Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal

By

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Submitted in partial fulfillment of the academic requirementsfor the degree of MMED in the Department of Internal Medicine, School of Clinical Medicine, College of Health Sciences

University of KwaZulu-Natal

Durban 2024

As the candidate's supervisors I have approved this thesis forsubmission.

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Declaration

I Sadaldin Mostafa Abokil declare that:

The research reported in this dissertation, except where otherwise indicated, is my original work.

This dissertation has not been submitted for any degree or examination at any other university.

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Student Signature: Sadaldin Mostafa Abokil Date: 23-05-2024

Supervisor Signature: [redacted] Date: 27/05/2024

Supervisor Signature: _____ Date: _____

Dedication

To my loving wife, Amira, our precious children, and our cherished family, I dedicate this thesis to each of you. Your unwavering support, unrelenting patience, and boundless love have been my guiding light throughout this journey. Your unshakeable belief in me, even in the darkest moments, has been a constant source of strength. I am eternally grateful for your unwaveringsupport, your understanding of the sacrifices required, and your unyielding presence by my side. To all those who have offered a helping hand, words of encouragement, or a supportive ear, I extend my deepest gratitude. Your contributions, whether big or small, have left an indelible mark on my journey,and I am forever thankful. With all my heart, I express my sincerest appreciation.

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Thank you all for being instrumental in this journey.

Overview of the Thesis

Background of the study

The epidemiological overview of Chronic Obstructive Pulmonary Disease (COPD) reflects its widespread impact, with a rising prevalence globally. Smoking is still the primary risk factor, although non-smoking-related causes, such as occupational exposures and environmental causes are increasingly recognized. As a progressive and irreversible condition, COPD presents with symptoms such as shortness of breath, chronic cough, and sputum production, greatly impacting patients' quality of life.

Aims:

To assess the clinical presentation, lung function, radiological findings, and comorbidities in patients with chronic obstructive pulmonary disease (COPD) managed by the Respiratory Clinic at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal, at the initial evaluation and after a two-year follow-up of pulmonary function tests, with the aim of determining the impact of these factors on disease progression, treatment response, and overall patient outcomes.

Methods:

We conducted a retrospective electronic chart review of patients with COPD who attended the Inkosi Albert Luthuli Central Hospital Pulmonology clinic between January 2013 and December 2019.

This is a referral clinic accepting patients throughout the KwaZulu-Natal province. The study excluded patients where electronic data could not be retrieved due to technical challenges.

Demographics, clinical data, lung function testing and radiological imaging were captured retrospectively from medical records. Demographic data

included age, gender, and race. Clinical data captured were presenting symptoms, pre-existing medical conditions, underlying co-morbidities, and modality of treatment. Imaging included chest X Ray and HRCT chest.
Ethical approval was granted by university of KwaZulu-Natal's Human Research Ethics Committee (ref: BREC00005794/2023) and the KwaZulu-Natal department of health (ref no KZ202308-018)

Statistical analysis:

Demographic data with a normal distribution is reported as means with standard deviation (SD).
The change in FEV1 at the initial and final visit was calculated. ANOVA was used to examine demographic and other risk factors associated with mean change in FEV1. The change in FEV1 was also categorized as an increaseor decrease. Factors associated with the percentage of patients with an increased FEV1 were examined using Chi square tests or Fisher's exact test. Statistical significance was regarded as a p-value <0.05 unless otherwise stated.
Stata v17 statistical software was used for statistical analysis.

Results:

There were 151 subjects (male =76.2% n= 115). Most were aged 50-69 years (72.2% n=109). Patients of Indian descent comprised (37.7%; n=57), followed by whites (27.2%; n=41), then Black African (25.2%; n=38). The most common risk factor was smoking (97.4 %; n=147), followed by occupational hazard (45.7%; n= 69). 7.3 % were HIV positive.

The average FEV1% predicted for the patients was 44.17 (SD 18.07), with a mean FVC of 1.36 L (SD 0.8) and an average FEV1/FVC ratio of 32.15 (SD 14.9).

The main finding on CT chest was fibrosis (36.3%.). Thirty-two-point three percent of the patients had pan lobular emphysema. and 30.3% had centrilobular emphysema. Eighty-eight-point seven percent (134 patients) had been managed with the triple therapy (LABA+LAMA+ICS), 9.3 % (n=14) with LABA +ICS, and 2% (n=3) with LAMA alone.
Eleven-point nine percent (18 patients) were dependent on oxygen.

Conclusion:

This is the first study on patients with COPD in KwaZulu-Natal, South Africa. Smoking is the predominant risk factor, but occupational risk was also high in this cohort, regardless of age, gender, or race.

This study adds to the understanding of COPD etiotypes (classifications) and management trends in South Africa, highlighting the significance of managing risk factors and the continual necessity for early diagnosis and treatment.

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List of Abbreviations:

COPD: Chronic obstructive pulmonary disease
IALCH: Inkosi Albert Luthuli Central Hospital. SA:
South Africa.
BOLD: Burden of obstructive lung disease
GOLD: Global initiative for chronic obstructive lung disease
PFT: Pulmonary function testing
FEV1: Forced Expiratory Volume in 1 Second
FVC: forced Vital capacity.
DLCO: Diffusing Capacity of the Lung for Carbon MonoxideCT:
computed tomography
HRCT: High Resolution Computerized Tomography ScanCXR:
chest X-ray
mMRC: Modified Medical Research Council score
CAT: COPD Assessment test.
BMI: Body mass index
LAMA: Long-Acting Muscarinic Antagonists
LABA: Long-acting B2 agonists
ICS: inhaled corticosteroids 6MWT:
six minutes walking testUK: United
Kingdom
USA: United States of America
IHD: ischemic heart disease
HIV: human Immunodeficiency virus
PTB: pulmonary tuberculosis
SD: standard deviation
LMIC: low middle-income countries

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Part 1: The Review of Literature

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production, exacerbations) due to abnormalities of the airways and/or alveoli that cause persistent, often progressive, airflow obstruction (1).

COPD is one of the main causes of morbidity and mortality in the world (2). It is estimated that there are over 380 million cases of the disease worldwide, with approximately 3.2 million deaths annually, making it the third-leading cause of death globally.

A significant number of these cases remain undiagnosed (1, 3). The prevalence of COPD is projected to rise owing to increased exposure to risk factors and population aging (3). A recent meta-analysis of 123 COPD studies estimated that the global prevalence was 11.7% (8.4–15.0%) (3).

Chronic obstructive pulmonary disease has a prevalence rate of around 13.4% in Africa, with estimates of around 20% for South Africa (SA) (4).

The Burden of Obstructive Lung Disease (BOLD) study performed in 2005 was conducted in the township suburbs of Cape town. It found the prevalence of COPD (GOLD stage ≥2) in the greater than 40 years age group to be 22.2% in men, and in 16.7% in women, giving an overall prevalence of 19 %. This rate is notably higher than the global prevalence of approximately 10%.

Epidemiology of COPD:

The commonly identified risk factors for COPD include tobacco use, exposure to indoor and outdoor pollution and occupational exposure (5).

COPD is the third leading cause of death around the world (6) and accounted for around 544 million cases world-wide in 2017, accounting for 55.1% of chronic respiratory disease prevalence among men and 54.8% among women globally (6).

In 2015, the incidence of COPD was 174 million, with approximately 3.2 million deaths attributed to the disease (7). The prevalence of COPD in Europe ranges between 15% and 20% among adults over 40 years of age (8, 9).

Pathophysiology:

COPD results from the combined processes of peripheral airway inflammation and narrowing of the airways. This leads to airflow limitationand the destruction and loss of alveoli, terminal bronchioles, and surrounding capillary vessels and tissues, which adds to airflow limitation and leads to decreased gas transfer through airway narrowing and decreased lung recoil capacity. The extent of airflow limitation is determined by the severity of inflammation, the development of fibrosis within the airway, and the presence of secretions or exudates (7).

Reduced airflow on exhalation leads to air trapping, resulting in reduced inspiratory capacity, which may cause dyspnea on exertion and reduced exercise capacity.

Abnormalities in gas transfer occur due to reduced airflow and ventilation and because of loss of alveolar structure and the pulmonary vascular bed. Hypoxemia and hypercapnia result from impaired gas transfer and can worsen as the disease progresses (10).

Risk factors:

Cigarette smokers have a higher prevalence of respiratory symptoms and pulmonary function test (PFT) abnormalities, a higher annual rate of decline in FEV1, and a higher COPD mortality rate than non-smokers (11). The starting age, total pack-years smoked, and current smoking status are predictive of COPD morbidity and mortality (12), Other types of tobacco (e.g., pipe, cigar, water pipe) and marijuana are also risk factors for COPD. Smoking during pregnancy may predispose to asthma and COPD by decreasing lung growth and development in the fetus (13).

Occupational exposures including organic and inorganic dust, chemical agents, and fumes, are under-appreciated risk factors for COPD. They have been identified as an independent cause of COPD (14).

The population-based National Health and Nutrition Examination Survey (NHANES III) done in 2002 estimated the fraction of COPD prevalence. related to work to be 19.2% overall and 31.1% among nonsmokers (14, 15).

Air pollution such as indoor burning of biomass and fossil fuels in poorly ventilated spaces leads to remarkably high levels of indoor air pollution. Biomass exposure begins in early childhood and may continue throughout life with significant negative health effects including COPD (15).

On the other hand, outdoor air pollution, mainly from motor vehicles, factory emissions in cities, and biomass smoke is associated with loss of lung function and COPD.

Genetic factors play a role. Severe hereditary deficiency of alpha-1 antitrypsin (AATD); the gene encoding matrix metalloproteinase 12 (MMP- 12) and glutathione S-transferase have also been related to a decline in lung function and or risk of COPD (7).

Increased age, particularly 45 years and older, is associated with worse COPD symptoms and reduced physical activity. Female sex is associated with an increased risk of developing COPD (10).

Regarding lung growth and development, any factor that affects lung growth during gestation and childhood (low birth weight, respiratory infections, etc.) has the potential to increase an individual's risk of developing COPD.

Poverty is consistently associated with airflow obstruction (4), and lower socioeconomic status is associated with an increased risk of developing COPD (16).

Recent studies have increasingly established a clear link between a history of tuberculosis (TB) and an increased risk of developing COPD. TB can cause

significant lung damage, which may lead to the development or worsening of COPD. The inflammation and scarring from TB can impair lung function, contributing to the pathophysiology of COPD, which in many settings is stronger than the association between smoking and COPD (4). However, the two conditions may co-exist within an individual. The association between tuberculosis and COPD is strongest in high-incidence countries, among the young and never smokers. Post-tuberculosis bronchiectasis should be excluded as a cause of airflow limitation before the tuberculosis-associated obstruction is presumed (17, 18).

HIV infection has been shown to accelerate the onset of smoking-related emphysema (19). In addition, viral and bacterial infections may contribute to the pathogenesis and progression of COPD (20).

Clinical diagnosis:

The medical history and the physical examination are not valid for a diagnosis of COPD and the clinical presentation of COPD is nonspecific (21).

However, inquiries should focus on symptoms such as cough, sputumproduction, dyspnea (shortness of breath), wheezing, and history of exacerbations, or history of hospital admissions (22). It is crucial to assessrisk factors such as smoking history, occupational exposures, and family history.

Physical examination may reveal signs of respiratory distress, cyanosis, hyperinflation, and wheezing. In advanced cases, muscle wasting, asterixis, and peripheral edema may be seen (23).

During an exacerbation, COPD symptoms can worsen rapidly. Depending on the severity of these symptoms, the patient's condition may deteriorate over a few days and often requires additional treatment (24).

Pulmonary function testing is the basic diagnostic test for COPD. Spirometry is critical for the detection, assessment, and management of patients with COPD. It must be performed by adequately trained personsusing a spirometer of approved standard and quality that is calibrated frequently (25).

Measurements used in the diagnosis of COPD are pre- and post-bronchodilator FEV1, FVC, and FEV1/FVC%. A ratio of less than 70% confirms COPD (7), Measurement of diffusing capacity (DLCO) provides information on the functional impact of emphysema in COPD andis often helpful in patients with breathlessness that may seem out of proportion to the degree of airflow limitation (25, 26).

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has categorized the severity of airflow limitation in COPD into four groups based on specific cut off points for forced expiratory ratio (FER). The FER is defined as FEV1/FVC <0.7 after bronchodilator use, and the FEV1 categories are as follows: mild (≥80% of predicted), moderate (50-79% of predicted), severe (30-49% of predicted), and very severe (<30% of predicted) (1).

A chest x-ray is recommended at the time of diagnosis of COPD. It may show evidence of hyperinflation, but a normal chest x-ray does not exclude the diagnosis (27).

Computed tomography (CT) of the chest is not routinely recommended except for the detection of bronchiectasis and COPD patients who meet the criteria for lung cancer risk assessment. It may show the presence of emphysema or bullae. However, CT scanning may be helpful in the differential diagnosis where concomitant diseases are present (26).

In chronic bronchitis, CT findings may include bronchial wall thickening, fibrotic changes, and enlarged vessels (28).

