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Do Tobacco and Cannabis Use and Co-use Predict Lung Function: A Longitudinal Study

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Author Contributions

JMN was responsible for conceptualisation, methodology and data analysis, writing and editing of the manuscript. SB, GMW, AMC, JGS, TRM and AAM all contributed to conceptualisation, methodology and data analysis, and editing.

Background

Use of tobacco and cannabis is common and has been reported to predict lung function. Less is known about co-use of tobacco and cannabis and their impact on changes in lung function to early adulthood.

Research Question

The study examines whether cigarette smoking or cannabis use and co-use are each associated with lung function in a population sample of young adults.

Study Design and Methods

Data are from a prospective cohort study of cigarette smoking, cannabis use and co-use at 21 and 30 years of age and lung function (FVC, FEV₁, FEV₁/FVC) measured at 30 years. Lung function results are transformed using Global Lung Function Formulae. Subjects are the children of pregnant women who were recruited into the cohort study over the period 1981-3. Respondents were administered a spirometry assessment at 21 and 30 years of age. These respondents completed a smoking and cannabis use questionnaire at 21- and 30-year follow-ups.

Results

Cigarette smoking (with or without cannabis use) is associated with reduced airflow. There is no consistent association between cannabis use and measures of lung function. The co-use of tobacco and cannabis appears to entail no additional risk to lung function beyond the risks associated with tobacco use alone.

Interpretation

Persistent cigarette smoking is associated with reduced airflow even in young adults. Cannabis use does not appear to be related to lung function even after years of use.

Key Words

Cohort; young adults; tobacco smoking; cannabis use; FVC; FEV₁

Abbreviations

- FEV1 Forced expiratory volume. How much air a person exhales during a forced breath. The amount exhaled in the first second is FEV1
 FVC Forced vital capacity is the total amount of air exhaled during the FEV test.
 FEV./EVC The ratio representing the proportion of a person's vital capacity that they are able
- **FEV₁/FVC** The ratio representing the proportion of a person's vital capacity that they are able to expire in the first second of forced expiration (FEV₁) to the full, forced vital capacity (FVC).

Introduction

While a good deal is known about the impact of cigarette smoking on lung function, less is known about the impact of cannabis use on lung function and there have been few attempts to determine whether the co-use of tobacco and cannabis may have consequences which differ from their separate use. Further, previous studies have not addressed the possibility that the use/co-use of tobacco and cannabis may predict changes in lung function from late adolescence to young adulthood.

Tobacco smoking and cannabis use may have different impacts on lung function (Hancox et al., 2022; Pletcher et al., 2012), however there has been limited attention to the co-use of tobacco and cannabis and lung function (Subramaniam, McGlade, & Yurgelun-Todd, 2016). The effects of tobacco smoking and cannabis use are likely to depend upon the pattern of use (duration, intensity). While a small number of studies have addressed the likely lung function consequences of the smoking of cigarettes and the use of cannabis very few of these studies explicitly consider co-use as a distinct pattern of use in a population/community sample. We have only found two community-based studies which address the joint impact of tobacco smoking and cannabis use. The CARDIA study found that tobacco smoking was associated with lower levels of FVC and FEV₁ while for cannabis use FVC and FEV₁ increased (Mark J. Pletcher et al., 2012). The Dunedin longitudinal study has a longer follow-up but a smaller sample and reports that tobacco smoking is associated with lower FEV₁ and lower FEV₁/FVC ratios and that the effects of cannabis on lung function are different from and independent of the effects of tobacco smoking (Hancox et al., 2022).

Most tobacco and cannabis users begin using in adolescence or young adulthood (Degenhardt et al., 2008). For tobacco and cannabis, the median age of onset (for seventeen countries) is between 16 and 19 years (Degenhardt et al., 2008). This is in a context where the worldwide rates of cigarette smoking have been declining (Navas-Acien, 2018; WHO, 2017) while rates of cannabis use have been increasing (Leung, Gravely, Lim, Hall, & Chan, 2022; Manthey, Freeman, Kilian, López-Pelayo, & Rehm, 2021). As cannabis users frequently co-use with tobacco (Hindocha, Freeman, Ferris, Lynskey, & Winstock, 2016), rates of co-use are an issue of continuing concern and there is a possibility that cigarette-cannabis co-users are a unique group with a high risk of adverse outcomes (Gravely et al., 2020). It is particularly important that co-use of tobacco and cannabis be compared to the use of tobacco only or cannabis only as well as no use of either.

