analysed using IBM SPSS® version 26 in Phase 4.

2.3 RESEARCH PROTOCOL WITHIN CLINICAL SETTING

This section describes the research protocol undertaken to support the research methodology used during the different phases of the study design within the clinical setting. Patients admitted with COPD and potential candidates within the inpatient cohort were identified by the participating clinicians' team.

The patients were introduced to the research and consent was sought (Appendix III). The team obtained each patient's respective consent and liaised with the researcher. The Clinical Patient Administration System (CPAS) was used to confirm location (in wards) of the flagged and consented patients. The researcher visited identified patients and confirmed whether patients met the inclusion criteria. The data collection tool (Appendix II) developed and validated for the purpose of the study was used to collect the data. The same group of patients were followed up for early readmissions defined as 30-day post-discharge all-cause admission. The control group involved recruiting patients from the COPD outpatient clinic. The control group consisted of COPD patients who had not been admitted during the previous year. The researcher visited COPD outpatient clinics on a weekly basis on pre-identified dates. Patients who met the inclusion criteria were approached and consented by the clinicians' team. Subsequently the researcher collected data from the patient using the Data Collection Tool (Appendix II).

2.4 PHASE 1: PRELIMINARY WORK

Phase 1 focused on the preliminary work required to compile tools and documents which were essential for the testing carried out in the pilot study (Phase 2) and the subsequent implementation on a larger scale within the main study at Phase 3.

2.4.1 *Development and validation of Data Collection Tool*

A literature review on risk factors for COPD, risk factors for COPD exacerbations necessitating hospital admissions and early COPD readmissions was conducted in order to develop a Data Collection Tool which would assist in identification of risk factors for exacerbations leading to hospitalisations. COPD protocols, practice guidelines, evidence-based research, compliance tools and inhaler technique assessment tools were reviewed. Appendix II lists the literature review used.

The compiled data collection tool entitled: *“COPD exacerbation risk factors management and prevention”* (Appendix II) was developed with the intention of gathering information on contributing factors for COPD exacerbation necessitating hospitalisation and identifying potential pharmaceutical interventions in this group of patients. The English version was first compiled followed by a Maltese version using forward translation and backward translation technique to ensure accuracy and repeatability between different versions of the same questionnaire. The *“COPD exacerbation risk factors management and prevention”* was validated by an expert panel consisting of the lead respiratory clinician at Mater Dei Hospital, a resident specialist in respiratory diseases, a clinical pharmacist, and a community pharmacist.

The scope of the validation process was to assess appropriateness towards the intended research and readability. The objectives for the validation exercise were to ensure that the tool covers all the different aspects of COPD pharmaceutical care and that the questions are clear, to the point and not misleading. Feedback was evaluated and incorporated within the final data collection tool (Appendix II).

2.5 PHASE 2: PILOT STUDY

The data collection sheet: *“COPD exacerbation risk factors management and prevention”* (Appendix II) was piloted to establish feasibility and applicability of study design within a busy clinical scenario.

2.5.1 Implementation of the pilot study

For the purpose of the pilot study, the first 5 in-patients (case cohort) and the first 5 out-patients (control cohort) were recruited in the pilot phase. In view of time constraints to carry out the study, it was estimated that between 50 and 70 patients will be recruited in the main study. On the basis of this, the sample size of the pilot was set at 10 participants in order to represent approximately 15% of the target study population whilst providing adequate information feasibility aspects. Patients were considered eligible to participate if they satisfied the following criteria namely were diagnosed as COPD patients confirmed by spirometry airflow obstruction, aged 18 years and over, under the care of the participating respiratory consultant, able to understand English or Maltese and mentally stable. Palliative patients and cognitively impaired patients were excluded from the study. Following consent, the researcher administered the *“COPD exacerbation risk factors management and prevention”* face to face to the participating patients. The patients were offered an individualised pharmaceutical care session which included medication review and medication reconciliation. Pharmaceutical interventions were dictated by the patients’ responses, areas of patient care necessitating attention or improvement as identified by the investigator whilst conducting the questionnaire-led interview, and difficulties expressed by the patients themselves.

2.6 PHASE 3: IMPLEMENTATION WITHIN THE CLINICAL SCENARIO

The study was conducted over a period of 5 months. Figure 2.2 schematically represents the flow of the study based on a case-control design. Patients admitted to MDH hospital due to acute exacerbation of COPD and who met the eligibility criteria were recruited to the case cohort. Patients who attended outpatient visits at the Medical Outpatient Clinics at MDH who met the set eligibility criteria and had not experienced COPD exacerbation necessitating hospitalisation during the previous year were recruited to the control cohort. Depending on the patients' language preference, the English or Maltese version of the tool, *"COPD exacerbation risk factors management and prevention"* was utilised in both patient groups. Medication reconciliation was carried out for both case and control groups. All data compiled was inputted manually by the researcher onto a password protected Microsoft® Excel spreadsheet. The electronic version was compiled to enable data analysis using IBM SPSS® Statistics software. In order to facilitate ease of reference, patients were coded in the format of a letter and number. The letters used were 'I' for patients recruited within the inpatient cohort and 'O' for patients recruited within the outpatient cohort. A number was also denoted to every patient interviewed. The case cohort patients were followed up at 30-day post discharge to note any readmissions within 30 days timeframe.

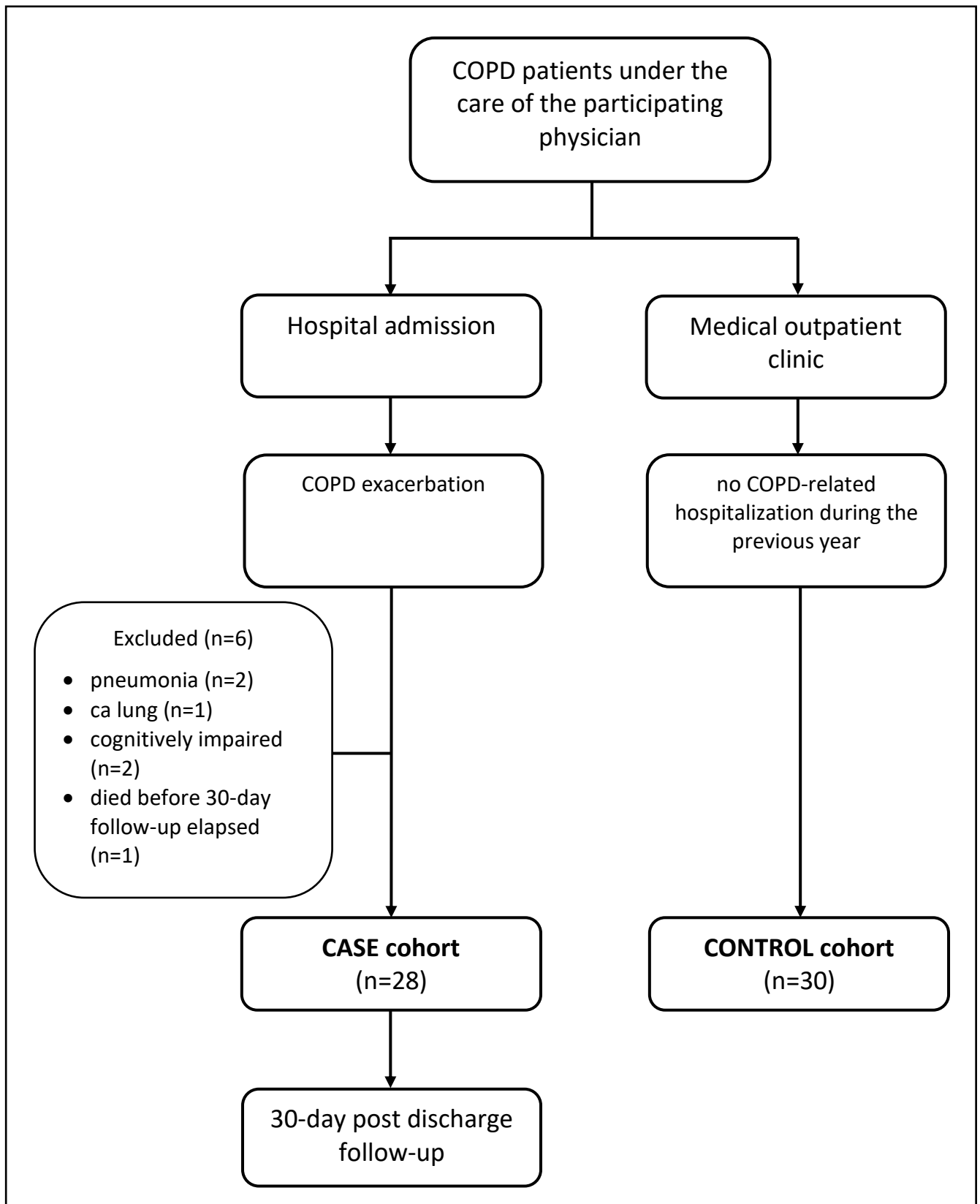


Figure 2.2: Flow diagram of participation selection distinguishing between inpatient and outpatient cohort

2.6.1 Case cohort

Case briefing was done prior to approaching the patient in order for the researcher to familiarise oneself with the admission details and patient history. In cases where patients were resting, being attended to, or have relatives visiting, the researcher revisited at an alternative and convenient time for the patient. Patient confidentiality was secured through identification of appropriate consultation area at the ward thus enabling the patient was comfortable and at ease to discuss in a friendly manner.

2.6.2 Control cohort

COPD patients were requested to perform a pulmonary function test on the day of outpatient review so that the latest spirometry results were available. Patient were first reviewed by the respiratory firm for their normal follow-up consultations. Subsequently potential study patients were asked to participate. All patients expressed enthusiasm towards participating and collaborating to the research. These patients were introduced to the researcher. The data collection tool was completed within a designated area at the Medical Outpatients premises to ensure patient confidentiality. Demonstration inhalers and spacers or patient's own were used to revise and improve device-specific inhaler techniques. In cases where an interview with one patient was ongoing whilst another had been flagged, the nurse in charge of appointments would ask the patient to wait until that interview was over.

2.7 PHASE 4: STATISTICAL ANALYSIS

All the data compiled was inputted in Microsoft® Excel spreadsheet software and converted into numerical data in order to facilitate transfer of information into IBM SPSS® Statistics 26 software for statistical analysis. The choice of statistical tests was discussed with the research group including a statistician. In order to compare between the two independent cohorts (inpatient versus outpatient) several different statistical tests were conducted depending primarily on the variable's characteristics (categorical, ordinal, or continuous). Parametric tests were conducted for data of normal distribution whilst non-parametric tests were conducted for data in which such an assumption cannot be made.

2.7.1 *Chi-Square test*

The Chi-square test was used to investigate the association between two categorical variables. One of these variables indicated the group (inpatient/outpatient) while the other variable provided some demographic or health related information about the patient. The null hypothesis specifies that there is no association between the two categorical variables and is accepted if the p value exceeds the 0.05 level of significance. The alternative hypothesis specifies that there is a significant association between the two categorical variables and is accepted if the p value is less than 0.05 criterion.

2.7.2 Shapiro-Wilk Test

The Shapiro-Wilk test was used to determine whether the variable's distribution is normally skewed. The null hypothesis specifies that the variable's distribution is normal and is accepted if the p-value exceeds the 0.05 level of significance. The alternative hypothesis specifies that the variable's distribution is skewed (not normal) and is accepted if the p-value is less than the 0.05 criterion.

2.7.3 Independent Sample T-test

The Independent Sample T-test was used to compare the mean value for a continuous variable of normal distribution between two independent groups. The null hypothesis specifies that the mean varies marginally between the two groups and is accepted if p-value exceeds the 0.05 level of significance. The alternative hypothesis specifies that the mean varies significantly between the two groups and is accepted if the p value is less than the 0.05 criterion.

2.7.4 Mann-Whitney Test

The Mann-Whitney Test was used to compare the mean value for a continuous variable of non-normal distribution (skewed distribution) between two independent groups. The null hypothesis specifies that the mean varies marginally between the two groups and is accepted if p-value exceeds the 0.05 level of significance. The alternative hypothesis specifies that the mean varies significantly between the two groups and is accepted if the p value is less than the 0.05 criterion.

2.7.5 *Two-proportions Z-test*

The difference of the two-proportions Z-test was used to compare two proportions and determines whether they differ significantly. The null hypothesis specifies that the 2 proportions are comparable and is accepted if the p-value exceeds the 0.05 level of significance. The alternative hypothesis specifies that the 2 proportions vary significantly and is accepted if the p-value is less than the 0.05 criterion.

CHAPTER 3

RESULTS

The results of this research focus on the compilation of a validated tool developed for investigation of risk factors in COPD exacerbation and early readmissions. The tool *“COPD exacerbation risk factors management and prevention”* was used as part of an individualised pharmaceutical care plan and consisted of 3 sections each targeting different aspects of COPD care and management. A sample of 58 patients selected from a population of approximately 20,000 patients guaranteed a maximum margin of error of 12.85% assuming a 95% confidence level. Statistical analysis of the data compiled through face to face questionnaire-led interviews was conducted using IBM SPSS® Statistics 26 software. Inferences and conclusions were drawn according to the p-value achieved with the intention of identifying associations between different factors possibly contributing towards COPD exacerbation leading to hospitalisation. There were no readmissions at 30 days post discharge for the case cohort group.

3.1 PHASE 1 AND PHASE 2: VALIDATION OF DATA COLLECTION TOOL AND PILOT STUDY

The developed tool entitled: *“COPD exacerbation risk factors management and prevention”* consists of three sections. Section A records the patient demographics and includes medicine reconciliation. One member of the expert panel suggested the inclusion of documenting oxygen flow rate and number of hours used per day in addition to whether patient has been prescribed medical oxygen or not. For patients hospitalised during the past year, it was established to record whether this was COPD related or not and quantify when possible COPD-related visits. As part of patient’s active involvement in condition management, if patient missed any outpatient reviews during the past year, this was to be recorded. The clinicians forming part of the expert group suggested to capture whether patient’s residence is in the vicinity to the sea, countryside, or garden and level of humidity, all of which are factors known to effect COPD exacerbations, in addition to the location. When identifying whether patients had any pets at home, these were to be categorized into furred pets versus non-furred pets. In relation to the healthcare professionals’ involvement, all members of the expert group suggested the identification of any input from respiratory physiotherapists. Section B recorded patient adherence to inhaled therapy and their behaviour in cases of symptom worsening. The pharmacist members of the group suggested to record where and to whom patients report first when symptoms worsen. Section C incorporated marking schemes developed to evaluate inhaler and nebulization techniques. The lead respiratory consultant recommended to distinguish inhalation techniques and the respective marking scheme such as using a metered dose inhaler (MDI) without a spacer versus using a spacer. A scoring scheme for hard

capsule inhalers and patient advice tips to pass over to patient when discussing proper inhaler handling were also developed. The data collection tool was well received by the expert panel who suggested to incorporate references to increase the robustness of the tool and which could aid for future amendments to the tool as new guidelines emerge.

No further amendments were carried out during Phase 2 which was the pilot study consisting of 10 participants.

3.2 PHASE 3: STUDY FINDINGS

A total of 58 patients were recruited for the study. The case (inpatient) cohort group consisted of 28 patients who met the inclusion criteria. The control (outpatient) group consisted of 30 patients. Table 3.1 compares the two groups in accordance with age. No statistically significant difference was noted between the two groups.

