DETERMINANTS OF SMOKING CESSATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Lindokuhle Goqwana

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment for the degree of Master of Medicine in the division of Internal Medicine

Johannesburg, 2020

DECLARATION

I, Lindokuhle Goqwana, declare that this research report is my own work. It is being submitted for the degree Master of Medicine (in the submissible format and extended literature review) in the branch of Internal Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

……..day of ……2020

ACKNOWLEDGEMENTS

I gratefully acknowledge the staff of Helen Joseph Hospital, Mr Tshegofatso Magano and Dr Kapila Hari on their assistance with this project.

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a preventable burden on international health with unavoidable risk factor in the form of smoking. Smoking cessation plays a major role in the morbidity and mortality of COPD. Determining factors that influence smoking cessation thus plays a huge role in establishing successful smoking cessation and reducing morbidity and mortality associated with COPD.

Objectives

Cross sectional survey of patients with COPD at the Helen Joseph Hospital, conducted between June and August 2018. Questionnaires were given to the patients in a confidential manner, where details like whether they were still smoking or not and the number of years they had been smoking for were interrogated. Determinants such socio-economic standing, highest level of education and symptomatology were amongst the few determinants that were included in the questionnaire.

Results

Of the 50 respondents, 33 had successfully stopped smoking and 17 were still smoking at the time they took the questionnaire. We found that 74% of patients (82.3% of smokers and 69.7% of ex-smokers) who took part in the study had severe disease according to their Global Initiative for Obstructive Lung Disease (GOLD) score. In our study the most significant finding was the relationship between the socio-economic status and COPD. The majority (75.8% and 76.6% of current and ex-smokers respectively) were unemployed. We were unable to demonstrate statistical significance between other well recognized factors that have been shown to influence smoking cessation (age; level of education and severity of disease) in our cohort. This may be due to the limited number of patients in our study. We did demonstrate the benefit of counselling by a doctor, even though this was not significant.

Conclusion

Smoking cessation is an important aspect in the management of COPD and by understanding these determinants we can reduce the morbidity and mortality associated with COPD. The significance of a low socio-economic status as highlighted by our study needs to be considered as a broader public health initiative but counselling by health professionals is an easier intervention and should be emphasized.

TABLE OF CONTENTS

LIST OF TABLES

Chapter 1

Chapter 2

LIST OF FIGURES

Chapter 1

Chapter 2

ABBREVIATIONS

Acetylcholine Receptors	AchR
COPD	Chronic Obstructive Pulmonary Disease
Forced Expiratory Volume	FEV
GOLD	Global Initiative for Chronic Obstructive Lung Disease
Modified Medical Research Council	mMRC
Nicotine Replacement Therapy	NRT
Ventral Tegmental Area	VTA

CHAPTER 1: PROTOCOL WITH EXTENDED LITERATURE REVIEW

Introduction

Chronic Obstructive Pulmonary Disease (COPD) - "A common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/ or alveolar abnormalities usually caused by significant exposure to noxious particles or gasses." (1)

According to the Global Initiative for Chronic Obstructive Lung Disease, COPD is classified into four groups (GOLD 1,2,3,4) based on post bronchodilator Forced Expiratory Volume in the first second (FEV1) and further into another four groups (GOLD A,B,C,D) based on symptoms and risk of exacerbation.(1)

Please see tables below where the classifications are illustrated.

Table 1.1 Airflow Limitation in COPD (Global Initiative for Obstructive Lung Disease, 2018, p29)

Classification of Airflow limitation in COPD (Based on post-bronchodilator FEV1)		
GOLD 1	Mild	FEV1>80% predicted
GOLD 2	Moderate	50%< FEV1 < 80% predicted
GOLD 3	Severe	30%< FEV1 <50% predicted
GOLD 4	Very Severe	FEV1< 30%

Table 1.2 The ABCD assessment tool (Global Initiative for Obstructive Lung Disease, 2018, p33)

>2 or >1 exacerbation leading to hospitalization	D	D
0 or 1 exacerbation (not leading to hospitalization)	A	B

	MRC 0 -1*	MRC >/=2*

Table 1.3 Modified Medical Research Council (mMRC) Dyspnoea Scale (Global Initiative for Obstructive Lung Disease, 2018, p29)

Grade	Description of Breathlessness
mMRC Grade 0	Breathlessness with strenuous exercise
mMRC Grade 1	Breathlessness when hurrying on level ground or walking up a slight hill
mMRC Grade 2	Have to stop for breath when walking at own pace
mMRC Grade 3	Breathlessness after 100m of walking
mMRC Grade 4	Breathlessness on mild functions of daily living

Epidemiology

545 million people in the world suffer from chronic respiratory disease of which the most prevalent is COPD and Asthma. This number has increased by 39.8% from 1990. (3) In 2017 3,9 million global deaths were due to chronic respiratory diseases. The leading cause of deaths worldwide were COPD and Asthma in 2017. (3) Sub-Saharan Africa had the lowest mortality due to chronic respiratory diseases. The epidemiological evidence may however be underrepresented, due to lack of spirometry which was required previously for diagnosis. The prevalence of COPD in the Sub-Saharan region is estimated at 11%, with an estimated figure of 29 million people within this region.(4)

Smoking has been identified as an important risk factor in the development of COPD. Epidemiological studies have shown that at least 64% of patients with COPD have either previously smoked or are currently smoking.(5) Smokers are 3-5 times more likely to develop

COPD than non-smokers. Cigarette smoke contains 4700 constituents that increase the production of endogenous reactive oxygen species.(6)

Risk Factors for COPD

Multiple risk factors for COPD have been outlined. Understanding the risk factors may help with reducing disease progression as this is an irreversible disease process.

- Cigarette smoking is probably the most well described risk factor for COPD. The relationship between smoking and COPD has been considered for the last 50 years, the British being the first to establish it in a study that followed smokers for 8 years. They found that susceptible smokers showed a decline in their lung function.(7)
- Smoking both Marijuana and cigarettes together shows an increase in COPD and symptomatology.(8)
- There are multiple devices which are used in smoking and not just the traditional cigarette. Different cultures use different ways to smoke tobacco for example the hookah which has the tobacco smoke go through water before reaching the smokers lungs. It was previously thought that this device was safer but this was found not to be true as this may have other additives besides tobacco that may be harmful. (7)
- An association with second hand smoking and development of COPD has been found with multiple reviews showing that people exposed to second hand smoke have a 2.5 greater risk of developing COPD than those that have no exposure.(9)
- The concept of biomass fuel exposure is an extremely important one in the South African setting where 20% of the population lives in informal and traditional dwellings. This is where cheaper less clean fuels are used such as: wood, animal dung, fossil coal etc. These fuels are harmful because they release numerous air pollutants, which results in endogenous reactive oxygen species formation and airway inflammation and remodeling.(7)
- Genetic factors play a role in the development of COPD. The most readily described genetic disorder associated with COPD is Alpha 1 Antitrypsin deficiency, first described in 1963 by Laurell and Erikson. They found an absence of alpha 1 antitrypsin in serum protein electrophoresis. This deficiency is associated with early

onset of COPD and/or liver cirrhosis, and is associated with panacinar emphysematous changes. (10)

- The following forms of industrial exposure are shown to carry an increased risk for COPD:
    - Dust exposure
    - Animal farming
    - Crop farming
    - Chemical Exposure(7)
- Outdoor Air pollution, mainly from car emissions and industrial pollution have also been shown to be risk factors for COPD. (7)
- Females seem to be more susceptible to developing COPD than males. Women with the same degree of disease as men are found to have smoked substantially less than men.(11)
- Persistent and severe childhood asthma may predispose to development of COPD.(1)

Biology of Cigarette Smoking

The hallmark of COPD is airflow limitation, and this may be as a result of small airway disease or emphysema. The airflow limitation is due to mucous accumulation and lung fibrosis causing airway narrowing. (12)

The pathogenesis of emphysema is based on four processes. See Figure1 below.

1. Cigarette smoke exposure interacting with possible genetic host factors - leading to inflammatory and immune cell activation and recruitment within the terminal air spaces of the lung (12)
2. These immune cells release proteases and elastolytic substances resulting in damage of the extracellular matrix of the lung (12)
3. Endothelial and epithelial cell death occurs secondary to free radical exposure from the cigarette smoke (12)
4. The lung is unable to repair the airway resulting in alveolar wall destruction and air space enlargement which is characteristic of emphysema as well as chronic bronchitis (12)

Nicotine addiction is an important factor as 3 million smoking related deaths are reported annually worldwide. (13) Nicotine, a mediator of addictions, acts on endogenous acetylcholine receptors (AChRs) found in the nervous system of all vertebrate and invertebrates. Nicotine has rewarding motivational effects by acting on the Ventral Tegmental Area (VTA), similar to that of cocaine, alcohol. The major neurotransmitters implicated in this reward process are Dopamine and Gamma Aminobutyric Acid (GABA). Dopamine is released from the VTA and sends projections to the nucleus accumbens and the prefrontal cortex, resulting in the reward effect that cigarette smoking has. Multiple factors play a role in nicotine addiction and non-dopamine pathways are also implicated in the role of nicotine addiction. (13)

Smoking Cessation Determinants

Multiple studies have been done in investigating the determinants of smoking cessation in patients with COPD (14) (15). A retrospective cohort done in Denmark showed multiple variables that could hinder or improve smoking cessation in these patients. (16)

- Mental Health – Psychiatric illness patients were less likely to stop smoking, this may be due to the theory that smoking cessation may exacerbate mental illness. (14)
- Low socio-economic status – Lower cessation rates were documented in patients of low socio-economic standing, this was thought to be due to lack of funds for pharmacological interventions to assist with cessation. (16)
- Marital Status – Patients who live alone are less likely to stop smoking. (16)
- Unemployment - Patients who were unemployed had a lower incidence of smoking cessation, this was attributed to the amount of free time individuals had and the psychological stressors imposed by the status of being unemployed. (16)
- Severity of Disease - Patients with severe COPD were found to have better abstinence possibly attributable to the functional limitation associated with this stage of disease. (16)
- Level of Education - Education was another determinant. They found that subjects that had only obtained a high school education smoked more than those that had obtained a university degree. (16)

- Co-Morbidities – Patients with concomitant malignancy were found to be less likely to stop smoking than those without malignancy. It is important to note that patients with other medical diseases were more likely to stop smoking than those that only have COPD. (16)
- Age – Younger patients were more unlikely to quit smoking than older patients. (16)

Benefits of Smoking Cessation

A study from the United Kingdom looked at the effects that smoking cessation had on patients FEV1 and Computed Tomography Scan changes at baseline, 6 weeks, 12 weeks and a year after smoking cessation. (17) They showed transient positive changes. These changes though, stabilized by 1 year post smoking cessation. The study showed that smoking cessation combined with pharmacological management could improve presence of micronodular disease further.(17)

In the Lung Health Study (LHS), patients with mild to moderate COPD were evaluated. The patients who had successfully quit were in one arm, those who intermittently quit were in the second arm and those who had not quit were in the third arm. Those who had quit showed reduction in morbidity (in the form of recurrent lower respiratory tract infections), improvement in their FEV1 and reduction in all-cause mortality. (18) The benefits of smoking cessation include a reduction in mortality. It has been reported that smokers die 13 to 14 years earlier than non-smokers. Causes of mortality equal that of non-smokers within 15 years of smoking cessation. One of the downsides of smoking cessation is the associated weight gain. Patients that stop smoking have an average weight gain of 5 kg within the 1st year of stopping. In the LHS the authors concluded that the health benefits of smoking cessation outweigh the risk of weight gain. (18)

Smoking Cessation Methods

Multiple modalities are used in order to assist with smoking cessation. They can be grouped into pharmacological and non-pharmacological methods.

Non-pharmacological measures include public health measures such as, tobacco taxes, bans on advertising and bans on smoking in public areas. These steps have all shown some reduction in smoking. The European regions have shown the lowest increase in the prevalence of COPD between 1990 and 2010. This figure has been attributable to the intensive public health campaigns that these countries have implemented. (19) These methods are growing in favor in South Africa as a smoking ban is currently being reviewed in the

South African National Assembly. Supportive efforts are another form of non-pharmacological interventions. This includes educational, motivational and behavioral interventions.