Cigarette Smoking and Lung Function

Cigarette/tobacco smoking is a cause of impaired lung function. Tobacco is a bronchoconstrictor (Nadel & Comroe, 1961). Studies with longer duration of smoking behaviour or higher levels of smoking confirm a dose-response association with impaired lung function (Camilli, Burrows, Knudson, Lyle, & Lebowitz, 1987; Chandrashekhar, Anandkumar, Jayalakshmi, & Babu, 2020). The smoking of

pipes or cigars or tobacco using water pipes (Raad et al., 2011; Waziry, Jawad, Ballout, Al Akel, & Akl, 2017) has similar effects on lung function to the smoking of cigarettes. Cessation of cigarette smoking is associated with some restoration of lung function, however the impairment of lung function after cessation of smoking may continue for many years and restoration of full lung function may be limited (Camilli et al., 1987; Fletcher & Peto, 1977; Yoon et al., 2021).

In contrast, smoking in a young sample of heavier smokers has been associated with reduced airflow (FEV₁/FVC) and with larger lung size (FVC) (Gold et al., 1996). It has been suggested that inhaling tobacco "trains" the lungs to expand. Other studies have suggested there is little evidence of an impact of cigarette smoking on lung function in younger samples and/or those who smoker fewer cigarettes (Camilli et al., 1987). These latter findings are consistent with evidence that there may be a dose-response association between cigarette smoking and lung function (Gold et al., 1996; Thacher et al., 2018) with young adult smokers experiencing no measurable impairment of lung function. For young smokers the age at which they first show evidence of changes in lung function is not known.

Cannabis Use and Lung Function

Interest in the health consequences of cannabis use reflect the increase in cannabis use observed in many countries (Manthey et al., 2021). Cannabis was used as a bronchodilator in the 19th century (Tashkin, 2013; Tashkin, Shapiro, & Frank, 1973) and in the treatment of asthma (Lee & Hancox, 2011). The acute bronchodilator effects peak 15 minutes after consumption of THC and last for some hours after use (Ribeiro & Ind, 2016; Tashkin et al., 1973). There is greater interest in whether lung function may be affected on a more permanent basis. In population/community samples, most users of cannabis are also cigarette smokers (Hancox et al., 2009; Moore, Augustson, Moser, & Budney, 2005) and both products are inhaled, often together. A large majority of US cannabis users also smoke cigarettes (Agrawal, Budney, & Lynskey, 2012). In this context there is a need to distinguish the effects of tobacco smoking from those of cannabis use. While tobacco and cannabis share many characteristics, both involve the inhalation of tar and similar volatile chemicals including hydrocyanic acid and procarcinogens like benzopyrene (Moore et al., 2005; Pletcher et al., 2012; Tashkin, 2013). Cannabis smoke also contains nitrous oxide, nitrogen dioxide and aromatic amines, all of which may lead to longer term harms for the cannabis user (Moir et al., 2008; Hancox et al., 2022). Further, those who smoke cannabis inhale a greater quantity of carbon monoxide and tar per cigarette smoked (Wu, Tashkin, Djahed, & Rose, 1988). However, tobacco and cannabis use differ in a number of important respects. Cigarettes (nicotine) are primarily a stimulant which is addictive (Nutt, King, Saulsbury, & Blakemore, 2007). Cannabis is a hallucinogen and sedative which is also addictive (Nutt et al., 2007). Cannabis users do not tend to use a filter when smoking, inhale more deeply than cigarette smokers and tend to retain the smoke in their lungs for a longer period of time (Wu et al., 1988). Importantly, the patterns of tobacco and cannabis use in population samples are different. Cigarette smokers

generally smoking multiple cigarettes daily while cannabis use is more episodic (Pletcher et al., 2012). Cannabis users may use only a few times a week or less often (Moore et al., 2005). The majority of cannabis users also smoke cigarettes but many tobacco smokers do not consume cannabis. Few studies have specifically addressed the pattern of co-use (Tashkin, 2013), as distinct from the separate effects of tobacco and cannabis. There is good reason to expect, firstly, that the effects of tobacco and cannabis on lung function may be different (Hancox et al., 2009) and secondly, that co-use may involve distinct effects on lung function (Pletcher et al., 2012).