Emphysema is diagnosed by alveolar septal destruction and airspace enlargement, the distribution of these regions of low attenuation and thedegree to which they involve the secondary pulmonary lobule can be characterized as centrilobular, pan lobular, and para-septal emphysema Centrilobular emphysema is predominantly seen in the upper lobes with pan lobular emphysema predominating in the lower lobes. Para septal emphysema tends to occur near lung fissures and pleura (29).

The formation of bullae may lead to compression of mediastinal structures, while rupture of pleural blebs may produce spontaneous pneumothorax and pneumomediastinum (30).

Assessment and Management:

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy has been providing recommendations for the prevention, diagnosis, treatment, and follow-up of patients with COPD since 1998. In the 2023 report, they introduced the GOLD ABE tool (31), which replaced the old ABCD assessment tool created in 2011. The A and B groups remain unchanged, but the C and D groups have been combined into a single E group.

Group A: patients with 0–1 moderate exacerbation in the previous year and mMRC 0–1, CAT <10.

Group B: patients with 0–1 moderate exacerbation in the previous year and mMRC ≥2 and/or CAT ≥10.

Group E: patients with ≥2 moderate exacerbations or ≥1 leading to hospitalization in the previous year, irrespective of the symptom burden (26).

The severity of the symptoms was evaluated using the modified British Medical Research Council (mMRC) questionnaire (and the COPD Assessment Test (CAT) (16, 26). The mMRC questionnaire assesses the degree of breathlessness on a scale of 0-4 with 4 being the most severe.

The COPD Assessment Test (CAT) provides a score on eight functional parameters to measure the impact of the disease on a patient's daily life (27), and exacerbation history in the past twelve months as criteria to use to grade severity. Both are recommended to guide appropriate pharmacological treatment.

Management:

As there is no cure for COPD, the primary goals of treatment are to slow the progression of symptoms, improve quality of life, reduce exacerbation rates,

decrease the risk of complications, and decrease mortality (7).

Non-pharmacological approaches:

1 -Smoking Cessation

This is the most crucial intervention to slow disease progression. The patients who quit smoking within two years after COPD diagnosis have lower risks of all-cause and cardiovascular mortality relative to persistentsmokers (32). This can be facilitated by counseling, nicotine replacement therapy, or another pharmacotherapy as needed.

2- Pulmonary Rehabilitation

In COPD patients, pulmonary rehabilitation has been demonstrated to provide beneficial effects on dyspnea, improvement in muscle strength and endurance, improvement of psychological status, reduction of hospital admissions, and quality of life (33).

3- Oxygen Therapy

Supplemental oxygen should be used for patients with:

- Severe hypoxemia (PaO_2 < 55 mmHg or SaO_2 < 88% at rest).
- Resting PaO_2 < 59 mmHg or SaO_2 89% or less if there is evidence of cor pulmonale, right heart failure, or polycythemia (hematocrit greater than 55%) at rest (34).

4- Vaccinations

Vaccines are effective preventive measures to reduce respiratory infections and exacerbations in COPD patients. It is important to administer the pneumococcal, influenza, and SARS-CoV-2 vaccines (35).

5- Nutritional Support

Malnutrition and weight loss are common in advanced COPD. Patients with COPD must have a healthy diet regimen that includes antioxidants, anti-inflammatory foods like fruits and vegetables, other sources of dietary fiber, vitamins D and E, and avoidance of unhealthy fats and simple carbohydrates (36).

Medications:

The patients must be educated on inhaler techniques, symptom recognition, and self-management strategies.

Bronchodilators are the mainstay of treating COPD and include inhaled beta-2 agonists and muscarinic antagonists. Oral theophylline additionally has some bronchodilator effect. Individuals vary in responsiveness to each, and combinations may have additive effects (27).

For the initial treatment of patients at minimal risk of exacerbation (0–1 prior moderate exacerbation), the GOLD 2023 recommends starting with a long-acting β2-agonist (LABA) or a long-acting muscarinic antagonist (LAMA) for those with low dyspnea and health status impairment scores (mMRC 0–1, CAT < 10). For

those with higher dyspnea and health status impairment scores, the recommendation is to start with a LAMA + LABA combined bronchodilator (26)

For the initial treatment of patients at high risk of exacerbation (≥ 2 moderate or 1 severe exacerbation), GOLD recommends starting with a LAMA + LABA combined bronchodilator, irrespective of the degree of dyspnea and health status impairment scores (GOLD E patients), except for those with blood eosinophils ≥300 cells/μL, where a LAMA + LABA + ICS triple inhaler could be considered.

For the follow-up treatment of those patients with a substantial risk of exacerbations, GOLD recommends that treatment be increased to a LAMA + LABA + ICS triple inhaler only if blood eosinophils ≥100. Otherwise, roflumilast or azithromycin should be added to the LAMA + LABA combined bronchodilator. Commence treatment in symptomatic patients with an inhaled short-acting bronchodilator on a PRN basis (mild COPD/GOLD A). Thereafter, increase treatment stepwise to include inhaled long-acting bronchodilators, slow-release theophylline (moderate COPD/GOLD B), and ICS in those with more severe symptoms and exacerbations (severe COPD/GOLD D) (1, 26).

Comorbidities:

Chronic Obstructive Pulmonary Disease (COPD) frequently occurs withvarious comorbidities, which are additional health conditions that co-existalongside the primary disease. These comorbidities can significantly impact the management and prognosis of COPD patients.

Cardiovascular Disease

COPD patients have a significantly higher prevalence of cardiovascular disease (CVD) compared to those without COPD (59.6% vs. 28.4%) (37). This includes conditions such as coronary artery disease, with estimates of ischemic heart disease (IHD) prevalence in COPD patients ranging from less than 20% to over 60%. Heart failure frequently coexists with COPD, with prevalence estimates ranging from 10% to 30% (38). The association between COPD and CVD is influenced by smoking, inflammation, and shared risk factors.

Lung Cancer

COPD patients have a higher risk of developing lung cancer, especially ifthey are smokers. The lifetime risk of developing lung cancer is 17.2% formales and 11.6% for females in smokers compared with 1.3% and 1.4% respectively for non-smokers (39). Chronic inflammation and impaired lung function play roles in this association.

Osteoporosis

COPD patients are at increased risk of osteoporosis. Various risk factors explaining the prevalence of osteoporosis in COPD patients include aging, smoking, physical inactivity, systemic inflammation, malnutrition, low body-mass index (BMI), hypogonadism, vitamin D deficiency, and the frequent use of corticosteroids (40).

Anxiety and Depression

COPD patients frequently experience anxiety and depression, which canworsen COPD symptoms and decrease quality of life. The frequency of depression varies greatly among patients with stable COPD in a primary care setting ranging, from 10% to 57%, while the prevalence of anxiety varies widely, between 7% and 50% (41).

Metabolic Syndrome and Diabetes

There is a higher prevalence of metabolic syndrome and diabetes in COPD patients, likely due to shared risk factors such as smoking, inflammation, and physical inactivity.

These comorbidities often necessitate a comprehensive approach tomanaging COPD patients, addressing not only respiratory symptoms butalso managing associated conditions to optimize patient outcomes. Regular monitoring and appropriate management of these comorbidities are crucial in the overall care of COPD patients.

Prognosis:

The prognosis for individuals with Chronic Obstructive Pulmonary Disease (COPD) can vary widely depending on several factors.

The BODE index, a simple multidimensional grading system, is a prognostic index for predicting the risk of death from any cause and respiratory causes among patients with COPD (42).

It utilizes four factors that predict the risk of death: the body-mass index (B), the degree of airflow obstruction (O) and functional dyspnea (D), and exercise capacity (E) as assessed by the six-minute-walk test.

The BODE Index is a simple multi-dimensional grading system that scores the systemic components of COPD.

The BODE Index's components:

- Body mass index BMI (kg.m-2) if > 21
- Respiratory function using FEV1% predicted.
- Dyspnea: using MMRC score 0-5
- Exercise tolerance: using 6 MWT.

These components are graded on a simple 10-point scale, with the more severe the symptoms the higher the score.

The BODE Index is a better predictor of mortality than FEV1 alone and can be useful in predicting readmission to hospital (43).

The BODE index is sensitive to change following pulmonary rehabilitation, with a reduction of 1 point (or more) in the score indicating a 'responder' to the program (42).

Other prognostic factorsAge and Gender

Older age and male gender are associated with a poorer prognosis in COPD, although individual factors such as disease severity and comorbidities also play significant roles (44).

Overall, while COPD is a progressive and incurable disease, prognosis can vary widely depending on multiple factors. Early diagnosis,appropriate management, smoking cessation, regular monitoring, and lifestyle modifications can all help improve outcomes and quality of life forindividuals living with COPD. However, it is essential to recognize that COPD is a chronic condition that requires ongoing management and support.

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Part 2: A submission readymanuscript.

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Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.

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Abstract:

Background: The epidemiological overview of Chronic Obstructive Pulmonary Disease (COPD) reflects its widespread impact, with a rising prevalence globally. Smoking is still the primary risk factor, although non-smoking-related causes, such as occupational exposures andenvironmental causes are increasingly recognized. As a progressive and irreversible condition, COPD presents with symptoms such as shortness of breath, chronic cough, and sputum production, greatly impacting patients' quality of life.

Aims: To assess the clinical presentation, lung function, radiological findings, and comorbidities in patients with chronic obstructive pulmonary disease (COPD) managed by the Respiratory Clinic at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal. at the initial evaluation and after a two-year follow-up of pulmonary function tests, with the aim of determining the impact of these factors on disease progression, treatment response, and overall patient outcomes.

Methods: We conducted a retrospective electronic chart review of patients with COPD who attended Inkosi Albert Luthuli Central Hospital Pulmonology clinic between January 2013 and December 2019. Demographics, clinical data, lung function testing and radiological imaging were captured retrospectively from medical records. Demographic data included age, gender, and race. Clinical data captured were presenting symptoms, pre-existing medical conditions, underlying co-morbidities,and modality of treatment. Imaging included chest X Ray and HRCT chest.

Results:

There were 151 subjects (male =76.2% n= 115). Most were aged 50-69 years (72.2% n=109). Patients of Indian descent comprised (37.7%; n=57), followed by whites (27.2%; n=41), then Black African (25.2%; n=38). The most common risk factor was smoking (97.4 %; n=147), followed by occupational hazard (45.7%; n= 69). 7.3 % were HIV positive.

The average FEV1% predicted for the patients was 44.17% (SD 18.07), with a mean FVC of 1.36 L (SD 0.8) and an average FEV1/FVC ratio of 32.15 (SD 14.9).

The main finding on CT chest was fibrosis (36.3%.). Thirty-two-point three percent of the patients had pan lobular emphysema. and 30.3% had centrilobular emphysema. Eighty-eight-point seven percent (134 patients) had been managed with the triple therapy (LABA+LAMA+ICS), 9.3 % (n=14) with LABA +ICS, and 2% (n=3) with LAMA alone.

Eleven-point nine percent (18 patients) were dependent on oxygen.

Conclusion: This is the first study on patients with COPD in KwaZulu- Natal, South Africa. Smoking is the predominant risk factor, but occupational risk was also high in this cohort., regardless of age, gender, or race.

This study contributes to the data on COPD classifications and management trends in South Africa and emphasizes the importance of controlling the risk factors, as well as the ongoing need for early diagnosis and treatment.

Material and Methods:

We conducted a retrospective electronic chart review of patients with COPD who attended the Inkosi Albert Luthuli Central Hospital Pulmonology clinic between January 2013 and December 2019.

This is a referral clinic accepting patients throughout the KwaZulu-Natal province. The study excluded patients where electronic data could not beretrieved due to technical limitations.

Demographics, clinical data, lung function testing and radiological imaging were captured retrospectively from medical records. Demographic data included age, gender, and race. Clinical data captured were presenting symptoms, pre-existing medical conditions, underlying co-morbidities, and modality of treatment. Imaging included chest X Ray and HRCT chest.

Ethical approval was granted by university of KwaZulu-Natal's Human Research Ethics Committee (ref: BREC00005794/2023) and the KwaZulu-Natal department of health (ref no KZ202308-018)

Statistical analysis:

Demographic data with a normal distribution is reported as means with standard deviation (SD).

The change in FEV1 at the initial and final visit was calculated. ANOVA was used to examine demographic and other risk factors associated withmean change in FEV1. The change in FEV1 was also categorized as an increase or decrease. Factors associated with the percentage of patientswith an increased FEV1 were examined using Chi square tests or Fisher'sexact test.

Statistical significance was regarded as a p-value <0.05 unless otherwisestated.

Stata v17 statistical software was used for statistical analysis.

Demographic details of the study population: Table 1

We collected data from 151 subjects who met the inclusion criteria for our study, (male = 115). Most were aged 50-69 years (72.2%, n=109). The other age groups were 70-90 years (17.2%, n=26) and less than 50 years(10.6 %, n = 16). Patients of Indian descent comprised 37.7% (n=57), followed by whites (27.2%, n=41), then Black African (25.2%; n=38). Table 1

The most common risk factor was cigarette smoking (97.4 %; n=147, with 42.9% of smokers having a history of more than 40 pack-years.

The second most common risk factor was occupational exposure (45.7%;n= 69). Of the occupational exposures, mining was the most common with34.8%, followed by construction workers and chemical workers, each with24.6%. Workers in fabric and cotton factories constituted 15.9% of the study population, while 6% (n=9) had a history of exposure to biomass fuel. Additionally, 28.5% (n=43) of patients had a history of pulmonary tuberculosis, and 7.3% were HIV positive, with all HIV-positive individuals receiving antiretroviral therapy.