Table 3.1: Age comparison between case and control cohorts

			Group		
			Inpatient	Outpatient	Total
Age	65 years or less	Count	12	7	19
		Percentage	42.9%	23.3%	32.8%
	66-75 years	Count	10	15	25
		Percentage	35.7%	50.0%	43.1%
	76 years or more	Count	6	8	14
		Percentage	21.4%	26.7%	24.1%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$\chi^2(2) = 2.536$, $p = 0.281$ (Chi square test)

There is a larger percentage of inpatients (42.9%) compared to outpatients (23.3%) who are aged 65 years or less. There is a higher percentage of outpatients (76.7%) who are aged at least 66 years compared to the inpatient group (57%). The percentage differences are not statistically significant since the p-value 0.28 exceeds the 0.05 level of significance.

In general, both cohorts consisted of a larger percentage of males (77.6%) than females (22.4%). Table 3.2 denotes a non-statistical difference between the case and control groups when considering gender.

Table 3.2: Gender comparison between case and control cohorts

			Group		
			Inpatient	Outpatient	Total
Gender	Male	Count	22	23	45
		Percentage	78.6%	76.7%	77.6%
	Female	Count	6	7	13
		Percentage	21.4%	23.3%	22.4%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(1) = 0.030$, $p = 0.862$ (Chi square test)

A higher percentage of males (77.6%) than females (22.4%) was observed in both groups. There was no statistically significant difference between the groups since the p-value 0.86 exceeds the 0.05 level of significance and thus the null hypothesis is accepted.

The study population (N=58) indicates that the male gender was possibly a predisposing factor for developing COPD but not a risk factor for hospitalisation. The difference of 2 proportions Z-tests indicated that the differences between males and females recruited was significant with a p-value < 0.001 less than the 0.05 criterion (Table 3.3).

Table 3.3 Proportions for Gender using the difference of 2 proportions Z-test

Percentage 1 (Male)	Percentage 2 (Female)	Z-Score	P-value
77.6%	22.4%	5.942	$p < 0.001$

3.2.1 Comparing Body mass index between cohorts

Figure 3.1 represents the study findings relating BMI for both cohort groups.

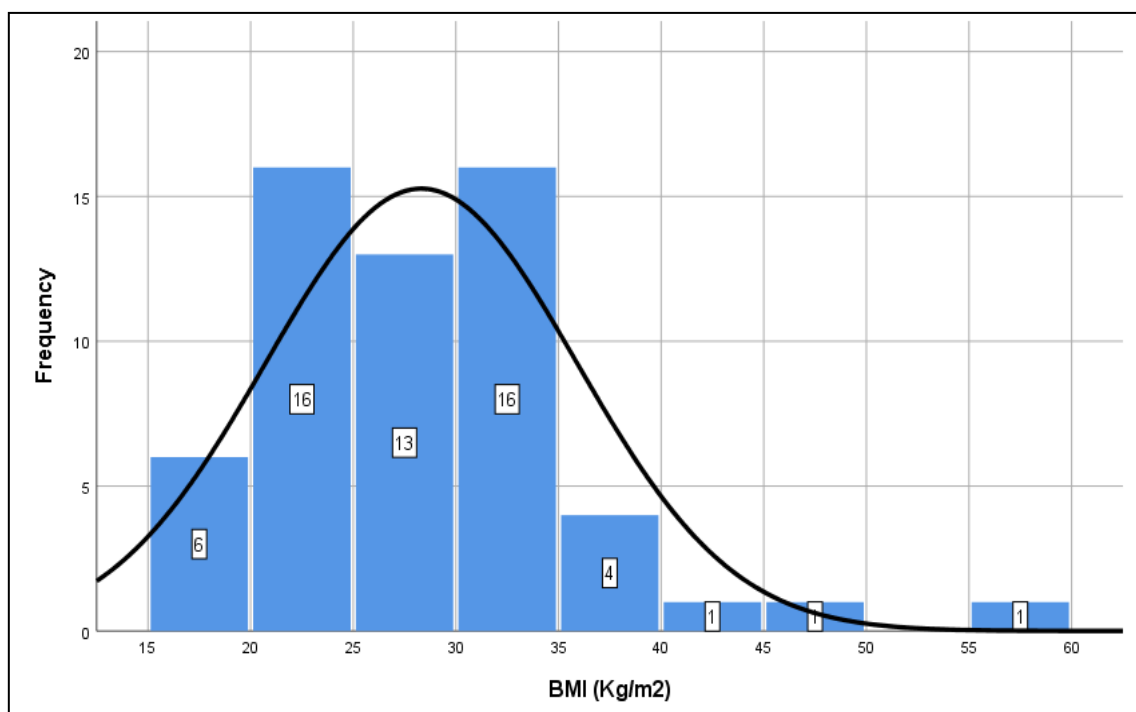


Figure 3.1: Histogram illustrating BMI distribution for both cohorts

The Shapiro-Wilk p-value (0.002) is less than the 0.05 level of significance indicating that the BMI distribution is skewed (as displayed in the histogram) and does not satisfy the normality assumption. For this reason, the Mann-Whitney Test was used to compare mean BMI between the two groups supporting a non-statistically significant result (Table 3.4).

Table 3.4: Mann-Whitney Test – BMI SPSS OUTPUT

Group	Sample size	Mean BMI	Std. Deviation	P-value
Inpatient	28	28.71	7.685	0.744
Outpatient	30	27.94	7.585	

Figure 3.2 displays the 95% confidence interval of the actual mean BMI of inpatients and outpatients if the sample size had to be increased considerably. The fact that the two confidence intervals overlap indicate that mean BMI of the two groups did not vary significantly. This means that BMI was not a risk factor for hospitalisation.

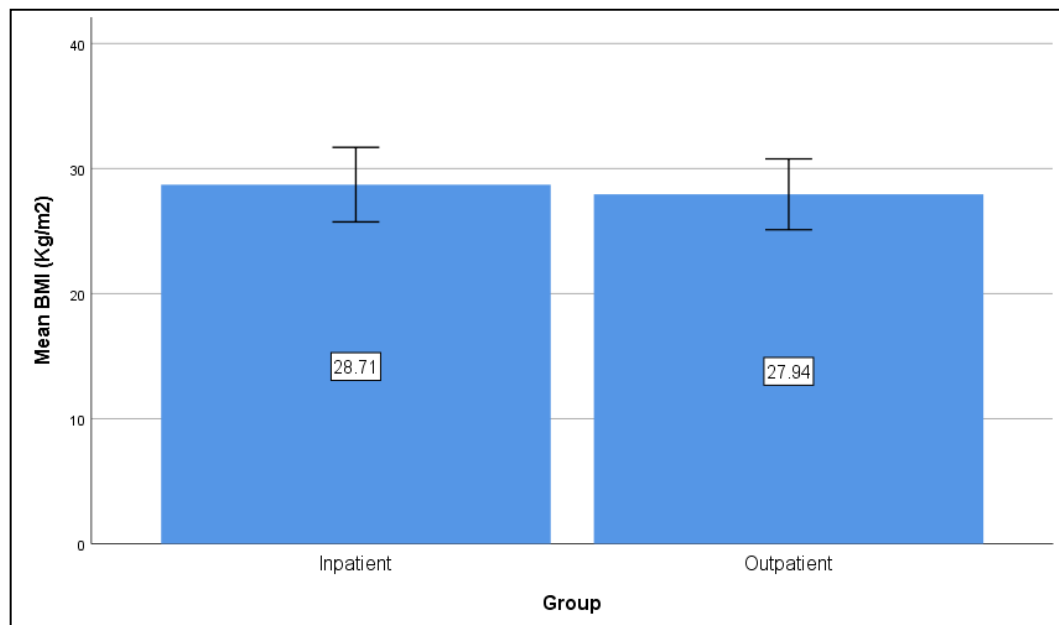


Figure 3.2: Error bar graph comparing the mean BMI which displays the 95% confidence interval for the actual mean BMI if the sample size had to be increased considerably

3.2.2 *Locality of residence*

In order to facilitate analysis of locality of residence, data was classified according to the Geographical Classification for the Republic of Malta (GCM) as recommended by the National Statistics Office (NSO)⁶. A greater percentage of patients hospitalised reside in the Southern Harbour district (35.7%) and Northern Harbour district (32.1%) as compared to outpatient group (16.7%) and (23.3%) respectively. All patients residing within the Western district (12.2%) were not hospitalised and did not experience an exacerbation necessitating hospitalisation within the previous year. The percentage differences were almost statistically significant since the p-value 0.055 exceeds the 0.05 criterion (Table 3.5). This result warrants further investigation with a larger sample size.

⁶ National Statistics Office (NSO) – Malta. Regional Statistics MALTA 2019 edition [Internet]. Valletta: NSO; 2019 [cited 2020 Jan 25]. Available from URL: <https://nso.gov.mt/en/nso/Media/Salient-Points-of-Publications/Pages/Regional-Statistics-MALTA-2019-Edition.aspx>

Table 3.5: Locality of residence across groups

			Group		
			Inpatient	Outpatient	Total
Locality	Southern harbour	Count	10	5	15
		Percentage	35.7%	16.7%	25.9%
	Northern harbour	Count	9	7	16
		Percentage	32.1%	23.3%	27.6%
	South eastern	Count	5	5	10
		Percentage	17.9%	16.7%	17.2%
	Western	Count	0	7	7
		Percentage	0.0%	23.3%	12.1%
	Northern	Count	4	6	10
		Percentage	14.3%	20.0%	17.2%
Total	Count	28	30	58	
	% within Group	100.0%	100.0%	100.0%	

$X^2(4) = 9.259$, $p = 0.055$ (Chi Square Test)

The majority of inpatients (68%) resided either within the Southern harbour district or the Northern harbour district. None of the hospitalised patients recruited resided within the Western district with all patient from this district (23%) recruited within the outpatient cohort. Further investigations are required to understand why no patients residing in Gharghur, Mellieħa, Mgarr, Mosta, Naxxar, and San Pawl il-Baħar were hospitalised due to COPD exacerbation and recruited as part of the inpatient cohort. A larger sample size will be required to investigate such events and identify if this difference holds.

3.2.3 Educational Standard

The majority of patients (88%) had an educational standard of either primary or secondary level. The outpatient cohort consisted of a greater percentage of patients with primary level of education (53.3%) compared to inpatients (39.3%). However, the percentage differences were not significant with a p-value of 0.210 exceeding the 0.05 criterion (Table 3.6).

Table 3.6: Level of Education across both groups

			Group		
			Inpatient	Outpatient	Total
Education Standard	Primary	Count	11	16	27
		Percentage	39.3%	53.3%	46.6%
	Secondary	Count	12	12	24
		Percentage	42.9%	40.0%	41.4%
	Post-secondary	Count	5	1	6
		Percentage	17.9%	3.3%	10.3%
	Graduate	Count	0	1	1
		Percentage	0.0%	3.3%	1.7%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(3) = 4.529$, $p = 0.210$ (Chi square test)

Advanced or basic level of education was not associated with an increased chance for exacerbation and hospitalisation. This indicates that any patient with any type of background is capable of taking control of his/her medical condition if appropriately managed. The data collected also suggests that locally COPD can be associated more with individuals of primary and secondary level of education rather than individuals with post-secondary and graduate educational standard. For such a correlation to be identified and confirmed, a separate study altogether, possibly with a larger sample size needs to be conducted to assess COPD diagnosis and risk factors in the local setting. Variables to be assessed may include patient-specific factors, environmental factors, and socioeconomic factors.

3.2.4 *Occupation and Job history*

Different classifications and groupings were used in order to study any possible correlation between the patient's line of work and hospitalisation due to COPD exacerbations. The first tool used was the latest version of the International Standard Classification of Occupations (ISCO-08).⁷ The ISCO is an international labour organization which classifies jobs into groups according to duties and tasks involved. Reported job descriptions were grouped according to the ISCO classification for statistical analysis (Table 3.7).

Study findings analysis indicate that elementary occupations (22.4%) were the most common job descriptions encountered, followed by clerical support workers (19%), plant and machine operators/assemblers (15.5%) and service/sales workers (12.1%). The percentage difference between inpatient and outpatient cohorts was not significant with a p-value of 0.640 exceeding the 0.05 criterion (Table 3.8).

⁷ International Labour Organization (ILO). ISCO. International Standard Classification of Occupations [Internet]. ILO; 2010 [cited 2020 Feb 10]. Available from: <https://www.ilo.org/public/english/bureau/stat/isco/index.htm>

Table 3.7: Classification of jobs encountered according to the International Labour Organization

International Standard Classification of Occupations (ISCO-08)	Jobs encountered in the study and included under the specified groupings
Managers	Hotel Manager
	Restaurant manager
Professionals	Computer Programmer
	Engineer
Technicians and associate professionals	Ship Repairs
	Dockyard worker
	Gym instructor
	Supervisor
Clerical support workers	Motor claims officer
	Clerk
	Support worker
	Administration
Service and sales workers	Watchman
	Automotive salesperson
	Health shop owner
	Family Business
	Bartender
	Caterer
Skilled agricultural, forestry and fishery workers	Wheat industry
	Flour mill
Craft and related trades workers	Plumber
	Printing workers
	Carpenter
	Painter
Plant and machine operators and assemblers	Factory worker
	Minibus Driver
	Grand Harbour officer
	Heavy Vehicle Driver
	Driver
	Sailor
	Machine operator
	Film industry
Elementary occupations	Construction Worker
	Housewife
	Cleaner
	Unemployed
	Tile layer
	Plaster worker
Armed forces occupations	Armed forces of Malta

Table 3.8: Occupation across cohorts

			Group		
			Inpatient	Outpatient	Total
Occupation	Managers	Count	1	1	2
		Percentage	3.6%	3.3%	3.4%
	Professionals	Count	3	0	3
		Percentage	10.7%	0.0%	5.2%
	Technicians and associate professionals	Count	1	4	5
		Percentage	3.6%	13.3%	8.6%
	Clerical support workers	Count	6	5	11
		Percentage	21.4%	16.7%	19.0%
	Service and sales workers	Count	4	3	7
		Percentage	14.3%	10.0%	12.1%
	Skilled agricultural, forestry and fishery workers	Count	1	1	2
		Percentage	3.6%	3.3%	3.4%
	Craft and related trades workers	Count	2	3	5
		Percentage	7.1%	10.0%	8.6%
	Plant and machine operators and assemblers	Count	4	5	9
		Percentage	14.3%	16.7%	15.5%
	Elementary occupations	Count	5	8	13
		Percentage	17.9%	26.7%	22.4%
	Armed forces occupations	Count	1	0	1
		Percentage	3.6%	0.0%	1.7%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(9) = 6.977$, $p = 0.640$ (Chi square test)

No particular occupations category or previous job history could be attributed to either cohorts. Jobs involving manual work, exposure to industrial materials and pollutants were encountered in both inpatient and outpatient cohort in comparable percentages such that no statistical significance was observed. This indicates that individuals with particular job descriptions were possibly at risk of developing COPD, but their line of work did not actually contribute to exacerbation and hospital admissions. A limitation in assessing the implications of this factor on exacerbation and hospitalisation was that a greater percentage of patients recruited were over 65 years of age (67.2%) and are no more full-time workers in their trade. Investigation into patient pastimes, leisure activity, and community work is a niche to consider further studies.

A second method of classification was undertaken. This classification looked at the type of occupation involved subdivided into three categories namely office work, industrial work, or any other type of work (Table 3.9).

Table 3.9: Occupation classified into 3 groups according to type of work

Group 1: Office work	Group 2: Industrial work	Group 3: Other
Hotel Manager	Engineer	Gym instructor
Restaurant manager	Ship Repairs	Watchman
Computer Programmer	Dockyard worker	Health shop owner
Motor claims officer	Supervisor	Bartender
Clerk	Wheat industry	Caterer
Support worker	Flour mill	Minibus Driver
Administration	Plumber	Grand Harbour officer
Automotive salesperson	Carpenter	Heavy Vehicle Driver
Family Business	Painter	Driver
Printing workers	Factory worker	Sailor
	Machine operator	Film industry
	Construction Worker	Housewife
	Tile layer	Unemployed
	Plaster worker	Armed forces of Malta
	Cleaner	

A greater percentage of inpatients (35.7%) reported that their profession involved office work compared to outpatients (23.3%). On the other hand, industrial workers comprised (50%) of the outpatient cohort and (28.6%) of the inpatient cohort. The percentage differences between cohorts were not statistically significant with a p-value of 0.245 exceeding the 0.05 level of significance (Table 3.10).