There have only been a small number of studies that have specifically addressed the likely impact of cannabis use on the lung function of adolescent/young adult users, with inconsistent results (Aldington et al., 2007; Ghasemiesfe et al., 2018; Hancox et al., 2009). Some of these studies suggest that cannabis smoking leads to larger lung volumes, ie, FVC (Hancox et al., 2009; Pletcher et al., 2012) while others suggest it may (Aldington et al., 2007) or may not (Hancox et al., 2009) lead to reduced airflow (FEV₁/FVC). It has also been suggested that there may be short term increases in FVC but that with continued use there is a decline in FVC over time (Hancox et al., 2022). The CARDIA study finds that the effects of cannabis smoking on lung function depend upon the level of cannabis use with low levels of use predicting substantial increases in lung volume (FVC) while heavier levels of use predict lower levels of increased lung volume, compared to a sample of non-cannabis users (Pletcher et al., 2012). One review notes that there are insufficient studies to answer questions about the effects of cannabis use on lung function (Ghasemiesfe et al., 2018). The possible consequences of quitting cannabis use on lung function does not appear to have been addressed in previous studies.

Material and Methods

Respondents in this study are the offspring of pregnant women who were recruited into the study over the period 1981-4 (Najman et al., 2015). Multiple births, still births and neonatal deaths have been excluded. Of the N=7223 children in the birth cohort, N=3805 (52.7%) responded to a face-to-face or paper and pencil interview when they were 21 years of age. These offspring were again interviewed at 30 years of age (N=2900, 40% of original sample). At 21 years, N=2601 respondents undertook a spirometry assessment. At 30 years, N=1713 respondents completed the spirometry assessments. Some N=1173 respondents completed a spirometry assessment at both the 21- and 30-year follow-ups (see Figure 1). While some questionnaire data was obtained using a hard copy questionnaire, all spirometry assessments were administered by a trained interviewer. Some respondents completed the questionnaire but did not participate in the spirometry, while some completed the spirometry but not parts of the questionnaire. The issue of possible bias attributable to selective participation is discussed in the study limitations.

Analytic Strategy

The selection of the analytic sample has involved decisions based upon the differing response rates to the questionnaires at 21 and 30 years, as well as the spirometry assessments. For comparisons of tobacco and cannabis use at 21 and 30 years we select the cohort with data available on both occasions. For the assessment of the combined use of tobacco and cannabis at 30 years we use the cohort available at 30 years.

We first present descriptive details of cigarette smoking and cannabis use at 21 and 30 years, with lung function assessments (FVC, FEV₁, FEV₁/FVC). We then use analyses of variance and covariance to test the associations between tobacco and cannabis use and lung function at 30 years. We adjust for potential confounders, respondent BMI, physical activity score and education, all at 30 years. For continuing use to tobacco and cannabis (at 21 and 30 years) we also adjust for lung function at 21 years, and cannabis use (adjusted for cigarette smoking) and tobacco use (adjusted for cannabis use). In sensitivity analyses using multinomial logistic regression and with categorial cut-offs (eg 20%/25%) we find that the results are similar and consistent to those we report here using analysis of variance and covariance.