Clinical data:

Exertional dyspnea had been recorded at the initial visit using the mMRCscore. 3 patients (2%) had a score of 1; 66 patients (43.7%) scored 2; 57 patients (37.7%) scored 3 and 25 patients (16.6%) had a score of 4.

Clubbing was found in 23.5 % (n=35) of the cases.

Table 1: Demographic details of the study population.

Age	Number	%
30-49	16	10.6%
50-69	109	72.2%
70-90	26	17.2%
Sex		
Male	115	76.2%
Female	36	23.8%
Race		
Black African	38	25.2%
Colored	15	9.9%
Indian	57	37.7%
White	41	27.2%

Pulmonary function tests: Table 2

121 patients had pulmonary function testing for the first visit and on the 2years follow-up visit. The GOLD criteria for the diagnosis of COPD (fixed ratio FEV1/FVC < 0.70) were met in 92.6% (n=112) of the patients.64.5%(n=78) had a mixed pattern on pulmonary function test, and 28 % (n=34) had an obstructive pattern on PFT.

The GOLD score was used to grade the severity of the airflow limitation according to FEV1%P. Of the participants, 30.5% (n=37) were classified with GOLD score 2, 35.5% (n=43) with GOLD score 3, 31.5% (n=38) with GOLD score 4, and 2.5% (n=3) with GOLD score 1.

The overall mean forced expiratory volume in one second (FEV1) at first presentation was 1.14 ± 0.54 L. The FEV1 mean after 2 years declined to 1.04 ± 0.47 L. Bronchodilator responsiveness (the increase in FEV1 ≥12% and 200 mL after 15 min of inhaling 200 µg of salbutamol) was present in9.3% (n=14).

As the decline in (FEV1) is one of the most important outcome measuresto assess disease progression, we calculated the difference in FEV1 at presentation with FEV1 after 2 years (FEV1-diff) and compared that with the risk factors for COPD. 67.8 % (n= 82) had a decline in FEV1 after 2 years.

The rate of decline in FEV1 over 2 years was highest in the age group 30 - 49 years with a mean of - 0.2 ± 0.38L. This was significantly higher thanthe > 70 years age group (mean decline = 0.10 ± 0.17L, p= 0.03). Patients with no occupational risk factors were more likely to show an increase in FEV1 after 2 years (p = 0.02).
There was a correlation between higher initial lung function and a more significant decline in FEV1 over time. A decline of 70mls occurred in those with FEV1%p > 80, while individuals with an initial FEV1%p less than 30 experienced a much smaller decline of only 2mls over the same period (p=0.001).

We examined the effect of Body Mass Index (BMI) on FEV1 -diff (independent of

height and age). We found that the participants who wereoverweight and obese had a better FEV1 at presentation, with a mean of
1.29 L and 1.32 L respectively, compared with an FEV1 mean of 0.81 L inpatients with a low BMI.

Patients with a higher BMI also had a greater proportion who had an improvement in FEV1 over 2 years. Specifically, 54.5% of patients with a BMI of 25-29.9 and 46.7% of those with a BMI greater than 30 experienced an improvement in FEV1.This was significantly less than the <18.5 BMI group in which 13.6% had an improvement (p=0.01).

Table 2:

Detailed data analysis of decline in FEV1 compared with the risk factors:

-

		FEV1		FEV1_2yr		FEV1 - diff		p value
	n	mean	SD	mean	SD	mean	SD	
	121	1,14	0,54	1,04	0,47	-0,10	0,27	
Age group								
30-49	14	1,07	0,75	0,87	0,45	-0,20	0,38	0,08
50-69	86	1,18	0,54	1,07	0,5	-0,11	0,27	
70-90	21	1,03	0,33	1,04	0,35	0,00	0,17	
Gender								
F	31	0,96	0,32	0,89	0,28	-0,07	0,18	0,37
M	90	1,21	0,58	1,09	0,52	-0,12	0,3	
Race								
A	27	1,08	0,46	0,93	0,43	-0,15	0,24	0,48
C	14	1,07	0,46	0,91	0,34	-0,16	0,32	
I	47	1,16	0,59	1,10	0,56	-0,06	0,24	
W	33	1,20	0,57	1,10	0,41	-0,10	0,32	
Smoking								
N	3	1,44	0,32	1,27	0,30	-0,17	0,03	0,67
Y	118	1,14	0,54	1,03	0,48	-0,11	0,28	
Smoking Cannabis								
N	113	1,16	0,54	1,07	0,47	-0,09	0,28	0,42
Y	8	0,86	0,40	0,68	0,32	-0,18	0,17	
Biomass								
N	113	1,15	0,55	1,05	0,48	-0,10	0,28	0,99
Y	8	1,0	0,41	0,9	0,35	-0,10	0,08	
Occupational risk								
N	65	1,21	0,58	1,12	0,49	-0,09	0,30	0,6
Y	56	1,07	0,48	0,95	0,44	-0,12	0,24	
IHD								
N	106	1,14	0,54	1,02	0,46	-0,12	0,27	0,048
Y	15	1,16	0,53	1,19	0,53	0,03	0,25	
RVD state								
N	112	1,15	0,53	1,05	0,47	-0,10	0,27	0,51
Y	9	1,11	0,61	0,95	0,54	-0,16	0,37	
PTB								
N	87	1,17	0,55	1,08	0,48	-0,09	0,28	0,53
Y	33	1,09	0,50	0,96	0,45	-0,13	0,25	
BMI								
<18.5	22	0,81	0,36	0,66	0,22	-0,15	0,22	0,29
18.5-24.9	62	1,17	0,53	1,04	0,44	-0,13	0,27	
25.0-29.9	22	1,32	0,59	1,29	0,58	-0,03	0,33	
>=30	15	1,29	0,52	1,25	0,37	-0,04	0,26	
FEV1P								
>80	3	2,4	0,92	1,7	0,52	-0,70	0,57	< 0.001
50-79	37	1,64	0,4	1,47	0,41	-0,17	0,31	

30-49	43	1,05	0,26	0,97	0,33	-0,08	0,24	
<30	38	0,67	0,19	0,65	0,21	-0,02	0,16	
Responsiveness								
N	109	1,13	0,55	1,04	0,49	-0,09	0,28	0,2
Y	12	1,24	0,37	1,04	0,35	-0,20	0,25	

Radiology:

Most of the chest x rays used in the assessment of the COPD patients had been reported electronically as they had been done at the base hospital. A chest x ray had been reported in 85 patients, with 78.8% reported as hyperinflation.

Ninety-nine patients had HRCT reports available. Emphysema was identified in 78 of these patients. Among them, 32.3% had pan lobular emphysema, 30.3% had centrilobular emphysema, and 10.6% had para-septal emphysema.

Bronchial wall thickening/ fibrosis was reported in 36.3% of patients. Bullae was described in 6.6% of cases. 18 patients had a lung mass on CT scan, with12 of them diagnosed as malignancy.

The main comorbidity amongst these patients was ischemic heart disease(13.2%, n=16). Pulmonary hypertension was observed in 8.2% (n=10) of the patients.

Treatment:

Most patients were managed with the triple regimen, LABA+LAMA+ ICS (88.7 %, n=134). 9.3%(n=14) were on LAMA monotherapy, and 2% on dual therapy (LABA+ICS).

Theophylline was prescribed in 31 patients, and 11.9% (n=18) were on long term domiciliary oxygen therapy (LTOT). At the 2-year follow-up, 61% (n=92) of patients had received an influenza vaccine.

Discussion:

COPD is a slow progressive disease with no cure. This study aimed to assess the clinical status, treatment and outcomes of patients seen at a tertiary hospital, IALCH, in Durban, KwaZulu Natal. at the initial evaluation and after a two-year follow-up of pulmonary function tests, with the aim of determining the impact of these factors on disease progression, treatment response, and overall patient outcomes.

In this retrospective study, we evaluated COPD patients referred to the respiratory clinic from different hospitals in the province. These patients had poorly controlled or severe COPD.

Seventy-two-point two percent of the patient population was within the age range of 50 to 69 years. This is similar to studies done in developing countries like Türkiye and India (1, 2), but in contrast to a study done in UK by *Landis et al*, where most patients were > 70 years of age (58.1%).

Most of our patients were males (76.2%), as reported in many studies (1- 3). The study done by *Abdool-Gaffar et al*. states that COPD prevalence is greateramong men and reflects previous smoking patterns. The prevalence is now equalizing in developed countries (4).

In our study, we found that patients of Indian descent constituted the highest proportion, followed by whites, then Black African. This finding is not in line with the demographics of KwaZulu Natal and South Africa, in which Black Africans comprise more than 80% of the total population. However, a study done by *Alexander et al*. in London found that Black people in London were half as likely as whites to have COPD after adjusting for lower smoking rates in Black people (5).

The GOLD 2023 report emphasizes that cigarette smokers have a higherprevalence of symptoms and greater decline in FEV1 than non-smokers (6). In our cohort we highlight that smoking was the most prevalent risk factor for COPD and a large proportion were heavy smokers, as 42.9% smoked more than 40 pack years.

Similar findings were made in many other studies like with *Brianet* al. in the USA (7), where they found the majority (96.2%) of the patients had a history of smoking. According to Fang et al (8), smoking is the most important risk factor for the high incidence of COPD in China. Conversely, Salvi et al. found that an estimated 25-45% of patients with COPD have never smoked; especially in developing countries (9).

The second most common risk factor in our study was occupational exposure. Interestingly, most of these patients had been smokers, and just one patient was not a smoker. *Blanc et al*. found that those with combined smoking and occupational risk exposure had a significantly higher risk of developing respiratory diseases compared to those with only one of these risk factors by a 14-fold increased risk of COPD (10). A study done by Esther et al. (11), in Spain found that patients who had worked in a job with high exposure to mineral or other dust, gas, or fumes were associated with an FEV1 of < 30% of predicted. This may explain the higher number of patients with occupational exposure seen at our clinic, which was a referral center for severe disease. The American Thoracic Society reported that about 15% of COPD cases might be attributable to workplace exposure (12).

In the current study, 6% of patients had a history of biomass fuel use. This may not include exposure to indoor air pollution, where poorly functioning stoves are used in insufficiently ventilated rooms. It also does not include outdoor pollution from motor vehicles. Exposure to biomass smoke might be the biggest risk factor for COPD globally (4).

In our study, we found 28.5%(n=43) of patients had a history of previous pulmonary tuberculosis. This is similar to a study by Aggarwal et al. which found that TB-associated COPD constituted a sizable proportion of COPD patients (32.4%) (13)

Finger clubbing is not typically associated with COPD. However, it can indicate the presence of another lung condition that may occur alongside COPD, such as lung cancer, pulmonary tuberculosis (PTB), or bronchiectasis. Our study found a high prevalence of clubbing, with 43% of patients with PTB exhibiting this symptom. Several case reports have documented clubbing in TB patients. Research from TB-endemic regions has reported a 30% prevalence of clubbing among smear-positive TB patients (14,15).

Despite the high prevalence of HIV in South Africa and the risk of up to 25% of HIV-infected people having COPD (16), we found 7.3% of patient's HIV reactive. A likely explanation is the underdiagnosis of COPD in HIV patients.

As our study was in a tertiary hospital, the majority of COPD patients had advanced stages of the disease, with a significant proportion in GOLD stage 3 (35.5%) and GOLD stage 4 (31.5%).

As the decline in (FEV1) is one of the most important outcome measures to assess disease progression, we calculated the difference in FEV1 at presentation vs FEV1 at the 2-year follow-up, and calculated risk factors for this decline (FEV1-diff) (17).

The natural history of COPD often involves a decline in FEV1 during adulthood. In normal middle-aged adults, the rate of decline in FEV1 is typically around 30 mL per year in men and 25 mL per year in women. However, this rate of decline can increase in current smokers, patients with bronchodilator responsiveness, and those with emphysema (18).

In our cohort the overall mean annual post bronchodilator FEV1 decline was 100ml ± 47ml. However, a decline occurred in just 67.8 % (n= 82). This rate of decline exceeds that reported by *Jorgen et al* (18), where the means rate of decline in FEV1 was 33±2 mL·year 1. This very significant difference in rate of decline could be multifactorial. South Africa is a LMIC (low middle-income countries) and socioeconomic factors such as poverty, unemployment, poor nutrition, poor housing, recurrent chest infections could be playing a major in this rapid decline.

A study conducted by *Rehman et al* in 2021 (19), found the mean annual decline in FEV1 was 27.35 (11.34) ml/year, with 30.27% of patients having a more than 60 ml/year decline. Another study reported a mean decline of 28 ml/year in all patients, with a decline of > 66 ml/year in FEV1 in 58.7% of the patients (20).

In our cohort, the decline in FEV1 in 2 years was greatest in the age group 30 - 49 years. This contradicts the normal progression of the disease, with longer exposure to risk factors leading to an increased rate of decline, *Kim et al*. suggests that the annual decline in FEV1 in COPD patients is accelerated in older patients compared to younger ones (21).