Spontaneous smoking cessation rates annually are 3-5 %, but with health professional advice this rate can be increased to 5.5-7.5%. (20) Motivational strategies have shown some benefit. A method of counselling called the 5 As and 5 Rs is a standardized method being widely used for smoking cessation. (see table below)(20)

Table 1.4 The 5 As and 5 Rs of smoking cessation (African tobacco smoking cessation clinical practice guideline, SAMJ, 2013)

The 5 As and 5 Rs smoking cessation strategy	
Ask	Enquire about smoking status
Advise	Firmly urge smokers to quit
Assess	Determine willingness to quit
Assist	Counsel as per 5 Rs. Start Pharmacotherapy
Arrange	Follow up by phone or office visit
Relevance	Patient to indicate why quitting is personally relevant
Risks	Identify negative consequences of tobacco use
Rewards	Identify benefits to smoking cessation
Roadblocks	Identify Barriers to quitting

The 5 As and 5 Rs smoking cessation strategy	
Repetition	Apply the 5 Rs again with relapsed and unmotivated patients

Pharmacological approaches can assist in smoking cessation. Two classes of pharmacotherapy have been approved for this: namely Nicotine Replacement Therapy (NRT) and drugs that reduce addiction namely Buproprion and Varenicline.

- NRT is aimed at reducing withdrawal symptoms in patients with nicotine addiction. It may be used alone or in combination with bupropion. It has been found to be effective, however 1 in 4 smokers will relapse within 4 years. (17) NRT comes in multiple forms (gum, lozenges, nasal spray) and pricing is similar to that spent on cigarettes, making it affordable. (19) The NRT can be titrated to symptom severity. (20)
- Bupropion is a dopamine, serotonin and norepinephrine reuptake blocker. It assists with the depressive symptoms that occur with smoking cessation. Bupropian mono-therapy has been found to be comparable to NRT mono therapy and superior to placebo in smoking cessation trials. (17) It may also be used in conjunction with NRT. (18) Buproprion is the drug of choice in the management of post cessation depression and weight gain. It is however contraindicated in patients with seizure disorders or with a high risk of seizures. Also, it is advisable that this drug not be used in patients with bipolar mood disorder as the anti-depressant effect will then unmask mania. (19) The dosing of Bupropion in smoking cessation is 150mg twice a day for 7 to 12 weeks. (20)
- Varenicline, first discovered during World War 2 is an alpha4beta2 nicotine receptor agonist-antagonist. It causes dopamine release which leads to less craving. Varenicline currently has a boxed warning for adverse psychiatric effects such as depression, worsening of schizophrenia, to name a few. (19)

In the face of limited local data we set out to determine the factors that affect smoking cessation in patients with COPD.

Study Objectives

Overall objective

To determine the factors that affect smoking cessation in patients with COPD

Specific aims

1. To investigate the proportion of patients that have quit smoking after a diagnosis of COPD (secondary to smoking) has been confirmed.
2. To describe the demographic, health and smoking related factors that determine smoking cessation in patients with COPD secondary to smoking

Methods

We will conduct a cross sectional study at the Helen Joseph Hospital. This hospital consists of 21 inpatient wards and functions as a referral hospital and provides tertiary services to the west of Johannesburg and parts of the neighboring North West province.

The patients will be approached during their out-patient clinic visit where a written consent will be sought from them before proceeding to interview them. Relevant data will be extracted from the respiratory clinic files following their out-patient visit.

Data will be collected over a four month period. We estimate that 300 patients will be evaluated during this period.

Study Populations

All patients with a diagnosis of COPD (based on spirometry and a history of smoking) attending the out-patient Respiratory clinic at the Helen Joseph Hospital

Inclusion Criteria:

- Smoking history
- Proven COPD by lung function testing
- Adult Patients (>18years)
- Patients who have had any smoking exposure

Exclusion Criteria

- Patients who do not consent

Data Analysis

Data will be put into GraphPad Instat, a commercial statistics software, for cleaning and identification of inconsistencies. Proportions will be represented with percentages and means with Standard deviations. A chi square test will be used to analyse associations between smoking cessation patient characteristics.

Ethics

Ethics approval will be applied for from the Human Research Ethics Committee. Consent will be obtained from all subjects involved in the study. The management staff of the

hospital will be approached for consent and ethical approval. All questionnaires will have a code and no use of names will occur in order to protect the confidentiality of the subjects

Gantt Chart

	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep
literature review														
Protocl Preparation														
Protocol assessment														
Ethics application														
Collecting Data														
Data Analysis														

	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sep
Writing up														

Budget

Printing	R5000
Transport	R3000

Limitations

Nicotine assays are unavailable in out setting due to financial constraints.

The sample size may be smaller than anticipated, depending on the clinic attendees during the designated period.

Reference List

1. Global Initiative For Obstructive Lung Disease. GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf [Internet]. [cited 2019 Jan 31]. Available from: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf

2. Fletcher CM, Elmes PC, Fairbairn AS. THE SIGNIICANCE OF RESPIRATORY SYMPTOMS AND THE DIAGNOSIS OF CHRONIC BRONCHITIS IN A WORKING POPULATION. :10.

3. Labaki WW, Han MK. Chronic respiratory diseases: a global view. Lancet Respir Med [Internet]. 2020 Jun [cited 2021 Feb 11];8(6):531–3. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213260020301570

4. Lopez AD. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J [Internet]. 2006 Feb 1 [cited 2019 Jan 31];27(2):397–412. Available from: http://erj.ersjournals.com/cgi/doi/10.1183/09031936.06.00025805

5. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet [Internet]. 2012 Dec 15 [cited 2019 Feb 3];380(9859):2095–128. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61728-0/abstract

6. Bai J, Chen X, Liu S, Yu L, Xu J. Smoking cessation affects the natural history of COPD. Int J Chron Obstruct Pulmon Dis [Internet]. 2017 Nov [cited 2019 Jan 31];Volume 12:3323–8. Available from: https://www.dovepress.com/smoking-cessation-affects-the-natural-history-of-copd-peer-reviewed-article-COPD

7. Salvi S. Tobacco Smoking and Environmental Risk Factors for Chronic Obstructive Pulmonary Disease. Clin Chest Med [Internet]. 2014 Mar 1 [cited 2019 Feb 3];35(1):17–27. Available from: http://www.sciencedirect.com/science/article/pii/S027252311300141X

8. Tan WC, Lo C, Jong A, Xing L, FitzGerald MJ, Vollmer WM, et al. Marijuana and chronic obstructive lung disease: a population-based study. CMAJ Can Med Assoc J [Internet]. 2009 Apr 14 [cited 2019 Feb 3];180(8):814–20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665947/

9. He Y, Jiang B, Li LS, Li LS, Ko L, Wu L, et al. Secondhand Smoke Exposure Predicted COPD and Other Tobacco-Related Mortality in a 17-Year Cohort Study in China. Chest [Internet]. 2012 Oct [cited 2021 Feb 13];142(4):909–18. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0012369212605595

10. Stoller JK, Aboussouan LS. A Review of α_1-Antitrypsin Deficiency. Am J Respir Crit Care Med [Internet]. 2012 Feb [cited 2019 Apr 21];185(3):246–59. Available from: http://www.atsjournals.org/doi/abs/10.1164/rccm.201108-1428CI

11. Hardin M, Foreman M, Dransfield MT, Hansel N, Han MK, Cho MH, et al. Sex-specific features of emphysema among current and former smokers with COPD. Eur Respir J [Internet]. 2016 Jan

[cited 2019 Feb 3];47(1):104–12. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5374719/

12. Harrison's Principles of Internal Medicine, 20e | AccessMedicine | McGraw-Hill Medical [Internet]. [cited 2019 Feb 3]. Available from: https://accessmedicine.mhmedical.com/book.aspx?bookid=2129

13. Laviolette SR, van der Kooy D. The neurobiology of nicotine addiction: bridging the gap from molecules to behaviour. Nat Rev Neurosci [Internet]. 2004 Jan [cited 2019 Feb 3];5(1):55–65. Available from: https://www.nature.com/articles/nrn1298

14. Tashkin DP, Murray RP. Smoking cessation in chronic obstructive pulmonary disease. Respir Med [Internet]. 2009 Jul [cited 2020 Oct 11];103(7):963–74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0954611109000651

15. Yang JJ, Song M, Yoon H-S, Lee H-W, Lee Y, Lee S-A, et al. What Are the Major Determinants in the Success of Smoking Cessation: Results from the Health Examinees Study. Wei Q-Y, editor. PLOS ONE [Internet]. 2015 Dec 3 [cited 2021 Feb 13];10(12):e0143303. Available from: https://dx.plos.org/10.1371/journal.pone.0143303

16. Tøttenborg SS, Thomsen RW, Johnsen SP, Nielsen H, Lange P. Determinants of Smoking Cessation in Patients With COPD Treated in the Outpatient Setting. CHEST [Internet]. 2016 Sep 1 [cited 2019 Feb 3];150(3):554–62. Available from: https://journal.chestnet.org/article/S0012-3692(16)49107-5/abstract

17. Dhariwal J, Tennant RC, Hansell DM, Westwick J, Walker C, Ward SP, et al. Smoking Cessation in COPD Causes a Transient Improvement in Spirometry and Decreases Micronodules on High-Resolution CT Imaging. Chest [Internet]. 2014 May [cited 2019 Apr 21];145(5):1006–15. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921534592X

18. Anthonisen NR. Lessons from the Lung Health Study. Proc Am Thorac Soc [Internet]. 2004 Apr 1 [cited 2020 Oct 15];1(2):143–5. Available from: http://pats.atsjournals.org/cgi/doi/10.1513/pats.2306033

19. Chandler MA, Rennard SI. Smoking Cessation. Chest [Internet]. 2010 Feb [cited 2019 Apr 21];137(2):428–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921060089X

20. Van Zyl-Smit RN, Allwood B, Stickells D, Symons G, Abdool-Gaffar S, Murphy K, et al. South African tobacco smoking cessation clinical practice guideline. S Afr Med J [Internet]. 2013 Sep 30 [cited 2019 Apr 21];103(11):869. Available from: http://www.samj.org.za/index.php/samj/article/view/7484

21. Statistics South Africa - 2015 - Census 2011 income dynamics and poverty status of.pdf.

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a preventable burden on international health with unavoidable risk factor in the form of smoking. Smoking cessation plays a major role in the morbidity and mortality of COPD. Determining factors that influence smoking cessation thus plays a huge role in establishing successful smoking cessation and reducing morbidity and mortality associated with COPD.

Objectives

Cross sectional survey of patients with COPD at the Helen Joseph Hospital, conducted between June and August 2018. Questionnaires were given to the patients in a confidential manner, where details like whether they were still smoking or not and the number of years they had been smoking for were interrogated. Determinants such socio-economic standing, highest level of education and symptomatology were amongst the few determinants that were included in the questionnaire.

Results

Of the 50 respondents, 33 had successfully stopped smoking and 17 were still smoking at the time they took the questionnaire. We found that 74% of patients (82.3% of smokers and 69.7% of ex-smokers) who took part in the study had severe disease according to their Global Initiative for Obstructive Lung Disease (GOLD) score. In our study the most significant finding was the relationship between the socio-economic status and COPD. The majority (75.8% and 76.6% of current and ex-smokers respectively) were unemployed. We were unable to demonstrate statistical significance between other well recognized factors that have been shown to influence smoking cessation (age; level of education and severity of disease) in our cohort. This may be due to the limited number of patients in our study. We did demonstrate the benefit of counselling by a doctor, even though this was not significant.

Conclusion

Smoking cessation is an important aspect in the management of COPD and by understanding these determinants we can reduce the morbidity and mortality associated with COPD. The significance of a low socio-economic status as highlighted by our study needs to be considered as a broader public health initiative but counselling by health professionals is an easier intervention and should be emphasized.