Measures of Lung Function

Lung function was assessed by a trained interviewer at the 21- and 30-year follow-up phase. The interviewers were trained by a clinician who was an investigator in the study with subsequent interviewers trained by other interviewers. A Spirobank G spirometer was used, attached to a laptop computer. We used the American Thoracic Society Guidelines with 3 to 5 trials and data from the best trial (unsatisfactory trial data discarded) used for the current analyses. For the current study we used recorded forced vital capacity (FVC) and forced expiratory volume (FEV₁) and calculated FEV₁/FVC. Once satisfactory readings of FVC and FEV₁ had been recorded, they were converted using age, gender and height values based upon criteria established by the Global Lung Initiative (Quanjer et al., 2012). Based upon these values each respondent is ascribed a percent predicted value reflecting norms for their age, gender and height. Following this conversion, it became apparent that the distribution of values (only at 30 years) was about 10% below those expected. The spirometry assessments were used in conjunction with a bacterial/viral respiratory filter, discarded after use by each respondent. The use of this filter is recommended but has been associated with a modest reduction in the estimates of lung function with this reduction likely providing a small (and not clinically significant) reduction in the estimates of lung volume (Fuso et al., 1995; Kamps, Vermeer, Roorda, & Brand, 2001). Following an inspection of the consistency of the lower values across the range of scores, the data were adjusted to bring them to expected values. Analyses were undertaken first using percent predicted values on the filter-based values and then with these values adjusted for the estimated impact of the respiratory filter. The findings were identical for both analyses.

Measures of Tobacco and Cannabis Use

At the 21- and 30-year data collections, respondents were asked two questions about how many cigarettes they smoked per day in the last week (this was repeated at 30 years). At 21 years respondents were asked how often they had used cannabis in the last month with response options including cannabis had been used but not in the last month, or had never been used. At 30 years, respondents were asked whether they had used cannabis in the last 12 months and how much cannabis they usually consumed on days they used. For data collected at 21 and 30 years we have created a composite tobacco smoking or cannabis use variable. The combined variable is of tobacco and cannabis used at the same age. Tobacco and cannabis use were counted if either or both were being used. For these latter comparisons we select a cohort responding at both 21 and 30 years.

Results

Table 1 presents descriptive data for the cohort selected in this study. At 21 years, 34.8% of respondents were smoking cigarettes, and at 30 years it was 23.1% (Wilcoxin Ranked Pairs, p<.001). At 21 years, 21.7% were using cannabis compared to 16.9% at 30 years of age (Wilcoxin Ranked Pairs, p<.001). Of those smoking cigarettes at 21 years (cohort only being compared), 53.8% were smoking cigarettes at 30 years. Of those using cannabis at 21 years, 49.1% reported using cannabis at 30 years. For cigarette smoking, 17.8% of the cohort reported smoking cigarettes at both 21 and 30 years, 20.1% at either 21 or 30 years (not both) and those not smoking at both 21 and 30 years, 17.6% at either 21 or 30 years and 72.7% not using cannabis at 21 and 30 years.

Cigarette smoking at 21 or 30 years is not associated with FVC but is associated with reduced FEV_1 at 30 years and smoking at 21 and 30 years are both associated with reduced airflow at 30 years. By contrast, cannabis use at 21 or 30 years is not significantly associated with measures of lung function. For those using both cigarettes and cannabis at 30 years, the data suggest that lung function (FEV₁) of tobacco smokers is poorer than non-users, with cannabis only users appearing to have lung function very similar to the lung function of those not using either tobacco or cannabis.

(Table 1 about here)

Table 2 presents the associations between cigarette smoking and cannabis use and lung function, all at 30 years of age. There is adjustment for potential confounders as well as lung function at 21 years of age (the latter to assess whether any observed associations may reflect a change in lung function since the 21-year follow-up). Use of both tobacco and cannabis at 30 years is not associated with lung function or evidence of a change in lung function. Use of tobacco only is associated with reduced FEV₁ means as well as reduced FEV₁/FVC suggesting that cigarette smoking only is associated with a reduction in lung airflow. Use of cannabis only appears to be associated with better lung volume (FVC) and forced expiratory volume but not airflow.

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Journal Pre-proof (Table 2 about here)

We next examine cigarette smoking over the 21- and 30-year follow-ups (Table 3). Those who report smoking cigarettes at both 21 and 30 years have lower FEV₁ as well as reduced airflow (FEV₁/FVC). These differences are not observed for those who had ceased smoking by 30 years, or were not smoking at 21 years but were smoking at 30 years. The data suggest that it is a longer duration of smoking that is predicting impairment in lung function particularly forced expiratory volume in 1 second as well as reduced airflow (FEV₁/FCV). Adjustment for pre-existing lung function at 21 years does not affect the observed associations.