A previous history of PTB in 64.3% who were within the age group 30-49 years may explain the higher decline in FEV1. A study done in Korea by *Rhee et al*. observed the decline in FEV1 during and after PTB treatment, and found a mean FEV1 decline of 38.2±8 mL/year in patients with PTB was higher compared to a mean FEV1 decline of 33±2 mL/year without PTB (22). This highlights the importance of early screening and management for COPD in patients with PTB.

A significant finding was that patients with no occupational risk factors are more likely to show an increase in FEV1 after 2 years (P = 0.02). *Möhner et al.* (23), they found that cumulative exposure was linearly negatively correlated with FEV1%. The higher the cumulative exposure to occupational risk factors, the worse the patient's lung function was.

In our study overweight and obese participants had a higher FEV1 at presentation, with mean 1.29L and 1.32L respectively, compared to patients with low BMI (0.81 L). This is similar to a study done in China by *Tang et al*. which concluded being underweight is a risk factor for impaired lung function in all participants, and severe obesity was a risk factor for FEV1 decline (24, 25).

A study done in Vermont university in 2015 recommended CT scan as screening for COPD, as they found spirometry missed 10.4% of patients with clinical COPD who had significant emphysema on chest CT scan. (26). Our study reported emphysema in 78.7% of patients, which was more than one study done at the University of Leicester, where emphysema occurred in 67 % of cases, and bronchial wall thickening was found in 27% of subjects (27). Another important use for CT scan is screening for

lung masses. In our cohort a lung mass was noted in eighteen patients, twelve of which were diagnosed as malignancy.

GOLD and the South African COPD guideline recommend smoking cessation as the most crucial intervention to slow disease progression.

Triple inhaler therapy was used for 85% of our patients. This is supported by the IMPACT study, which recommends using triple Therapy in severe COPD patients to increase FEV1, reduce exacerbation frequency and improve symptoms (28).

This is also recommended by GOLD 2024 where it is the only pharmacotherapy agent that reduces mortality for symptomatic patients with a history of multiple exacerbations (6).

Long-acting muscarinic antagonists (LAMA) or long-acting beta-2 agonists (LABA) are the mainstay of pharmacotherapy as bronchodilators for mild and moderate COPD 4(6). There was no LABA use as monotherapy in our study, and this is in keeping with some studies showing a greater effect on exacerbation rates for LAMA compared to LABA treatment. However, the use of LAMA as monotherapy had been seen in just 9.3% of cases (6, 29).
The use of the LABA+ICS combination had been recommended in GOLD guidelines 2013 for Group C or D to improve lung function and health status in patients with 2 or more exacerbations and moderate to severe COPD. However, we had just 2% of patients treated with this combination.

Limitations of this study:

This study is an electronic retrospective review of data. It has a small sample size at a single center with missing data, which made it difficult to determine any associations or lack thereof. There is the possibility of overestimation as the study was conducted at a tertiary hospital in a specialized clinic, which may have resulted in referral bias. This is not anaccurate estimation of all patients with COPD in KZN, as the mild cases would not have been referred. Another limitation is the use of the GOLD strategy as the primary reference for spirometric detection and staging of COPD, rather than the ERS/ATS standards, which reflects the practices at IALCH.

Conclusion and recommendation:

This is the first study on patients with COPD in KwaZulu-Natal, South Africa. Smoking is the predominant risk factor, but occupational risk was also high in this cohort, regardless of age, gender, or race. This study contributes to the data on COPD taxonomy and management trends in South Africa and emphasizes the importance of controlling the risk factors, as well as the ongoing need for early diagnosis and treatment.

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Appendix 1: The final Study Protocol:

The final Study Protocol

Title of study

Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.

Student: Dr Sadaldin Mostafa Abokil
Student No: 210556904

Supervisor: Dr Zaid Hoosen
Co-Supervisor: Dr Mohammed Mitha
Co-Supervisor: Prof Kennedy Nyamande

2.2 Identify the problem that is motivating your research.

Chronic obstructive pulmonary disease (COPD) is one of the main causes of morbidityand mortality in the world. It is estimated that there are currently over 380 million casesin the world, of which about 3.2 million die each year, making it the third-leading causeof death worldwide. As a progressive and irreversible condition, COPD manifests through symptoms like dyspnea, chronic cough, and sputum production, significantly affecting patients' quality of life.

2.3 What is the research question or the hypothesis?

Chronic obstructive pulmonary disease demographic records, disease spectrum,

radiological findings and clinical features and outcome in Inkosi Albert Luthuli central Hospital

In all patients with severe COPD managed by the Respiratory clinic at IALCH:

- ❖ Symptoms are present for at least 1 year before the diagnosis is made.
- ❖ The rate of decline in pulmonary function is the same as in other countries.
- ❖ The majority of patients have established pulmonary hypertension at the timeof presentation.
- ❖ Risk for deterioration includes smoking pack years, number of exacerbations,male gender, and comorbidities.

The aim of this study?

To assess the clinical presentation, lung function, radiological findings, and comorbidities in patients with chronic obstructive pulmonary disease (COPD) managed by the Respiratory Clinic at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal, at the initial evaluation and after a two-year follow-up of pulmonary function tests, with the aim of determining the impact of these factors on disease progression, treatment response, and overall patient outcomes.

The objectives of the study.

To describe the radiological, and echocardiogram parameters at baseline.
To describe lung function parameters at baseline, and at 12 and 24 months afterpresentation.
To assess symptoms, signs, and severity at the time of presentation.To determine the time to diagnosis.
To examine the demographic profile of the study cohort.
To assess the outcomes of different management modalities.
To determine the association with co-morbidities including (HIV, diabetes mellitus, andHypertension).
To determine risk factors for severity at presentation.
To determine risk factors for the decline in FEV1 over 2 years.

Background and Literature review:

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung conditioncharacterized by chronic respiratory symptoms (dyspnea, cough, sputum production,

exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction (1) COPD is one of the main causes of morbidity and mortality in the world (2). It isestimated that there are currently over 380 million cases in the world, of which about 3.2 million die each year, making it the third-leading cause of death worldwide, a significant proportion of whom are undiagnosed (1,3). The prevalence of COPD is projected to rise owing to increased exposure to risk factors and population aging (3).A recent meta-analysis of 123 COPD studies estimated that the global prevalence was11.7% (8.4–15.0%) (3).
The chronic obstructive pulmonary disease has a prevalence rate of around 13.4% inAfrica, with estimates of around 20% for South Africa (SA) (4)

Risk factors:
Cigarette smokers have a higher prevalence of respiratory symptoms and pulmonary function test (PFT) abnormalities, a most annual decline in FEV1, and a most mortality rate from COPD compared to non-smokers. The starting age, total pack-years smoked, and current smoking status are predictive of COPD morbidity and mortality (5).
Occupational exposures including organic and inorganic dust, chemical agents, and fumes, are under-appreciated risk factors for COPD. It has been identified as an independent cause of COPD (6).
Air pollution such as indoor burning of biomass and fossil fuels in poorly ventilated spaces leads to very high levels of indoor air pollution. Biomass exposure begins in early childhood and may continue throughout life with significant negative health effects including COPD (7). On the other hand, outdoor air pollution, mainly from motorvehicles, factory emissions in cities, and biomass smoke is associated with loss of lung function.
Genetic factors play a role. Severe hereditary deficiency of alpha-1 antitrypsin (AATD);the gene encoding matrix metalloproteinase 12 (MMP-12) and glutathione S- transferase have also been related to a decline in lung function16 or risk of COPD. (1,8)
Age and sex: increase age, 45 years old and over were more likely to have worse COPD symptoms and less physically active, and the female sex had increased COPD risk. (1,9)
Socioeconomic status: Poverty is consistently associated with airflow obstruction (4),

and lower socioeconomic status is associated with an increased risk of developing COPD. (10)

Infections: There is now unequivocal evidence of the association between previous tuberculosis and COPD, which in many settings is stronger than the association between smoking and COPD. (4).

HIV infection has been shown to accelerate the onset of smoking-related emphysema (11).In addition, viral and bacterial infections may contribute to the pathogenesis and progression of COPD (12).

Pulmonary function testing: Spirometry is critical for the detection, assessment, and management of patients with COPD. It must be performed by adequately trained persons using a spirometer of approved standard and quality that is calibratedfrequently (13). Measurements used in the diagnosis of COPD are pre- and post-bronchodilator FEV1, FVC, and FEV1/FVC%. Less than 70% confirm COPD. (1, 8) Chest Radiography: A chest x-ray is recommended at the time of diagnosis of COPD.It may show evidence of hyperinflation, but a normal chest x-ray does not exclude thediagnosis.

Computed tomography (CT) of the chest is not routinely recommended except for the detection of bronchiectasis and COPD patients that meet the criteria for lung cancer risk assessment or identifying the presence of emphysema.

The primary goals of treatment are to control symptoms, improve the quality of life, and reduce exacerbations and mortality. The non-pharmacological approach includessmoking cessation and pulmonary rehabilitation.

Annual influenza vaccination is recommended for all patients with COPD Bronchodilators are the mainstay of the treatment of COPD and include inhaled beta-2 agonists and muscarinic antagonists. Oral theophylline additionally has some bronchodilator effect. Individuals vary in their responsiveness to each, andcombinations may have additive effects (14). Commence treatment in symptomatic patients with an inhaled short-acting bronchodilator on a PRN basis (mild COPD/GOLD A). Thereafter, increase treatment stepwise to include inhaled long- acting bronchodilators, slow-release theophylline (moderate COPD/GOLD B) and ICSin those with more severe symptoms and exacerbations (severe COPD/GOLD D)

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Research design: Retrospective chart review.

Study sample: All adult patients diagnosed with COPD managed by the departmentof pulmonology at lALCH during the study period will be included in the study. The projected sample size is approximately 120 patients.

Sampling technique: Electronic chart review.

Sampling strategy: The study population will include all adult patients aged 18 years and older who were diagnosed with COPD in the pulmonology department between January 1, 2013, and December 31, 2019.

Variables: Confounding factors that may affect the study outcomes include all these variables:

A) Demographic data:
Age, Gender, Race

B) History of:
Cigarette Smoking
Cannabis smoking
Smoking pack-year smoking
Number of Hospital Admission
History of Pulmonary TB
HIV statues
HIV patients on Antiretroviral
Exacerbation
Occupational history
Exposure to biomass fuel
Vaccination

C) Clinical data:
mMRC score / NYHA score
weight, height, Body mass index
Clubbing
Signs of pulmonary hypertension
Oxygen saturation
Six-minute Walk test distance

D) Lung function parameters:
Forced Vital Capacity (FVC)
Forced expiratory Volume in 1 second (FEV1)
FEV1/FVC
Total Lung Capacity (TLC)
Diffusion Capacity for carbon monoxide (DLCO)
Peak expiratory flow
Degree of reversibility

E) Radiological Parameters: Chest X-ray and CT scan

F) Echocardiogram Parameters
Ejection Fraction (EF)
Pulmonary arterial systolic pressure (PAS)
Right ventricle dilatation

G) Medication
LABA
LAMA
ICS

Inclusion criteria

All adult patients diagnosed with COPD managed by the department of pulmonologyat IALCH during the study period will be included in the study.
COPD diagnosis is based on the GOLD definition.

Exclusion criteria

Cases where electronic data sets cannot be retrieved.
Patients with COPD/Asthma overlap
Patients in whom the diagnosis of COPD is doubtful.

Data collection methods and Tools:

Research method: data capture sheet.

Retrospective electronic chart review between January 2013 and December 2019 in the department of pulmonology at Inkosi Albert Luthuli Central Hospital, Durban, KZN,South Africa.

Data analysis techniques

All data and the subsequent analysis will be discussed with a statistician. Descriptive statistics will be used to summarize the data. Frequencies and percentages will be used for categorical data. Numeric data will be checked for normality and parametric(means) or nonparametric (medians). Subgroup comparisons will be made using t- tests or Wilcoxon rank sum tests for numeric data and chi-square tests for categoricaldata. A paired analysis will be used to estimate changes in patient parameters over time (paired t-test) or sign rank test. Data will be analysed in Stata v13 and a p-valueof <0.05 will be considered statistically significant.

Statistical analysis:

Research data will primarily be analysed within a quantitative framework. Data willbe entered into IBM SPSS, version 24 (Statistical Packages for the Social Sciences). A p-value <0.05 will be considered as statistically significant. Continuous variables willbe expressed as mean ± standard deviation or medians (interquartile range) and compared using Student's t-test or Wilcoxon-Mann-Whitney test as appropriate. Proportions and categorical variables will be compared using Pearson's chi-square test or Fisher's exact test as appropriate.

Study location:

The study location will include adult patients who were diagnosed with COPD at the Inkosi Albert Luthuli Central Hospital, in the period between January 2013 and December 2019.

Study period:

The study population will include adult patients who diagnosed with COPD at the Inkosi

Albert Luthuli Central Hospital, in the period between January 2013 and December 2019.

Limitations of the study

The study is limited to one center. This may not be truly representative of the general population, it has a small sample size at a single center with missing data, which madeit difficult to determine any associations or lack thereof. There is the possibility of overestimation as the study was conducted at a tertiary hospital in a specialized clinic,which may have resulted in referral bias. This is not an accurate estimation of all patients with COPD in KZN, as the mild cases would not have been referred.