Chapter 2: Submissible Article

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation. This limitation is due to airway and/ or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.(1) In 2005, three million people died from COPD making it the fifth leading cause of death in the world.(2)

In the period between 1990 and 2010 there has been a significant documented increase in the number of patients with COPD in Africa.(3) The epidemiological evidence may however be underrepresented, due to limited availability of spirometry which was previously required for diagnosis. The prevalence of COPD in the Sub-Saharan region is estimated at 11%, with an estimated 29 million people affected within this region.(4)

Smoking is the foremost modifiable risk factor and smoking cessation is the main intervention shown to modify the course of COPD.(5) Cigarette smoke contains 4700 constituents that increase the production of endogenous reactive species which predispose to the development of COPD.(6) Smokers are 3-5 times more likely to develop COPD than non-smokers. Epidemiological studies have shown that at least 64% of patients with COPD have either smoked or are currently smoking. (7)

The benefits of smoking cessation have been well documented. In the Lung Health Study (LHS), patients who had quit smoking showed reduction in morbidity (in the form of recurrent lower respiratory tract infections), improvement in their Forced Expiratory Volume in 1 second (FEV1) and reduction in all-cause mortality.**(8)** Mortality rates equal those of non-smokers within 15 years of smoking cessation. Smoking cessation also decreases the risk of developing the co-morbidities associated with smoking and COPD such as cardiovascular disease and malignancies (both lung and non- lung). These findings emphasize the importance of encouraging patients with COPD to stop smoking.(9)

Multiple modalities are used to assist with smoking cessation. It has been shown that the combination of pharmacological and non-pharmacological interventions improve outcomes. (10) Two classes of pharmacotherapy have been approved for assistance in smoking cessation. They are classified into nicotine replacement therapy (NRT) and drugs that reduce

addiction, namely, Buproprion and Varenicline. These drugs are unavailable in the South African state sector. Non-pharmacological measures include public health measures such as, tobacco taxes, ban on advertising, and ban on smoking in public areas, all of which have shown some reduction in smoking.(11) These methods are growing in favour in South Africa.(12) Supportive efforts are an additional form of non-pharmacological interventions. These include educational, motivational, and behavioral interventions. Motivational strategies have shown some benefit. A method of counselling called the 5 As and 5 Rs is a standardised method widely used for smoking cessation.(13) Spontaneous smoking cessation rates annually are 3-5 % but with health professional advice this rate can be increased to 5.5-7.5%.(14)

Numerous studies have been done to investigate the determinants of smoking cessation in patients with COPD. A retrospective study done in Denmark showed multiple variables that could hinder or improve smoking cessation in these patients. These included, mental health, low socio-economic status, unemployment, severity of disease and level of education.(15)

Smoking pervasiveness is higher in deprived populations and smokers from these communities could face an increased risk for the deleterious effects of tobacco. Smoking cessation is less likely in persons of lower socioeconomic standing and their attempts to quit are not as successful. Possible reasons cited in the literature include poor social support, decreased motivation, worse addiction to tobacco, higher risk of defaulting pharmacotherapy and counselling sessions and targeted marketing by the tobacco industry.(16) A previous South African study identified female gender, increased age, a higher number of cigarettes smoked per day, a smoke-free home, recognition that cigarettes cause harm and previous alcohol dependence increased cessation success. (15)

In this study we analyzed determinants of smoking cessation in patients with COPD at the Helen Joseph Hospital. We determined the number of patients who had quit after a diagnosis of COPD and describe the demographic, health and smoking related factors that determine smoking cessation in patients with COPD. This study was approved by the Human Research Ethics Committee (Medical) University of the Witwatersrand (Appendix A;Approval M180635)

Methods

We conducted a cross sectional study at the Helen Joseph Hospital. This hospital consists of 21 inpatient wards and functions as a referral hospital. It provides tertiary services to the west of Johannesburg and parts of the neighboring North West province. Patients were approached either during their out-patient clinic visits or during their admission. They were interviewed, and the researcher completed the questionnaire. Relevant data was extracted from the respiratory clinic files and inpatient files.

Data was collected over a 3month period, between June 2018 and August 2018. Fifty patients agreed to participate in the study.

Study Population

All patients with a diagnosis of COPD (based on spirometry and a history of symptoms according to the GOLD classification) at the Helen Joseph Hospital. Patients were included if they had a history of smoking, diagnosed COPD on symptoms or spirometry and were 18 years or older. They were excluded if they did not consent to participation in the study.

Data Analysis

Data was entered into GraphPad Instat, a commercial statistics software. Proportions were represented with percentages and means with standard deviations. A chi square test was used to analyze associations between smoking cessation and patient characteristics.

Results

The cohort was made up of 50 respondents. The group was divided into those who continued to smoke (Smokers) versus those that had ceased to smoke (Ex-smokers). The results revealed that most of the respondents i.e. 33 (66%) had stopped smoking while 17 (34%) of were still smoking. Chi square tests were conducted to assess whether there was an association between smoking and the other variables such as age, economic status, level of education to name a few. The results are summarised below.

Table 1 Socio-demographic Data

		Smokers	Ex-smokers	Total	P-value
Age	30-65 years old	14 (82%)	22 (66%)	36 (72%)	0.327
	>65	3 (17.6%)	11 (33.3%)	14 (28%)	
Current Employment	Yes	4 (23.5%)	8 (24.2%)	12 (24%)	1.000
	No	13 (76.5%)	25 (75.8%)	38 (76%)	
Highest level of education	No Tertiary Education	17 (100%)	28 (84.4%)	45 (90%)	0.112
	Tertiary Education	0 (0%)	5 (15.2%)	5 (10%)	
Annual household income	No income	6 (35.3%)	2 (6.1%)	8 (16%)	0.039
	R1 - R 19 200	8 (47.1%)	27 (81.8%)	35 (70%)	
	R 19 201 - 307 200	1 (5.9%)	2 (6.1%)	3 (6%)	
	R 307 201 and above	2 (11.8%)	2 (6.1%)	4 (8%)	

Table 2 Smoking History

	Smokers	Ex-smokers	Total	P-value
No of cigarettes/day currently or previously				
<15	6	12		1.00
≥15	11	21		
No. of years smoking/ previously smoked				
>10	0	4		0.285
<10	17	29		
Pack year history				
5-10	0	7		0.079
≥10	19	25		

Table 3 COPD History

		Smokers	Ex smokers	Total	P Value
		Yes	No		
Initial COPD diagnosis	<5 years	13 (76.5%)	18 (54.5%)	31 (62%)	0.062
	5-10 years	1 (5.9%)	12 (36.4%)	13 (26%)	
	>10 years	3 (17.6%)	3 (9.1%)	6 (12%)	
Perception of COPD as a problem	Yes	13 (76.5%)		13 (76.5%)	
	No	4 (23.5%)		4 (23.5%)	
No. of admissions in the past year (COPD related)	<1	12 (70.6%)	20 (60.6%)	32 (64%)	0.548
	≥2	5 (29.4%)	13 (39.4%)	18 (36%)	

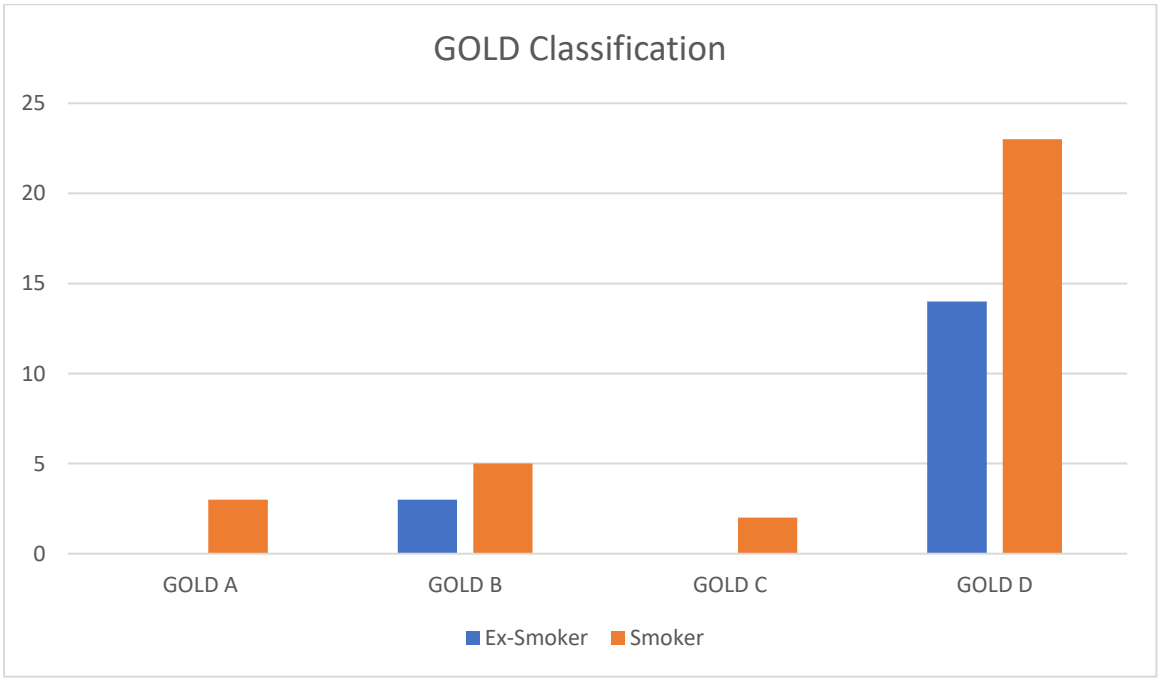

Figure 1 – GOLD Classification of patients

Table 4 Activity Level and GOLD Classification

		Smokers	Ex-smokers	Total	P-value
Dyspnoea Scale	Walking <100m	8 (47.1%)	11 (33.3%)	19 (38%)	0.357
	Stop when walking on level ground	6 (35.3%)	7 (21.2%)	13 (26%)	
	Daily activities	2 (11.8%)	6 (18.2%)	8 (16%)	
	Minimal exercise or going up an incline	1 (5.9%)	7 (21.2%)	8 (16%)	
GOLD Classification	GOLD A	0	3 (9%)	3(6%0	0.413
	GOLD B	3 (17.6%)	5 (15%)	8 (16%)	
	GOLD C	0	2 (6%)	2 (4%)	
	GOLD D	14 (82.3%)	23 (69.7%)	37 (74%)	

Table 5 Co-morbidities

		Smokers	Ex-smokers	Total	P-value
Associated chronic illnesses	Cardiovascular disease alone	6 (35.3%)	11 (33.3%)	17 (34%)	0.387
	Cardiovascular & other diseases	2 (11.8%)	3 (6%)	2 (4%)	
	Endocrine Disease	1 (5.9%)	3 (9.1%)	4 (8%)	
	HIV	2 (11.8%)	1 (3%)	3 (6%)	
	Musculoskeletal Disease	2 (11.8%)	1 (3%)	3 (6%)	
	None	3 (17.6%)	11 (33.3%)	14 (28%)	
Current/previous mental illness?	Yes	2 (11.8%)	3 (9.1%)	5 (10%)	1.000
	No	15 (88.2%)	30 (90.9%)	45 (90%)	

Smoking Cessation

Amongst the 17 smokers, 16 (94%) had attempted cessation. In this sub-group 13 (76%) perceived their continued smoking as a problem whilst 4 (24%) patients did not.

Table 6 Smoking Cessation Motivation (Ex-smokers)

Motivation Factor	**Number (%)**	**P-value**
Family intervention	2 (6.1%)	0.198
Appropriate time	1 (3%)	
Dyspnoea on speaking	12 (36.4%)	
Hospital admission	7 (21.2%)	
Counsel by doctor	7 (21.2%)	
None	4 (12.1%)	

Discussion

Smoking cessation has been shown to be the most effective way to stop the progression of COPD, in addition to improving survival and decreasing morbidity. Smoking cessation should therefore take precedence in the management of COPD. (17) In our patients with COPD (both smokers and ex-smokers) the majority of patients smoked for more than 10 years and had pack year histories in excess of 10 years. This observation confirms the long established relationship between increased smoking exposure and COPD, and re-affirms the findings of Bhatt et al who showed that smoking on its own provides the biggest risk factor for COPD. (18)

The only statistically significant factor that influenced the likelihood of smoking cessation in our cohort was the household income of the study participant. Patients with lower household incomes were less likely to stop smoking. These findings are consistent with the conclusions

of a review on the effects of socioeconomic status and smoking. The authors decided that amongst people with a lower socio-economic status smoking cessation attempts are less likely to succeed.(16) Our results are similar to those of Hymowitz et al. They conducted a telephonic survey of 13415 "smokers" in 1993 and repeated the survey in 1998. They concluded that a high income was significantly associated with successful smoking cessation. (19) The influence of income was further ratified by Wilcox et al. They studied 703 smokers over a six month period and determined that smokers with higher incomes are more likely to quit smoking. (20) It has been suggested that social context or life circumstances such as poverty may result in the smoker giving quitting a low priority. (15,21)

In our study employment status did not have a significant effect on the likelihood of smoking cessation. This mirrors a Brazilian study where employment status did not significantly affect smoking cessation. That study was however biased in that their cohort consisted only of patients who had actively sought help for smoking cessation. (22).