(Table 3 about here)

Persistent cannabis use, by contrast with cigarette smoking, does not appear to be associated with any impairment of lung function. While the tests are at the borderline of significance, they are consistent and raise the possibility that those using cannabis at either 21 or 30 years may have better lung volume (FVC) than non-cannabis users. The other borderline significant associations in Table 4 are not consistent. While not strong the findings imply that use of cannabis, either at 21 or 30 years may enhance lung volumes.

(Table 4 about here)

While the above findings address the possibility of a dose-response type association, they do not explicitly test this possibility. To explicitly address the question of dose-response we have undertaken some additional analyses limited to those who smoke cigarettes and use cannabis at 30 years. In both these instances we have related the frequency of use to FVC, FEV₁ and FEV₁/FVC percentages predicted. The frequency of tobacco use is very different (N=340, 1-9 pd 47.9%; 10-19 pd 36.2%; 30+ pd 15.9%) from the frequency of cannabis use (N=231; less than once per month – 80.1%/about once per month – 11.3%/more than once per month – 8.7%). We found no associations between the frequency of cigarette smoking and FVC, FEV₁ or FEV₁/FVC. For frequency of cannabis use at 30 years of age (there are very small numbers using more frequently), we found no consistent pattern of association with the three measures of lung function. In this sample of young adults, we see no support for a dose-response association between cigarette smoking, cannabis use and lung function at 30 years of age.

Discussion

First, we find that cigarette smoking is associated with impairment of lung function by 30 years of age. We find no support for the possibility that co-use of tobacco and cannabis is associated with greater lung impairment than the use of tobacco alone. There is some evidence that cigarette smoking alone is associated with poorer lung function (FEV₁) and FEV₁/FVC, while cannabis use only may be associated with better lung function (FVC and FEV₁). Our findings add to the literature by not only focussing on tobacco and cannabis co-use but by stratifying for tobacco smoking and cannabis use at 21 years of age.

More persistent patterns of use are addressed in tables 3 and 4. Smoking of cigarettes at both 21 and 30 years consistently predicts lower FEV₁/FVC ratio (suggesting airways obstruction). Cessation of cigarette smoking before the 30-year follow-up is not associated any reduction in lung function. Those who cease smoking cigarettes by 30 years of age do not appear to manifest impairment of airflow. By contrast cannabis users at both 21 and 30 years have no evidence of impairment lung function (after adjustment) either in lung capacity, volume or FEV₁/FVC ratio. Cannabis users who were using at 21 years but are more recent users, show some evidence of better lung capacity (after adjustment). Those cannabis users who had ceased using by 30 years do not appear to differ in their lung function from those who have never used cannabis. Perhaps the most remarkable difference between cigarette smokers and cannabis users is the obstruction of airflow (FEV₁/FVC ratio) observed in smokers but not observed in cannabis users.

There is a need to consider the implications of the findings from a clinical and public health perspective. In this sample of young adults, tobacco smoking is associated with early evidence of potential airflow obstruction (reduced FEV₁/FVC ratio). Cessation of smoking to prevent longer-term impact of lung function is indicated as recommended in the Global Initiative for Chronic Obstructive Lung Disease (Albitar & Iyer, 2020). The low levels of cannabis use (typical in community samples) do not appear to be associated with the lung function of users. From a clinical perspective the cessation of cigarette smoking may prevent lung function loss while cannabis use has no apparent impact.

Limitations

In this population study there are a number of caveats to consider. First, the bronchodilator effects of cannabis are evident for some hours after use (Tashkin et al., 1973). In the current study few, if any, respondents are likely to have used cannabis within the past few hours, suggesting that evidence of improved FVC potentially associated with the use of cannabis may reflect the method of cannabis use (inhaling deeper and for a longer period of time).

Second, this study only spans a nine-year period of the life course. Many of the consequences of tobacco and cannabis use will only become apparent in the longer term. Third, the benefits and harms we identify are limited to lung function with harms for other conditions (eg. lung cancer, heart disease) not addressed. There are many harms associated with tobacco and cannabis use that are not detected using spirometry (eg. emphysema). Fourth, while levels of tobacco smoking are broadly reflective of the population, cannabis use may not be because (i) rates and patterns of cannabis use have been changing (ii) the level of active ingredients in cannabis has been increasing over time (iii) there have been changes in use likely a consequence of legislative changes relating to cannabis use specifically

and recreational use of cannabis more generally. Further, cannabis use is more episodic than tobacco use and our data for cannabis use may be less accurate than for tobacco use.

