

## Worse Chronic Obstructive Pulmonary Disease Outcomes in Patients Who Smoke Both Tobacco and Marijuana

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### ABSTRACT

**Objective:** To compare clinical course and outcomes in patients admitted for Chronic Obstructive Pulmonary Disease (COPD) who smoke tobacco plus marijuana versus tobacco only.

**Methods:** A retrospective chart review was conducted for patients admitted to the Victoria and St Jude Hospitals from January 2014 to June 2016 with a primary discharge diagnosis of Chronic Obstructive Pulmonary Disease (COPD). Select biographic data, self-reported substance use, clinical course and adverse outcomes related to COPD were reviewed. The study was reviewed by the St Lucia Medical and Dental Council Ethics Committee and ethical approval granted.

**Results:** A total of 100 patient charts were reviewed; 70 patients in the tobacco plus marijuana group and 30 in the tobacco only group. There were significant differences in clinical course and outcomes between the two groups with poorer outcomes noted in tobacco plus marijuana smokers ( $p < .001$ ). Tobacco plus marijuana smokers required admission for COPD at a younger age (M = 45.4 years, SD = 9.4) compared to tobacco only smokers (M = 72.6 years, SD = 11.6). Tobacco plus marijuana smokers were more likely to be diagnosed with cor pulmonale (OR 15.7, 95% CI 3.47-71.01), which was associated with increased mortality (OR 8.2, 96% CI 3.2-20.8). Lastly, tobacco plus marijuana smokers died at an earlier age, mean age at death 47.6 years (SD = 7.2) versus 73.6 years (SD = 12.8) in tobacco only smokers. Worse clinical outcomes in tobacco plus marijuana smokers were seen despite lower cumulative tobacco consumption; mean of 11.8 pack years (SD = 14.3) versus 34.3 pack years (SD = 29.1) in tobacco only smokers.

**Conclusion:** Worse clinical outcomes were seen in tobacco smokers who also smoke marijuana. There was an increased risk of admission for COPD at a younger age and more frequent progression to cor pulmonale and death in tobacco plus marijuana smokers despite lower cumulative tobacco consumption compared with tobacco only smokers.

**Keywords:** COPD, chronic obstructive pulmonary disease, cor pulmonale, tobacco and marijuana smoking

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## **INTRODUCTION**

Physicians at St Lucia's general hospitals have noted a steady increase in the number of young patients admitted with severe Chronic Obstructive Pulmonary Disease (COPD) and its complications. Both hospitals have raised the concern that patients who smoke tobacco mixed with marijuana seem to develop and die from COPD and its complications at a significantly younger age than tobacco only smokers. The smoking of marijuana mixed with tobacco is a common practice among the youth in St Lucia and further study is required to investigate the adverse effects of combined marijuana and tobacco smoking in this patient population. Tan et al observed that smoking both tobacco and marijuana synergistically increased the risk of respiratory symptoms and COPD<sup>1</sup>.

Tan's Vancouver population based study suggested that concurrent use of tobacco and marijuana was associated with an increased risk of respiratory symptoms and COPD if the lifetime dose of marijuana exceeded 50 marijuana cigarettes. This increased risk is consistent with the trend of earlier onset of chronic lung disease in our population and underscores the need for further research to better assess the relationship between combined tobacco plus marijuana use and chronic lung disease in our patients. This study could inform future public health interventions aimed at decreasing the health burden of Chronic Obstructive Pulmonary Disease in St Lucia and other countries.

## **SUBJECTS AND METHODS**

A retrospective cohort study was used to investigate patients admitted to the Victoria and St Jude Hospitals from January 1<sup>st</sup> 2014 to June 30<sup>th</sup> 2016 with a primary discharge diagnosis of Chronic

Obstructive Pulmonary Disease (COPD). Patients were required to have a documented history of tobacco or tobacco plus marijuana use for inclusion. One hundred and seventeen (117) patient charts were reviewed. Exclusion criteria included pre-existing other lung disease (except asthma), significant pulmonary infectious disease, cocaine abuse, occupational or other environmental exposures known to cause lung disease, congenital and/or significant valvular heart disease and pulmonary hypertension from non-pulmonary causes. Seventeen (17) patients were excluded with pulmonary sarcoidosis (1), rheumatoid lung disease (1), pulmonary tuberculosis (1), occupational exposure from coal making (2), concomitant use of cocaine (11) and valvular heart disease (1). Of the remaining 100 patients included in the study 70 reported smoking tobacco plus marijuana and 30 reported smoking tobacco only.