Another limitation is the use of the GOLD strategy as the primary reference for spirometric detection and staging of COPD, rather than the ERS/ATS standards, which reflects the practices at IALCH.

Ethical considerations

This is a retrospective chart review. Therefore, there will be no risk to the patients, norwill this study impact their management. Consent will not be obtained from individual patients. The data will be anonymized, ensuring complete protection of patient confidentiality. Consent will be obtained from IALCH hospital management, the Department of Health, and the University of KwaZulu-Natal Biomedical Research Ethics Committee.

There is no conflict of interest.

Data Sheet

KZ number: _____

Year of diagnosis: _____

Year of symptoms:
Clinical Cough

Smoking ☐

Clubbing ☐

mMRC Grade (presentation): ☐

mMRC Grade (12 Months visit):mMRC

Grade (24 Months Visit):

Pulmonary hypertension signs (presentation): ☐

Pulmonary hypertension signs (last visit): ☐

Demographic data:	
Age	
Gender	
Race	

History of:	
Cigarette Smoking	
Cannabis smoking	
Smoking pack-year smoking	
Number of Hospital Admission	
History of PTB	
HIV statues	
HIV patients on ARVs	
Exacerbation	
Occupational history	
Exposure to biomass fuel	

Clinical data:	
mMRC score / NYHA score	
weight	
height	
Body mass index	
Clubbing	
Signs of pulmonary hypertension	

Lung function parameters:	First Visit	12 months visit	24 months
Forced Vital Capacity (FVC)			
Forced expiratory Volume in 1second (FEV1)			
FEV1/FVC			
Total Lung Capacity (TLC)			
Diffusion Capacity for carbonmonoxide (DLCO)			
Oxygen saturation			
Six-minute Walk test distance			
Peak expiratory flow			
Degree of reversibility			

Radiological parameters:	Chest X-Ray	CT scan
Hyperinflation		
Air trapping		
Bronchiectasis		
Emphysema		
Lung mass		
Fibrosis		

Echocardiogram Parameters	First Visit	12 months Visit	24 months visit
Ejection Fraction (EF)			
Pulmonary arterial systolicpressure (PAS)			
Right ventricle dilatation			

Medication	
LABA	
LAMA	
Single inhaler (LABA and LAMA)	
ICS	
Home Oxygen	
Theophylline	
Others	

Vaccination	
Pneumococcal conjugate vaccine (PCV 13)	
Pneumococcal polysaccharide vaccinePPSV 23)	
Influenza Vaccine	

Appendix 2: The Guidelines for Authorship for the Journal selected for submission of themanuscript:

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include ananonymized version of the manuscript. The exceptions to this requirement are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, soplease be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines willbe returned to the author(s) for correction prior to being sent for review, which will delay publication.
General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contactdetails of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g., 'intravenous (IV)' or 'Department of Health (DoH)'.
- Scientific measurements must be expressed in SI units except blood pressure (mmHg)and hemoglobin (g/dL).
- Liters is denoted with an uppercase L e.g., 'mL' for milliliters).
- Units should be preceded by a space (except for % and ºC), e.g., '40 kg' and '20 cm' but '50%'and '19ºC'.
- Please be sure to insert proper symbols e.g., µ not u for micro, a not for alpha, b not B for beta,etc.
- Numbers should be written as grouped per thousand-units, i.e., 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If you wish material to be in a box, simply indicate this in the text. You may use the table format. -this is the *only* exception. Please DO NOT use fill, format lines and so on.

AJTCCM is a medical journal covering all aspects of respiratory health, therefore for articlesinvolving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g., TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins, and related shorthand terms at first mention, e.g., '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008; 17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results, and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion, and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study areto fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables.
- A max of 20 - 25 references

Structured abstract

- This should be no more than 250words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.

- **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they arenot the most significant findings of the study.
- **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to themain body of the article.
- Do not include any references in the abstracts.

Click Here for an example of a good abstract.

Case reports/Scientific letters/Short reports

These include side effects of drugs and brief or negative research findings.

Guideline word limit: 1500 words

- Abstract: unstructured, of about 100-150 words
- May include only one illustration or table.
- A maximum of 6 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider andpeer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles.

Contributors are encouraged to write to the Editor about possible papers to be considered forreview, and where appropriate a review outline will be submitted to experts in the field for consideration before a full review is commissioned. It is expected that an author or authors have substantial experience and track record in the field that the review is about.

*Guideline word limit: 3 500 words (*unless an alternative word limit has been arrangedwith the Chief Editor)

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important

- Methods: Outline the sources and selection methods, including search strategy and keywordsused for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations and provideadvice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (usedfor CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Contributors are encouraged to include tables and figures in their reviews to keep to themaximum word count.

Guidelines

Must be endorsed by an appropriate body prior to consideration and all conflicts of interestexpressed.

- A structured abstract not exceeding 250 words.
- Recommended sub-headings: Background, Recommendations, Conclusion is required.
- Sections and sub-sections must be numbered consecutively (e.g., 1. Introduction; 1.1 Definitions. 2. etc.) and summarised in a Table of Contents.
- References, appendices, figures, and tables must be kept to a minimum.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the AJTCCM or to a topical issue of particular relevance to the journal's readership.

- May include only one illustration or table.
- Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death and may beaccompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g., '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.

- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g., 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g., *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show thetumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections or offer a large table as anaddendum to the publication, but available in full on request from the author.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e., not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make ‘new rows’:

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:

Rather:

Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that do not overlap:

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. Ifreference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting.*

- Authors must verify references from original sources.

- Citations should be inserted in the text as superscript numbers between square brackets, e.g., These regulations are endorsed by the World Health Organization,[2] and others. [3,4-6]

- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the firstthree names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI)link). Authors are encouraged to use the DOI lookup service offered.

by CrossRef:

- On the Crossref homepage, paste the article title into the 'Metadata search' box.
- Look for the correct, matching article in the list of results.
- Click Actions > Cite.
- Alongside 'url =' copy the URL between {}.
- Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms ofDisease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - ReducingRisks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the noticenumber in this Gazette.

- Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment andLand Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicineservices. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa.2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned 1949:

Date of decision (or when the case was heard) (4): Volumenumber.

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G)Gauteng, and so on.

NOTE: no. after the v

- *Other references (e.g., reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications. e.g., '... (Prof. Michael Jones, personal communication)'.

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  - Author Agreement form [forthcoming]
  - Manuscript
  - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
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Appendix 3: EthicalApprovals

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

11 October 2023

Dr Sadaldin Mostafa Saad Abokil (210556904)
School of Clinical Medicine
Medical School

Dear Dr Abokil,

Protocol reference number: BREC/00005794/2023
Project title: Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.
Degree: MMed

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application.

The conditions have been met and the study is given full ethics approval and may begin as from 11 October 2023. Please ensure that any outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is valid for one year from 11 October 2023. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on RIG on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2020) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on 14 November 2023.

Yours sincerely,

[redacted]

Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

KWAZULU-NATAL PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

DIRECTORATE:
OFFICE OF THE MEDICAL MANAGER
INKOSI ALBERT LUTHULI CENTRAL HOSPITAL

Physical Address 800 Vusi Mzimela Road, Mayville - 4058
Postal Address: Private bag X03 Mayville – 4058
Tel: 031 240 1124 Fax: 031 240 1005 Email: linda.mtshali@ialch.co.za
www.kznhealth.gov.za

Reference: BREC00005794/2023
Enquiries: Dr L P Mtshali

8 August 2023

Dr S M S Abokil (210556904)
School of Clinical Medicine
Medical School

Dear Dr Abokil

Re: Approved Research: Ref No: BREC/00005794/2023: Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.

As per the policy of the Provincial Health Research Committee (PHRC), you are hereby granted permission to conduct the above-mentioned research once all relevant documentation has been submitted to PHRC inclusive of Full Ethical Approval.

Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

- The application is an online process by logging on to: HTTP://NHRD.HEALTH.GOV.ZA and follow the steps as indicated on the Provincial Health Research page.

Yours faithfully

.....[redacted].....

Dr L P Mtshali
Acting Medical Manager

KWAZULU-NATAL PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

DIRECTORATE:
NKOSI ALBERT LUTHULI CENTRAL HOSPITAL
OFFICE OF THE MEDICAL MANAGER
Private Bag X03, Mayville, 4058
000 Vusi Mzimela (Bellair) Road, Mayville,4091
Tel: 031 240 1059 Fax: 031 240 1005 Email: Ursula.john@ialch.co.za

Reference: BREC 00005794/2023
Enquiries: Medical Management

8 August 2023

Dr S M S Abokil (210556904)
School of Clinical Medicine
Medical School

Dear Dr Abokil

RE: PERMISSION TO CONDUCT RESEARCH AT IALCH

I have pleasure in informing you that permission has been granted to you by the Medical Manager to conduct research on: **Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.**

Kindly take note of the following information before you continue:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Kindly ensure that this office is informed before you commence your research.
4. The hospital will not provide any resources for this research.
5. You will be expected to provide feedback once your research is complete to the Medical Manager.

Yours faithfully

....[redacted].
Dr L P Mtshali
Medical Manager

KWAZULU-NATAL PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

DIRECTORATE:

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email:

Health Research & Knowledge Management

NHRD Ref: KZ_202308_018

Dear Dr SM Abokil
(UKZN)

Approval of research

1. The research proposal titled '**Review and outcomes of patients with Chronic Obstructive Pulmonary Disease managed by the Department of Pulmonology at Inkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal.**' was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at Inkosi Albert Luthuli Central Hospital.

2. You are requested to take note of the following:
   a. ***Kindly liaise with the facility manager BEFORE your research begins.***
      This is to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.
   b. *All research conducted in KwaZulu-Natal must comply with government regulations relating to Covid-19. These include but are not limited to: regulations concerning social distancing, the wearing of personal protective equipment, and limitations on meetings and social gatherings.*
   c. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   d. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za*
   e. *Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.*

For any additional information please contact Mr. X Xaba on 033-395 2805.

Yours Sincerely

[redacted]

Dr E Lutge
Chairperson, Provincial Health Research Committee
Date: 11/09/2023

Appendix 4: Data collection tools:

KZ NO	Age at pre	gender	race	Smoking	Smoking p	Smoki	ng C	Biomass	Occupetina	Type of oc
KZ00575 92	65	M	I	Y	40	Y	N	N		
KZ00575 78	70	F	C	Y	22	N	Y	N		
KZ00569 36	62	F	A	N	N		Y	N		
KZ00568 47	68	M	I	Y	44	N	N	Y		2
KZ00566 00	53	M	A	Y	35	N	N	N		
KZ00557 26	77	M	W	Y	30	N	N	Y		2
KZ00552 77	59	F	W	Y	45	N	N	N		
KZ00549 71	60	M	I	Y	30	N	N	N		
KZ00545 73	63	M	I	Y	35	Y	N	N		
KZ00544 74	77	M	I	Y	25	N	N	N		
KZ00544 04	61	M	A	Y	60	N	N	N		
KZ00543 40	68	F	W	Y	80	N	N	N		
KZ00543 32	66	M	A	N	N		N	Y		3
KZ00541 69	75	F	W	Y	55	N	N	N		
KZ00541 14	59	M	A	N	N		Y	Y		1
KZ00540 17	46	M	I	Y	25	N	N	Y		3
KZ00537 68	57	M	I	Y	37	N	N	N		
KZ00537 54	59	M	A	Y	10	N	N	Y		1
KZ00536 83	41	M	A	Y	1.5	N	Y	Y		1
KZ00536 54	45	M	A	Y	10	N	N	N		
KZ00534 40	64	F	W	Y	40	N	N	N		
KZ00531 72	52	M	A	Y	15	N	N	N		
KZ00530 36	56	M	A	Y	15	N	N	Y		1
KZ00530 09	63	F	W	Y	65	N	N	N		
KZ00527 59	62	M	A	Y	4	N	Y	Y		2
KZ00527 21	77	M	I	Y	10	N	N	Y		1
KZ00527 16	40	M	A	Y	7.5	N	N	N		
KZ00526 78	70	M	W	Y	40	N	N	N		
KZ00526 27	56	M	I	Y	45	N	N	Y		1
KZ00526 14	55	M	A	Y	40	N	N	Y		1
KZ00525 60	54	F	C	Y	30	N	Y	Y		4
KZ00525 37	61	M	A	Y	36	N	N	Y		2
KZ00524 78	90	M	A	Y	22	N	N	Y		1
KZ00524	57	M	A	Y	30	N	N	N		

56									
KZ00523	68	F	W	Y	25	N	N	N	
38									
KZ00523	71	M	I	Y	40	N	N	N	
09									
KZ00522	63	M	I	Y	25	N	N	Y	1
60									
KZ00521	69	M	I	Y	112	N	N	N	
72									
KZ00521	51	M	A	Y	30	N	N	N	
41									
KZ00521	54	M	A	Y	18	N	N	Y	4
25									
KZ00521	77	M	A	Y	60	N	N	Y	1
06									
KZ00520	54	M	I	Y	40	N	N	Y	2
85									
KZ00520	48	M	A	Y	27	N	N	Y	1
35									
KZ00520	55	M	I	Y	40	N	N	Y	4
12									
KZ00519	54	M	W	Y	46	N	N	Y	2
63									
KZ00518	58	F	C	Y	40	Y	N	N	
23									