Table 3.10: Occupation across cohorts (type of work)

			Group		
			Inpatient	Outpatient	Total
Occupation	Office work	Count	10	7	17
		Percentage	35.7%	23.3%	29.3%
	Industrial work	Count	8	15	23
		Percentage	28.6%	50.0%	39.7%
	Other	Count	10	8	18
		Percentage	35.7%	26.7%	31.0%
Total	Count	28	30	58	
	Percentage	100.0%	100.0%	100.0%	

$\chi^2(2) = 2.816$, $p = 0.245$ (Chi square test)

3.2.5 Analysis of Comorbidities

In general, a greater percentage of inpatients suffered from Hypertension (46.4%), Gastro-Oesophageal Reflux Disease (28.6%), Diabetes Mellitus (21.4%), Chronic Heart Failure (21.4%), Benign Prostatic Hyperplasia (17.9%), Psychosis and Depression (21.4%) as compared to outpatients for Hypertension (43.3%), Gastro-Oesophageal Reflux Disease (3.3%), Diabetes Mellitus (10%), Chronic Heart Failure (13.3%), Benign Prostatic Hyperplasia (10%), and Psychosis and Depression (3.3%). Chi Square test was used to analyse percentage differences in the frequency of comorbidities between inpatient and outpatient cohorts. A p-value of 0.351 indicates that there was no statistical significance in frequency of comorbidities between the cohorts.

Table 3.11: Comorbidities across the cohorts

		Group	
		Inpatient	Outpatient
Comorbidities	Hypothyroidism	3.6%	10.0%
	Hypertension	46.4%	43.3%
	Atrial Fibrillation	10.7%	6.7%
	Benign Prostatic Hyperplasia	17.9%	10.0%
	Glaucoma	7.1%	6.7%
	Hyperthyroidism	0.0%	3.3%
	Diabetes Mellitus	21.4%	10.0%
	Dyslipidaemia	7.1%	20.0%
	Allergic Rhinitis	0.0%	3.3%
	Chronic Heart Failure	21.4%	13.3%
	Anxiety	0.0%	6.7%
	Depression	10.7%	3.3%
	Chronic Kidney Disease	3.6%	3.3%
	Gastro-Oesophageal Reflux Disease	28.6%	3.3%
	Sleep Apnoea	3.6%	3.3%
	IHD/Coronary Artery Disease	14.3%	6.7%
	Abdominal Aortic Aneurysm	0.0%	3.3%
	Psychosis	10.7%	0.0%
	Rheumatoid Arthritis	3.6%	0.0%
	Pleural Plaque	0.0%	3.3%
	Insomnia	0.0%	3.3%
	History of Pulmonary Embolism	3.6%	0.0%
	Bronchiectasis	0.0%	3.3%
	Pulmonary Hypertension	3.6%	0.0%
	History of Chronic Alcoholism	3.6%	0.0%
	History of Acute Kidney Injury	3.6%	0.0%
	Psoriasis	0.0%	3.3%
	Impaired hearing	0.0%	3.3%
	Gastric Ulceration	0.0%	3.3%
	Neuropathic pain	0.0%	3.3%
	Penicillin Allergy	3.6%	0.0%
	Anaemia	0.0%	3.3%
	Liver Disease	3.6%	0.0%
	IBD	3.6%	0.0%

$\chi^2(33) = 35.51$, $p = 0.351$ (Chi square test)

3.2.5.1 Number of Comorbidities

A larger percentage of outpatients had no comorbidities (26.7%) compared to inpatients (14.3%) whilst more inpatients reported three or more comorbidities (46.4%) than outpatients (36.7%). Similar percentages were observed for both cohorts for patients with one or two comorbidities (39.3%) inpatients and (36.7%) outpatients. The percentage differences were not statistically significant with a p-value of 0.489 exceeding the 0.05 criterion (Table 3.12).

Table 3.12: Number of comorbidities across cohorts

			Group		
			Inpatient	Outpatient	Total
Number of comorbidities	no comorbidities	Count	4	8	12
		Percentage	14.3%	26.7%	20.7%
	one or two	Count	11	11	22
		Percentage	39.3%	36.7%	37.9%
	three or more	Count	13	11	24
		Percentage	46.4%	36.7%	41.4%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(2) = 1.433$, $p = 0.489$ (Chi square test)

The number of comorbidities per se did not contribute towards exacerbation of COPD necessitating hospitalisation. Further investigations would be required to specifically assess and determine effect of comorbidity management on COPD exacerbation and hospitalisation.

3.2.6 Use of LAMA therapy across cohorts

There is a higher percentage of outpatients (20%) than inpatients (14.3%) who are buying and using LAMA therapy. Percentage of patients not on LAMA therapy are comparable with (85.7%) inpatient and (80%) outpatient. The percentage differences between cohorts are not significant since the p-value 0.565 exceeds the level of significance (Table 3.13).

Table 3.13: LAMA therapy across cohort

			Group		
			Inpatient	Outpatient	Total
LAMA therapy	Yes	Count	4	6	10
		Percentage	14.3%	20.0%	17.2%
	No	Count	24	24	48
		Percentage	85.7%	80.0%	82.8%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(1) = 0.331$, $p = 0.565$ (Chi square test)

The use of LAMA therapy has been shown to improve COPD management. Lack of LAMA availability on the government formulary presents prescribing challenges. A protocol for the introduction and use of LAMAs on the Maltese National Health Service was compiled as a patient-prioritisation tool by Spiteri, 2018 as part of her doctorate studies.

3.2.7 Vaccination History

A large percentage of patients (62.1%) received the annual influenza vaccine. A higher percentage of inpatients (71.4%) had received the vaccine when compared to outpatients (53.3%). A greater percentage of outpatients (46.7%) were not vaccinated compared to (28.6%) of inpatients. The percentage differences were not significant since the p-value exceeds the 0.05 level of significance (Table 3.14).

Table 3.14: Flu Vaccine history across the cohorts

			Group		
			Inpatient	Outpatient	Total
Influenza vaccine	Yes	Count	20	16	36
		Percentage	71.4%	53.3%	62.1%
	No	Count	8	14	22
		Percentage	28.6%	46.7%	37.9%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 2.014$, $p = 0.156$ (Chi square test)

A smaller percentage of patients received the pneumococcal vaccine at least once (32.8%) compared to (67.2%) who never did. A larger percentage of outpatients (40%) had taken the pneumococcal vaccine versus inpatients (25%). The percentage differences were not significant since the p-value 0.224 exceeds the 0.05 criterion (Table 3.15).

Table 3.15: Pneumococcal Vaccine history across the cohorts

			Group		
			Inpatient	Outpatient	Total
Pneumococcal vaccine	Yes	Count	7	12	19
		Percentage	25.0%	40.0%	32.8%
	No	Count	21	18	39
		Percentage	75.0%	60.0%	67.2%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 1.479$, $p = 0.224$ (Chi square test)

3.2.8 Oral corticosteroid courses

A greater percentage of inpatients (78.6%) received one or more oral corticosteroid courses during the previous year as compared to outpatients (43.3%). The difference was statistically significant with a p-value of 0.006 exceeding the 0.05 criterion (Table 3.16).

Table 3.16: Oral corticosteroid therapy prescribing across cohorts

			Group		
			Inpatient	Outpatient	Total
Were you prescribed any oral corticosteroid courses during the previous year	Yes	Count	22	13	35
		Percentage	78.6%	43.3%	60.3%
	No	Count	6	17	23
		Percentage	21.4%	56.7%	39.7%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(1) = 7.515$, $p = 0.006$ (Chi square test)

3.2.8.1 Number of oral corticosteroid courses prescribed

On comparison between cohorts (72.7%) of inpatients and (76.9%) of outpatients received one or two courses of oral corticosteroids during the previous year. Percentage differences between cohorts were not statistically significant with a p-value 0.963 exceeding the 0.05 level of significance (Table 3.17).

Table 3.17: Number of oral corticosteroid courses prescribed across cohorts

			Group		
			Inpatient	Outpatient	Total
Number of oral corticosteroid courses prescribed	1 or 2 courses	Count	16	10	26
		Percentage	72.7%	76.9%	74.3%
	3-5 courses	Count	4	2	6
		Percentage	18.2%	15.4%	17.1%
	6 courses or more	Count	2	1	3
		Percentage	9.1%	7.7%	8.6%
Total	Count	22	13	35	
	Percentage	100.0%	100.0%	100.0%	

$X^2(2) = 0.075$, $p = 0.963$ (Chi square test)

Data analysis established that there was no significant difference in the number of oral corticosteroids courses received during the previous year between cohorts. On the contrary, a statistically significant difference was demonstrated when assessing between cohorts whether patients received at least one oral corticosteroid course during the previous year. This indicates that hospitalised patients had a greater chance of having had an oral corticosteroid course prescribed some time that year prior to the current hospitalisation. Patients recruited within the outpatient cohort had a greater chance of not having had an oral corticosteroid course prescribed during the previous year. One can infer that irrespective of the number of oral corticosteroid courses prescribed, patients who required at least once course were at risk for another exacerbation which might necessitate hospitalisation. A correlation between oral corticosteroid courses and exacerbation was demonstrated. Such prescribing could have indicated that patients required clinical attention and review of treatment to avoid another exacerbation possibly necessitating hospitalisation.

3.2.9 Oral antibiotic courses

A greater percentage of inpatients (71.4%) received an antibiotic course during the previous year as compared to outpatient cohort (40%). On the other hand, a greater percentage of outpatients (60%) did not receive an antibiotic course when compared to inpatient cohort (28.6%). The percentage differences were significant with a p-value of 0.016 that is less than the 0.05 level of significance (Table 3.18).

Table 3.18: Oral antibiotic therapy across cohorts

			Group		
			Inpatient	Outpatient	Total
Were you prescribed any antibiotic courses during the previous year	Yes	Count	20	12	32
		Percentage	71.4%	40.0%	55.2%
	No	Count	8	18	26
		Percentage	28.6%	60.0%	44.8%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 5.784$, $p = 0.016$ (Chi square test)

3.2.9.1 Comparing number of oral antibiotic courses

A greater percentage of outpatients (75%) received one course of oral antibiotics as compared to inpatients (65%). On the other hand, a greater percentage of inpatients (35%) received 2 course or more of oral antibiotics versus outpatients (25%). The percentage differences were not statistically significant with a p-value of 0.811 exceeding the 0.05 criterion (Table 3.19).

Table 3.19: Number of oral antibiotic courses prescribed across cohorts

			Group		
			Inpatient	Outpatient	Total
Number of antibiotic courses	1 course	Count	13	9	22
		Percentage	65.0%	75.0%	68.8%
	2 courses	Count	4	2	6
		Percentage	20.0%	16.7%	18.8%
	3 courses or more	Count	3	1	4
		Percentage	15.0%	8.3%	12.5%
Total	Count	20	12	32	
	Percentage	100.0%	100.0%	100.0%	

$X^2(1) = 0.420$, $p = 0.811$ (Chi square test)

An association was observed between hospitalisation and prescribing of oral antibiotics during the previous year, but no significant difference between cohorts was observed in the number of oral antibiotic courses prescribed. This analysis followed the same observation and inferences for the prescribing of oral corticosteroid courses possibly since both are prescribed concomitantly for moderate exacerbations. Systemic corticosteroids and antibiotics, when indicated can shorten hospital stay and shorten recovery time (GOLD, 2020). Identifying exacerbation symptoms, following a written action plan, and when to refer for professional healthcare are key concepts which patients need to understand. Such patient education can be incorporated in a pharmaceutical care plan for COPD patients.

3.2.10 Emergency Nebulized Treatment

(46.6%) of the participants claimed that they required emergency nebulized treatment at Health centres while (53.4%) did not require the service during the previous year. These percentages vary marginally between inpatients and outpatients for emergency nebulized treatment visits at health centres and differences were not significant since the p-value 0.986 exceeds the 0.05 level of significance (Table 3.20).

Table 3.20: Emergency nebulized treatment from Health Centres across cohorts

			Group		
			Inpatient	Outpatient	Total
Emergency nebulized treatment at Health Centres	Yes	Count	13	14	27
		Percentage	46.4%	46.7%	46.6%
	No	Count	15	16	31
		Percentage	53.6%	53.3%	53.4%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.000$, $p = 0.986$ (Chi square test)

Data collected showed that there was no significant difference between hospitalised patients (inpatient cohort) and patients not hospitalised during the previous year (outpatient cohort) in their need to request nebulized therapy from Healthcare centres. This implies that one cannot identify patients frequently visiting healthcare centres for nebulized therapy as at risk for exacerbation and hospitalisation. These patients can still be flagged for a pharmaceutical review in order to identify why they are frequently necessitating nebulized therapy. One possible explanation for this observation may be patient attitudes. Upon worsening respiratory symptoms, patients tend to visit healthcare centres rather than having a set self-management plan prior to visiting primary healthcare centres.

The inpatient cohort visited healthcare centres for nebulized treatment as much as patients in the outpatient cohort. A statistically significant difference was that patients who were hospitalised also indicated that when symptoms worsen, they report first to MDH Accident and Emergency. A possible explanation for this is that hospitalised patients tend to visit Healthcare centres as part of their routine COPD management (mismanagement of their medical condition). On the other hand, the outpatient cohort visited Healthcare centres as part of their COPD management to seek medical advice when symptoms worsen. These different notions as to why patients in the two cohorts possibly visited Healthcare centres might explain why no difference between cohorts in this scenario could be established. Specific studies into patient practices and disease management might provide more insight as to why no statistically significant difference between inpatient and outpatient cohorts was recorded in this regard. One cannot infer that patients frequently visiting Healthcare centres due to worsening respiratory symptoms for emergency nebulized treatment may be at an increased risk of hospitalisation.

3.2.10.1 Comparing the number of visits to Healthcare centres for emergency nebulized

A larger percentage of outpatients only required emergency nebulized treatment once (42.9%) during the previous year as compared to inpatients (23.1%). On the other, a greater percentage of inpatients required such interventions twice (30.8%) or even three time or more (46.2%) when compared to outpatients (21.4%) and (35.7%) respectively. The percentage differences were not statistically significant with a p-value of 0.549 that exceeds the 0.05 level of significance (Table 3.21).

Table 3.21: Number of visits to Healthcare centres for emergency nebulized treatment across cohorts

			Group		
			Inpatient	Outpatient	Total
Number of times emergency nebulizer treatment was required from Health centres	once	Count	3	6	9
		Percentage	23.1%	42.9%	33.3%
	twice	Count	4	3	7
		Percentage	30.8%	21.4%	25.9%
	three times or more	Count	6	5	11
		Percentage	46.2%	35.7%	40.7%
Total	Count		13	14	27
	Percentage		100.0%	100.0%	100.0%

$X^2(2) = 1.198$, $p = 0.549$ (Chi square test)

Irrespective of the number of times that patients visited health care centres for emergency nebulized treatment, one could not make a differentiation between the two cohorts. This further supports the notion that patients might be inadequately managing their worsening symptoms and resorting to healthcare centres for nebulized therapy rather than having a self-management plan.

3.2.11 Environmental Factors

Environmental factors assessed for any possible contribution to exacerbations were the type of main residence and residential environment, whether the individual is a pet owner and if yes, the type of pet.