### **Measurements and definitions**

Patient charts were reviewed by the principal investigator for select biographic information, substance use, clinical course and adverse outcomes related to COPD including death. Cumulative tobacco exposure was calculated in "pack years" with one pack year defined as smoking one pack of 20 cigarettes per day for one year. Cumulative marijuana exposure was calculated in "joint years" with one joint year defined as smoking one joint per day for one year.

Eighty percent of tobacco plus marijuana smokers mixed the two substances into a single joint or "tobacco spliff". The most common ratio of tobacco to marijuana in mixed joints was 1:4 with five mixed joints having the equivalent of 0.7 grams of tobacco or one tobacco cigarette. Cumulative tobacco pack year calculations included the tobacco content of mixed joints. Charts were reviewed to validate the diagnosis of cor pulmonale and ensure consistency in application of criteria for the diagnosis. Cor pulmonale was defined as clinical evidence of right heart failure, (increased jugular venous pressure, peripheral edema and hepatomegaly +/- ultrasound evidence

of passive liver congestion), plus electrocardiogram (ECG) evidence of right chamber enlargement and/or chest x-ray evidence of pulmonary hypertension/right heart enlargement. Chest x-ray evidence for a diagnosis of cor pulmonale was independently confirmed by a board certified consultant radiologist. Echocardiograms were used to confirm the diagnosis where available. Patient chart review and death certificates were used to determine whether COPD and its complications were significant contributors to or causes of mortality.

### **Statistical analysis**

All analyses were performed using IBM SPSS Statistics version 22. Levene's test was initially applied to assess the equality of variance in our study population; followed by independent samples *t*-Test to compare differences in mean values between the two groups. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for associations between substance use and cor pulmonale and cor pulmonale and death.

**RESULTS**

Table 1: Characteristics of the study population

	<b>Tobacco and marijuana Smokers (n=70)</b>		<b>Tobacco only Smokers (n=30)</b>		<i>p</i> value
	<b>n</b>	<b>Mean (SD)</b>	<b>n</b>	<b>Mean (SD)</b>	
Age at first admission, years	70	45.4 (9.4)	30	72.6 (11.6)	<0.001
Marijuana Joint Years‡	63	130.1 (121.5)		na	
Tobacco Pack Years†	64	11.8 (14.3)	24	34.3 (29.1)	<0.001
Age when started smoking, years	66	17.9 (6.2)	26	25.5 (9.7)	<0.001
Years from start of smoking to first admission	66	26.8 (8.6)	24	45.9 (12.2)	<0.001
Age at death, years	26	47.6 (7.2)	8	73.6 (12.8)	<0.001
Years from start of smoking to death	26	29.8 (8.2)	6	55.3 (15.4)	<0.001

‡ One marijuana joint year is equivalent to smoking one joint per day for one year

† One tobacco pack year is equivalent to smoking one pack of 20 cigarettes per day for one year

One hundred patients were included, 70 patients smoked tobacco plus marijuana and 30 patients smoked tobacco only. There were 84 males and 16 females with a mean age of 53.6 years (SD = 16.1). Mean values and standard deviations (SD) for all variables are listed in table 1 below.

**Tobacco plus marijuana smokers**

Seventy (70) patients reported smoking tobacco plus marijuana, 61 males and 9 females, with a mean age of 45.4 years (SD = 9.4) at first admission for COPD. Fifty four reported smoking tobacco mixed with marijuana (tobacco spliff) while sixteen reported smoking tobacco and

marijuana separately. The mean joint year history was 130 (SD = 121.5) and mean tobacco pack year history 11.8 (SD = 14.3). Cor Pulmonale was a common clinical complication in this group diagnosed in over half (53%) of the patients. COPD with cor pulmonale was the most common cause of mortality directly contributing to 23 of the 26 recorded deaths (88%).