While we find no evidence of a dose-related association between tobacco/cannabis use and lung function as other have (Pletcher, et al., 2012; Tan et al, 2019) this may reflect the modest number of more frequent users and the young age of our sample. There is evidence from other studies that heavy lifetime use of cannabis impacts on lung function (Pletcher et al., 2012; Tan et al., 2019). It is important that young age of use suggests little evidence of impairment and provides support for the likely benefits of tobacco cessation by 30 years of age. While the use of cannabis requires further investigation. There remains a need to consider the potential for dependence as well as the harmful consequences of the co-use of tobacco and cannabis, as well as the changing composition of cannabis itself. The current study has no data on the way cannabis was consumed. We are unable to distinguish cannabis smoking (with or without tobacco), use of cannabis in food, as an oil supplement involving vaping, or otherwise in food products. Smoking of cannabis, often mixed with tobacco are the most common methods of cannabis consumption (Smith et al., 2021; Steigerwald et al., 2018) however cannabis use involving vaporisers or in edible form (often multimode use) may have become more common (Smith et al., 2021).

There is also some evidence that the uptake of cannabis by older persons (Kaskie, Ayyagari, Milavetz, Shane, & Arora, 2017) has been substantial in recent years and it is likely that cannabis use by older persons is at a higher frequency (Yang et al., 2021) than recreational use by younger persons. The impact of cannabis use on lung function by older persons is an important issue about which little appears to be known (Barjaktarevic et al., 2022; Tan et al., 2019).

There is also a need to address the possibility that loss to follow-up has led to findings which are unrepresentative. There is a distinction here between results which describe population parameters (eg. percent who smoke/use cannabis) and results which provide details of the associations within a sample (does cigarette smoking or cannabis use affect lung function?) While sample bias is likely to impact on the former (eg. non-responders at follow-up may be unhealthier persons who are heavier smokers), it is less likely that this bias impacts on estimates of association within the study. We have previously tested this possibility in a series of analyses comparing associations of economic disadvantage and mental illness for respondents who were retained in the study and those subsequently lost to follow-up (Saiepour et al., 2019). Despite high levels of sample attrition, associations remain effectively identical. This finding has since been replicated in an unrelated cohort study (Steinhausen, Spitz, Aebi, Metzke, & Walitza, 2019).

Rothman et al (Rothman, Gallacher, & Hatch, 2013) adds to the debate about the representativeness of samples by noting that (i) all samples are collected at a particular time and place (ii) and are arguably

not directly comparable to other "representative" samples and (iii) that in any event the issue of representativeness needs to be understood in a broader context. The research question, he suggests, is not whether the sample is representative of the population in all respects but rather whether the sample is representative from the perspective of the variables involved and the research question. In any event, replication of findings provides better protection from misleading results and conclusions than does a reliance on the claimed representativeness of a sample.

Conclusions

Cigarette smoking and cannabis use are common behaviours which may affect lung function. The longterm impacts of impaired lung function may be substantial and the early age of onset of both cigarette smoking and cannabis use represent early life behaviours which are able to be addressed and modified. Our findings are consistent in suggesting impairments in lung function (early age of airflow impairment) associated with cigarette smoking. Our findings regarding cannabis use are suggestive of few if any harms associated with relatively low levels of cannabis use evident in a young adult sample. The combined (co-use) of tobacco smoking and cannabis use does not appear to be associated with harms that are greater than the use of tobacco smoking alone.