3.2.11.1 Type of residence

Apartments (43.1%) were the most common type of residence encountered followed by houses of character (22.4%). Percentage differences in the type of residence between cohorts was not significant with a p-value of 0.593 exceeding the 0.05 level of significance (Table 3.22).

Table 3.22: Type of Residence across cohorts

			Group		
			Inpatient	Outpatient	Total
Type of residence	Maisonette	Count	5	1	6
		Percentage	17.9%	3.3%	10.3%
	House of Character	Count	6	7	13
		Percentage	21.4%	23.3%	22.4%
	Apartment	Count	11	14	25
		Percentage	39.3%	46.7%	43.1%
	Farmhouse	Count	1	1	2
		Percentage	3.6%	3.3%	3.4%
	Terraced House	Count	2	4	6
		Percentage	7.1%	13.3%	10.3%
	Town House	Count	3	3	6
		Percentage	10.7%	10.0%	10.3%
Total	Count	28	30	58	
	Percentage	100.0%	100.0%	100.0%	

$X^2(5) = 3.706$, $p = 0.593$ (Chi square test)

3.2.11.2 Residential environment

A larger percentage of inpatients reside in close proximity to the sea (28.6%) and have humidity issues (32.1%) than outpatients. Comparable percentage of cases were recorded for inpatients and outpatients residing in main roads (46.4%) and (40%) respectively. On the other hand, a greater percentage of outpatients reside in village cores (16.7%) and countryside (16.7%). Chi Square test was used to analyse percentage differences in the type of residential environment patients reside in, between inpatient and outpatient cohorts. The differences were not statistically significant with a p-value of 0.125 exceeding the 0.05 criterion (Table 3.23).

Table 3.23: Residential environment comparison across cohorts

			Group		Total
			Inpatient	Outpatient	
Residential Environment	Village core	Count	2	5	7
		Percentage	7.1%	16.7%	
	Main road	Count	13	12	25
		Percentage	46.4%	40.0%	
	Sea	Count	8	5	13
		Percentage	28.6%	16.7%	
	Humidity	Count	9	3	12
		Percentage	32.1%	10.0%	
	Countryside	Count	1	5	6
		Percentage	3.6%	16.7%	
	Garden	Count	0	1	1
		Percentage	0.0%	3.3%	
Total		Count	28	30	58

$\chi^2(5) = 8.631$, $p = 0.125$ (Chi square test)

The most prevalent residential environment was main roads for both inpatients and outpatients. This is probably due to the fact that Malta being a relatively small island, a good proportion of the residential areas are within main roads which exposes individuals to more air pollution, a known risk factor for COPD. Although not statistically significant, patients residing in main roads, in close proximity to the sea, and have humidity issues in their residence could potentially be more susceptible to COPD exacerbations and subsequent hospitalisations.

3.2.11.3 Pet owners

A greater percentage of inpatients (42.9%) are pet owners as compared to outpatients (33.3%). The percentage difference whether patients are pet owners between the 2 cohorts was not significant with a p-value of 0.455 exceeding the 0.05 criterion.

Table 3.24: Pet owners' comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Pet owner	Yes	Count	12	10	22
		Percentage	42.9%	33.3%	37.9%
	No	Count	16	20	36
		Percentage	57.1%	66.7%	62.1%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 0.558$, $p = 0.455$ (Chi square test)

Whether or not patients had pets at home was not associated with an increased risk of exacerbation and hospitalisation.

3.2.11.4 Type of pet

The most common type of pet owned by patients recruited were birds. A greater percentage of inpatients had birds (66.7%), dogs (25%) and pigeons (8.3%) as pets compared to outpatients. Chi Square test was used to analyse percentage differences in the types of pet patients owned between inpatient and outpatient cohorts. The percentage differences were not statistically significant with a p-value of 0.707 exceeds the 0.05 criterion (Table 3.25).

Table 3.25: Type of pet comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Type of pet	Birds	Count	8	6	14
		Percentage	66.7%	60.0%	
	Cats	Count	2	2	4
		Percentage	16.7%	20.0%	
	Dogs	Count	3	2	5
		Percentage	25.0%	20.0%	
	Pigeons	Count	1	0	1
		Percentage	8.3%	0.0%	
	Turtles	Count	0	1	1
		Percentage	0.0%	10.0%	
Total	Count	12	10	22	

$X^2(4) = 2.157$, $p = 0.707$ (Chi square test)

No association was observed between type of pet and inpatient/outpatient cohort. One cannot infer that a particular type of pet imposed an increased risk for exacerbation and hospitalisation.

3.2.12 Who is involved in the patient's care?

A greater percentage of patient (72.4%) have a general practitioner who follows them for their COPD and refer to for advice compared to (27.6%) who do not communicate with general practitioners for COPD consultations. Approximately 75% percent of hospitalised patients and 70% of outpatients confirmed that they have a general practitioner with whom they discuss issues relating to general disease management and medication. Percentage differences between inpatient and outpatient cohorts both for patients who have a GP involved in their COPD management and for those who do not, were not statistically significant with a p-value of 0.670 exceeding the 0.05 level of significance (Table 3.26).

Table 3.26: General practitioner involvement comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
GP involvement	Yes	Count	21	21	42
		Percentage	75.0%	70.0%	72.4%
	No	Count	7	9	16
		Percentage	25.0%	30.0%	27.6%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(1) = 0.181$, $p = 0.670$ (Chi square test)

The data suggests that most of the patients (72.4%, $n=42$) have a general practitioner they usually refer to. No major differences were observed in the number of patients between cohorts who reported involvement of general practitioners in their COPD management. An association between GP involvement and inpatient or outpatient cohort was not established.

A larger percentage of patients recruited (72.4%) were not routinely reviewed by respiratory physiotherapists as part of the non-pharmacological management plan. Involvement of respiratory physiotherapists was to a larger extent within the inpatient cohort (39.3%) rather than the outpatient cohort (16.7%). No involvement of respiratory physiotherapists was reported in (60.7%) of the inpatient cohort and (83.3%) of the outpatient cohort. The percentage differences were almost statistically significant with a p-value of 0.054 exceeding the 0.05 level of significance (Table 3.27).

Table 3.27: Respiratory Physiotherapists involvement comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Respiratory physiotherapist involvement	Yes	Count	11	5	16
		Percentage	39.3%	16.7%	27.6%
	No	Count	17	25	42
		Percentage	60.7%	83.3%	72.4%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$\chi^2(1) = 3.709$, $p = 0.054$ (Chi square test)

An association between whether or not respiratory physiotherapists are involved in patient care and inpatient/outpatient cohort could possibly be established with a larger sample size. This is in view that a greater percentage of hospitalised patients were being followed up by physiotherapists (39.3%) compared to outpatients (16.7%) whilst a smaller percentage of hospitalised patient were not being reviewed by physiotherapists at time of admission (60.7%) compared to outpatients (83.3%).

In order to identify whether percentage differences within the same cohort were significant, the difference of 2 proportions Z-tests was carried out. At time of admission, a greater percentage of patients were not undergoing review sessions with respiratory physiotherapists (60.7%) compared to (39.3%) who were. The difference of 2 proportions Z-tests conducted for inpatient cohort achieved a p-value of 0.174 that exceeds the 0.05 level of significance and indicates that there was no statistical significance. The percentage difference for the outpatient cohort was statistically significant with a p-value of <0.001 less than the 0.05 criterion (Table 3.28).

Table 3.28: Proportions for respiratory physiotherapist involvement using the difference of 2 proportions Z-test

Percentage 1 (Yes)	Percentage 2 (No)	Z-Score	P-value
39.3%	60.7%	1.604	p = 0.109
16.7%	83.3%	5.164	p < 0.001
27.6%	72.4%	4.828	p < 0.001

Statistical significance was not established between hospitalised patients who at time of admission were attending respiratory physiotherapy sessions and hospitalised patients who were not receiving such intervention.

3.2.13 Comparing the ABCD Status between cohorts

The ABCD scheme is independent of spirometry results and considers patient symptoms through dyspnoea assessment using the mMRC score or CATTM score and exacerbation history. The pre-defined cohort-specific inclusion and exclusion criteria automatically segregated patients with an ABCD status of A and B to be included only within the outpatient cohort (Table 3.29). This is because what distinguishes GOLD groups A and B labelling from C and D is exacerbation history. Those patients who were recruited within the outpatient cohort and identified as GOLD groups C and D were patient who experienced 2 or more exacerbations in the previous year not necessitating hospitalisation.

Table 3.29: ABCD status comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
ABCD Status	Group A	Count	0	15	15
		% within Group	0.0%	50.0%	25.9%
	Group B	Count	0	9	9
		% within Group	0.0%	30.0%	15.5%
	Group C	Count	3	2	5
		% within Group	10.7%	6.7%	8.6%
	Group D	Count	25	4	29
		% within Group	89.3%	13.3%	50.0%
Total		Count	28	30	58
		% within Group	100.0%	100.0%	100.0%

$X^2(3) = 39.385$, $p = 0.000$ (Chi square test)

3.2.14 Smoking history

Factors related to smoking history assessed for any possible contribution to exacerbations were patient's current smoking status, number of years since stopped smoking, and pack years.

3.2.14.1 Comparing smoking status

A larger percentage of patients recruited have quit smoking (74.1%) than those who still smoke (25.9%). When comparing between cohorts for the same smoking status a p-value of 0.649 was achieved indicating that the difference was not significant since p-value exceeds the 0.05 criterion (Table 3.30).

Table 3.30: Smoking status comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Smoking status	Smoker	Count	8	7	15
		Percentage	28.6%	23.3%	25.9%
	Ex-smoker	Count	20	23	43
		Percentage	71.4%	76.7%	74.1%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 0.207$, $p = 0.649$ (Chi square test)

Irrespective of whether patient still smokes or has stopped smoking, no correlation could be established between smoking status and exacerbations leading to hospitalisation. Other smoking-related factors might be contributing towards increased risk for hospitalisation, possibly pack years.

The difference of 2 proportions Z-tests conducted for the inpatient cohort, outpatient cohort and overall recruited patients all achieved a p-value less the 0.05 level of significance and indicates that there was a statistical significance difference (Table 3.31). This implies that the difference in smoking status within the same cohort was significant and smoking cessation recommendations from date of diagnosis were in general adopted by patients.

Table 3.31: Proportions for smoking status using the difference of 2 proportions Z-test

Percentage 1 (Yes)	Percentage 2 (No)	Z-Score	P-value
28.6%	71.4%	3.2071	p = 0.001
23.3%	76.7%	4.131	p < 0.001
25.9%	74.1%	5.120	p < 0.001

3.2.14.2 Comparing mean number of years since stopped smoking between cohorts

The independent sample t-test was used to assess the mean number of years since ex-smokers stopped smoking and compare between cohorts. A p-value of 0.675 exceeds the 0.05 criterion which indicates that the difference in mean number of years since stopped smoking was not statistically significant (Table 3.32).

Table 3.32: Independent sample T-test – mean number of years since stopped smoking SPSS OUTPUT

Group	Sample size	Mean number of years since stopped smoking	Std. Deviation	P-value
Inpatient	20	11.23	15.193	0.675
Outpatient	23	12.91	10.892	

3.2.14.3 Comparing number of years since patients stopped smoking between cohorts

A greater percentage of patients (55%) who stopped smoking up to 5 years ago were admitted versus (26.1%) who were not. When analysing patients who stopped smoking between 6 and 10 years ago, less patients (15%) were hospitalised compared to (34.8%) who were not. For patient who stopped smoking over 10 years ago, also less patients (30%) were admitted compared to (39.1%) who were not. The percentage differences were not statistically significant with a p-value 0.125 exceeding the 0.05 criterion (Table 3.33).

Table 3.33: Number of years since patients stopped smoking across cohorts

			Group		
			Inpatient	Outpatient	Total
Number of years since stopped smoking	5 years or less	Count	11	6	17
		Percentage	55.0%	26.1%	39.5%
	6 - 10 years	Count	3	8	11
		Percentage	15.0%	34.8%	25.6%
	10 years or more	Count	6	9	15
		Percentage	30.0%	39.1%	34.9%
Total	Count	20	23	43	
	Percentage	100.0%	100.0%	100.0%	

$\chi^2(2) = 4.154$, $p = 0.125$ (Chi square test)

A statistically significant association could not be inferred between the number of years since ex-smokers stopped smoking and reduced risk of exacerbation leading to hospitalisation. If smoking cessation had to have an effect on risk reduction for exacerbation and hospitalisation, data analysis suggests that this might be the case for patients who have stopped smoking at least 6 years ago. Recruiting a larger sample size might be necessary to confirm or negate such a correlation.

3.2.14.4 Analysis of pack years between cohorts

A greater percentage of patients (39.7%) recorded 40 pack years or less followed by (34.5%) of patients with 41-80 pack years, and (25.9%) of patients with 81 pack years or more. The percentage differences between inpatient and outpatient cohorts were not statistically significant with a p-value of 0.886 exceeding the 0.05 level of significance (Table 3.34).

Table 3.34: Pack year comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Pack Years	40 pack years or less	Count	11	12	23
		Percentage	39.3%	40.0%	39.7%
	41-80 pack years	Count	9	11	20
		Percentage	32.1%	36.7%	34.5%
	81 pack years or more	Count	8	7	15
		Percentage	28.6%	23.3%	25.9%
Total	Count		28	30	58
	Percentage		100.0%	100.0%	100.0%

$X^2(2) = 0.241$, $p = 0.886$ (Chi square test)

There was no association between pack years and exacerbation necessitating hospitalisation which infers that more pack years were not associated with a greater chance of exacerbation related hospitalisation.

3.2.15 Seasonality

In general (46.6%) of patients recruited explained that they perceived no difference in worsening symptoms between summer and winter. A greater percentage of inpatients (39.3%) claimed that symptoms deteriorated mostly during the summer period versus outpatients (26.7%). On the other hand, a greater percentage of outpatients (56.7%) claimed that there was no difference in disease progression and symptom burden between summer and winter. The percentage differences were not statistically significant with a p-value of 0.279 exceeding the 0.05 level of significance (Table 3.35).

Table 3.35: Seasonality comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Seasonality: During which period of the year do symptoms usually worsen	Summer	Count	11	8	19
		Percentage	39.3%	26.7%	32.8%
	Winter	Count	7	5	12
		Percentage	25.0%	16.7%	20.7%
	No difference	Count	10	17	27
		Percentage	35.7%	56.7%	46.6%
Total	Count	28	30	58	
	Percentage	100.0%	100.0%	100.0%	

$\chi^2(2) = 2.556$, $p = 0.279$ (Chi square test)

Malta is a Subtropical-Mediterranean country with mild winters and dry hot summers. Relative humidity in Malta is highest in December and lowest in July with the annual average percentage of humidity 76%. Precipitations is highest in December and lowest between June and August⁸. Several studies report that frequency of COPD exacerbation and hospitalisation were highest during winter (Donaldson et al, 1999; Jenkins et al, 2012; Rabe et al 2013) and that the effect of seasonality was independent of other risk factors such as history of prior exacerbation, low BMI, older age, and lower FEV₁ % predicted (Jenkins et al, 2012). With (46.6%) of recruited patients describing that they perceive no difference in worsening symptoms between seasons warrants further investigation as to how local weather variations effect respiratory conditions such as COPD. In this manner one can target pharmaceutical interventions in a way to pre-empt seasonal increase in symptoms if any, particularly deterioration in lung function.

⁸ National Statistics Office (NSO) – Malta. The Climate of Malta: statistics, trends, and analysis 1951-2010 [Internet]. Valletta: NSO; 2014 [cited 2020 April 20]. Available from URL: <https://nso.gov.mt/en/publicatons/Pages/Publications-by-Date.aspx>

3.3 MEDICATION COMPLIANCE

Assessment of medication compliance was conducted through evaluation of the following variables: frequency of missed doses and subsequent strategy adopted for missed doses, occurrence of side effects and side effect profile, patient attitudes and action plan for worsening symptoms, and salbutamol requirements.