The majority (74%) of our patients had severe disease and were in GOLD class D. Previous publications have noted that the GOLD classification of patients influenced their likelihood of smoking cessation. Patients with more severe disease were more likely to stop smoking. (7,8). We did not show a significant difference in the cessation rates between patients in GOLD classes A; B; C and D. The small numbers of patients in each of the GOLD sub-groups, except D make our results open to bias.

The link between smoking cessation and age was not significant in our cohort. The effects of age on smoking cessation is varying. A Danish study found that the likelihood of discontinuing smoking is higher in the elderly (>70years). (15) In an English study smoking cessation was more common in adults >50years, however the authors also noted that young adults (<30years) had similar rates of smoking cessation.(20)

In the sub-group of smokers 16 of the 17 patients (94%) had attempted smoking cessation but failed, although only 13 (76%) admitted to perceiving their continued smoking as a problem. Methods used by the subjects in the 2 groups included no support; counselling and/or pharmacological therapy. Most patients did not have any pharmacological support, which can be attributed to the unavailability of the drugs at our facility and the prohibitive costs of obtaining the drugs privately.

A Cochrane review on individual behavioural counselling for smoking cessation found that health care provider counselling increased the likelihood of smoking cessation. (23) Participants in our study were asked to comment on their health care provider counselling. Most subjects replied yes to this question but on further questioning on how often this was done and what methods were offered health care providers fared dismally. They did not comply with the recommendations of the South African smoking cessation guidelines.(13) This further testifies to the lack of smoking cessation supportive measures in the South African public health care sector.

Conclusion

Household income significantly influenced the success of patients in their efforts to quit smoking and whilst we are unable to influence this, as physicians we should be advocating for additional supportive measures for our patients with COPD. Further research is needed to facilitate smoking cessation, especially in disadvantaged communities.

Limitations

Our small sample size limited our analyses. The cross-sectional nature of the study limits the reproducibility of our data, specifically the proportion of patients who continue to refrain from smoking. We were unable to secure funding for nicotine testing and were forced to rely on self-reporting to determine whether patients had stopped smoking.

Reference List

1. Global Initiative For Obstructive Lung Disease. GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf [Internet]. [cited 2019 Jan 31]. Available from: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf

2. Bousquet J, Weltgesundheitsorganisation, editors. Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. Geneva: WHO; 2007. 146 p.

3. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. J Glob Health [Internet]. [cited 2019 Jan 31];5(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693508/

4. Lopez AD. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J [Internet]. 2006 Feb 1 [cited 2019 Jan 31];27(2):397–412. Available from: http://erj.ersjournals.com/cgi/doi/10.1183/09031936.06.00025805

5. Wu J, Sin DD. Improved patient outcome with smoking cessation: when is it too late? Int J Chron Obstruct Pulmon Dis [Internet]. 2011 [cited 2019 May 7];6:259–67. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3144846/

6. Bai J, Chen X, Liu S, Yu L, Xu J. Smoking cessation affects the natural history of COPD. Int J Chron Obstruct Pulmon Dis [Internet]. 2017 Nov [cited 2019 Jan 31];Volume 12:3323–8. Available from: https://www.dovepress.com/smoking-cessation-affects-the-natural-history-of-copd-peer-reviewed-article-COPD

7. Laniado-Laborín R. Smoking and Chronic Obstructive Pulmonary Disease (COPD). Parallel Epidemics of the 21st Century. Int J Environ Res Public Health [Internet]. 2009 Jan [cited 2020 Oct 1];6(1):209–24. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2672326/

8. Tashkin DP, Murray RP. Smoking cessation in chronic obstructive pulmonary disease. Respir Med [Internet]. 2009 Jul [cited 2020 Oct 11];103(7):963–74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0954611109000651

9. Warnier MJ, van Riet EES, Rutten FH, De Bruin ML, Sachs APE. Smoking cessation strategies in patients with COPD. Eur Respir J [Internet]. 2013 Mar [cited 2019 Aug 12];41(3):727–34. Available from: http://erj.ersjournals.com/lookup/doi/10.1183/09031936.00014012

10. Dhariwal J, Tennant RC, Hansell DM, Westwick J, Walker C, Ward SP, et al. Smoking Cessation in COPD Causes a Transient Improvement in Spirometry and Decreases Micronodules on High-Resolution CT Imaging. Chest [Internet]. 2014 May [cited 2019 Apr 21];145(5):1006–15. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921534592X

11. Chandler MA, Rennard SI. Smoking Cessation. Chest [Internet]. 2010 Feb [cited 2019 Apr 21];137(2):428–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921060089X

12. Reddy P, Sewpaul R. Tobacco control and health. Policy brief. Human Sciences Research Council. June 2014

13. Van Zyl-Smit RN, Allwood B, Stickells D, Symons G, Abdool-Gaffar S, Murphy K, et al. South African tobacco smoking cessation clinical practice guideline. S Afr Med J [Internet]. 2013 Sep 30 [cited 2019 Apr 21];103(11):869. Available from: http://www.samj.org.za/index.php/samj/article/view/7484

14. Nicotine Withdrawal - an overview | ScienceDirect Topics [Internet]. [cited 2020 Aug 2]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/nicotine-withdrawal

15. Tøttenborg SS, Thomsen RW, Johnsen SP, Nielsen H, Lange P. Determinants of Smoking Cessation in Patients With COPD Treated in the Outpatient Setting. CHEST [Internet]. 2016 Sep 1 [cited 2019 Feb 3];150(3):554–62. Available from: https://journal.chestnet.org/article/S0012-3692(16)49107-5/abstract

16. Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. Ann N Y Acad Sci [Internet]. 2012 [cited 2020 Oct 1];1248(1):107–23. Available from: https://nyaspubs.onlinelibrary.wiley.com/doi/abs/10.1111/j.1749-6632.2011.06202.x

17. Tonnesen P. Smoking cessation and COPD. Eur Respir Rev [Internet]. 2013 Mar 1 [cited 2019 Aug 12];22(127):37–43. Available from: http://err.ersjournals.com/cgi/doi/10.1183/09059180.00007212

18. Bhatt SP, Kim Y, Harrington KF, Hokanson JE, Lutz SM, Cho MH, et al. Smoking duration alone provides stronger risk estimates of chronic obstructive pulmonary disease than pack-years. Thorax [Internet]. 2018 May 1 [cited 2020 Jul 26];73(5):414–21. Available from: https://thorax.bmj.com/content/73/5/414

19. Hymowitz N, Cummings K, Hyland A, Lynn W, Pechacek T, Hartwell T. Predictors of smoking cessation in a cohort of adult smokers followed for five years. Tob Control [Internet]. 1997 Jun [cited 2019 Aug 13];6(Suppl 2):S57–62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1766209/

20. Wilcox NS, Prochaska JO, Velicer WF, DiClemente CC. Subject characteristics as predictors of self-change in smoking. Addict Behav [Internet]. 1985 Jan 1 [cited 2019 Aug 13];10(4):407–12. Available from: http://www.sciencedirect.com/science/article/pii/0306460385900371

21. CDCTobaccoFree. Cigarette and Tobacco Use Among People of Low Socioeconomic Status [Internet]. Centers for Disease Control and Prevention. 2019 [cited 2020 Aug 2]. Available from: https://www.cdc.gov/tobacco/disparities/low-ses/index.htm

22. França SA de S, Neves ALF das, Souza TAS de, Martins NCN, Carneiro SR, Sarges E do SNF, et al. Factors associated with smoking cessation. Rev Saúde Pública [Internet]. 2015 [cited 2019 Aug 13];49(0). Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102015000100203&lng=en&tlng=en

Chapter 3: Appendices

Appendix A: Smoking Cessation Questionnaire

Patient Questionnaire

1. How old are you?

30-55 ☐

55-65 ☐

>65 ☐

2. When were you diagnosed with COPD?

<5 years ago ☐

5-10 years ago ☐

>10 years ago ☐

3. Do you currently smoke?

Yes ☐

No ☐

4. If yes do you see it as a problem?

Yes ☐

No ☐

5. How many cigarettes do you smoke per day?

5- 10 ☐

10-15 ☐

15-20 ☐

>20 ☐

6. How many years have you been smoking for?

<5 ☐

5-10 ☐

>10 years ☐

7. Pack year history

<5 ☐

5-10 ☐

>10 years ☐

8. How many admissions have you had in the past year?

(NB! COPD-related)

None ☐

Once ☐

More than twice ☐

9. When are you short of breath?

With strenuous exercise (jogging, cycling etc) ☐

With minimal exercise or when going up an incline ☐

I have to stop when walking on level ground ☐

I am breathless when walking a distance less than 100m ☐

I am breathless while doing daily activities ☐

(e.g. getting dressed)

10. Are you employed?

Yes ☐

No ☐

11. What is your highest level of education?

I never went to school ☐

Primary school ☐

High School ☐

Tertiary education ☐

12. If you currently smoke, have you attempted to stop?

Yes ☐

No ☐

13. What motivated you to stop?

I was admitted to hospital ☐

I was counselled by my doctor ☐

I feel ill when I smoke ☐

Family intervention ☐

Other measures ☐

14. Do you have any other illness besides chronic obstructive lung disease?

Cardivoscular disease ☐

Respiratory (lung disease)

Endocrine Disease ☐

(e.g Diabetes, Thyroid disease)

Musculo-Skeletal Disease ☐

(e.g arthritis)

15. Do you currently suffer or have you previously suffered from any form of mental illness?

Yes ☐

No ☐

16. What is your annual household income?

No income ☐

R1- R 19200 ☐

R 19 201 - R 307 200 ☐

R307 201 and above ☐

17. What Methods have you used to stop smoking?

Counselling ☐

Prescription Medications ☐

Electronic Cigarettes ☐

Nicotine Replacement therapy ☐

(eg. nicotine gum)

18. Did your health care provider counsel you on quitting?

Yes ☐

No ☐

19. How often did your doctor speak to you about smoking cessation?

Once ☐

Every Visit ☐

Never ☐

Occasionally ☐

(more than once but not at every visit)

20. If yes, what methods did he/she offer you?

_____

Comments:

_____

_____

_____

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

R14/49 Dr Lindokuhle Goqwana

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180635

NAME: Dr Lindokuhle Goqwana
(Principal Investigator)
DEPARTMENT: Internal Medicine
Helen Joseph Hospital

PROJECT TITLE: Determinants of smoking cessation in patients with Chronic Obstructive Pulmonary Disease (COPD)

DATE CONSIDERED: 29/06/2018

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr Kapila Hari

APPROVED BY: P B Penny
Professor CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 23/08/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorize to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **June** and will therefore be due in the month of **June** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

L. Goqwana
Principal Investigator Signature

21/08/2018
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Turnitin Originality Report

Processed on: 22-Oct-2020 4:07 PM SAST
ID: 1423117887
Word Count: 3866
Submitted: 1

0705245v:Determinants_of_Smoking_Cessation_in_Patients_with_COPD_Submissable_Article.pdf
By Lindokuhle Goqwana

Similarity Index	Similarity by Source
11%	Internet Sources: 8% Publications: 7% Student Papers: 3%

1% match (Internet from 10-Oct-2020)
https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2909-8

1% match (Internet from 06-Nov-2017)
https://cris.maastrichtuniversity.nl/portal/files/14386777/c5679.pdf

1% match (publications)
"Chronic Obstructive Pulmonary Disease", Springer Science and Business Media LLC, 2017

< 1% match (Internet from 28-Feb-2020)
http://wiredspace.wits.ac.za/bitstream/handle/10539/15258/MPH-research%20report-Patrick%20Sofohlo-2014-final%20-%20PS.pdf?isAllowed=y&sequence=1

< 1% match (student papers from 27-Apr-2020)
Submitted to University of Technology, Sydney on 2020-04-27

< 1% match (Internet from 25-Jan-2020)
https://www.dovepress.com/front_end/enlightening-chronic-obstructive-pulmonary-disease-through-patients-an-peer-reviewed-fulltext-article-COPD