### **Tobacco only smokers**

Thirty patients reported smoking tobacco only, 23 males and 7 females, with a mean age of 72.6 years (SD = 11.6) at first admission for COPD. The mean tobacco pack year history was 34 (SD 29). Cor pulmonale was diagnosed in 2 of the 30 patients in this group. There were 8 deaths in this group with cancer of the respiratory tract being the most common cause of mortality (3 patients) 37.5% of deaths. One patient death was secondary to COPD with cor pulmonale.

### **Comparative analysis**

Two thirds of tobacco plus marijuana smokers required admission for COPD prior to the age of 50 as compared to none in the tobacco only group. The mean age at first admission for tobacco plus marijuana smokers was significantly younger (Fig. 1), 45.4 years versus 72.6 years in tobacco only smokers ( $p < 0.001$ ).

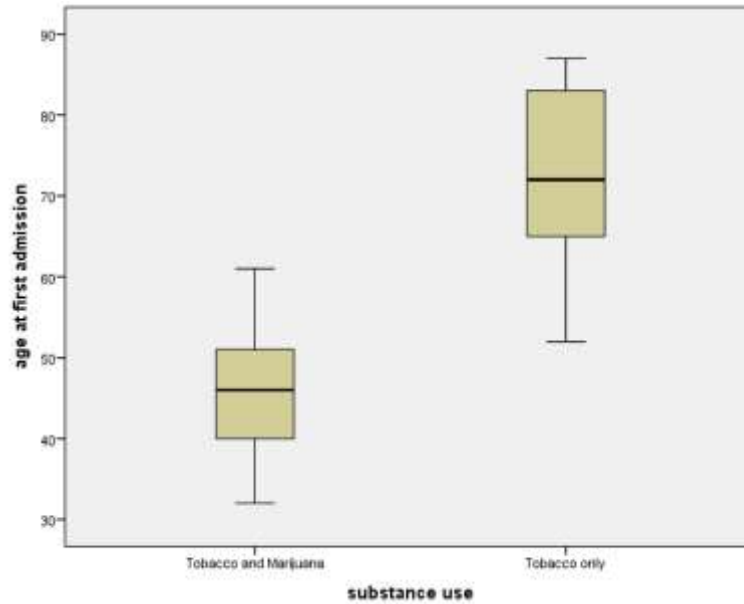


Fig. 1: Age at first admission for tobacco plus marijuana smokers versus tobacco only smokers.

Tobacco plus marijuana smokers also had a shorter lag time from smoking initiation to first admission, an average of 26.8 years (SD = 8.6) versus 45.9 years (SD = 12.2) in tobacco only smokers signifying a more rapid progression to advanced lung disease with concurrent use of tobacco and marijuana ( $p < .001$ ).

Cor Pulmonale was a significant cause of morbidity and mortality among tobacco plus marijuana smokers as compared to tobacco only smokers. Fifty three percent (53%) of tobacco plus marijuana smokers were diagnosed with cor pulmonale compared to 6% of tobacco only smokers (OR 15.7, 95% CI 3.47-71.01). Cor pulmonale also contributed significantly to mortality in tobacco plus marijuana smokers with right heart failure as a listed complication in 23 of the 26 deaths (88%) compared to 1 of the 8 deaths (12.5%) in the tobacco only group. Patients who smoked tobacco and marijuana died at a younger age (Fig. 2), median age at time of death 47.6 years (SD = 7.2) versus 73.6 years (SD = 12.8) for tobacco only smokers ( $p < 0.001$ ).