3.3.1 *How often do patients forget to use their inhalers?*

A higher percentage of inpatients (28.6%) sometimes forget to use their inhalers when compared to outpatients (10%). A higher percentage of outpatients (46.7%) rarely forget to use their inhalers when compared to inpatients (28.6%). The percentage differences were not statistically significant with a p-value of 0.183 exceeding the 0.05 criterion (Table 3.36).

Table 3.36: Frequency of missed inhalations comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Do you ever forget to use your inhaled medication?	Frequently	Count	0	1	1
		Percentage	0.0%	3.3%	1.7%
	Sometimes	Count	8	3	11
		Percentage	28.6%	10.0%	19.0%
	Rarely	Count	8	14	22
		Percentage	28.6%	46.7%	37.9%
	Never	Count	12	12	24
		Percentage	42.9%	40.0%	41.4%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$X^2(3) = 4.846$, $p = 0.183$ (Chi square test)

(79.3%) of the sample population (n=46) never or rarely forget to use their inhaled medication. Although this is an encouraging observation, it is a patient reported measure with a high degree of subjective error.

3.3.2 What patients do when they miss a dose

A greater percentage of inpatients (39.3%) skip doses completely when they miss a dose as compared to outpatients (33.3%). Approximately 66.7% of the outpatients administer immediately the skipped dose when they remember. Percentage differences were not statistically significant with a p-value 0.637 exceeding the 0.05 level of significance (Table 3.37).

Table 3.37: Strategy adopted for missed doses comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
What do you do when you miss a dose	Skip dose completely	Count	11	10	21
		Percentage	39.3%	33.3%	36.2%
	Administer when I remember	Count	17	20	37
		Percentage	60.7%	66.7%	63.8%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 0.222$, $p = 0.637$ (Chi square test)

3.3.3 Occurrence of side effects from inhaled therapy

A greater percentage of inpatients (71.4%) experienced side effects as a result of their inhalers when compared to outpatient cohort (33.3%). The percentage differences in whether side effects from inhalers occurred or not was statistically significant with a p-value 0.004 less than the 0.05 criterion (Table 3.38).

Table 3.38: Comparison of side effects occurrence across cohorts

			Group		
			Inpatient	Outpatient	Total
Have you ever experienced any side effects with the use of inhalers	Yes	Count	20	10	30
		Percentage	71.4%	33.3%	51.7%
	No	Count	8	20	28
		Percentage	28.6%	66.7%	48.3%
Total		Count	28	30	58
		Percentage	100.0%	100.0%	100.0%

$X^2(1) = 8.417$, $p = 0.004$ (Chi square test)

A significant difference between cohorts was observed in whether patients have experienced side effects from their inhaled medication. Inpatient cohort reported to have experienced side effects more than the outpatient cohort. The reported side effects were dry cough, hoarseness, oral candidiasis, and dry mouth.

3.3.4 Side effects profile

More than half of the patients (53.3%) reported dry mouth as the main side effect encountered. A greater percentage of inpatients reported oral candidiasis (30%) and dry cough (10%) as side effect. Percentage differences between cohorts was not statistically significant with a p-value 0.599 exceeding the 0.05 criterion (Table 3.39).

Table 3.39: Side effect profile comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Type of side effect	Dry cough	Count	2	0	2
		Percentage	10.0%	0.0%	6.7%
	Hoarseness	Count	2	2	4
		Percentage	10.0%	20.0%	13.3%
	Oral candidiasis	Count	6	2	8
		Percentage	30.0%	20.0%	26.7%
	Dry mouth	Count	10	6	16
		Percentage	50.0%	60.0%	53.3%
Total		Count	20	10	30
		Percentage	100.0%	100.0%	100.0%

$X^2(3) = 1.875$, $p = 0.599$ (Chi square test)

A significant difference was observed between cohorts in whether patients experienced side effects or not from inhalers, but the difference in type of side effects experienced was not significant. This implies that no particular side effect was associated with increased risk for exacerbation and hospitalisation but rather whether the side effects were flagged, addressed, and resolved.

3.3.5 Worsening symptoms – Action Plan

The majority of patients (62.1%) endure symptoms when these worsen. Approximately one third of the patients recruited (29.3%) seek medical advice with only a few patients (8.6%) having a set written management plan. Percentage differences in patient's action plan towards worsening symptoms between cohorts was not statistically significant with a p-value 0.718 exceeding the 0.05 level of significance (Table 3.40).

Table 3.40: Strategy adopted for worsening symptoms across cohorts

			Group		Total
			Inpatient	Outpatient	
What do you do in case of worsening symptoms	Have a set management plan	Count	3	2	5
		Percentage	10.7%	6.7%	8.6%
	Endure symptoms	Count	18	18	36
		Percentage	64.3%	60.0%	62.1%
	Seek medical advice	Count	7	10	17
		Percentage	25.0%	33.3%	29.3%
Total	Count	28	30	58	
	Percentage	100.0%	100.0%	100.0%	

$X^2(2) = 0.661$, $p = 0.718$ (Chi square test)

Lack of a set management plan was observed across both cohorts.

3.3.6 Worsening symptoms – Patient Attitudes

A larger percentage of inpatients (50%) when compared to the outpatients (20%) confirmed that when symptoms worsen, they report first to Mater Dei Hospital. A greater percentage of patients recruited as outpatients (56.7%) reported that they visit healthcare centres first compared to inpatients (39.3%). None of the patients recruited reported to visit pharmacists for advice on worsening symptoms. Percentage differences between cohorts were found to be statistically significant with a p-value of 0.049 which is less than 0.05 criterion (Table 3.41).

Table 3.41: Where patients report to first comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Where do patients report to first when symptoms worsen?	GP	Count	3	7	10
		Percentage	10.7%	23.3%	17.2%
	H/C	Count	11	17	28
		Percentage	39.3%	56.7%	48.3%
	MDH A&E	Count	14	6	20
		Percentage	50.0%	20.0%	34.5%
Total	Count	28	30	58	
	Percentage	100.0%	100.0%	100.0%	

$\chi^2(2) = 6.024$, $p = 0.049$ (Chi square test)

A statistically significance difference was observed between inpatients and outpatient cohort symptom management attitudes. (80%) of the patients recruited within the outpatient cohort visited either a general practitioner (23.3%) or Healthcare centre (56.7%). On the contrary, (50%) of patients recruited within the inpatient cohort reported to MDH A&E for medical attention and advice.

3.3.7 Salbutamol requirements

A larger percentage of outpatients (60%) required salbutamol inhaler one day per week or less as compared to hospitalised patients (17.9%). A greater percentage of inpatients (64.3%) required reliever inhaler on a daily basis as compared to outpatients (23.3%). The percentage differences were statistically significant with a p-value 0.002 less than the 0.05 criterion (Table 3.42).

Table 3.42: Salbutamol requirement comparison across cohorts

			Group		
			Inpatient	Outpatient	Total
Days per week patient required reliever inhaler	one day per week or less	Count	5	18	23
		% within Group	17.9%	60.0%	39.7%
	2-6 days per week	Count	5	5	10
		% within Group	17.9%	16.7%	17.2%
	daily	Count	18	7	25
		% within Group	64.3%	23.3%	43.1%
	Total	Count	28	30	58
		% within Group	100.0%	100.0%	100.0%

$X^2(2) = 12.133$, $p = 0.002$ (Chi square test)

Data suggests that patients using salbutamol for symptom relief on a daily basis could potentially be at risk of exacerbation and hospital admission. Further investigation would be required to distinguish whether this scenario is due to the actual use of salbutamol on a daily basis or due to the need to use salbutamol on a daily basis. A simple pharmaceutical intervention incorporated with the dispensing of inhalers can be introduced to identify how often patients are resorting to their reliever inhaler. Through this intervention we can flag patients earlier and either offer them pharmaceutical advice or refer them for consultation.

3.4 ASSESSMENT OF INHALER/NEBULIZER TECHNIQUE

This section reports the study findings related to the patients' technique of using inhalers or nebulizers accordingly.

3.4.1 MDI technique score (*with or without spacer*)

Overall, 38.2% of the patients recruited scored 7 points followed by 32.7% who scored 8 points from a total of 10 points. This means that 70.9% of patients recruited skipped 3 or 2 steps when demonstrating their MDI technique to the investigator. A greater percentage of outpatients (22.2%) scored 10 points when compared to inpatients (7.1%) whilst a larger percentage of inpatients (14.3%) scored 6 points compared to outpatients (3.7%). The percentage differences were not statistically significant with a p-value 0.384 exceeding the 0.05 level of significance (Table 3.43).

Table 3.43: MDI technique score with or without spacer across cohorts

		Group		
		Inpatient	Outpatient	Total
MDI Technique score with or without spacer	Count	4	1	5
	Percentage	14.3%	3.7%	9.1%
	7 points	Count	11	10
	Percentage	39.3%	37.0%	38.2%
	8 points	Count	9	9
	Percentage	32.1%	33.3%	32.7%
	9 points	Count	2	1
	Percentage	7.1%	3.7%	5.5%
	10 points	Count	2	6
	Percentage	7.1%	22.2%	14.5%
Total	Count	28	27	55
	Percentage	100.0%	100.0%	100.0%

$X^2(4) = 4.164$, $p = 0.384$ (Chi square test)

Differences in MDI technique scores were not associated with increased risk of exacerbation necessitating hospitalisation. However, irrespective of whether patient was hospitalised or not, areas for improvement with regards to inhaler technique were evident. Only 16.1% of patients recruited scored 10 points which emphasizes the need to continuously assess patient's inhaler technique and implement interventions to optimize the administration of inhaled therapies.

3.4.2 Evaluation of MDI technique

The most common 3 missed steps for patients not using a spacer with their MDI were step 4, step 7, step 6 for both cohorts. A p-value of 0.927 indicates that there was no statistical significance in the missed steps between the cohorts (Table 3.44).

Table 3.44: Comparison of skipped steps in MDI technique without spacer across cohorts

			Group		Total
			Inpatient	Outpatient	
Steps skipped during inhaler technique demonstration	Step 3	Count	1	0	1
		Percentage	12.5%	0.0%	
	Step 4	Count	7	4	11
		Percentage	87.5%	80.0%	
	Step 5	Count	2	1	3
		Percentage	25.0%	20.0%	
	Step 6	Count	5	2	7
		Percentage	62.5%	40.0%	
	Step 7	Count	5	4	9
		Percentage	62.5%	80.0%	
	Step 8	Count	1	0	1
		Percentage	12.5%	0.0%	
	Step 9	Count	2	2	4
		Percentage	25.0%	40.0%	
Total		Count	8	5	13

$\chi^2(6) = 1.919$, $p = 0.927$

The most common 3 missed steps for patients using a spacer with their MDI were step 4, step 7, step 9 for both cohorts. A p-value of 0.805 indicates that there was no statistical significance in the missed steps between the cohorts (Table 3.45).

Table 3.45: Comparison of skipped steps in MDI technique with spacer across cohorts

			Group		Total
			Inpatient	Outpatient	
Steps skipped during inhaler technique demonstration with spacer	Step 2	Count	3	1	4
		Percentage	16.7%	6.3%	
	Step 3	Count	2	0	2
		Percentage	11.1%	0.0%	
	Step 4	Count	14	11	25
		Percentage	77.8%	68.8%	
	Step 5	Count	3	5	8
		Percentage	16.7%	31.3%	
	Step 6	Count	7	5	12
		Percentage	38.9%	31.3%	
	Step 7	Count	8	9	17
		Percentage	44.4%	56.3%	
	Step 8	Count	2	2	4
		Percentage	11.1%	12.5%	
	Step 9	Count	8	7	15
		Percentage	44.4%	43.8%	
Total		Count	18	16	34

$\chi^2(7) = 3.780$, $p = 0.805$

40 patients used a spacer with their MDI (Table 3.46) out of which 6 patients scored 10 points and missed no steps in their inhalation technique.

For both groups (patients who use a spacer and patients who do not use a spacer with their MDI) the most common missed technique was step 4, that is to exhale fully (or as much as comfortable) away from device. This was followed by step 7, that is to hold breath for as long as comfortable (5 to 10 seconds) and remove device from the mouth or for when using a spacer to use 'tidal breathing technique'. The 3rd most common missed step for patients who use a spacer, and which distinguished the two cohorts was step 9, that is to wait 5 to 30 seconds between actuations if more than 1 actuation is to be administered. Potential pharmaceutical interventions in such circumstances include: to advocate the use of spacer to all patients using MDIs and reiterate the most commonly missed steps identified.

3.4.3 Use of spacer with MDI

From the study sample, N=58 patients, a sample of n=55 patients use an MDI and should be using a spacer to facilitate delivery of inhaled therapy. A greater percentage of patients (72.7%) use a spacer with their MDI compared to (27.3%) who do not. A larger percentage of outpatients (81.5%) use a spacer compared to inpatients (64.3%) whilst a greater percentage of inpatients (35.7%) do not use a spacer compared to outpatients (18.5%). The percentage differences were not statistically significant since the p-value 0.152 exceeds the 0.05 criterion (Table 3.46).

Table 3.46: Comparison of spacer use with MDI across cohorts

			Group		
			Inpatient	Outpatient	Total
Use of spacer with MDI	Yes	Count	18	22	40
		Percentage	64.3%	81.5%	72.7%
	No	Count	10	5	15
		Percentage	35.7%	18.5%	27.3%
Total	Count		28	27	55
	Percentage		100.0%	100.0%	100.0%

$X^2(1) = 2.049$, $p = 0.152$ (Chi square test)

Percentage differences between patients who use a spacer and patients who do not within the same cohort, for both inpatients and outpatients were statistically significant with a p-value of 0.032 and < 0.001 respectively, less than the 0.05 level of significance (Table 3.47).

Table 3.47: Proportions for use of spacer with MDI using the difference of 2 proportions Z-test

Percentage 1 (Yes)	Percentage 2 (No)	Z-Score	P-value
64.3%	35.7%	2.138	p = 0.032
81.5%	18.5%	4.627	p < 0.001
72.7%	27.3%	4.767	p < 0.001

The difference of 2 proportions Z-tests indicated that the differences between patients who use a spacer and those who do not for inpatients and outpatients vary significantly and were statistically significant. A greater percentage of patients recruited use a spacer with their MDI (74.5%). For patients admitted due to COPD exacerbation, (35.7%) did not use a spacer with their MDI whilst (64.3%) did. For the outpatient cohort, (14.8%) did not use a spacer with their MDI whilst (85.2%) did.

3.5 SUMMARY OF FINDINGS

In the study population (N=58), statistically significant differences between cohorts were observed ($p < 0.05$) for the following parameters:

- Corticosteroid prescribing
- Antibiotic prescribing
- Side effects (irrespective of type of side effect)
- Where patients report to first when symptoms worsen
- Number of days per week patients required salbutamol

An almost statistically significant difference between cohorts was observed for the following parameters:

- Locality of residence
- Involvement of respiratory physiotherapists

Parameters of interest for which statistically significant difference was not achieved between cohorts but are nonetheless of interest include:

- Smoking status between cohorts (nor did pack years or number of years since stopped smoking)
- Metered dose inhaler technique score

No all-cause readmissions within 30 days from date of discharge were recorded for the inpatient group.