KZ00517 20	58	M	W	Y	5	Y	N	Y		1
KZ00514 83	57	F	C	Y	14	N	N	Y		4
KZ00513 93	59	M	W	Y	35	N	N	Y		2
KZ00513 44	73	M	I	Y	50	N	N	N		
KZ00511 44	69	F	W	Y	80	N	N	N		
KZ00510 96	65	M	W	Y	45	N	N	Y		4
KZ00508 33	68	M	W	Y	30	N	N	Y		3
KZ00506 32	59	F	W	Y	43	N	N	N		
KZ00504 89	39	M	A	Y	10	N	N	Y		1
KZ00504 69	33	M	I	Y	20	Y	N	N		
KZ00503 18	53	M	A	Y	5	N	N	Y		1
KZ00500 33	81	M	A	Y	25	N	N	N		
KZ00373 86	58	M	I	Y	80	N	N	Y		2
KZ00373 62	57	M	I	Y	104	N	N	N		
KZ00372 78	61	F	A	Y	40	N	N	N		
KZ00372 34	60	F	W	Y	40	N	N	N		
KZ00370 84	62	M	I	Y	30	N	N	N		
KZ00368 84	65	F	I	Y	40	N	N	N		
KZ00366 19	50	M	A	Y	15	N	Y	Y		4
KZ00366 11	67	F	W	Y	50	N	Y	N		
KZ00365 85	36	M	I	Y	10	N	N	Y		2
KZ00360 87	70	M	W	Y	35	N	N	N		
KZ00357 18	63	M	A	Y	10	N	N	Y		2
KZ00356 11	53	M	I	Y	40	N	N	Y		4
KZ00356 02	73	M	I	Y	32	N	N	N		
KZ00354 89	62	M	I	Y	7	Y	N	Y		4
KZ00352 46	58	M	W	Y	40	N	N	Y		1
KZ00352 18	53	F	W	Y	60	N	N	N		
KZ00348 91	53	M	A	Y	2	N	N	N		
KZ00348 44	59	M	I	Y	40	N	N	Y		2
KZ00347 96	60	M	A	Y	30	N	N	Y		4
KZ00346 01	58	M	I	Y	80	N	N	N		
KZ00343 91	68	F	A	Y	2.5	N	Y	Y		3
KZ00343 25	67	M	I	Y	17	N	N	Y		4
KZ00342	53	M	C	Y	40	N	N	Y		4

65									
KZ003424	52	M	A	Y	26	N	N	N	
42									
KZ003404	50	M	A	Y	25	N	N	Y	1
75									
KZ003363	41	M	W	Y	30	N	N	N	
21									
KZ003343	72	F	W	Y	32	N	N	N	
17									
KZ003325	37	F	C	Y	20	N	N	N	
53									
KZ003319	64	M	I	Y	50	N	N	N	
96									
KZ003317	61	M	W	Y	14	N	N	Y	1
76									
KZ003303	73	F	W	Y	20	N	N	N	
37									
KZ003298	53	M	W	Y	25	N	N	Y	1
88									
KZ003263	64	M	I	Y	50	N	N	N	
30									
KZ003216	50	M	I	Y	40	N	N	Y	3
63									
KZ003216	54	M	C	Y	15	N	N	Y	4
62									

KZ00321 22	72	M	I	Y	30	N	N	N	
KZ00321 09	66	F	I	Y	25	N	N	Y	3
KZ00320 67	58	M	I	Y	50	Y	N	N	
KZ00319 10	79	M	W	Y	50	N	N	Y	4
KZ00316 24	59	F	W	Y	40	N	N	N	
KZ00314 81	62	M	A	Y	15	N	N	N	
KZ00312 76	75	M	I	Y	40	N	N	N	
KZ00310 63	53	M	A	Y	10	N	N	Y	2
KZ00307 50	76	M	C	Y	60	N	N	Y	2
KZ00306 77	56	M	W	Y	60	N	N	Y	1
KZ00305 35	47	M	I	Y	30	N	N	N	
KZ00304 97	57	M	I	Y	60	N	N	N	
KZ00302 88	52	M	I	Y	40	N	N	Y	2
KZ00300 38	66	F	W	Y	20	N	N	N	
KZ00299 97	65	M	I	Y	20	N	N	N	
KZ00299 88	65	M	I	Y	20	Y	N	Y	2
KZ00296 76	61	F	W	Y	80	N	N	N	
KZ00293 77	59	F	C	Y	15	N	N	N	
KZ00293 34	52	M	I	Y	30	Y	N	Y	1
KZ00293 28	58	M	I	Y	40	N	N	N	
KZ00292 20	48	M	A	Y	20	N	N	N	
KZ00291 44	86	F	I	Y	5	N	N	Y	3
KZ00291 28	64	F	I	Y	20	N	N	Y	3
KZ00290 76	69	M	I	Y	18	N	N	Y	3
KZ00290 24	69	M	I	Y	22	N	N	Y	2
KZ00289 68	72	F	I	Y	15	N	N	N	
KZ00289 18	68	M	W	Y	50	N	N	N	
KZ00288 56	60	M	W	Y	10	N	N	N	
KZ00287 38	62	M	I	Y	40	N	N	N	
KZ00287 35	69	M	C	Y	75	N	N	Y	1
KZ00286 81	63	M	A	Y	40	Y	N	Y	3
KZ00285 69	69	M	C	Y	50	N	N	N	
KZ00285 68	51	F	W	Y	40	N	N	N	
KZ00285 22	74	M	I	Y	40	N	N	N	
KZ00284	62	M	I	Y	50	N	N	N	

16									
KZ0028207	64	M	A	Y	25	N	N	N	
KZ0028190	68	F	I	N		N	N	Y	3
KZ0028087	39	M	I	Y	20	Y	N	N	
KZ0027979	47	F	W	Y	30	N	N	N	
KZ0027974	62	M	I	Y	40	N	N	N	
KZ0027764	43	M	A	Y	15	N	N	Y	1
KZ0027671	68	M	C	Y	124	N	N	Y	4
KZ0027593	59	M	W	Y	40	N	N	Y	1
KZ0027588	63	M	C	Y	15	N	N	N	
KZ0027491	77	F	W	Y	25	N	N	N	
KZ0027487	67	M	C	Y	40	N	N	N	
KZ0027176	47	M	A	Y	30	N	N	N	

KZ0026846	81	M	W	Y	4	N	N	Y	4
KZ0026844	62	M	C	Y	45	N	N	Y	4
KZ0026489	70	F	W	Y	20	N	N	N	
KZ0026366	74	M	W	Y	50	N	N	Y	2
KZ0026155	69	M	I	Y	30	N	N	Y	4
KZ0025996	56	M	I	Y	20	N	N	N	
KZ0025992	65	M	I	Y	22	N	N	N	
KZ0025980	67	F	W	Y	47	N	N	N	
KZ0025801	54	M	W	Y	29	N	N	Y	1
KZ0025735	66	M	I	Y	40	N	N	N	
KZ0025676	62	M	I	Y	20	N	N	N	

RVD st	ate PTB	O2 sat at p O2	sat afte COPD	Gold score	Gold score		Gro Gro	COPD	mMRC sco mM	RC 1 y
N	N	96		3	C				3	
N	N	99		2	B				2	
N	N	95	98	2	2	B	B		2	2
N	N	98		3	C				4	
N	Y	97		2	B				2	
N	N	96	97	2	3	A	C		2	2
N	N	96	98	3	3	D	D		4	2
N	Y	90		2	D				4	
N	N	88		3	D				4	
N	N	99	99	2	2	B	C		2	1
N	Y	96		2	C				3	
N	N	98		2	B				3	
N	N	97		3	C				3	
N	N	93	96	3	3	C	C		2	2
N	Y	98	100	2	2	B	C		2	1
N	Y	96		1	D				4	
N	N	96	95	3	3	C	B		3	1
N	N	98		2	B				3	
N	Y	97	98	3	3	D	C		3	2
Y	Y	93		3	C				3	
N	N	96	98	3	C				2	2
N	N	94	96	4	D				2	2
N	N	96	98	2	B				3	2
N	N	83	96	3	D				4	4
N	N	93	96	3	3	B	C		3	2
N	N	97	97	2	2	A	B		2	1
N	Y	91	96	4	4	D	D		4	4
N	Y	95		4	C				3	
N	N	98		2	B				2	
N	Y	100	98	3	4	B	C		2	2
N	N	95	95	2	2	C	C		4	2
Y	Y	98	97	4	4	D	D		3	3
N	N	98		3	D				3	
N	Y	98		2	B				2	
N	N	96	97	3	3	D	D		3	3
N	N	99		2	B				2	
N	N	89		3	D				4	
N	N	92	96	2	2	B	B		2	3
Y	Y	95		2	B				2	
N	N	81		4	D				4	
N	N	94	95	3	4	D	D		4	4
N	N	95		3	C				3	
Y	Y	94	92	3	3	D	D		3	4
N	N	91	94	4	4	D	D		4	4
N	Y	95		4					4	
N	N	93	98	2	2	B	B		2	2

N	Y	95		2				2	
N	N	100	97	3	3	D	D	2	3
N	N	99		2		B		2	
N	N	94	97	2		B		3	4
N	N	96	97	2	3	C	B	2	2
N	Y	97	95	4	3	D	C	2	4
N	N	98	97	3	3	D	C	3	3
N	N	98	96	3	3	C	D	3	2
N	Y	90	83	4	4	D	D	2	4
N	Y	97	98	4	3	D	D	2	4
Y	N	97	95	4	4	D	D	2	2
N	Y	96	97	2	2	C	B	2	2
N	N	98	96	2	3	D	C	3	3
N	N	99	98	2	2	D	D	4	4
N	N	98	95	3	3	D	C	2	2
N	N	99	100	3	3	C	C	2	2
N	N	99	98	2	2	B	A	2	1
N	N	97	99	2	2	B	B	3	2
Y	Y	95	99	3	3	D	D	3	4
N	N	96	89	2	2	D	C	4	4
N	Y	99	100	2	3	A	A	1	1
N	N	93	94	3	3	D	D	2	3
N	N	96	100	3	3	B	B	2	2
N	N	98	98	2	2	B	B	3	2
N	N	100	100	2	2	A	B	2	2
N	N	99	100	2	2	B	B	2	2
N	N	93	96	2	2	D	B	3	3
N	N	97	97	2	2	C	B	3	1
Y	Y	84	86	3	3	D	D	4	2
N	N	95	95	2	2	C	D	4	4
N	Y	96	92	3	3	C	C	2	2
N	N	95	98	2	3	D	C	4	2
N	Y	100	99	2	2	B	C	2	2
N	N	94	95	4	4	D	D	4	3
N	Y	99	97	3	3	C	D	2	2
Y	Y	60	98	2	2	D	C	4	2
N	Y	98	93	2	2	C	B	2	3
N	N	97	94	2	3	B	D	2	4
N	N	93	67	3	3	D	D	3	3
N	Y	92	97	3	2	B	B	1	1
N	N	98	95	2	2	D	B	2	2
N	N	95	92	2	2	C	D	2	1
N	N	95	97	2	2	D	D	2	3
N	Y	96	97	3	3	D	C	2	2
N	N	99	99	2	2	D	B	2	2
N	N	94	95	3	3	D	D	4	3
N	N	99	96	4	4	D	C	3	3

N	Y	98	99	3	3	B	B	2	1
N	N	96	100	2	3	D	D	2	2
N	N	92	92	3	3	D	D	2	3
N	N	94	88	4	4	D	D	3	4
N	N	95	99	2	2	D	B	3	2
Y	Y	97	98	2	3	D	D	3	4
N	N	98	98	2	2	C	B	2	3
N	Y	100	100	2	2	B	B	2	2
N	Y	94	92	3	4	C	D	2	2
N	N	97	98	3	4	D	D	2	3
N	N	97	98	3	3	D	C	3	3
N	N	98	97	2	2	B	C	3	2
N	N	96	97	2	2	B	B	2	2
N	N	96	98	2	3	D	D	3	3
N	N	98	96	3	3	D	C	3	3
N	N	96	97	3	3	D	D	3	3
N	N	87	97	2	2	D	C	3	3
N	N	90	94	3	4	D	D	3	3
N	Y	97	95	3	3	D	D	3	3
N	N	93	96	2	2	C	B	2	2
N	N	99	99	2	2	B	B	3	2
N	N	98	98	2	2	B	B	2	2
N	N	97	97	2	2	C	B	2	3
N	Y	99	96	3	3	D	B	2	2
N	N	95	98	4	3	D	D	4	3
N	N	96	99	2	2	B	C	3	3
N	N	94	95	2	2	A	A	2	2
N	N	94	97	2	2	B	A	2	1
N	N	100	97	4	4	D	C	3	3
N	N	98	97	2	2	C	B	2	2
N	N	98	98	3	3	C	D	3	4
N	N	92	97	2	3	C	C	2	3
N	N	98		2		D		3	
N	N	98	99	3	3	D	C	3	2
N	N	98	95	3	2	D	D	3	3
N	Y	96	98	3	3	D	C	3	2
N	Y	99	98	2	3	B	B	3	2
N	N	98	98	3	3	D	D	3	3
N	N	95	94	4	4	D	D	3	3
N	N	93	91	3	3	D	D	3	3
Y	Y	96	95	3	3	D	D	4	2
N	N	95	95	3	2	C	C	1	2
N	N	94	92	3	3	C	D	2	4
N	N	97	100	3	3	C	C	2	2
N	N	93	99	2	2	C	B	3	2
N	N	98	96	3	3	D	D	3	3
N	Y	99	98	3	3	C	B	2	2