< 1% match (Internet from 01-Mar-2016)
http://amzeweb01.blackbookinformation.com/EZCredit/ca_Questionnaire1.aspx?DealerPACode=07890&PrimaryLeadSource=DC+Trade-in&QuestionnaireVersionId=3&SecondaryID=Desktop&SecondaryLeadSource=Website&VendorBrand=Ford&_width=1547&dealerid=1141004&

< 1% match (publications)
Kolawole S. Okuyemi, Hui Zheng, Hongfei Guo, Jasjit S. Ahluwalia. "Predictors of Adherence to Nicotine Gum and Counseling among African-American Light Smokers", Journal of General Internal Medicine, 2010

< 1% match (publications)
Francesca Wuytack, Declan Devane, Elizabeth Stovold, Melissa McDonnell et al. "Comparison of outpatient and home-based exercise training programmes for COPD: A systematic review and meta-analysis", Respirology, 2018

< 1% match ()
https://hdl.handle.net/10216/119423

< 1% match (Internet from 14-Sep-2020)
https://www.scielo.br/scielo.php?pid=S1806-37132019000300400&script=sci_arttext&tlng=en

< 1% match (Internet from 28-Jul-2020)
https://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0119948

< 1% match (Internet from 05-Jan-2020)
https://www.researchsquare.com/article/e1f75d66-168c-408b-a980-4b31a14e3376/v1

< 1% match (Internet from 20-May-2020)
https://es.scribd.com/document/404062866/TOB-G-BOOK-DIGITAL-VERSION-pdf

< 1% match (Internet from 23-Nov-2019)
https://www.filtermist.com/news/post/2018/11/14/World-COPD-Day-21st-November-2018

< 1% match (publications)
Monden, C.W.. "How important are parents and partners for smoking cessation in adulthood? An event history analysis", Preventive Medicine, 200302

< 1% match (Internet from 25-Aug-2020)
https://link.springer.com/content/pdf/10.1007%2F978-3-662-47178-4.pdf

< 1% match (Internet from 02-Feb-2020)
https://www.tandfonline.com/doi/full/10.1080/20018525.2017.1421389

< 1% match (Internet from 10-Oct-2020)
https://journals.lww.com/jaids/Fulltext/2008/04010/Sexual_Behavior_and_Reproductive_Health_Among.11.aspx

< 1% match (Internet from 29-Jul-2020)
https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-019-6694-4

< 1% match (Internet from 15-Oct-2019)
https://www.tandfonline.com/doi/full/10.3109/15412555.2014.898049

< 1% match (Internet from 21-Oct-2020)
https://www.researchsquare.com/article/rs-43678/v1

< 1% match (Internet from 26-Jul-2020)
https://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0192451

< 1% match (Internet from 27-Dec-2019)
https://academic.oup.com/ije/article/47/6/1887/5086723

< 1% match (publications)
Do Sun Kwon, Tae Hee Kim, Min Kwang Byun, Hyung Jung Kim, Hye Sun Lee, Hye Jung Park. "Positive Effects of the National Cigarette Price Increase Policy on Smoking Cessation in South Korea", Tuberculosis and Respiratory Diseases, 2020

< 1% match (publications)
Soheir Mohamed Wehieda. "Effect of Implementation of Teaching Modules about Physiological and Psychological Parameters on Expected Clinical Outcomes of Patients with Chronic Obstructive Pulmonary Disease", American Journal of Nursing Science, 2017

< 1% match (publications)
Antoni Sicras-Mainar, Javier Rejas-Gutiérrez, Ruth Navarro-Artieda, Jordi Ibáñez-Nolla. "The Effect of Quitting Smoking on Costs and Healthcare Utilization in Patients with Chronic Obstructive Pulmonary Disease: A Comparison of Current Smokers Versus Ex-Smokers in Routine Clinical Practice", Lung, 2014

< 1% match (publications)
Ivan Kopitovic, Aleksandar Bokan, Ilija Andrijevic, Miroslav Ilic, Sanja Marinkovic, Dragana Milicic, Marija Vukoja. "Frequency of COPD in health care workers who smoke", Jornal Brasileiro de Pneumologia, 2017

ABSTRACT Chronic Obstructive Pulmonary Disease (COPD) is a preventable burden on international health with often a preventable risk factor in the form of smoking. Smoking cessation plays a major role in morbidity and mortality of COPD. Determining factors that influence smoking cessation thus plays a huge role in establishing successful smoking cessation and reducing morbidity and mortality associated with COPD. Objectives Cross sectional survey of patients with COPD at the Helen Joseph Hospital, conducted between June and August 2018. Questionnaires were given to the patients in a confidential manner, where details like whether they were still smoking or not and the number of years they had been smoking for were interrogated. Determinants such Socio-economic standing, highest level of education and symptomatology were amongst the few determinants that were included in the questionnaire. Results Of the 50 respondents, 33 had successfully stopped smoking and 17 were still smoking at the time they took the questionnaire. We found that 74% of patients who took part in the study and severe diseases according to their Global Initiative for Obstructive Lung Disease (GOLD) score, this also related to the subject's smoking exposure expressed in pack years. Where both smoking and ex-smoker patients had more than 10 pack year history of smoking. We found that the most statistically significant result was the socio-economic standing of our subjects. Where 76.6% and 75.8% in the ex-smoker and smoking groups were unemployed respectively, where majority earned below R19 200 per annum. Conclusion Smoking cessation is an important aspect in the management of COPD and by understanding these determinants a lot can be done to reduce COPD morbidity and mortality. A lot though still needs to be done in smoking cessation interventions. This study reveals the areas in which interventions may be targeted. Chapter 2: Submissible Article Introduction Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation. This limitation is due to airway and/ or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.(1) In 2005, three million people died from COPD making it the fifth leading cause of death in the world.(2) In the period between 1990 and 2010 there has been a significant documented increase in the number of patients with COPD in Africa.(3) The epidemiological evidence may however be underrepresented, due to limited availability of spirometry which was previously required for diagnosis. The prevalence of COPD in the Sub-Saharan region is estimated at 11%, with an estimated 29 million people affected within this region.(4) Smoking is the foremost modifiable risk factor and smoking cessation is the main intervention shown to modify the course of COPD.(5) Cigarette smoke contains 4700 constituents that increase the production of endogenous reactive species which predispose to the development of COPD.(6) Smokers are 3-5 times more likely to develop COPD than non- smokers. Epidemiological studies have shown that at least 64% of patients with COPD have either smoked or are currently smoking. (7) The benefits of smoking cessation have been well documented. In the Lung Health Study (LHS), patients who had quit smoking showed reduction in morbidity (in the form of recurrent lower respiratory tract infections), improvement in their Forced Expiratory Volume (FEV1) and reduction in all-cause mortality.(8) Mortality rates equal those of non-smokers within 15 years of smoking cessation. Smoking cessation also decreases the risk of developing the co-morbidities associated with smoking and COPD such as cardiovascular disease and malignancies (both lung and non- lung). These findings emphasize the importance of encouraging patients with COPD to stop smoking.(9) Multiple modalities are used to assist with smoking cessation. It has been shown that the combination of pharmacological and non-pharmacological interventions improve outcomes. (10) Two classes of pharmacotherapy have been approved for assistance in smoking cessation. They are classified into nicotine replacement therapy (NRT) and drugs that reduce 17 addiction, namely, Buproprion and Varenicline. These drugs are unavailable in the South African state sector. Non-pharmacological measures include public health measures such as, tobacco taxes, ban on advertising, and ban on smoking in public areas, all of which have shown some reduction in smoking.(11) These methods are growing in favor in South Africa.(12) Supportive efforts are an additional form of non-pharmacological interventions. These include educational, motivational, and behavioral interventions. Motivational strategies have shown some benefit. A method of counselling called the 5 As and 5 Rs is a standardized method widely used for smoking cessation.(13) Spontaneous smoking cessation rates annually are 3-5 % but with health professional advice this rate can be increased to 5.5- 7.5%.(14) Numerous studies have been done to investigate the determinants of smoking cessation in patients with COPD. A retrospective study done in Denmark showed multiple variables that could hinder or improve smoking cessation in these patients. These included, mental health, low socio-economic status, unemployment, severity of disease and level of education.(15) Smoking pervasiveness is higher in deprived populations and smokers from these communities could face an increased risk for the deleterious effects of tobacco. Smoking cessation is less likely in persons of lower socioeconomic standing and their attempts to quit are not as successful. Possible reasons cited in the literature include poor social support, decreased motivation, worse addiction to tobacco, higher risk of defaulting pharmacotherapy and counselling sessions and targeted marketing by the tobacco industry.(16) A previous South African study identified female gender, increased age, a higher number of cigarettes smoked per day, a smoke-free home, recognition that cigarettes cause harm and previous alcohol dependence increased cessation success. (15) In this study we analyzed determinants of smoking cessation in patients with COPD at the Helen Joseph Hospital. We determined the number of patients who had quit after a diagnosis of COPD and describe the demographic, health and smoking related factors that determine smoking cessation in patients with COPD. This study was approved by the Human Research Ethics Committee (Medical) University of the Witwatersrand (Appendix A; Approval M180635) Methods We conducted a cross sectional study at the Helen Joseph Hospital. This hospital consists of 21 inpatient wards and functions as a referral hospital. It provides tertiary services to the west of Johannesburg and parts of the neighboring North West province. Patients were approached either during their out-patient clinic visits or during their admission. They were interviewed, and the researcher completed the questionnaire. Relevant data was extracted from the respiratory clinic files and inpatient files. Data was collected over a 3month period, between June 2018 and August 2018. Fifty patients agreed to participate in the study. Study Population All patients with a diagnosis of COPD (based on spirometry and a history of symptoms according to the GOLD classification) at the Helen Joseph Hospital. Patients were included if they had a history of smoking, diagnosed COPD on symptoms or spirometry and were 18 years or older. They were excluded if they did not consent to participation in the study. Data Analysis Data was entered into GraphPad Instat, a commercial statistics software. Proportions were represented with percentages and means with standard deviations. A chi square test was used to analyze associations between smoking cessation and patient characteristics. Results The cohort was