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Table 1: Cigarette Smoking, Cannabis Use and Sociodemographic Characteristics with Lung
Function at 30 Years
(Analysis of Variance)

	Percent Predicted FVC 30 Years		Percent Predicted FEV ₁ 30 Years		FEV ₁ /FVC Ratio Percent Predicted 30 Years	
	Mean	F-ratio p-value	Mean	F-ratio p-value	Mean	F-ratio p-value
Cigarette Smoking 21 Years						
Yes (N=446)	97.7	F=2.44,	96.1	F=.053,	97.9	F=6.47,
No (N=911)	96.5	P=ns	96.8	P=ns	99.6	P=.01
Cigarette Smoking 30 Years						
Yes (N=347)	96.7	F=.001,	94.6	F=6.74,	97.5	F=9.54,
No (N=1157)	96.7	P=ns	99.9	P=.01	99.6	P<.01
Cannabis Use 21 Years						
Yes (N=279)	98.2	F=3.31,	96.6	F=.001,	97.9	F=3.6,
No (N=1350)	96.6	P=.07	96.6	P=ns	99.3	P=.058
Cannabis Use 30 Years						
Yes (N=254)	98.1	F=3.79,	97.5	F=1.58,	99.0	F=0.028,
No (N=1246)	96.4	P=.052	96.2	P=ns	99.2	P=ns
Cigarette Smoking/Cannabis			Ó			
Use at 30 Years						
Use Both Tobacco and	07.0		05.7		07.0	F=3.44, P=.016
Cannabis (N=139)	97.6		95.7		97.9	
Use Tobacco Only (N=206)	96.0	F=1.51,	93.8	F=4.18,	97.3	
Use Cannabis Only (N=115)	98.7	P=ns	99.6	P=.006	100.4	
Not Used Tobacco or Cannabis (N=1040)	96.4		96.6		99.5	
Cigarette Smoking 21 to 30 Yr						
Smoking 21, Smoking 30 (N=240)	97.3		94.8		97.1	F=3.35, P=.018
Smoking 21, No Smoking 30 (N=702)	98.1	F=1.02,	97.6	F=1.61, p=ns	98.9	
No Smoking 21, Smoking 30 (N=70)	96.7	p-ns	p=ns 96.4		99.2	F010
No Smoking 21, No Smoking 30 (N=835)	96.5		96.8		99.1	
Cannabis Use 21 to 30 Years						
Cannabis 21, Cannabis 30 (N=130)	97.6		96.2		98.2	
Cannabis 21, No Cannabis 30 (N=142)	98.4	F=2.18,	96.6	F=0.71, p=ns	97.6	F=1.39, P=ns
No Cannabis 21, Cannabis 30 (N=94)	98.9	P=.09	98.7		99.3	
No Cannabis 21, No Cannabis 30 (N=972)	96.4		96.4		99.4	

Lung Function	Use both tobacco & cannabis (N=139)	Use tobacco only (N=206)	Use cannabis only (N=115)	Not use tobacco or cannabis (N=1040)	F-ratio, p-value
FVC (% of predicted – mean)					
Unadjusted	97.6 ^{ns}	96.0 ^{ns}	98.7 ^{=.071}	96.4 ^{ref}	1.51, p=ns
Adjusted ⁺	97.5 ^{ns}	96.0 ^{ns}	99.1 ^{=.024}	96.5 ^{ref}	2.24, p=.08
Adjusted ⁺⁺	97.7 ^{ns}	97.1 ^{ns}	98.0 ^{ns}	96.5 ^{ref}	0.32, p=ns
FEV ₁ (% of predicted – mean)					
Unadjusted	95.7 ^{ns}	93.8 ^{=.012}	99.6 ^{=.038}	96.6 ^{ref}	4.18, p<.01
Adjusted ⁺	95.3 ^{ns}	94.8 ^{=.051}	99.1 ^{=.066}	96.5 ^{ref}	1.40, p=ns
Adjusted ⁺⁺	96.5 ^{ns}	95.1 ^{ns}	99.3 ^{ns}	97.0 ^{ref}	2.15, p=.09
FEV ₁ /FVC					
(% of predicted – mean)					
Unadjusted	97.9 ^{ns}	97.3 <.01	100.4 ^{ns}	99.5 ^{ref}	3.44, p<.02
Adjusted ⁺	98.4 ^{ns}	97.4 ^{=.06}	99.9 ^{ns}	99.5 ^{ref}	1.41, p=ns
Adjusted ⁺⁺	98.4 ^{ns}	97.4 ^{=.03}	101.0 ^{ns}	99.8 ^{ref}	2.41, p=.07

Table 2: Tobacco Smoking and Cannabis Use at 30 Years and Lung Function at 30 Years (Analysis of Variance and Covariance*)

* contrasts are post-hoc with not tobacco or cannabis as the comparison

+ adjusted for respondent BMI, level of physical activity and education all at 30 years

++ adjusted for same measure of lung function at 21 years.