CHAPTER 4

DISCUSSION

4.1 THE CHALLENGING OUTCOMES OF THE RESEARCH

This chapter brings up a concise conclusion to this modest research which started off through a collaborative discussion between a clinician and a pharmacist-researcher during an experiential placement. The sharing of ideas focused on potential pharmacist roles to aid in identifying and subsequently pre-empting hospitalisations or early readmissions for diagnosed COPD patients. The research presented attempts to present a tool which was developed and validated against the Maltese logistic scenario specifically to identify potential risk factors for COPD hospitalisations and early readmissions. The research does not focus on the pharmaceutical care interventions as one would traditionally refer to. This research puts a tool as a means of exploring the possibility of having the pharmacist within a holistic pharmaceutical service who is proactively taking up a role in trying to reduce readmission and hospitalisation rates. The tool can be embedded in a pharmaceutical care framework within community and hospital settings as part of the pharmacist's interventions. Through the developed tool entitled: *"COPD exacerbation risk factors management and prevention"* pharmacists can identify factors which could lead to exacerbations.

The research indicated a number of factors which could be identified as red flag alert. Comorbidities in COPD are common, can significantly impact prognosis, and are either casually related or arise independently. Common comorbidities documented in the research include cardiovascular, osteoporosis, and gastroesophageal reflux disease (GERD). This is in line with results from international literature. GOLD recommendations for follow up specifically suggest providing a management plan for

comorbidities and subsequently follow up and record comorbidities status. The extended role of pharmacists within an interdisciplinary setting needs to be substantiated. Pharmacists are easily accessible healthcare professionals and yet the study indicated that none of the patients recruited visited pharmacists for COPD management advice. Does this stem from an underestimation to seek COPD advice from the pharmacists? Is it time for the pharmacists to be more proactive and reactive towards COPD patients and reach out to their patients? The strategy of reaching out to the patients can be adopted in COPD management and subsequently extrapolated to other chronic conditions. PHARM-CHF⁹, a pharmacy based randomised controlled trial assessed whether weekly interdisciplinary interventions improved medication adherence, QoL, mortality, and hospitalisation rates. Schulz et al, (2019) concluded that additional pharmacy care provision contributed to patient's quality of life and improved medication adherence in chronic heart failure patients. Following an exacerbation, clinical and community pharmacists can be involved in implementing appropriate measures to prevent further exacerbations. In the case of COPD patients, pulmonary rehabilitation for patients with symptoms and/or high risk of exacerbations is which is recommended by GOLD can be supported by pharmacist's interventions. The use of data collection tools such the COPD Assessment Test - CAT TM (Jones et al, 2009) and the developed *"COPD exacerbation risk factors management and prevention"* can be used by pharmacists to formulate trends and take up an enhanced role in COPD management eventually putting forward an individualised care plan.

⁹ PHARMacy-based interdisciplinary program for patients with Chronic Heart Failure

The latest GOLD 2020 guideline highlights the need of self-management skills and written management plans for symptom control. Against this scenario, the pharmacist should prompt and empower COPD patients towards better self-management. Pharmaceutical interventions should prompt patients to express concern regarding their treatment plan. Pharmacy outreach to COPD patients needs to incorporate therapy strategies for missed inhaled doses. Missed doses should be administered as soon as patient remembers or if patient is due for the next dose, missed dose should be skipped altogether. This aspect needs to be highlighted to patients.

Another set of interventions revolve around optimization of inhaler techniques through identification and correction of critical and non-critical errors, for which distinction and consensus has yet to be determined by international expert bodies in respiratory (Makhinova et al, 2020). In this study, a greater proportion of admitted patients (inpatient cohort) did not use a spacer whilst a greater proportion of patients not admitted during the previous year (outpatient cohort) did use a spacer with their MDI. This implies that there was an association between lack of spacer use with MDI and exacerbation leading to hospitalisation. Recruitment of a larger sample size could potentially acquire statistical significance for the use of spacers with MDI. This would substantiate the notion that lack of use of spacers with MDI can be associated with an increased risk for exacerbation and hospitalisation. This study finding highlights the potential benefit of pharmacists advising the proper use of the inhalers in addition to the use of spacers.

Smoking cessation is central to patient empowerment and education for COPD patients. The pharmacist is in a position to assist patients in smoking cessation. Smoking and smoking cessation modalities can have clinically significant effects on other treatments and chronic comorbidities. The ever-increasing advancements in software technology presents an innovative approach for pharmacists to make use of visuals to disseminate information to patients accordingly. One possible medium for sharing interactive educational material with patients is through short video clips to consolidate verbal advice and which can also be repeatedly seen by patients at their own leisure. Pharmacists can also contribute towards encouraging the administration of vaccines particularly influenza vaccine annually and pneumococcal polysaccharide vaccine. This service could be taken up by pharmacists within the community setting.

The developed tool *“COPD exacerbation risk factors management and prevention”* can assist pharmacists’ outreach to help identify patients requiring the clinical assistance of other healthcare professionals such as respiratory physiotherapists. Study findings indicated that a larger percentage of the inpatient cohort were not reviewed by physiotherapists. One asks whether their respiratory physiotherapists regular interventions in patient care might prevent exacerbations resulting in hospitalisation? Further investigation as to whether additional respiratory physiotherapy follow-ups can prevent COPD exacerbations leading to hospitalisation or to what extent may be warranted. One could argue for respiratory physiotherapy visits be combined with a pharmaceutical care session as happens in other chronic conditions such as the rheumatology.

The collaborative model between pharmacists and physiotherapists worked out effectively in the rheumatology clinic where the researcher had the opportunity of undertaking a placement during the years of study as a pharmacist. This model would create an area for improvement in the service offered to COPD patients as part of the non-pharmacological COPD management care plan. It also presents an opportunity for improvement for the different stakeholders involved in patient care whilst at the same time providing an increased efficient and safe holistic service for COPD patients.

The “*COPD exacerbation risk factors management and prevention*” tool presents to pharmacists an aid to assess medication compliance and pick up issues related to medication compliance or medication accessibility problems. Understanding barriers to medication adherence can provide insight on areas for improvement. Within a busy outpatient setting, clinical pharmacists can conduct medication reconciliations, inhaler adherence assessments, and inhaler technique evaluation. Such data collection and records can guide the multidisciplinary team on therapeutic decisions following thorough clinical review by physicians.

The 30-day post discharge follow up potentially could indicate another niche for pharmacists. The 30-day all-cause unplanned readmissions is one outcome measure that can be used to identify any deficiencies in the discharge process and ensure smooth transition of care. Upon discharge, focus should be shifted towards developing a follow-up plan. Recent studies evaluating this matter such as Fernández-Villar et al, (2018) recommend spirometry tests to be conducted prior to discharge. A study was conducted by Hansen et al, (2011) to analyse interventions to reduce 30-day readmission risk. The study concluded that flexible and patient-specific interventions with the aim of accommodating individual patient needs were the most successful. From the data collected in this study, there were no admission within 30 days from date of discharge. This complements well to the multidisciplinary team with whom the researcher was assigned and is indicative of appropriate and timely discharge interventions. However, one does not exclude the possibility of studying readmissions at a longer period within 60 days or during seasonality of increased exacerbations. Follow up could be implemented through regular phone calls and the setting up of an assistance line where COPD patients can get through to the pharmacists within the hospital setting for guidance. This model of having a “hot line” was implemented within the rheumatology department and the day care unit for patients post-surgery. The model operated on an inter-collaborative approach where the line is manned by a specialised nurse and pharmacist working together. This model was noted by the researcher during his working experience as a pharmacist within the hospital setting.

4.2 LIMITATIONS OF THE STUDY

Every study has its limitations. A major limitation was the time allocated to carry out the fieldwork and the fact that the researcher was working with one respiratory firm. Incorporating more respiratory firms is one potential approach to recruit a larger group of patients and capture more data in view of the time constraints to conduct the study might have led to more robust data. Statistical power of findings might have been compromised due to the small sample size, underestimating the effect of some parameters studied. Recruitment at outpatient and inpatient settings proposed some logistical challenges. The lack of appropriate technological equipment and facilities hindered the possibility of using short video clips to consolidate advice given with regards to inhaler technique.

A substantial contribution to the successful recruitment of the patients was due to the collaboration of the respiratory firm who flagged patients meeting the inclusion criteria. This needs to be acknowledged.

4.3 CONTRIBUTION TO THE PHARMACEUTICAL SERVICE

The innovative contribution of the study towards pharmaceutical was the identification of a tool to be incorporated in the implementation of a pharmaceutical service for COPD patients. The *COPD exacerbation risk factors management and prevention tool* developed in this research can be easily adapted for use within the community setting allowing the community pharmacist, who is very often the first port of call of patients to trigger off a mechanism for referring or advising the patients to proactively prevent hospitalisations related to COPD. The tool was developed specifically to meet the Maltese scenario but can be adapted to reflect international scenarios. The research methodology developed can be extrapolated to other chronic conditions putting pharmacists at the service of our patients.

4.4 RECOMMENDATIONS FOR FURTHER RESEARCH STUDIES

One recommendation would be to role out the *COPD exacerbation risk factors management and prevention tool* to a community setting. With the implementation of such a pharmaceutical care plan based on the use of this tool, one can possibly study the input and benefit of integrated care programs in COPD within the local setting. The concept behind the tool can be adapted and studied in other chronic conditions. Another potential study can reflect on the implementation of set management plans as a self-management strategy. Variables of interest would be patient perspectives and implementation hurdles. Main outcome measures would look at the association if any between written action plans and COPD-related hospitalization or all-cause hospitalisation. The interrelationship between seasonality and COPD in the local setting warrant further analysis with particular attention to different variables and their effect on COPD exacerbation. Parameters to investigate could include ambient temperature, humidity, and precipitation.

The data compiled from this study suggested that COPD effected mainly individuals of primary and secondary level of education. Lower socioeconomic statuses have been associated with increased risk of developing COPD as a result of higher smoking prevalence, type of occupation, and income (Gershon et al, 2011). This could warrant the possibility of developing pharmacist-led patient self management educational programs for COPD patients. Such programs would empower patients while regularly updating patients with knowledge on their conditions and innovative medication management. One aspect of COPD management gaining interest is the relationship between COPD and clinical nutrition. Prevalence of malnutrition in COPD patients has

been estimated to stand between 20% and 40% at an outpatient setting (Raguso & Luthy, 2011). Research in clinical nutrition practices locally and possible ways of advocating the importance of appropriate attention to nutrition can be conducted in light of previous studies associating appropriate nutritional support with improved grip strength, respiratory muscle strength, and physical strength (Aniwidyaningsih et al, 2008; Collins et al, 2012). A reduction in length of hospital stay by 21.5%, total hospital costs by 12.5%, and a 13.1% reduction in 30-day readmission rate was reported by Snider et al, (2015) when assessing to quantify the effect of oral nutritional supplementation on such domains in Medicare patients aged 65 years and over. Evaluation of specific factors relating to low socioeconomic statuses such as poor nutrition and the association with risk of developing COPD, length of hospital stay, readmission risk, and cost reduction can provide further insight on the relevance of oral nutritional supplementation and COPD in the local setting. Research in how and in what way, poor dental hygiene indices may impact respiratory symptoms in COPD and exacerbation rate. A prospective study conducted by Gaeckle et al, (2018) correlated poor dental health with worse daily respiratory symptoms. A 2-year, small, randomized controlled trial concluded that regular dental visits, root planning and tooth scaling was associated with a reduction in COPD exacerbations (Zhou et al, 2014).

Telehealth, telemedicine, and virtual exercise programs are becoming more common means of communication between healthcare workers and patients. Ringbæk et al, (2015) studied telemonitoring on high risk of exacerbation COPD patients and the effect of such intervention with the possibility of video conferencing on exacerbations and hospital admissions. The researchers applied the case-control technique, but no significant difference was achieved for hospital admissions, time to first admission, and all-cause admissions between the two groups. Although telehealth has not yet been proven to have significant impact on QoL (Gegersen et al, 2016; Hirani et al, 2017), the current COVID-19 circumstances are pushing the boundaries of telehealth services. Further investigation into how telehealth can be incorporated into a pharmaceutical care service as applied to the local demographic can be undertaken, utilising such unprecedented circumstances as a case study. One method of assessing this is through telehealth follow-up patient appointments at predetermined time frames such as 1 month, 3 months and 6 months. The ever-increasing interest in technology systems and health is also reflected by indexed scientific journals such as NPJ Primary Care Respiratory Medicine issuing calls for paper relating to 'Health IT and data-enabled transformation of respiratory health'. The integration of IT systems such as robotic technology in secondary healthcare management systems is the next trajectory for Mater Dei Hospital. Investigations into how this implementation will impact COPD exacerbation and readmission rates could provide insight on interventions necessary to integrate such technology with the primary healthcare setting.

4.5 CONCLUSION

The identification of variables contributing to COPD exacerbation admissions allow for evidence-based targeted interventions that ultimately benefit patients and the national healthcare system. In order to mitigate hospitalisations and readmissions, all healthcare sectors need to incorporate a series of pre-identified protocols for interventions rather than passively reacting to unwanted outcomes. Any form of pharmaceutical care service formulated with the aim of addressing exacerbations, hospital admissions, and readmission rates should incorporate an appropriate transitional care plan that revolves around person-centred interventions.

In conclusion, this research fulfilled its initial target of developing a tool which puts pharmacists in a central proactive role in relation to COPD patients. The study findings captured by the innovative tool shed light on potential risk factors associated with hospitalisations of Maltese COPD patients. This study provides unpretentious food for thought for future research. But then again this is what research is.

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APPENDIX I

ETHICS APPROVAL



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Tuesday 6th August 2019

Mr Daniel Joseph Gixti
69,
Arzella Triq l-Ghakrux,
St Peters Area,
Zabbar

Dear Mr Daniel Joseph Gixti,

Please refer to your application submitted to the Research Ethics Committee in connection with your research entitled:

**Pharmacists' interventions in Chronic Obstructive Pulmonary Disease related hospital
readmission**

The Faculty Research Ethics Committee granted ethical approval for the above mentioned protocol.