made up of 50 respondents. The group was divided into those who continued to smoke (Smokers) versus those that had ceased to smoke (Ex-smokers). The results revealed that most of the respondents i.e. 33 (66%) had stopped smoking while 17 (34%) of were still smoking. Chi square tests were conducted to assess whether there was an association between smoking and the other variables such as age, economic status, level of education etc. The results are summarised below. Table 1 Socio-demographic Data Age Current Employment Highest level of education? Annual household income? 30-65 years old >65 Yes No No Tertiary Education Tertiary Education No income R1 - R 19 200 R 19 201 - 307 200 R 307 201 and above Smokers 14 (82%) Ex-smokers 22 (66%) Total 36 (72%) P-value 0.327 3 (17.6%) 11 (33.3%) 14 (28%) 4 (23.5%) 8 (24.2%) 12 (24%) 1.000 13 (76.5%) 25 (75.8%) 38 (76%) 17 (100%) 28 (84.4%) 45 (90%) 0.112 0 (0%) 5 (15.2%) 5 (10%) 6 (35.3%) 2 (6.1%) 8 (16%) 0.039 8 (47.1%) 27 (81.8%) 35 (70%) 1 (5.9%) 2 (6.1%) 3 (6%) 2 (11.8%) 2 (6.1%) 4 (8%) Table 2 Smoking History Smokers Ex-smokers Total P-value No of cigarettes/day currently or previously <15 ≥15 No. of years smoking/ previously smoked >10 <10 Pack year history 5-10 >10 6 11 0 17 0 19 12 21 1.00 4 29 0.285 7 25 0.079 Initial COPD diagnosis Perception of COPD as a problem? No. of admissions in the past year (COPD related) <5 years 5-10 years>10 years Yes No Table 3 COPD History Smokers Ex smokers Yes No 13 (76.5%) 18 (54.5%) 1 (5.9%) 12 (36.4%) 3 (17.6%) 3 (9.1%) 13 (76.5%) 4 (23.5%) Total 31 (62%) 13 (26%) 6 (12%) 13 (76.5%) 4 (23.5%) P Value 0.062 <1 12 (70.6%) 20 (60.6%) 32 (64%) 0.548 ≥2 5 (29.4%) 13 (39.4%) 18 (36%) GOLD Classification 25 20 15 10 5 0 GOLD A GOLD B GOLD C GOLD D Ex-Smoker Smoker Figure 1 – GOLD Classification of patients Table 4 Activity Level and GOLD Classification Dyspnoea Walking Scale <100m Stop when walking on level ground Daily activities Minimal exercise or going up an incline GOLD GOLD A Classification GOLD B GOLD C GOLD D Smokers Ex-smokers Total 8 (47.1%) 11 (33.3%) 19 (38%) 6 (35.3%) 7 (21.2%) 13 (26%) P-value 0.357 2 (11.8%) 6 (18.2%) 8 (16%) 1 (5.9%) 7 (21.2%) 8 (16%) 0 3 (17.6%) 0 14 (82.3%) 3 (9%) 5 (15%) 2 (6%) 23 (69.7%) 3(6%0 0.413 8 (16%) 2 (4%) 37 (74%) Associated chronic illnesses Current/prev ious mental illness? Cardiovascular disease alone Cardiovascular & other diseases Endocrine Disease HIV Musculoskeletal Disease None Yes No Table 5 Co-morbidities Smokers Ex-smokers 6 (35.3%) 11 (33.3%) 2 (11.8%) 1 (5.9%) 2 (11.8%) 2 (11.8%) 3 (17.6%) 2 (11.8%) 15 (88.2%) 3 (6%) 3 (9.1%) 1 (3%) 1 (3%) 11 (33.3%) 3 (9.1%) 30 (90.9%) Total 17 (34%) 2 (4%) 4 (8%) 3 (6%) 3 (6%) 14 (28%) 5 (10%) 45 (90%) P-value 0.387 1.000 Smoking Cessation Amongst the 17 smokers, 16 (94%) had attempted cessation. In this sub-group 13 (76%) perceived their continued smoking as a problem whilst 4 (24%) patients did not. Table 6 Smoking Cessation Motivation (Ex-smokers) Motivation Factor Number (%) P-value Family intervention 2 (6.1%) Appropriate time 1 (3%) Dyspnoea on speaking 12 (36.4%) Hospital admission 7 (21.2%) 0.198 Counsel by doctor 7 (21.2%) None 4 (12.1%) Discussion Smoking cessation has been shown to be the most effective way to stop the progression of COPD, in addition to improving survival and decreasing morbidity. Smoking cessation should therefore take precedence in the management of COPD. (17) In our patients with COPD (both smokers and ex-smokers) the majority of patients smoked for more than 10 years and had pack year histories in excess of 10 years. This observation confirms the long established relationship between increased smoking exposure and COPD, and re-affirms the findings of Bhatt et al who showed that smoking on its own provides the biggest risk factor for COPD. (18) The only statistically significant factor that influenced the likelihood of smoking cessation in our cohort was the household income of the study participant. Patients with lower household incomes were less likely to stop smoking. These findings are consistent with the conclusions of a review on the effects of socioeconomic status and smoking. The authors decided that amongst people with a lower socio-economic status smoking cessation attempts are less likely to succeed.(16) Our results are similar to those of Hymowitz et al. They conducted a telephonic survey of 13415 "smokers" in 1993 and repeated the survey in 1998. They concluded that a high income was significantly associated with successful smoking cessation. (19) The influence of income was further ratified by Wilcox et al. They studied 703 smokers over a six month period and determined that smokers with higher incomes are more likely to quit smoking. (20) It has been suggested that social context or life circumstances e.g. poverty may result in the smoker giving quitting a low priority. (15,21) In our study employment status did not have a significant effect on the likelihood of smoking cessation. This mirrors a Brazilian study where employment status did not significantly affect smoking cessation. That study was however biased in that their cohort consisted only of patients who had actively sought help for smoking cessation. (22). The majority (74%) of our patients had severe disease and were in GOLD class D. Previous publications have noted that the GOLD classification of patients influenced their likelihood of smoking cessation. Patients with more severe disease were more likely to stop smoking. (7,8). We did not show a significant difference in the cessation rates between patients in GOLD classes A; B; C and D. The small numbers of patients in each of the GOLD sub- groups, except D make our results open to bias. The link between smoking cessation and age was not significant in our cohort. The effects of age on smoking cessation is varying. A Danish study found that the likelihood of discontinuing smoking is higher in the elderly (>70years). (15) In an English study smoking cessation was more common in adults >50years, however the authors also noted that young adults (<30years) had similar rates of smoking cessation.(20) In the sub-group of smokers 16 of the 17 patients (94%) had attempted smoking cessation but failed, although only 13 (76%) admitted to perceiving their continued smoking as a problem. Methods used by the subjects in the 2 groups included no support; counselling and/or pharmacological therapy. Most patients did not have any pharmacological support, which can be attributed to the unavailability of the drugs at our facility and the prohibitive costs of obtaining the drugs privately. A Cochrane review on individual behavioural counselling for smoking cessation found that health care provider counselling increased the likelihood of smoking cessation. (23) Participants in our study were asked to comment on their health care provider counselling. Most subjects replied yes to this question but on further questioning on how often this was done and what methods were offered health care providers fared dismally. They did not comply with the recommendations of the South African smoking cessation guidelines.(13) This further testifies to the lack of smoking cessation supportive measures in the South African public health care sector. Conclusion Household income significantly influenced the success of patients in their efforts to quit smoking and whilst we are unable to influence this, as physicians we should be advocating for additional supportive measures for our patients with COPD. Further research is needed to facilitate smoking cessation, especially in disadvantaged communities. Limitations Our small sample size limited our analyses. The cross-sectional nature of the study limits the reproducibility of our data, specifically the proportion of patients who continue to refrain from smoking. We were unable to secure funding for nicotine testing and were forced to rely on self-reporting to determine whether patients had stopped smoking. Reference List 1. Global Initiative For Obstructive Lung Disease. GOLD-2018-v6.0-FINAL-revised-20- Nov_WMS.pdf [Internet]. [cited 2019 Jan 31]. Available from: https://goldcopd.org/wp- content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf 2. Bousquet J, Weltgesundheitsorganisation, editors. Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. Geneva: WHO; 2007. 146 p. 3. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. J Glob Health [Internet]. [cited 2019 Jan 31];5(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693508/ 4. Lopez AD. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J [Internet]. 2006 Feb 1 [cited 2019 Jan 31];27(2):397–412. Available from: http://erj.ersjournals.com/cgi/doi/10.1183/09031936.06.00025805 5. Wu J, Sin DD. Improved patient outcome with smoking cessation: when is it too late? Int J Chron Obstruct Pulmon Dis [Internet]. 2011 [cited 2019 May 7];6:259–67. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3144846/ 6. Bai J, Chen X, Liu S, Yu L, Xu J. Smoking cessation affects the natural history of COPD. Int J Chron Obstruct Pulmon Dis [Internet]. 2017 Nov [cited 2019 Jan 31];Volume 12:3323–8. Available from: https://www.dovepress.com/smoking-cessation-affects-the- natural-history-of-copd-peer-reviewed-article-COPD 7. Laniado-Laborín R. Smoking and Chronic Obstructive Pulmonary Disease (COPD). Parallel Epidemics of the 21st Century. Int J Environ Res Public Health [Internet]. 2009 Jan [cited 2020 Oct 1];6(1):209–24. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2672326/ 8. Tashkin DP, Murray RP. Smoking cessation in chronic obstructive pulmonary disease. Respir Med [Internet]. 2009 Jul [cited 2020 Oct 11];103(7):963–74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0954611109000651 9. Warnier MJ, van Riet EES, Rutten FH, De Bruin ML, Sachs APE. Smoking cessation strategies in patients with COPD. Eur Respir J [Internet]. 2013 Mar [cited 2019 Aug 12];41(3):727–34. Available from: http://erj.ersjournals.com/lookup/doi/10.1183/09031936.00014012 10. Dhariwal J, Tennant RC, Hansell DM, Westwick J, Walker C, Ward SP, et al. Smoking Cessation in COPD Causes a Transient Improvement in Spirometry and Decreases Micronodules on High-Resolution CT Imaging. Chest [Internet].

2014 May [cited 2019 Apr 21];145(5):1006–15. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921534592X 11. Chandler MA, Rennard SI. Smoking Cessation. Chest [Internet]. 2010 Feb [cited 2019 Apr 21];137(2):428–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921060089X 12. Reddy P, Sewpaul R. Tobacco control and health. Policy brief. Human Sciences Research Council. June 2014 13. Van Zyl-Smit RN, Allwood B, Stickells D, Symons G, Abdool-Gaffar S, Murphy K, et al. South African tobacco smoking cessation clinical practice guideline. S Afr Med J [Internet]. 2013 Sep 30 [cited 2019 Apr 21];103(11):869. Available from: http://www.samj.org.za/index.php/samj/article/view/7484 14. Nicotine Withdrawal - an overview | ScienceDirect Topics [Internet]. [cited 2020 Aug 2]. Available from: https://www.sciencedirect.com/topics/medicine-and-dentistry/nicotine-withdrawal 15. Tøttenborg SS, Thomsen RW, Johnsen SP, Nielsen H, Lange P. Determinants of Smoking Cessation in Patients With COPD Treated in the Outpatient Setting. CHEST [Internet]. 2016 Sep 1 [cited 2019 Feb 3];150(3):554–62. Available from: https://journal.chestnet.org/article/S0012-3692(16)49107-5/abstract 16. Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. Ann N Y Acad Sci [Internet]. 2012 [cited 2020 Oct 1];1248(1):107–23. Available from: https://nyaspubs.onlinelibrary.wiley.com/doi/abs/10.1111/j.1749-6632.2011.06202.x 17. Tonnesen P. Smoking cessation and COPD. Eur Respir Rev [Internet]. 2013 Mar 1 [cited 2019 Aug 12];22(127):37–43. Available from: http://err.ersjournals.com/cgi/doi/10.1183/09059180.00007212 18. Bhatt SP, Kim Y, Harrington KF, Hokanson JE, Lutz SM, Cho MH, et al. Smoking duration alone provides stronger risk estimates of chronic obstructive pulmonary disease than pack-years. Thorax [Internet]. 2018 May 1 [cited 2020 Jul 26];73(5):414–21. Available from: https://thorax.bmj.com/content/73/5/414 19. Hymowitz N, Cummings K, Hyland A, Lynn W, Pechacek T, Hartwell T. Predictors of smoking cessation in a cohort of adult smokers followed for five years. Tob Control [Internet]. 1997 Jun [cited 2019 Aug 13];6(Suppl 2):S57–62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1766209/ 20. Wilcox NS, Prochaska JO, Velicer WF, DiClemente CC. Subject characteristics as predictors of self-change in smoking. Addict Behav [Internet]. 1985 Jan 1 [cited 2019 Aug 13];10(4):407–12. Available from: http://www.sciencedirect.com/science/article/pii/0306460385900371 21. CDCTobaccoFree. Cigarette and Tobacco Use Among People of Low Socioeconomic Status [Internet]. Centers for Disease Control and Prevention. 2019 [cited 2020 Aug 2]. Available from: https://www.cdc.gov/tobacco/disparities/low-ses/index.htm 22. França SA de S, Neves ALF das, Souza TAS de, Martins NCN, Carneiro SR, Sarges E do SNF, et al. Factors associated with smoking cessation. Rev Saúde Pública [Internet]. 2015 [cited 2019 Aug 13];49(0). Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034- 89102015000100203&lng=en&tlng=en Chapter 3: Appendices Appendix A: Smoking Cessation Questionnaire Patient Questionnaire 1. How old are you? 30-55 □ 55-65 □ >65 □ 2. When were you diagnosed with COPD? <5 years ago □ 5-10 years ago □ >10 years ago □ 3. Do you currently smoke? Yes □ No □ 4. If yes do you see it as a problem? Yes No □ □ 5. How many cigarettes do you smoke per day? 5-10 □ 10-15 □ 15-20 □ >20 □ 6. How many years have you been smoking for? <5 □ 5-10 □ >10 years □ 7. Pack year history <5 5-10 >10 years □ □ □ 8. How many admissions have you had in the past year? (NB! COPD-related) None □ Once □ More than twice □ 9. When are you short of breath? With strenuous exercise (jogging, cycling etc) With minimal exercise or when going up an incline I have to stop when walking on level ground I am breathless when walking a distance less than 100m I am breathless while doing daily activities (e.g. getting dressed) □ □ □ □ □ 10. Are you employed? Yes No □ □ 11. What is your highest level of education? I never went to school □ Primary school □ High School □ Tertiary education □ 12. If you currently smoke, have you attempted to stop? Yes □ No □ 13. What motivated you to stop? I was admitted to hospital I was counselled by my doctor I feel ill when I smoke Family intervention Other measures □ □ □ □ □ 14. Do you have any other illness besides chronic obstructive lung disease? Cardivoscular disease □ Respiratory (lung disease) Endocrine Disease □ (e.g Diabetes, Thyroid disease) Musculo-Skeletal Disease □ (e.g arthritis) 15. Do you currently suffer or have you previously suffered from any form of mental illness? Yes □ No □ 16. What is your annual household income? No income □ R1- R 19200 □ R 19 201 - R 307 200 □ R307 201 and above □ 17. What Methods have you used to stop smoking? Counselling □ Prescription Medications □ Electronic Cigarettes □ Nicotine Replacement therapy □ (eg. nicotine gum) 18. Did your health care provider counsel you on quitting? Yes □ No □ 19. How often did your doctor speak to you about smoking cessation? Once □ Every Visit □ Never Occasionally (more than once but not at every visit) □ □ 20. If yes, what methods did he/she offer you? _____ Comments: _____ _____ _____ 16 18 19 20 21 22 23 24 25 26 27 28 29 30 31