N	N	92	88	4	3	D	D	4	4
N	N	100	97	3	3	D	B	3	2
Y	Y	98	96	3	3	B	D	2	3
N	N	94	95	4	4	D	D	3	3
N	N	100	98	3	2	C	C	2	3
N	N	99	96	2	2	C	B	3	2
N	N	97	93	2	2	C	B	3	2
N	N	97	99	2	2	B	B	2	2
N	Y	100	94	4	3	D	B	4	4
N	Y	98	100	2	2	D	C	2	2
N	N	94	95	4	4	D	D	3	3

Clubbing	signs of PH	weight	Height	BMI	FEV1	FEV1 P%	Reversibili FVC	FEV1\FVC
Y	N	57	163	21.45357	0.42	15.99	N	1.21	35.2
N	Y	65	155	27.05515	0.92	52.15	N	1.53	60.62
N	N	87.3	154	36.81059	1.42	73.37	N	1.89	74.96
N	N	62	167	22.23099	0.58	21.36	N	1.51	38.4
Y	N	43.8	161	16.8975	1.54	53.25	N	2.83	54.4
N	N	77	172	26.02758	1.35	50.59	N	2.6	52.7
N	N	55	157.5	22.17183	0.89	41.39	Y	2.04	43.6
N	Y	106.5	178	33.61318	1.07	31.38	N	1.63	63.8
N	N	57.9	168	20.51446	0.34	11.72	N	0.83	41.5
N	N	64	174	21.13886	1.59	57.59	N	2.4	66.07
Y	N	53	171.1	18.10405	1.29	41.55	N	2.33	55.3
Y	N	62.2	161	23.99599	0.84	40.86	N	1.39	60.6
N	N	50	174	16.51473	0.8	26.09	N	2.37	33.9
N	N	62	153	26.48554	1.39	90.02	N	2.88	48.2
N	N	71.2	170	24.63668	1.77	56.45	Y	2.43	72.8
Y	N	72.7	189	20.35217	2.4	55.88	N	2.99	80
N	N	67	163	25.21736	0.65	22.21	N	1.69	38.3
Y	Y	68	158.5	27.06764	1.98	76.47	Y	2.86	69
N	N	54.6	165	20.0551	0.62	17.9	Y	1.58	39.4
N	N	43.7	170	15.12111	0.49	13.96	N	1.34	36.7
N	N	58.3	163	21.94287	0.84	37.49	N	2.07	40.4
N	N	45.7	159	18.07682	0.57	20.12	N	2.22	25.7
Y	N	70	164	26.02617	2.11	71.7	N	2.85	73.9
N	Y	41	149	18.46764	0.49	28.72	N	1.2	40.8
N	N	90	169	31.5115	0.66	23.32	N	1.53	45
N	N	70	170	24.22145	0.98	38.39	N	1.67	58.6
N	N	49	181	14.95681	0.44	10.58	N	1.8	24
N	N	70	174	23.12062	0.76	25.85	N	2.58	29.4
Y	N	63.7	183	19.02117	3.04	80.9	Y	4.12	73.8
N	N	52	175	16.97959	1.33	38.54	Y	3.59	36
N	Y	54	153	23.06805	0.95	45.55	N	1.57	60.6
N	N	66.8	172	22.57977	0.66	20.89	N	2.67	25
N	Y	50.9	167	18.25092	0.75	36.96	N	2.39	31.2
Y	N	59	174	19.4873	1.86	64.02	N	2.9	62.6

				8				7	
N	N	44.1	167	15.81269	1.24	35.71	N	3	41.28
N	N	64	162.4	24.26654	1.21	49.58	N	2.24	54
N	N	47	160	18.35938	0.36	14.05	N	1.04	34
N	N	73	180	22.53086	2.63	80.53	N	3.75	70
Y	N	65.6	177	20.93907	2.87	79.49	N	4.45	64.6
Y	N	60	170	20.76125	0.37	11.27	N	1.43	25.5
N	N	53.5	163	20.13625	0.72	29.42	N	2.2	32.9
N	Y	57.5	168	20.37273	0.74	23.46	N	1.89	39.3
Y	N	59.8	165	21.96511	0.68	21.27	N	2.26	30.3
N	Y	47.7	172	16.12358	0.59	17.82	N	2.11	27
N	N	53.5	177	17.07683	0.85	23.8	N	3.31	25.5
N	N	60.7	163	22.84617	1.23	51.31	N	2.09	58.7

N	N	102	169	35.71304	1.57	50.65	N	2.43	64.1
N	N	46.4	165	17.04316	0.89	35.54	N	1.97	45
N	N	51.8	169	18.13662	1.21	39.57	N	2.18	55.7
N	N	58.5	166.5	21.10218	1.46	57.1	N	2.25	64.6
N	N	61.9	159	24.48479	0.86	43.46	N	1.44	59.6
Y	N	47	177	15.00207	0.79	24.18	N	2.8	28.1
N	N	60	180	18.51852	1.23	38.29	N	2.87	42
N	N	57.8	170	20	1.37	51.77	N	3.13	43.5
N	N	72	169	25.2092	0.81	21.98	Y	3.1	26.06
Y	N	49.7	180	15.33951	0.63	14.65	N	2.23	28.55
Y	N	68.2	172	23.053	0.74	22.07	N	2.8	29
Y	N	65	170	22.49135	1.43	55.2	N	2.07	69
N	N	57	171	19.49318	1.88	59.19	N	3.36	56
Y	N	130.8	191	35.85428	1.15	28.22	N	2.08	55
N	N	64	157.5	25.79995	0.89	42.24	N	2.9	30.5
N	N	53	170	18.3391	0.75	28.66	N	1.91	38
N	N	57	157	23.12467	1.72	69.75	N	2.55	67.2
N	Y	54.4	153	23.23893	0.44	24.02	N	0.72	60.5
N	N	74	175	24.16327	0.66	18.29	N	2.08	31.5
N	N	78	159	30.85321	0.98	48.74	N	1.65	59
N	N	76	181	23.19832	1.81	42.92	N	3.14	57
N	N	104	175	33.95918	0.89	29.57	N	2.36	37.5
N	N	91.8	170	31.76471	1.17	39.17	N	2.78	42.1
N	N	84.5	175	27.59184	2.06	59.02	N	3.04	68
N	N	84.8	175	27.6898	1.68	57.69	N	2.4	70
N	N	69.4	172	23.45863	1.59	51.2	N	3.1	51.28
Y	Y	77.8	170	26.92042	0.89	45.79	N	1.43	62
N	N	81	167	29.04371	1.3	48.48	N	2.14	60.5
N	N	61	169	21.3578	0.75	22.59	N	1.8	41.69
N	N	46.6	169	16.31596	1.03	33.54	N	1.96	52.4
N	N	69	172	23.32342	1.04	32.94	Y	3.4	30.1
N	Y	83.6	166	30.33822	0.77	26.06	N	1.51	51
N	Y	49	159	19.38214	0.96	48.49	N	1.39	68.8
N	N	52	185	15.19357	0.74	20.82	N	2.74	26.9
N	N	69.5	172	23.49243	1.24	36.73	N	3.42	36.2
N	N	69	173	23.05456	2.08	60.86	N	3.55	58.5
Y	Y	44.4	168	15.73129	0.79	24.06	N	1.31	60.49
N	N	73	171	24.9649	3.18	86.13	N	4.39	72.4

Y	Y	53.9	159	21.32035	0.54	29.74	N	1.36	40
N	N	39	150	17.33336	0.46	19.35	N	1.27	36
Y	N	65	178	20.51503	1.63	49.14	N	2.41	67.3
N	N	95.6	177	30.51486	2.66	79.6	N	4.07	60
N	Y	54.1	157	21.94815	1.19	66.72	N	2.16	54
N	N	67	179	20.91071	1.57	42.74	Y	3.74	41
N	N	81.8	171	27.97442	2.44	78.95	N	3.89	62
N	N	40	165	14.69238	0.42	13.43	N	1.27	33
N	N	39	169	13.65498	0.46	14.26	N	1.7	26.8

N	N	52	165	19.10009	0.9	36.29	N	2.27	39.7
N	N	43.6	144	21.02623	0.64	43.74	N	1.16	54.9
Y	N	42	174	13.87237	0.57	17.2	N	1.68	33.8
N	N	78	182	23.54788	0.92	30.33	N	3.41	27
N	N	49.5	153	21.14571	1.4	71.83	N	2.32	60
Y	N	70	167	25.0995	2.18	75.45	N	3.88	56.3
Y	N	72	161	27.77671	1.05	46.31	N	1.51	74.3
N	N	88	171	30.09473	1.47	44.27	Y	2.58	57.02
N	N	73.5	169	25.73439	1.24	48.17	Y	3.07	40.4
N	N	58	180	17.90123	0.9	28.63	N	2.79	32
Y	N	66.7	167	23.91624	1.03	30.98	Y	2.41	39.3
N	N	80	170	27.68166	2.04	64.36	N	2.66	76.5
N	N	87.5	173	29.23586	1.9	55.28	N	2.6	71.5
N	N	63	150	28	0.79	47	N	1.47	53.5
N	N	70.4	175	22.98776	1.17	34.48	N	2.58	49
N	N	51	169	17.85652	1.03	39.51	N	2.87	35
N	N	52	154	21.92613	0.68	34.73	N	1.29	52.5
N	N	52.9	135	29.02606	0.32	25.28	N	0.9	35
N	N	46	158	18.42653	0.37	15.9	N	0.82	45.6
N	N	67	164	24.91077	1.77	61.61	N	3.03	58.6
Y	N	64.5	172	21.80233	1.77	50.29	N	2.54	69
N	N	62	150	27.55556	0.64	49.23	N	0.86	74
Y	N	67	155	27.88762	1.12	58.47	N	1.84	61
Y	N	69.5	168	24.62443	0.63	22.95	N	1.87	33.4
N	N	55.3	168	19.59325	0.5	18.12	N	1.88	26.3
N	Y	97	157	39.35251	0.85	47.28	N	1.47	57.9
N	N	97.1	185	28.37107	2.17	61.73	N	3.49	62
N	N	127	164	47.21892	1.7	58.83	N	2.4	68.9
N	N	70.5	190	19.52909	1.04	23.3	N	3.95	26.4
N	N	104	176	33.57438	1.57	54.11	N	2.76	56.8
N	N	53.7	153	22.93989	0.83	37.38	N	2.03	41.1
Y	N	52.9	165	19.43067	1.07	41.5	N	1.96	54.4
N	N	73	153	31.18459	0.91	42	N	1.82	50
N	N	58	153	24.7768	0.67	32.32	N	1.49	44
N	N	58	165	21.30395	1.02	51.68	N	2.23	45
Y	Y	67	170	23.18339	1.08	52.1	N	2.89	37.22

N	N	47.6	150	21.15556	1.14	68.16	N	1.84	62.1
N	N	39	166	14.153	0.6	17.11	N	1.9	31.6
N	N	44.7	157	18.13461	0.71	29.14	N	2.48	28.7
Y	N	56.1	158	22.47236	0.77	30.37	N	2.14	35.9
Y	N	52.2	164	19.40809	0.96	28.84	N	2.26	42.3
Y	N	66.6	169	23.31851	1.78	61.63	N	3.56	49.9
N	N	58.4	168	20.69161	1.15	37.57	N	3.23	35.1
N	Y	72.6	162	27.66347	0.99	37.54	N	2.54	39.1
N	N	56.6	160	22.10938	0.96	53.39	N	1.71	56
N	N	60	156	24.65483	1.05	46.34	N	2.65	39.8
Y	N	43.8	160	17.10938	1.29	42.76	Y	2.9	43.6

N	N	63	166	22.86253	0.89	38.57	N	3.05	29.07
N	N	57	176	18.40134	1.78	54.4	Y	4.13	43
N	N	93	170	32.17993	1.3	55.06	N	2.84	45.9
N	N	56.5	166	20.5037	0.55	22.09	N	1.95	29
N	N	74	172	25.01352	1.1	37.71	N	2.24	48.87
N	N	60	158	24.03461	1.36	51.49	N	1.97	69
N	N	98.7	170	34.15225	1.83	61.81	N	2.7	67.8
N	N	55.2	158	22.11184	1.4	66.17	N	2.67	52.2
N	N	103	185	30.09496	0.87	22.77	N	3.15	27.6
N	N	54	167	19.36247	2.1	77.6	N	3.2	67
Y	N	56	173	18.71095	0.47	14.98	N	1.51	29.1