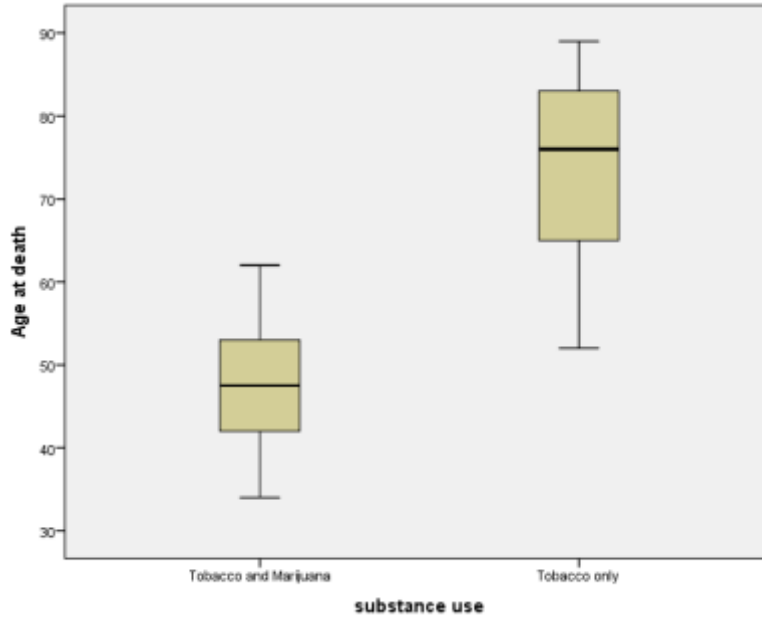


Fig. 2: Age at time of death for tobacco plus marijuana smokers versus tobacco only smokers.

Death in the tobacco plus marijuana group strongly correlated with the diagnosis of cor pulmonale (OR 8.2, 96% CI 3.2-20.8). Despite the earlier onset of COPD and its complications in tobacco plus marijuana smokers, this group had lower cumulative tobacco consumption when compared with the tobacco only group (6.5 versus 25 tobacco pack year history) ( $p < 0.001$ ).

## DISCUSSION

The results of our retrospective cohort study show worse clinical outcomes for patients admitted with COPD who smoke both tobacco and marijuana as compared with tobacco only. There is a growing body of evidence to suggest that individuals who smoke both tobacco and marijuana are at a greater risk for respiratory symptoms or COPD when compared with those who smoke tobacco only (1–3). However previous studies have primarily investigated outpatient populations through



general practice clinics and population based census activities (1–3). Our study demonstrated an earlier onset of pulmonary disease and an increased risk for the development of cor pulmonale in patients hospitalized with COPD who smoke both tobacco and marijuana as compared with tobacco only ( $p < 0.001$ ).

### **Strengths and limitations**

The reliance on chart reviews for substance use histories required certain assumptions to be made; based on common practices e.g. tobacco to marijuana ratios in mixed joints. Black tobacco is used regularly in mixed joints and further investigation is required to delineate risks specific to black tobacco versus regular tobacco. The number of marijuana only smokers was inadequate to serve as a control group; thus limiting our ability to assess for clinically significant respiratory disease in marijuana only smokers.

### **CONCLUSION**

This study demonstrated worse clinical outcomes for tobacco smokers who also smoke marijuana. In addition to an increased risk of earlier onset of moderate to severe COPD requiring admission, there was an increased risk of progression to cor pulmonale and death when compared to tobacco only smokers. Despite these poorer outcomes, cumulative tobacco consumption was lower in tobacco plus marijuana smokers as compared to tobacco only smokers. This is suggestive of a synergistic effect between tobacco and marijuana, as cited in earlier studies (1).

The significant morbidity and mortality risk seen in our study among patients who mix tobacco and marijuana highlights the need for further research into the mechanisms of early disease progression. This could allow for more targeted treatment and informed clinical advice for our

patients. Future public education campaigns would not only encourage tobacco cessation; but might also discourage the mixing of tobacco with marijuana.

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### **AUTHORS' NOTE**

LM Charles conceived paper, oversaw data collection, conducted data analysis, wrote manuscript and approved final version. M Ambrose participated in study design, manuscript revision and approval of final version. C Nathaniel participated in study design, manuscript revision and approval of final version. M Didier participated in study design, manuscript revision and approval of final version. The authors declare that they have no conflict of interest.

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