Turnitin Originality Report

Processed on: 22-Oct-2020 4:06 PM SAST
ID: 1423117761
Word Count: 3345
Submitted: 1

0705245v:Determinants_of_Smoking_Cessation_in_COPD_Extended_Literature_Review.pdf
By Lindokuhle Goqwana

Similarity Index
16%

Similarity by Source

Internet Sources:	12%
Publications:	11%
Student Papers:	8%

2% match (student papers from 26-Oct-2012)
Submitted to University of Newcastle upon Tyne on 2012-10-26

1% match (publications)
Michael A. Chandler, Stephen I. Rennard. "Smoking Cessation", Chest, 2010

1% match (publications)
David Lomas, Dickens. "Why has it been so difficult to prove the efficacy of alpha-1-antitrypsin replacement therapy? Insights from the study of disease pathogenesis", Drug Design, Development and Therapy, 2011

1% match (student papers from 10-Apr-2009)
Submitted to Indiana State University on 2009-04-10

1% match (publications)
Shiraz Shaikh, Asaad Ahmed Nafees, Vikash Khetpal, Abid Ali Jamali, Abdul Manan Arain, Akram Yousuf. "Respiratory symptoms and illnesses among brick kiln workers: a cross sectional study from rural districts of Pakistan", BMC Public Health, 2012

1% match (Internet from 18-Oct-2017)
http://scripties.umcg.eldoc.ub.rug.nl/FILES/root/geneeskunde/2015/JansenS/JansenS.pdf

1% match (student papers from 09-Nov-2015)
Submitted to University of Witwatersrand on 2015-11-09

1% match (student papers from 08-Apr-2009)
Submitted to University of New South Wales on 2009-04-08

1% match (publications)
Claus F. Vogelmeier, Gerard J. Criner, Fernando J. Martinez, Antonio Anzueto et al. "Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary", European Respiratory Journal, 2017

1% match (publications)
Heiko Golpon. "The Role of Proteases in the Pathogenesis of Lung Emphysema", Proteases in Tissue Remodelling of Lung And Heart, 2003

1% match (Internet from 11-Mar-2016)
http://not-so-great-northern-transmission-line.org/wp-content/uploads/2015/08/Legalectric_GNTL_DEISComment_8-10-2015.pdf

< 1% match (Internet from 01-Jul-2018)
https://bestpractice.bmj.com/topics/en-gb/8

< 1% match (Internet from 25-Jan-2020)
https://www.dovepress.com/front_end/enlightening-chronic-obstructive-pulmonary-disease-through-patients-an-peer-reviewed-fulltext-article-COPD

< 1% match (publications)
Sundeep Salvi, Ashish Kumar Deb, Mayank Agarwal, Venkateswara Reddy Tummuru et al. "Fixed-dose combination of three drugs, i.e. LABA/LAMA/ICS for COPD: results of a real-world study from India", Pulmonary Pharmacology & Therapeutics, 2020

< 1% match (Internet from 02-May-2016)
http://journal.publications.chestnet.org/article.aspx?articleid=1086255

< 1% match (Internet from 07-Apr-2016)
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693508/

< 1% match (Internet from 10-May-2020)
https://www.magonlinelibrary.com/doi/full/10.12968/bjhc.2017.23.6.252

< 1% match (Internet from 03-Aug-2020)
https://nursinganswers.net/essays/causes-effects-teenage-smoking-5062.php?vref=1%2F

< 1% match (publications)

Adam L. Friedlander, David Lynch, Liesel A. Dyar, Russell P. Bowler. "Phenotypes of Chronic Obstructive Pulmonary Disease", COPD: Journal of Chronic Obstructive Pulmonary Disease, 2009

< 1% match (Internet from 31-May-2009)
http://www.westernhealth.com/providers/downloads/GOLD%20Report%20COPD%20Guidelines%20Full%20Report%202007.

< 1% match ()
http://www.fedoa.unina.it/11594/1/deblasio_francesca_29.pdf

< 1% match (Internet from 05-Aug-2014)
http://www.tobaccoinaustralia.org.au/downloads/chapters/Ch3_Healtheffects.pdf

< 1% match (student papers from 11-Jun-2014)
Submitted to University of Newcastle upon Tyne on 2014-06-11

< 1% match ()
https://cris.maastrichtuniversity.nl/ws/files/11957480/v5649.pdf

< 1% match ()
http://bdigital.unal.edu.co/51402/

< 1% match (Internet from 06-Dec-2019)
https://www.powerpak.com/course/print/115436

< 1% match (Internet from 27-Apr-2020)
https://pdfs.semanticscholar.org/00e8/f657c08a46a95028b50857a688bc16847dd2.pdf

< 1% match (Internet from 12-Oct-2020)
https://hsag.co.za/index.php/hsag/article/download/1384/pdf

< 1% match (Internet from 04-Feb-2020)
https://www.cadth.ca/sites/default/files/pdf/OP0525_OSA_Treatment_HTA_Report.pdf

< 1% match (publications)
"Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary Updated 2003", COPD: Journal of Chronic Obstructive Pulmonary Disease, 2004

< 1% match (publications)
Wonnacott, S.. "Nicotine: from molecular mechanisms to behaviour", Current Opinion in Pharmacology, 200502

CHAPTER 1: PROTOCOL WITH EXTENDED LITERATURE REVIEW Introduction Chronic Obstructive Pulmonary Disease (COPD) - "A common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/ or alveolar abnormalities usually caused by significant exposure to noxious particles or gasses." (1) According to the Global Initiative for Chronic Obstructive Lung Disease, COPD is classified into four groups (GOLD 1,2,3,4) based on post bronchodilator Forced Expiratory Volume1 (FEV1) and further into another four groups (GOLD A,B,C,D) based on symptoms and risk of exacerbation.(1) Please see tables below where the classifications are illustrated. Table 1.1 Airflow Limitation in COPD (1) Classification of Airflow limitation in COPD (Based on post-bronchodilator FEV1) GOLD 1 Mild FEV1>80% predicted GOLD 2 Moderate 50%< FEV1 < 80% predicted GOLD 3 Severe 30%< FEV1 <50% predicted GOLD 4 Very Severe FEV1< 30% Table 1.2 The ABCD assessment tool (1) >2 or >1 exacerbation leading D to hospitalization D 0 or 1 exacerbation (not leading to hospitalization) A B MRC 0 -1* MRC >/=2* Table 1 .3 Modified Medical Research Council (mMRC) Dyspnoea Scale (2) Grade Description of Breathlessness mMRC Grade 0 Breathlessness with strenuous exercise mMRC Grade 1 Breathlessness when hurrying on level ground or walking up a slight hill mMRC Grade 2 Have to stop for breath when walking at own pace mMRC Grade 3 Breathlessness after 100 of walking mMRC Grade 4 Breathlessness on mild functions of daily living Epidemiology In 2005, three million people died from COPD making it the fifth leading cause of death in the world. (3) In the period between 1990 and 2010 there has been a significant documented increase in the number of patients with COPD in Africa.(4) The epidemiological evidence may however be underrepresented, due to lack of spirometry which was required previously for diagnosis. The prevalence of COPD in the Sub-Saharan region is estimated at 11%, with an estimated figure of 29 million people within this region.(5) Smoking has been identified as an important risk factor in the development of COPD. Epidemiological studies have shown that at least 64% of patients with COPD have either smoked or are currently smoking.(6) Smokers are 3-5 times more likely to develop COPD than non-smokers. Cigarette smoke contains 4700 constituents that increase the production of endogenous reactive species. (7) Risk Factors for COPD Multiple risk factors for COPD have been outlined. Understanding the risk factors may help with reducing disease progression as this is an irreversible disease process. • Cigarette smoking is probably the most well described risk factor for COPD. The relationship between smoking and COPD has been considered for the last 50 years, the British being the first to establish it in a study that followed smokers for 8 years. They found that susceptible smokers showed a decline in their lung function.(8) • Smoking both Marijuana and cigarettes together shows an increase in COPD and symptomatology.(9) • There are multiple devices which are used in smoking and not just the traditional cigarette. Different cultures use different ways to smoke tobacco for example the hookah which has the tobacco smoke go through water before reaching the smokers lungs. It was previously thought that this device was safer but this was found not to be true as this may have other additives besides tobacco that may be harmful. (8) • An association with second hand smoking and development of COPD has been found with multiple reviews showing that people exposed to second hand smoke have a 2. 5 greater risk of developing COPD than those that have no exposure.(8) The second hand smoke may be more harmful than actual cigarette smoke as this smoke is unfiltered, meaning it contains more harmful substances than direct smoke.(8) • The concept of biomass fuel exposure is an extremely important one in the South