FEV1 -FEV FE	V1 after FV	C after 2 FE	V1\FVC pe	ak expir Pe	ak expir		(XR	
				2.23		1	2	4
				2.8				5
0.15	1.27	1.67	75.8	5.77	5.89			
				1.92		1		
				2.8				3
0.25	1.1	2.31	47.83	4.16	3.47	1		1
-0.08	0.97	2.11	45.78	2.26	2.87	1		2
				4.71				
				0.74		1		
0.02	1.57	2.56	61.41	2.1	3.11	1		3
				3.74				6
				2.15				4
				2.22		1	3	1
0.27	1.12	2.64	42.44	4.11	3.19	1		
0.2	1.57	2.04	77.02	5.16	4.97	1		
				7.8		4		
-0.08	0.73	2.04	35.5	2.55	3.07			
				5.7		3		1
-0.03	0.65	1.63	39.83	2.4	1.7	3		5
				1.45		1		3
				2.9		1		
				1.26				2
				6.8				2
				1.12				3
0.05	0.61	1.5	40.81	3.16	2.96			5
-0.33	1.31	1.8	72.53	2.57	4.05			
0.05	0.39	1.69	23.2	1.29	1.23	1	5	3
				1.48		1		3
				8.9				4
0.5	0.83	3.31	25.2	2.8	1.98	3		1
0.09	0.86	1.55	55.54	2.97	3.28			
-0.09	0.75	3.23	23.37	1.8	1.59			3
				2.89				4
				3.74		1	3	3
0.42	0.82	1.7	48.24	3.02	2.77			
				4.5				
				2.25		1	3	
0.49	2.14	3.66	65	7.7	7.5			1
				6.3		2	3	3
				0.88		1		
0.05	0.67	2.27	29.46	2.8	3.44			
				3.17		3		5
0.26	0.42	1.35	30.87	2.26	1.58	1		3
0.12	0.47	1.95	24.2	2.03	1.99	1		
				2.36				6
0.52	0.71	1.27	55	4.1	2.8			

				5.6		2	3		
0.07	0.82	1.89	43	2.07	2.48				2
				2.7					4
				3.75					2
0.14	0.72	1.55	46.4	1.08	1.93	1			
0.14	0.65	2.06	31.6	2.97	2.23				3
-0.02	1.25	2.53	49.45	3.9	3.8				1
0.17	1.2	2.42	49.6	4.2	3.2	1			5
0.15	0.66	2.21	29.6	2.8	3.11				6
0.13	0.5	1.65	30.3	2.73	2.44				2
0.01	0.73	2.5	28.8	4.04	4.06				2
-0.11	1.54	2.53	61	5.1	4.91				3
0.54	1.34	2.76	48.69	5.23	3.85	1			1
0.07	1.08	2.03	53.18	4.5	3.9				4
0.24	0.65	2.03	31.6	3.19	2.45				
0.08	0.67	2.22	30	2.35	2.6				1
0.08	1.64	2.32	70.8	8.25	8.23				1
-0.15	0.59	0.88	66	1.95	1.9	1			3
0.08	0.58	1.94	30.1	2.62	2.27	1			
0.19	0.79	1.53	51.17	2.97	2.41				
0.22	1.59	3.23	49	7.5	6.23	1			3
-0.26	1.15	2.4	48	3.37	3.39	1	2	3	
0.01	1.16	2.77	42.03	3.8	4.44				
0.14	1.92	2.89	66.25	3.8	4.46				6
-0.09	1.77	2.6	68	5.9	6.3				
0.28	1.31	2.4	54.5	4.12	3.69				5
-0.64	1.53	2.8	53	3.06	4.73				5
-0.19	1.49	2.46	60.4	3.37	4.62				
0.01	0.74	1.51	49.02	2.44	2.43	1	2		3
0.44	0.59	0.98	60.5	2.22	2.16	3	5		3
0.08	0.96	2.67	35.86	2.66	3.22	5			3
-0.33	1.1	2.29	48.3	1.77	3.02				

0.11	0.85	1.25	67.52	2.9	2.99	1		2
0.1	0.64	2.28	27.89	3	2.48	1		
0.5	0.74	1.66	32	3.7	3.7			
-0.06	2.14	3.78	56.48	4.7	5.8	1		2
0.13	0.66	0.97	68.47	1.75	1.75			2
1.34	1.84	4	45.5	6.54	3.99			
-0.05	0.59	1.79	32.98	1.96	1.51	1	4	5
-0.39	0.85	1.67	51	1.3	2.4	1		
0.13	1.5	2.28	63	5.71	4.5	1		1
0.68	1.98	3.9	50.4	6.45	6.48			
0.04	1.15	2.01	57.1	3.1	3.2	1		2
0.07	1.5	4.28	35.04	3.26	4.61			1
-0.04	2.48	3.96	62	9.1	9.1	1		6
0.07	0.35	1.08	32	1.5	1.65	1		
0.09	0.37	1.39	26.8	1.87	2.24	1		3

-0.09	0.99	2.56	38.1	1.44	2.06	5		4
0.19	0.45	0.89	49.9	2	1.38			2
0.16	0.41	1.08	37	2.7	2	1		3
0.07	0.85	2.89	29.4	2.86	2.27	3		
0.17	1.23	1.96	63	3.5	3.2	1		5
1.05	1.13	2.78	40.5	5.9	3	1		1
-0.17	1.22	1.83	66.9	2.59	3.02	3	5	
-0.16	1.63	2.91	55.7	5.06	5.2	3	5	
0.35	0.89	3.03	29.5	2.8	3.4			
0.03	0.87	3.11	28	2.44	2.7	1		4
0.29	0.74	2.34	30	2.9	2.12			1
0.24	1.8	2.47	76	5.9	5.3	1		
-0.21	2.11	2.79	75.5	6.5	6.86			2
-0.08	0.87	1.96	44.5	2.3	2.4			
-0.21	1.38	2.87	48	3.57	4.8			
0.11	0.92	2.84	32	3.27	1.74	1		
0.03	0.65	0.99	65	2	2.7	1		3
-0.11	0.43	1.85	23	1.27	1.48	1		
0.09	0.28	0.62	46.2	1.44	1.32	1	2	3
0.55	1.22	2.14	57	5.37	4	1		2
0.28	1.49	2.17	68	7	6.75	1		3
0.1	0.54	0.81	66	2.5	1.3			5
0.13	0.99	1.63	60	3.59	3.06	1		5
0.1	0.53	1.65	31.9	1.89	1.99			3
-0.15	0.65	1.67	38	2.46	2.8	1		2
-0.03	0.88	1.4	62	3.17	2.74			5
-0.1	2.27	3.38	67	5	7.2	1		
0.4	1.3	2.1	60.5	5.9	5.7			
0.39	0.65	2.44	26.5	2.9	2.35	1		3
-0.11	1.68	3.38	61.1	4.57	4.86	2		
0.2	0.63	1.41	44.5	4.25	2.47			2
0.22	0.85	2.5	33.9	3	3.6	1		2

				3.5		1		2
0.08	0.59	1.19	49	2.39	2	1		
-0.62	1.64	2.8	58.3	3.3	5.5			
0.23	0.85	2.2	38.48	2.9	2.17	1	4	3
0.16	0.98	1.62	60.3	3.3	3.1			5
-0.06	0.66	1.87	35.6	1.75	2.3	3	5	
-0.08	0.79	2.7	29.39	1.53	1.88	1		
0.33	0.44	1.45	30.5	1.4	1.59			
0.33	0.63	1.67	37.6	1.74	1.76	1	5	5
0.51	1.27	2.36	53.9	5.5	3.9	1		1
0.31	0.84	2.23	37.8	3.28	2.27	1		
-0.26	1.25	2.85	43.8	2	2.9	3		3
-0.04	1	1.73	58.3	2.9	1.9			2
0.16	0.89	2.3	38.5	2.6	2.7	1		3
0.32	0.97	2.61	36.9	2.7	2.3			4

0.12	0.77	1.92	34.6	2.8	3.1	1	3	3
0.7	1.08	3.36	32	4.3	3	1		
-0.13	1.43	3.25	43.9	2.77	3.5	3	5	2
-0.08	0.63	1.94	25	2.6	2.4			
-0.36	1.46	2.89	50.9	2.2	3.8	1		1
-0.21	1.57	2.46	63.6	2.27	2.32	1		1
0.22	1.61	2.5	63	6.08	4.8			
0.08	1.32	2.44	54	3.5	2.69	1	3	2
-0.17	1.04	2.99	34.6	2.6	2.8	2	5	3
0.27	1.83	2.99	61.1	5.66	5.27	1	4	3
-0.05	0.52	2.2	23.6	0.89	1.29	1		4

CT scan	Mal gnanc	othe r com	Ejec teion f	Pul monary	Ha moglo	Esi nopheli	Mec ication	Theyophili
		1			13.9	0.05	5	
		2			10.5		5	
			62	26	13.4		1	
							5	Y
		3			9.9		5	
							5	
					14.3	0.1	5	
		4	60	50	12.2	0.09	1	
			51		17.6		5	
					13.6	0.13	5	
					11.6		1	
		2			12.9	0.17	5	
4		1			10.6	0.07	5	
					14.4	0.15	5	
					14.4		5	
		4	12	42	15.7	0.07	4	
			55		15	0.16	5	Y
2	5		45		14.9		5	
6					13.6	0.09	5	
6					12.9	0.11	1	
		1			8.9	0.48	5	
4					9		5	
							5	
			63	35	12.5	0.14	5	
							1	
		3	58	41	11.4	0.06	5	
6					12.7		5	Y
5					12	0.02	5	
		1			17.1	0.22	1	
2	5				14.4		5	
		4	58	45	14.4	0.32	5	
							5	
5					12.1	0.09	5	
5					6.1	0.04	5	
					15.2	0.18	5	Y
					14.8	0.17	5	
		2					5	
5					14.8	0.51	5	
5					13.6		1	
					14.8		5	
							5	Y
					15.9	0.35	5	
					12.5		5	
			66	53	14.9		5	
							5	
					13.2		5	

									1
						15.4		5	
		3				12.5		5	
4		1				12.5	0.03	5	
						13.5	0.08	5	
5						15.3	0.1	5	
2			5			14	0.29	5	Y
						13.7	0.48	5	
			2			12.4	0.24	5	Y
3	6					14.7		5	
4						14.2		5	
4		1				11.7	0.03	1	
2				60		15.9		5	Y
		2	4	55	29	10.8		5	
						16		5	
						17.2	0.03	5	Y
2	5		2			15.6		5	
			4	55	74	11.4		5	
						13.4		5	
						12.9	0.03	5	Y
								1	
						15.9	0.01	5	
								5	
			1	48		15.6		5	
			1			12.4		5	
			3			16.1		5	
				55	20	16.2		5	Y
				55	47	11.2		5	
5						13.6	0.04	5	
6			2			15.8	0.1	5	
5						15.3		5	Y
								5	
				47	46	11.6	0.04	1	
						13.9	0.35	5	Y
						8.8	0.26	5	Y
						14.6		5	
4	5					14.9	0.23	5	
						14.8	0.6	1	
			4	67	50	16.9		5	Y
						12.6		5	
						15		5	
						16.6		5	
5						12.8		5	
2	5					12.7	0.08	5	
								5	
						15		5	
5						16.4		5	Y

5		1			13.9		5
					12.4		5 Y
		1	48	24	14.1		5 Y
					13.3		5
		4			15.7	0.71	5
2					13.5		5
		5			10.8	0.45	5 Y
					13		5
							5
					11.7	1.1	5 Y
2					14.8	0.18	5 Y
		1					5
5					14.2		5
							5
		1			11.6		5
					17.1		5
		1			12.2		5
					14.7		5
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		1		50			5
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5		2			10.3		5
					14.1	0.15	5
		4	74		9.4	0.2	4
					10.5		5
		1			13.4		5
		5			14.4		5 Y
		2			12.4	0.05	5
3							5
					12.7		5
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		1			14.5		5 Y
		1			14.2		5
4	1				11	0.1	5
					11.4		1
		2					5
							5 Y
					14		5
					15.2		5
2							5
					15.4	0.04	5 Y
					11.7	0.68	5 Y
		4	60	47	14.8	0.09	5
					10.4		5
5					15		5

							5	Y
					14.9		5	
					13.4	0.05	5	
					15		5	Y
5			1		11.1		5	
4	5	2	1				5	
					14.6		1	
			1	60			4	
				51	9		5	Y
			4		13.3		5	Y
5			10		10.7		5	Y

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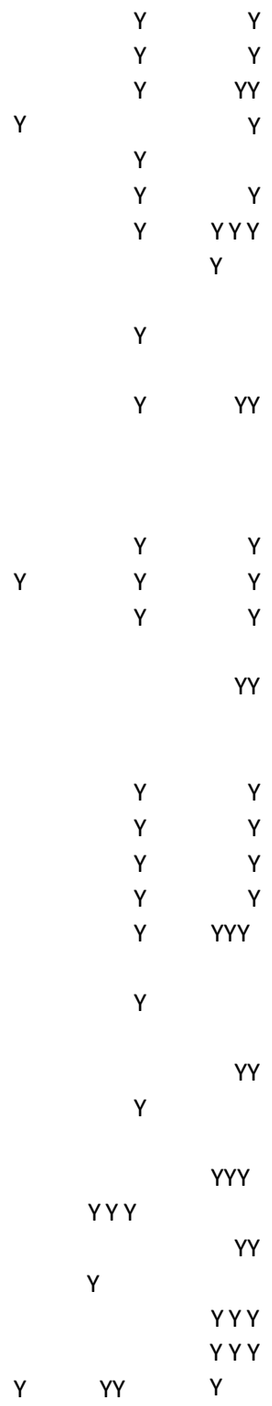

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