Yours sincerely,

Professor Pierre Mallia
Chairman
Research Ethics Committee

APPENDIX II

DATA COLLECTION TOOL

COPD PROTOCOLS, PRACTICE GUIDELINES, AND OTHER RESOURCES
REVIEWED TO COMPILE THE DATA COLLECTION TOOL

TYPE OF SOURCE AND REFERENCE
<p>COPD strategy document</p> <p>Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic pulmonary disease; 2019 Report [Internet]. Wisconsin: GOLD; 2019 [cited 2019 Jun 9]. Available from: https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf</p>
<p>Evidence-based clinical resource</p> <p>Hess D & Dhand R. The use of inhaler devices in adults. [Internet] Waltham, MA: UpToDate® Inc; 2019 [cited 2019 May 20]. Available from: https://www.uptodate.com. Subscription required.</p>
<p>Practice guidelines</p> <p>National Institute for Health and Care Excellence (NICE). Chronic obstructive pulmonary disease in over 16s: diagnosis and management [Internet]. London: NICE; 2019 [cited 2019 May 23]. Available from: https://www.nice.org.uk/guidance/ng115</p> <p>National Institute for Health and Care Excellence (NICE). NICE Bites – Medicines Optimisation [Internet]. London: NICE; 2015 [cited 2019 May 20]. Available from https://www.evidence.nhs.uk/search?ps=250&q=nice+bites</p>

TYPE OF SOURCE AND REFERENCE
<p>Dissertations</p> <p>Pizzuto M. Compliance and medication problems in chronic conditions. [dissertation] Msida (Malta); University of Malta. 2010</p> <p>Spiteri J. Chronic Obstructive Pulmonary Disease Exacerbations – Cost, Risk Factors, and Impact of Long-Acting Muscarinic Antagonists. [dissertation] Msida (Malta); University of Malta. 2018.</p>
<p>Research articles</p> <p>Fialko L, Garety PA, Kuipers E, Dunn G, Bebbington PE, Fowler D, et al. A large-scale validation study of the Medication Adherence Rating Scale (MARS). Schizophrenia research. 2008;100(1-3):53-59.</p> <p>Gauci J, Yamagata K, Bilocca D, Mifsud M, Montefort S. Current GOLD recommendations and its implementation within hospitalised COPD patients in Malta. Malta Medical Journal. 2015;27(1):33-39.</p> <p>Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. New England Journal of Medicine. 2010;363(12):1128-1138.</p> <p>Lau CS, Siracuse BL, Chamberlain RS. Readmission after COPD exacerbation scale: determining 30-day readmission risk for COPD patients. International Journal of Chronic Obstructive Pulmonary Disease. 2017;12:1891-1902.</p>

TYPE OF SOURCE AND REFERENCE
<p>Levy ML, Dekhuijzen PN, Barnes PJ, Broeders M, Corrigan CJ, Chawes BL et al. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). NPJ Primary Care Respiratory Medicine. 2016;26 [cited 2019 May 5]. Available from: https://www.nature.com/articles/npjpcrm201617</p> <p>Micallef LA. A review of the metered dose inhaler technique in asthmatic and COPD patients. Malta Medical Journal. 2015;27(1):22-28.</p> <p>Plaza V, Fernández-Rodríguez C, Melero C, Cosío BG, Entrenas LM, de Llano LP, et al. Validation of the ‘Test of the Adherence to Inhalers’(TAI) for Asthma and COPD Patients. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2016;29(2):142-52.</p> <p>Svarstad BL, Chewning BA, Sleath BL, Claesson C. The Brief Medication Questionnaire: a tool for screening patient adherence and barriers to adherence. Patient Education and Counselling. 1999;37(2):113-124.</p>

COPD EXACERBATION RISK FACTORS MANAGEMENT AND PREVENTION
TOOL

Section A - Data Collection Sheet

Setting: Inpatient / Outpatient

Reference number: _____

Patient Demographics

Patient Initials:		ID No:		Age:	
Weight (Kg):		Height (cm):		BMI (Kg/m2):	
Gender:		Locality:		Nationality:	

Educational standard (tick one):

☐ Primary ☐ Secondary ☐ Higher Secondary ☐ Undergraduate ☐ Postgraduate

Occupation: _____

Medication Reconciliation

Comorbidities	Medication	Regimen

***Include herbal and non-prescription medication**

Domiciliary oxygen therapy (tick accordingly):

<input type="checkbox"/> Short burst oxygen therapy	<input type="checkbox"/> Oxygen concentrator
What is the flow rate?	
Number of hours daily?	

Vaccinations

- i. Have you taken the Influenza vaccine this year? YES / NO
- ii. Have you ever taken the Pneumococcal vaccine? YES / NO

During the past year:

- i. How many courses of steroids were you prescribed? _____
- ii. How many antibiotic courses were you prescribed? _____
- iii. How many hospitalisations (inpatients cohort only) _____
- iv. If hospitalised, COPD related or not? YES / NO
- v. Have you missed any COPD outpatient clinics? YES / NO
- vi. Any visits for Emergency Nebulized Treatment? YES / NO
- vii. (If emergency nebulizer required) – How many times? _____

Environmental factors

- i. Type of residence? _____
- ii. Vicinity to sea/countryside/garden/humidity? _____
- iii. Any pets at home? _____
- iv. (If yes) what type? _____

Who is involved in the patient's care?

- i. Respiratory Physician YES / NO
- ii. General Physician (GP) YES / NO
- iii. (If GP is involved) – is it usually the same GP YES / NO
- iv. Respiratory Physiotherapists YES / NO

Lung Function Test or Spirometry

- i. Post-bronchodilator FEV₁/FVC ratio _____
- ii. FEV₁ (% predicted) _____
- iii. FVC _____
- iv. mMRC _____
- v. SpO₂ _____
- vi. Is the ABCD status recorded? YES / NO

Smoking History

- | | |
|--|----------|
| i. Smoking history | YES / NO |
| ii. Current smoker | YES / NO |
| a. Number of cigarettes smoked daily | _____ |
| b. Number of smoking years | _____ |
| c. Pack-years | _____ |
| iii. Ex-smoker | YES / NO |
| a. Number of cigarettes smoked daily | _____ |
| b. Number of smoking years | _____ |
| c. Pack-year | _____ |
| d. Number of years since stopped smoking | _____ |

Seasonality

During which period of the year do symptoms usually worsen (tick one)?

- ☐ Summer
- ☐ Winter
- ☐ No difference

Section B - Inhaler Adherence Assessment

1. Do you ever **forget** to take your inhaled medication?

All the time	Frequently	Sometimes	Rarely	Never

2. If you **miss a dose** do you (tick accordingly):

- ☐ Skip the dose completely
- ☐ Administer when you remember

3. Any other reasons why you would **miss/skip a dose**?

		YES	NO
4.	Do you stop your inhalers when you feel good?		
5.	Do you skip doses when you feel good?		
6.	Have you ever stopped using the inhalers without consulting your physician?		
7.	Have you ever reduced the dose yourself without consulting your physician?		
8.	Do you get your inhalers for free from the Pharmacy of Your Choice?		
9.	Do you buy any of the inhalers?		
10.	(If you buy your inhalers) have you ever stopped any inhalers because of financial burden ?		
11.	Do you find it difficult to adhere to the treatment regimen?		
12.	Do you feel that your inhalers are useful to treat your condition?		
13.	Have you ever experienced any side effects with the use of inhalers?*		

14. *If you experienced side effects, what type?

15. What do you do in case of **worsening symptoms** (tick accordingly)?

- ☐ Have a set management plan/set changes to inhalers
- ☐ Endure symptoms
- ☐ Seek medical advice

16. Where do you report to first when symptoms worsen (tick accordingly)?

- ☐ GP
- ☐ Pharmacist
- ☐ Health centre
- ☐ MDH Emergency

17. During the last month:

a) How many **days per week** did you require your reliever inhaler?

b) How many **times per day** did you require your reliever inhaler?

c) How many **puffs** of reliever inhaler each time?

Section C - Inhaler/Nebulizer Technique Evaluation Sheet

General Questions

Have you ever received inhaler technique education?

YES / NO

Do you know how to use your inhaler device?

YES / NO

Metered Dose Inhaler (MDI)

1. Remove mouthpiece cover. Score: _____
2. Shake MDI vigorously for five seconds.
3. Hold MDI upright (finger on canister and thumb at the bottom of inhaler).
4. Exhale fully (or as much as comfortable) away from device.
5. Place mouthpiece between teeth and use lips to create tight seal over mouthpiece.
6. Inhale slowly and deeply whilst activating canister.
7. Hold breath for as long as comfortable (5 to 10 seconds) and remove device from the mouth.
8. Breathe out normally away from device.
9. If more than 1 actuation required, wait 15 to 30 seconds between actuations.
10. Recap mouthpiece.

Metered Dose Inhaler (MDI) with Spacer

1. Remove mouthpiece cover and attach to spacer. Score: _____
2. Shake MDI vigorously for five seconds.
3. Hold assembled MDI and spacer in a vertical position.
4. Exhale normally (or as much as comfortable) away from device.
5. Place mouthpiece of spacer between teeth and use lips to create tight seal over mouthpiece.
6. Sequentially activate canister and then inhale slowly and deeply.
7. Hold breath for as long as comfortable (5 to 10 seconds) or 'use tidal breathing technique' and remove device from the mouth.
8. Breathe out normally away from device.
9. If more than 1 actuation required, wait 15 to 30 seconds between actuations.
10. Recap mouthpiece.

Dry Powder Inhaler (DPI)

1. Prepare the inhaler (depending on type of device). Score: _____
2. Load dose.
3. Hold DPI horizontal or upright.
4. Exhale fully (or as much as comfortable) away from device.
5. Place mouthpiece between teeth and use lips to create tight seal over mouthpiece.
6. Inhale forcefully and deeply.
7. Hold breath for as long as comfortable (5 to 10 seconds) and remove device from the mouth.
8. Breathe out normally away from device.
9. If second inhalation required, repeat steps 2-8.
10. Close device.

Inhalation powder, hard capsule

1. Pull off Cap. Score: _____
2. Open inhaler.
3. Insert capsule and close inhaler.
4. Hold inhaler upright.
5. Pierce capsule once by pressing both side buttons simultaneously and release.
6. Exhale fully away from the inhaler.
7. Place mouthpiece between teeth and use lips to create tight seal over mouthpiece.
8. Inhale quickly and as deeply as possible.
9. Hold breath for as long as comfortable (5 seconds) and remove device from the mouth.
10. Check capsule is empty.

Other Tips when using hard capsules for inhalation:

- Always store capsules in the blister card and removed only immediately before use.
- Peel open the blister to remove capsule. Do not push the capsule through the foil to remove it from the blister.
- Capsules are not to be swallowed.
- Capsules to be used only with the provided inhaler.
- Side buttons are not to be pressed more than once.
- Do not press side buttons during inhalation.
- Do not handle capsules with wet hands.
- Never wash inhaler with water.

Nebulizer Technique

1. Sit up or partially in supine position.
2. Assemble apparatus and add solution for nebulization in nebulizer cup.
3. Use a fill volume of 3mL to 6 mL.
4. Attach a compressor or a pressurized gas supply (eg, compressed air or oxygen) with a flow of 6 to 8 L/min.
5. Breathe through the mouth using either a mask or mouthpiece.
6. Inhale slowly and deep breaths.
7. Periodically tap nebulizer to return impacted droplets to reservoir.
8. Stop treatment when the nebulizer sputters despite tapping.

Score: _____

Note: Slow breathing pattern and an occasional deep breath improves treatment penetration and deposition of aerosol in the lower respiratory airways.

If using a mouthpiece, the patient can rest teeth on mouthpiece and close lips around it.

Do you have any questions or concerns regarding your treatment?

General Patient Advice:

When you need to prime MDI

- First use
- Not used for several days
- Dropped inhaler

How to prime MDI

- Shake and spray it into the air (away from your face) a total of up to four times

Method of administration for specific DPI

- Refer to Patient Information Leaflet

For glucocorticoid-containing inhalers

- Rinse and gargle your mouth with water after using the inhaler. Then spit out the water. Do not swallow it.

Benefits of using a spacer with MDI

- Improves drug delivery
- When used with ICS reduced potential for side effects.

How to clean spacer

- Clean every 1 - 2 weeks with warm water and dishwashing soap, rinse it, and let it air-dry. Do not put it in the dishwasher.
- New spacers may have static charge – wash as described above prior to initial use to eliminate the static charge.

General points

- Make sure tongue does not block mouthpiece.
- Wait for 15 to 30 seconds between puffs. Shake canister again before the next puff.

Sezzjoni A - Ġabra ta' Informazzjoni

Post: 'Inpatient' / 'Outpatient'

Numru ta' referenza: _____

Demografika

Inizjali tal-pazjent:		Numru ta' Identita' :		Eta':	
Piż (Kg):		Tul (cm):		BMI (Kg/m ²):	
Sess:		Lokalita:		Nazzjonalita':	

Livell ta' edukazzjoni (agħzel waħda):

- ☐ Primarja ☐ Sekondarja ☐ Post-sekondarja ☐ Gradwat/a bil-Baċcellerat
☐ Gradwat/a b'livell oltre l-Baċcellerat

Tip ta' impjeg: _____

Rikonċiljazzjoni tal-medicina

Kundizzjonijiet Mediċi	Mediċina u Doża	Frekwenza

*Inkludi medicini mil-ħxejjex u dawk li ma jirrikjedux riċetta

Użu tal-ossigenu mediku d-dar (agħzel skont il-bżonn):

<input type="checkbox"/> Ċilindru tal-ossigenu	<input type="checkbox"/> Kompresur tal-ossigenu
X'inhil- <i>flow rate</i> ?	
Numru ta' siegħat kuljum?	

Vaċċini

- i. Hadt l-vaċċin tal-influenza din is-sena? IVA / LE
ii. Qatt ħadt il-vaċċin tal-Pneumococcal? IVA / LE

Matul is-sena li għaddiet

- | | |
|--|----------|
| i. Kemm korsijiet ta' steroidi ġejt preskritt? | _____ |
| ii. Kemm korsijiet ta' antibijotiċi ġejt preskritt? | _____ |
| iii. Kemm-il darba d'hall l-isptar? (għal <i>inpatients</i> biss) | _____ |
| iv. Jekk ġejt rikoverat l-isptar, dan kien relatat ma' COPD? | IVA/ LE |
| v. Ikkancelajt xi appuntamenti l-klinika tas-COPD <i>outpatients</i> ? | IVA / LE |
| vi. Kellek bżonn trattamenti t'emergenza b' <i>nebuliser</i> ? | IVA / LE |
| vii. (Jekk ġejt bżonn <i>nebuliser</i>) – Kemm-il darba? | _____ |

Fatturi relatati ma' l-ambjent

- | | |
|--|-------|
| i. F'liema tip ta' residenza tgħix? | _____ |
| ii. Toqgħod viċin il-baħar/ħdura/ġnien/residenza umduża? | _____ |
| iii. Għandek xi annimali domestiċi d-dar? | _____ |
| iv. Jekk Iva, x'tip ta' annimali għandek? | _____ |

Min huwa nvolut fil-ħarsien u trattament tal-kundizzjoni medika tal-pazjent?

- | | |
|---|----------|
| i. Il-konsulent u t-tobba tan-nifs | IVA / LE |
| ii. It-tabib tal-famija | IVA / LE |
| iii. (Jekk it-tabib tal-familja huwa nvolut) – jinżamm dejjem l-istess tabib? | IVA / LE |
| iv. Fiżjoterapisti tan-nifs | IVA / LE |

Testijiet tan-nifs u funzjoni tal-pulmun

- | | |
|--|----------|
| i. Post-bronchodilator FEV ₁ /FVC ratio | _____ |
| ii. FEV ₁ (% predicted) | _____ |
| iii. FVC | _____ |
| iv. mMRC | _____ |
| v. SpO ₂ | _____ |
| vi. Huwa irrekordjat l-ABCD status? | IVA / LE |

Tipjip

- | | |
|---|----------|
| i. Qatt pejjipt? | IVA / LE |
| | |
| ii. Tpejjep bħalissa? | IVA / LE |
| a. Numru ta' sigaretti li tpejjep ta' kuljum | _____ |
| b. Numru ta' snin li ilek tpejjep | _____ |
| c. Pack-years | _____ |
| iii. Waqaft tpejjep? | IVA / LE |
| a. Numru ta' sigaretti li kont tpejjep ta' kuljum | _____ |
| b. Numru ta' snin li kont ilek tpejjep | _____ |
| c. Pack-years | _____ |
| d. Numru ta' snin kemm ilek li qtajt is-sigaretti | _____ |

Stagjonalita'

Meta normalment iaggravaw is-sintomi? (agħzel waħda)

- ☐ Matul is-Sajf
- ☐ Matul ix-Xitwa
- ☐ Ma narax differenza

Sezzjoni B - Evalwazzjoni għall-konformita' mad-doži tal-*inhalers*

1. Qatt **tinsa** tiehu l-medicina tal-*inhaler*?

Dejjem	Ta' spiss	Xi drabi	Rari	Qatt

2. Meta għal xi raġuni **taqbeż id-doża**, x'tagħmel? (aġżel waħda):

- ☐ Taqbeż id-doża kompletament?
- ☐ Tiehu d-doża x'hin tiftakar?