African setting where 20% of the population lives in informal and traditional dwellings. This is where cheaper less clean fuels are used for example: wood, animal dung, fossil coal etc. These fuels are harmful because they release numerous air pollutants, which results in endogenous reactive species formation and airway inflammation and remodeling.(8) • Genetic factors play a role in the development of COPD. The most readily described genetic disorder associated with COPD is Alpha 1 Antitrypsin deficiency. First described in 1963 by Laurell and Erikson. They found an absence of alpha 1 antitrypsin in serum protein electrophoresis. This deficiency is associated with early onset of COPD and/or liver cirrhosis, and is associated with panacinar emphysematous changes. (10) • The following forms of industrial exposure are shown to carry an increased risk for COPD: • Dust exposure (concrete, coal mining, construction etc.) • Animal farming • Crop farming • Chemical Exposure(8) • Outdoor Air pollution, mainly from car emissions and industrial pollution have also been shown to be risk factors for COPD. (8) • Females seem to be more susceptible to developing COPD than males. Women with the same degree of disease as men are found to have smoked substantially less than men.(11) • Persistent and severe childhood asthma may predispose to development of COPD.(1) Biology of Cigarette Smoking The hallmark of COPD is airflow limitation, and this may be as a result of small airway disease or emphysema. The airflow limitation is due to mucous accumulation and lung fibrosis causing airway narrowing. [9] The pathogenesis of emphysema is based on four processes. See Figure1 below. 1. Cigarette smoke exposure interacting with possible genetic host factors - leading to inflammatory and immune cell activation and recruitment within the terminal air spaces of the lung (12) 2. These immune cells release proteases and elastolytic substances resulting in damage of the extracellular matrix of the lung (12) 3. Endothelial and epithelial cell death occurs secondary to free radical exposure from the cigarette smoke (12) 4. The lung is unable to repair the airway resulting in alveolar wall destruction and air space enlargement which is characteristic of emphysema as well as chronic bronchitis (12) 4 Figure1.1 Pathophysiology of Chronic Obstructive Pulmonary Disease (13) Nicotine addiction is an important factor as 3 million smoking related deaths are reported annually worldwide. (14) Nicotine, a mediator of addictions, acts on endogenous acetylcholine receptors (AChRs) found in the nervous system of all vertebrate and invertebrates. Nicotine has rewarding motivational effects by acting on the Ventral Tegmental Area (VTA), similar to that of cocaine, alcohol etc. The major neurotransmitters implicated in this reward process are Dopamine and Gamma Aminobutyric Acid (GABA). Dopamine is released from the VTA and sends projections to the nucleus accumbens and the prefrontal cortex. Resulting in the reward affect that cigarette smoking has. Multiple factors play a role in nicotine addiction and non-dopamine pathways are also implicated in the role of nicotine addiction. (14) Smoking Cessation Determinants Multiple studies have been done in investigating the determinants of smoking cessation in patients with COPD. A retrospective cohort done in Denmark showed multiple variables that could hinder or improve smoking cessation in these patients. (15) • Mental Health – Psychiatric illness patients were less likely to stop smoking, this may be due to the theory that smoking cessation may exacerbate mental illness. (14) • Low socio-economic status – Lower cessation rates were documented in patients of low socio-economic standing, this was thought to be due to lack of funds for pharmacological interventions to assist with cessation. (15) • Marital Status – Patients who live alone are less likely to stop smoking. (15) • Unemployment - Patients who were unemployed had a lower incidence of smoking cessation, this was attributed to the amount of free time individuals had and the psychological stressors imposed by the status of being unemployed. (15) • Severity of Disease - Patients with severe COPD were found to have better abstinence possibly attributable to the functional limitation associated with this stage of disease. (15) • Level of Education - Education was another determinant. They found that subjects that had only obtained a high school education smoked more than those that had obtained a university degree. (15) • Co-Morbidities – Patients with concomitant malignancy were found to be less likely to stop smoking than those without malignancy. It is important to note that patients with other medical diseases were more likely to stop smoking than those that only have COPD. (15) • Age – Younger patients were more unlikely to quit smoking than older patients. (15) Benefits of Smoking Cessation A study from the United Kingdom looked at the effects that smoking cessation had on patients FEV1 and Computed Tomography Scan changes at baseline, 6 weeks, 12 weeks and a year after smoking cessation. (15) They showed transient positive changes. These changes though, stabilized by 1 year post smoking cessation. The study showed that smoking cessation combined with pharmacological management could improve outcomes further. (15) In the Lung Health Study (LHS), patients with mild to moderate COPD were evaluated. The patients who had successfully quit were in one arm, those who intermittently quit were in the second arm and those who had not quit were in the third arm. Those who had quit showed reduction in morbidity (in the form of recurrent lower respiratory tract infections), improvement in their FEV1 and reduction in all-cause mortality. (16) The benefits of smoking cessation include a reduction in mortality. It has been reported that smokers die 13 to 14 years earlier than non-smokers. Causes of mortality equal that of non-smokers within 15 years of smoking cessation. One of the downsides of smoking cessation is the associated weight gain. Patients that stop smoking have an average weight gain of 5 kg within the 1st year of stopping. In the LHS the authors concluded that the health benefits of smoking cessation outweigh the risk of weight gain. (16) Smoking Cessation Methods Multiple modalities are used in order to assist with smoking cessation. They can be grouped into pharmacological and non-pharmacological methods. Non-pharmacological measures include public health measures such as, tobacco taxes, bans on advertising and bans on smoking in public areas. These steps have all shown some reduction in smoking. The European regions have shown the lowest increase in the prevalence of COPD between 1990 and 2010. This figure has been attributable to the intensive public health campaigns that these countries have implemented. (17) These methods are growing in favor in South Africa as smoking ban is currently being reviewed in the South African National Assembly. Supportive efforts are another form of non-pharmacological interventions. This includes educational, motivational and behavioral interventions. Spontaneous smoking cessation rates annually are 3-5 % but with health professional advice this rate can be increased to 5.5-7.5%. (18) Motivational strategies have shown some benefit. A method of counselling called the 5 As and 5 Rs is a standardized method being widely used for smoking cessation. (see table below)(18) Table 1.4 The 5 As and 5 Rs of smoking cessation (18) The 5 As and 5 Rs smoking cessation strategy Ask Enquire about smoking status Advise Firmly urge smokers to quit Assess Determine willingness to quit Assist Counsel as per 5 Rs. Start Pharmacotherapy Arrange Follow up by phone or office visit Relevance Patient to indicate why quitting is personally relevant Risks Identify negative consequences of tobacco use Rewards Identify benefits to smoking cessation Roadblocks Identify Barriers to quitting Repetition Apply the 5 Rs again with relapsed and unmotivated patients Pharmacological approaches can assist in smoking cessation. Two classes of pharmacotherapy have been approved for this: namely Nicotine Replacement Therapy (NRT) and drugs that reduce addiction i.e. Buproprion and Varenicline. • NRT is aimed at reducing withdrawal symptoms in patients with nicotine

addiction. It may be used alone or in combination with bupropion. It has been found to be effective, however 1 in 4 smokers will relapse within 4 years. (17) NRT comes in multiple forms (gum, lozenges, nasal spray, etc) and pricing is similar to that spent on cigarettes, making it affordable. (17) The NRT can be titrated to symptom severity. (18) • Bupropion is a dopamine, serotonin and norepinephrine reuptake blocker. It assists with the depressive symptoms that occur with smoking cessation. Bupropian mono-therapy has been found to be comparable to NRT mono therapy and superior to placebo in smoking cessation trials. (17) It may also be used in conjunction with NRT. (18) Buproprion is the drug of choice in the management of post cessation depression and weight gain. It is however contraindicated in patients with seizure disorders or with a high risk of seizures. Also, it is advisable that this drug not be used in patients with bipolar mood disorder as the anti-depressant effect will then unmask mania. (17) The dosing of Bupropion in smoking cessation is 150mg twice a day for 7 to 12 weeks. (18) • Veranicline, first discovered during World War 2 is an alpha4beta2 nicotine receptor agonist-antagonist. It causes dopamine release which leads to less craving. Veranicline currently has a boxed warning for adverse psychiatric effects such as depression, worsening of schizophrenia etc. Other antidepressants may also be used, though that would constitute off label usage. (17) In the face of limited local data we set out to determine the factors that affect smoking cessation in patients with COPD. Study Objectives Overall objective To determine the factors that affect smoking cessation in patients with COPD Specific aims 1. To investigate the proportion of patients that have quit smoking after a diagnosis of COPD (secondary to smoking), has been confirmed. 2. To describe the demographic, health and smoking related factors that determine smoking cessation in patients with COPD secondary to smoking Methods We will conduct a cross sectional study at the Helen Joseph Hospital. This hospital consists of 21 inpatient wards and functions as a referral hospital and provides tertiary services to the west of Johannesburg and parts of the neighboring North West province. The patients will be approached during their out-patient clinic visit where a written consent will be sought from them before proceeding to interview them. Relevant data will be extracted from the respiratory clinic files following their out-patient visit. Data will be collected over a four month period. We estimate that 300 patients will be evaluated during this period. Study Populations All patients with a diagnosis of COPD (based on spirometry and a history of smoking) attending the out-patient Respiratory clinic at the Helen Joseph Hospital Inclusion Criteria: Smoking history Proven COPD by lung function testing Adult Patients (>18years) Patients who have had any smoking exposure Exclusion Criteria Patients who do not consent Data Analysis Data will be put into GraphPad Instat, a commercial statistics software, for cleaning and identification of inconsistencies. Proportions will be represented with percentages and and means with Standard deviations. A chi square test will be used to analyse associations between smoking cessation patient characteristics. Ethics Ethics approval will be applied for from the Human Research Ethics Committee. Consent will be obtained from all subjects involved in the study. The management staff of the hospital will be approached for consent and ethical approval. All questionnaires will have a code and no use of names will occur in order to protect the confidentiality of the subjects Gantt Chart Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun July Aug Sep literature review Protocl Preparation Protocol assessment Ethics application Collecting Data Data Analysis Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun July Aug Sep Writing up Budget Printing R5000 Transport R3000 Limitations Nicotine assays are unavailable in out setting due to financial constraints. The sample size may be smaller than anticipated, depending on the clinic attendees during the designated period. Reference List 1. Global Initiative For Obstructive Lung Disease. GOLD-2018-v6.0-FINAL-revised-20- Nov_WMS.pdf [Internet]. [cited 2019 Jan 31]. Available from: https://goldcopd.org/wp- content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf 2. Fletcher CM, Elmes PC, Fairbairn AS. THE SIGNIICANCE OF RESPIRATORY SYMPTOMS AND THE DIAGNOSIS OF CHRONIC BRONCHITIS IN A WORKING POPULATION. :10. 3. Bousquet J, Weltgesundheitsorganisation, editors. Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. Geneva: WHO; 2007. 146 p. 4. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. J Glob Health [Internet]. [cited 2019 Jan 31];5(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4693508/ 5. Lopez AD. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J [Internet]. 2006 Feb 1 [cited 2019 Jan 31];27(2):397–412. Available from: http://erj.ersjournals.com/cgi/doi/10.1183/09031936.06.00025805 6. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet [Internet]. 2012 Dec 15 [cited 2019 Feb 3];380(9859):2095–128. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61728-0/abstract 7. Bai J, Chen X, Liu S, Yu L, Xu J. Smoking cessation affects the natural history of COPD. Int J Chron Obstruct Pulmon Dis [Internet]. 2017 Nov [cited 2019 Jan 31];Volume 12:3323–8. Available from: https://www.dovepress.com/smoking-cessation-affects-the-natural-history-of- copd-peer-reviewed-article-COPD 8. Salvi S. Tobacco Smoking and Environmental Risk Factors for Chronic Obstructive Pulmonary Disease. Clin Chest Med [Internet]. 2014 Mar 1 [cited 2019 Feb 3];35(1):17–27. Available from: http://www.sciencedirect.com/science/article/pii/S027252311300141X 9. Tan WC, Lo C, Jong A, Xing L, FitzGerald MJ, Vollmer WM, et al. Marijuana and chronic obstructive lung disease: a population-based study. CMAJ Can Med Assoc J [Internet]. 2009 Apr 14 [cited 2019 Feb 3];180(8):814–20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665947/ 10. Stoller JK, Aboussouan LS. A Review of α 1 -Antitrypsin Deficiency. Am J Respir Crit Care Med [Internet]. 2012 Feb [cited 2019 Apr 21];185(3):246–59. Available from: http://www.atsjournals.org/doi/abs/10.1164/rccm.201108-1428CI 11. Hardin M, Foreman M, Dransfield MT, Hansel N, Han MK, Cho MH, et al. Sex-specific features of emphysema among current and former smokers with COPD. Eur Respir J [Internet]. 2016 Jan [cited 2019 Feb 3];47(1):104–12. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5374719/ 12. Harrison's Principles of Internal Medicine, 20e | AccessMedicine | McGraw-Hill Medical [Internet]. [cited 2019 Feb 3]. Available from: https://accessmedicine.mhmedical.com/book.aspx?bookid=2129 13. Chronic obstructive pulmonary disease (COPD) | McMaster Pathophysiology Review [Internet]. [cited 2019 Apr 21]. Available from: http://www.pathophys.org/copd/ 14. Laviolette SR, van der Kooy D. The neurobiology of nicotine addiction: bridging the gap from molecules to behaviour. Nat Rev Neurosci [Internet]. 2004 Jan [cited 2019 Feb 3];5(1):55–65. Available from: https://www.nature.com/articles/nrn1298 15. Tøttenborg SS, Thomsen RW, Johnsen SP, Nielsen H, Lange P. Determinants of Smoking Cessation in Patients With COPD Treated in the Outpatient Setting. CHEST [Internet]. 2016 Sep 1 [cited 2019 Feb 3];150(3):554–62. Available from: https://journal.chestnet.org/article/S0012- 3692(16)49107-5/abstract 16. Anthonisen NR. Lessons from the Lung Health Study. Proc Am Thorac Soc [Internet]. 2004 Apr 1 [cited 2020 Oct 15];1(2):143–5. Available from: http://pats.atsjournals.org/cgi/doi/10.1513/pats.2306033 17. Chandler MA, Rennard SI.

Smoking Cessation. Chest [Internet]. 2010 Feb [cited 2019 Apr 21];137(2):428–35. Available from: https://linkinghub.elsevier.com/retrieve/pii/S001236921060089X 18. Van Zyl-Smit RN, Allwood B, Stickells D, Symons G, Abdool-Gaffar S, Murphy K, et al. South African tobacco smoking cessation clinical practice guideline. S Afr Med J [Internet]. 2013 Sep 30 [cited 2019 Apr 21];103(11):869. Available from: http://www.samj.org.za/index.php/samj/article/view/7484 19. Statistics South Africa - 2015 - Census 2011 income dynamics and poverty status of.pdf. [cited 2019 Apr 21] Available from: http://www.statssa.gov.za/publications/Report-03-10-10/Report- 03-10-102014.pdf 1 2 3 5 6 7 8 9 10 11 12 13 14