3. X'raġunijiet ohra jista' jkun hemm biex **taqbeż id-doża**?

		IVA	LE
4.	Meta tħossok tajjeb, tibqa' teħodhom l-inhalers jew twaqqafhom?		
5.	Meta tħossok tajjeb, tibqa' teħodhom l-inhalers jew taqbiżhom?		
6.	Qatt waqft tuża l-inhalers mingħajr ma kkonsultajt mat-tabib tiegħek?		
7.	Qatt naqqast id-doża inti mingħajr ma kkonsultajt mat-tabib tiegħek?		
8.	Tiġbor l-inhalers b'xejn mil-ispizerija tal-għażla tiegħek?		
9.	Tixtri xi inhalers?		
10.	(Jekk tixtri xi inhalers) Qatt waqqaftom minħabba raġunijiet finanzjarji?		
11.	Issibha diffiċli li żżomm mad-doża u l-frekwenza tal-inhalers?		
12.	Tħoss li l-inhalers huma utli biex tikkontrolla l-kundizzjoni medika tiegħek?		
13.	Qatt esperjenzajt xi side effects bl-użu tal-inhalers?*		

14. *Jekk esperjenzajt xi *side effects*, x'kienu?

15. F'Kaz li **s-sintomi jiggravaw** x'tagħmel? (ağħzel waħda)

- ☐ Għandek pjan strutturat ta' emendi fl-*inhalers*
- ☐ Tissapporti s-sintomi
- ☐ Tfittex għajnuna professjonai

16. Fejn tirrikorri l-ewwel f'kas li jiggravaw is-sintomi tan-nifs? (ağħzel waħda)

- ☐ Tabib tal-familja
- ☐ Ċentru tas-Saħħa
- ☐ L-Emergenza ta' l-isptar Mater Dei
- ☐ Spiżjar

17. Matul ix-xahar li għadda:

- a) Kemm-il **darba fil-gimgha** kellek bżonn *reliever inhaler*? _____
- b) Kemm-il **darba fil-gurnata** kellek bżonn *reliever inhaler*? _____
- c) Kemm-il **għafsa** ta' *reliever inhaler* tagħmel kull darba? _____

Sezzjoni Ċ - Evalwazzjoni tat-Teknika tal-*Inhaler/Nebuliser*

Mistoqsijiet Ġenerali

Qatt ingħatajt edukazzjoni dwar it-teknika ta' kif għandu jiġi użat l-*inhaler*?
Taf kif għandek tuża l-*inhaler*?

IVA / LE
IVA / LE

Metered Dose Inhaler (MDI)

1. Neħhi t-tokka tal-*mouthpiece* Marka: ____
2. Hawn MDI b'mod vigoruż għal hames sekondi
3. Żomm MDI wieqaf (wieħed mis-swaba fuq il-*canister* u s-sebġha l-kbir fil-qiegħ tal-*inhaler*)
4. Hu nifs sew il-barra
5. Poġġi l-*mouthpiece* bejn is-snien u uża xufftejk biex tissigillaha
6. Hu nifs il-ġewwa bil-mod u fil-fond filwaqt li tagħfas il-*canister* l-isfel
7. Neħhi l-*inhaler* minn ma' ħalqek u, b'ħalqek magħluq, żomm in-nifs sakemm tibqa' tħossok komdu (minn 5 sa 10 sekondi)
8. Hu nifs il-barra
9. F'kaz li għandek bżonn iktar minn għafsa waħda, stenna bejn 15 u 30 sekonda bejn kull doża
10. Erga' poġġi t-tokka fuq il-*mouthpiece*.

Metered Dose Inhaler (MDI) permezz tat-Tubu

1. Neħhi t-tokka tal-*mouthpiece* u eġmizha mat-Tubu Marka: ____
2. Hawn MDI b'mod vigoruż għal hames sekondi
3. Żomm MDI u t-Tubu weqfin
4. Hu nifs sew il-barra
5. Poġġi l-*mouthpiece* bejn is-snien u uża xufftejk biex tissigillaha
6. Hu nifs il-ġewwa bil-mod u fil-fond filwaqt li tagħfas il-*canister* l-isfel
7. Neħhi l-*inhaler* minn ma' ħalqek u, b'ħalqek magħluq, żomm in-nifs sakemm tibqa' tħossok komdu (minn 5 sa 10 sekondi) jew uża *tidal breathing technique*
8. Hu nifs il-barra
9. F'kaz li għandek bżonn iktar minn għafsa waħda, stenna bejn 15 u 30 sekonda bejn kull doża
10. Erga' poġġi t-tokka fuq il-*mouthpiece*.

Dry Powder Inhaler (DPI)

1. Ipprepara l- inhaler (jiddependi mit-tip ta DPI) Marka: ____
2. Ipprepara d-doża
3. Żomm DPI wieqaf
4. Hu nifs sew il-barra
5. Poġġi l-*mouthpiece* bejn is-sniem u uża xufftejk biex tissigillaha
6. Hu nifs il-ġewwa u fil-fond
7. Neħhi l-*inhaler* minn ma' ħalqek u, b'ħalqek magħluq, żomm in-nifs sakemm tibqa' tħossok komdu (minn 5 sa 10 sekondi)
8. Hu nifs il-barra
9. F'każ li għandek bżonn iktar minn doża waħda, irrepeti l-proċess minn numru 2 sa 8.
10. Agħlaq l-*inhaler*.

Inhalation Powder, hard capsule

1. Neħhi t-tokka tal-*mouthpiece*. Marka: ____
2. Iftaħ l-*inhaler*.
3. Poġġi l-kapsola u għalaq l-*inhaler*.
4. Żomm l-*inhaler* wieqaf.
5. Taqqab il-kapsola darba billi tgħafas iz-żewġ buttuni tal-ġnub fl-istess ħin u mbgħad itlaqhom.
6. Hu nifs sew il-barra 'l bogħod mil-*inhaler*.
7. Poġġi l-*mouthpiece* bejn is-sniem u uża xufftejk biex tissigillaha.
8. Hu nifs il-ġewwa u fil-fond.
9. Neħhi l-*inhaler* minn ma' ħalqek u, b'ħalqek magħluq, żomm in-nifs sakemm tibqa' tħossok komdu (5 sekondi).
10. Iċċekja li l-kapsola hija vojta.

Rakommandazzjonijiet meta tuża hard capsule inhalers:

- Dejjem żomm il-kapsoli fil-kontenitur tagħhom. Neħhihom minnu biss qabel ma tużahom.
- Biex toħrog il-kapsola mill-kontenitur, qaxxar il-folja. Tipruvax tgħafas il-kapsola biex toħroġa.
- Il-kapsola m'għandiex tigi mibluha.
- Il-kapsoli għandom jiġu użati biss mal-inhaler provdut.
- Il-buttuni tal-ġnub m'għandhomx jiġu mgħafusin iktar minn darba.
- Il-buttuni tal-ġnub m'għandomx jiġu mgħafusin waqt li jittieħed in-nifs il-ġewwa.
- Tmissx il-kapsola b'idejk imxarbin.
- Qatt taħsel l-inhaler bl-ilma.

Nebuliser

1. Poġġi bil-qiegħda jew oqgħod parzjalment mimdud Marka: ____
2. Arma l-apparat u żid id-doża ġewwa it-tazza tan-*nebuliser*
3. Uża volum ta' bejn 3mL u 6 mL
4. Waħħal kompressur jew ossiġenu kkompressat u tih flow ta' bejn 6 u 8 L/min
5. Hu nifsijiet mil-ħalq filwaqt li tuża l-maskra jew il-*mouthpiece*
6. Hu nifs il-ġewwa bil-mod u fil-fond
7. Perjodikament taptap it-tazza tan-*nebuliser*
8. Waqqaf it-trattament meta t-tazza tan-*nebuliser* tibda tfaqqa' minkejja li tkun qiegħed itaptapha.

Nota: Nifsijiet bil-mod flimkien ma' xi nifs fil-fond kull tant ħin itejbu l-penetrazzjoni tat-trattament u d-depożizzjoni tal-medicina fil-pulmun.

Jekk qed jintuża l-*mouthpiece*, il-pazjent jista' jserraħ snien u fuqha u jagħmel xuftejh madwarha.

Għandek xi mistoqsijiet dwar it-trattament tiegħek?

Rakkomandazzjonijiet Ġenerali:

Meta għandek tipprepara l-MDI

1. Jekk qed tużah għall-ewwel darba
2. Jekk ma ntuzax għal numru ta' granet
3. Jekk waqqajt l-*inhaler*

X'għandek tagħmel biex tipprepara l-MDI

- Ħawwad u agħfas fl-arja (il-bogħod mill-wieċċ) għal madwar erba' darbiet, filwaqt li żżommu wieqaf.

Modi differenti ta' amministrazzjoni ta' DPIs differenti

- Irreferi għall-fuljett ta' informazzjoni għall-pazjent

Għal *inhalers* li fihom il-medicina *glucocorticoid*

- Laħlaħ u ggargarizza ħalqek bl-ilma wara li tuża l-*inhaler*. Tiblax l-ilma imma obżqu 'l barra.

Beneficcji tal-użu tat-tubu fil-MDI

- Ittejjeb il-mod ta' kif tiġi trażmessa l-medicina
- Meta tintużah ma' l-ICS, tnaqqas ir-riskju ta' *side effects*.

Kif tnaddaf it-tubu

- Naddfu kull ġimgħa jew ġimgħatejn b'ilma fietel u ftit sapun, laħlaħu u ħallih jinxef waħdu. Iddaħlux fid-*dishwasher*
- Tubi godda jaf ikollhom effett ta' *static charge* – naddaf it-tibu kif ġie deskritt qabel ma dan jigi użat għall-ewwel darba biex jtneħħa l-*static charge*.

Punti Ġenerali

- Kun ċert li l-ilsien ma jimblokkax il-*mouthpiece*
- Stenna 15 jew 30 sekonda bejn kull għafsa. Ħawwad l-*inhaler* darba oħra qabel l-għafsa li ikun imiss.

APPENDIX III

INFORMATION SHEET

Information Sheet

April 2019

Dear Sir /Madam,

I am currently reading for a Doctoral Degree in Pharmacy and as part of this course I am carrying out research on patients who have Chronic Obstructive Pulmonary Disease (COPD).

The purpose of this research is to study the patients admitted to hospital as a result of worsening of their COPD condition and to study the risk factors contributing towards COPD hospitalisation.

I require your consent to participate in this study. Once this is granted, I will be accessing data from your case file notes whilst also taking a few minutes of your time in order to conduct an interview.

Under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said Regulation, you have the right to obtain access to, rectify, and where applicable ask for the data concerning them to be erased.

Please note that all data will remain confidential.

Regards,

Daniel Joseph Gixti

Bsc. Pharm. Sci, M.Pharm

Ittra ta' Informazzjoni

April 2019

Għażiż Sinjur/a,

Bħalissa qiegħed nistudja għal-dottorat fil-farmaċija fejn parti mill-kors tikkonsisti f'riċerka. Jiena għażilt li nirriċerka l-marda tas-'COPD' magħrufa wkoll bħala 'Chronic Obstructive Pulmonary Disease', jew bronkite kronika.

L-iskop ta' din ir-riċerka hija li nistudjaw persuni li jinżammu l-isptar minħabba l-attakki tas-COPD. Se nkun qed inġares b'mod partikolari lejn il-fatturi u r-riskji li possibbilment qed jikkontribwixxu biex pazjenti b'din il-kundizzjoni jiġu rikoverati l-isptar.

Sabiex inwettaq dan l-istudju, għandi bzonn il-kunsens tiegħek. Wara li nikseb dan il-kunsens ser ninġtieg illi nagħmillek intervista filwaqt illi jkolli aċċess għan-noti tat-tobba.

Taħt il-General Data Protection Regulation (GDPR) u l-liġijiet tar-Repubblika ta' Malta li jimplimentaw u jispeċifikaw il-proviżjonijiet ta' dan ir-regolament, inti għandek id-dritt għall-aċċess, tikkoreġi, u fejn applikabbli, titlob li informazzjoni li tikkonċerna lilek tiġi eliminata.

Nassigurak li kull informazzjoni se tibqa' kunfidenzjali.

Grazzi bil-quddiem,

Daniel Joseph Grixti

Bsc. Pharm. Sci, M.Pharm

APPENDIX IV

CONSENT FORM

Consent Form for Research Interview Participation

I have been asked to participate in a research study entitled:

‘Pharmacists’ interventions in Chronic Obstructive Pulmonary Disease related hospital readmissions’

The purpose and details of the study have been explained to me by Mr. Daniel Joseph Grixti and any difficulties which I raised have been adequately clarified. I have been provided with an information sheet detailing the scope of the study.

I give my consent to the Principal Investigator to make the appropriate observations.

I understand that the results of this study may be used for medical or scientific purposes and that the results achieved from the study in which I am participating may be reported or published. Nevertheless, my personal identity (either individually or collectively) shall not be revealed with any parties other than the researcher, supervisor and the examiners without my consent in writing.

I am under no obligation to participate in this study and am doing so voluntarily. I may withdraw from the study at any time, without giving any reason. Withdrawal from the study will not influence in any way the care, attention and treatment normally given to me.

Under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said Regulation, you have the right to obtain access to, rectify, and where applicable ask for the data concerning them to be erased.

I am not in receipt of any remuneration for participating in this study. In case of queries during the study I may contact Mr Daniel Joseph Grixti on mobile number 79089414.

Signature of participant _____

Name of participant _____

ID number of participant _____

Signature of Chief Investigator _____

Name of Chief Investigator _____

ID number of Chief Investigator _____

Date _____

Formola tal-Kunsens Għall- Parteċipazzjoni f'Intervista

Jien ġejt mitlub/a sabiex nipparteċipa fi studju ta' riċerka bl-isem:

'Pharmacists' interventions in Chronic Obstructive Pulmonary Disease related hospital readmissions'

Il-għan u d-dettalji tal-istudju spjegagħomli s-Sur Daniel Joseph Grixti li wkoll iċċarali xi mistoqsijiet li għamilt. Ġejt mogħti wkoll ltra tal-Infurmazzjoni għall-Parteċipanti li fiha dettalji dwar l-istudju.

Jiena nagħti l-kunsens tiegħi lill-persuna responsabli għal din ir-riċerka biex jagħmel l-osservazzjonijiet meħtiega.

Jiena nifhem li r-rizultat ta' dan l-istudju jista' jigi ntuzat għal raġunijiet mediċi jew xjentifiċi, filwaqt illi ir-rizultat jista' jigi ppublikat. Madanakollu, bl-ebda mod ma nista' nkun identifikat/a, kemm individwalment kif ukoll kollettivament hliet għar-ricerkatur, il-persuna li ser twettaq is-supervizzjoni u l-eżaminatur mingħajr il-kunsens tiegħi bil-kitba.

Jiena qiegħed/a nipparteċipa f'dan l-istudju b'rieda ħielsa u nista' meta rrid nirtira l-parteċipazzjoni tiegħi minn dan l-istudju mingħajr il-htiega li nagħti raġuni. Jekk nirtira l-parteċipazzjoni tiegħi, dan mhux ser ikollu effett bl-ebda mod fuq il-kura, l-attenzjoni u t-trattament mediku li niġi offrut.

Taħt il-General Data Protection Regulation (GDPR) u l-liġijiet tar-Repubblika ta' Malta li jimplimentaw u jispeċifikaw il-proviżjonijiet ta' dan ir-regolament, inti għandek id-dritt għall-aċċess, tikkoreġi, u fejn applikabbli, titlob li infurmazzjoni li tikkonċerna lilek tiġi eliminata.

Jiena minix qiegħed niġi mħallas biex nipparteċipa f'dan l-istudju. F'kaz li jkolli xi diffikulta' waqt l-istudju nista' nikkuntatja lis-Sur Daniel Joseph Grixti fuq in-numru tal-mobajl 79089414.

Firma tal-parteċipant _____

Isem il-parteċipant _____

Numru tal-Identita' tal-participant _____

Firma tal-investigatur _____

Isem l-investigatur _____

Numru tal-Identita' tal-investigatur _____

Data _____