Lung Function	Smoking 21 and 30 years (N=240)	Smoking 21, not at 30 years (N=202)	Not smoking 21, smoking at 30 years (N=70)	Not smoking 21 and 30 years (N=835)	F-ratio, p-value
FVC (% of predicted –					
mean)					
Unadjusted	97.3 ^{ns}	98.1 ^{ns}	96.7 ^{ns}	96.5 ^{ref}	1.02, p=ns
Adjusted ⁺	97.4 ^{<.05}	97.9 ^{<.05}	97.3 ^{ns}	96.4 ^{ref}	2.15, p=.09
Adjusted ⁺⁺	97.3 ^{ns}	97.4 ^{ns}	97.7 ^{ns}	96.5 ^{ref}	0.23, p=ns
FEV ₁ (% of predicted – mean)			0		
Unadjusted	94.8 ^{=.06}	97.6 ^{ns}	96.4 ^{ns}	96.8 ^{ref}	1.61, p=ns
Adjusted ⁺	95.0 ^{ns}	97.1 ^{ns}	97.4 ^{ns}	96.7 ^{ref}	0.49 <i>,</i> p=ns
Adjusted ⁺⁺	95.3 ^{=.044}	97.9 ^{ns}	96.8 ^{ns}	97.0 ^{ref}	1.99, p=ns
FEV ₁ /FVC					
(% of predicted – mean)					
Unadjusted	97.1 ^{*<.001}	98.9 ^{ns}	99.2 ^{ns}	99.6 ^{ref}	3.35, p=.02
Adjusted ⁺	97.2 ^{=.03}	98.5 ^{ns}	99.6 ^{ns}	99.6 ^{ref}	1.64, p=ns
Adjusted ⁺⁺	97.5 ^{=.03}	99.8 ^{ns}	98.6 ^{ns}	99.9 ^{ref}	1.71, p=ns

Table 3: Tobacco Smoking at 21 and 30 Years and Lung Function at 30 Years(Analysis of Variance and Covariance)

+ adjusted for respondent cannabis use at 30 years

++ adjusted for same measure of lung function at 21 years

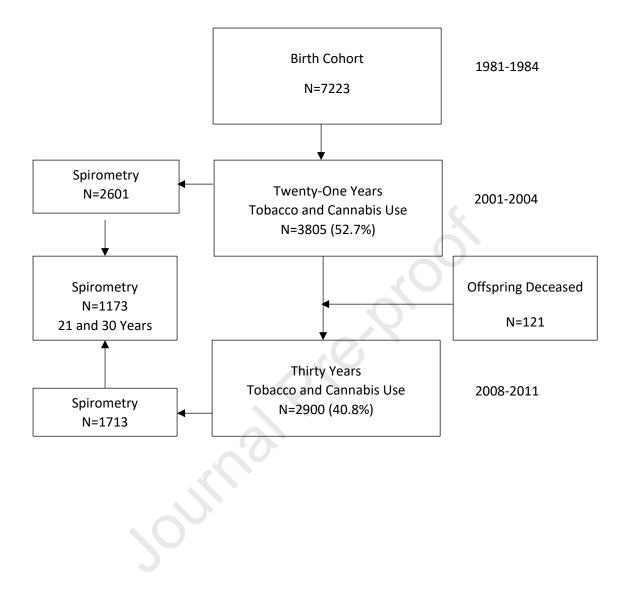
Lung Function	Cannabis 21 and 30 Years (N=130)	Cannabis 21, not at 30 Years (N=142)	Not Cannabis at 21, Cannabis at 30 (N=94)	Not Cannabis 21 and 30 Years (N=972)	F-ratio, p-value
FVC (% of predicted – mean)					
Unadjusted	97.6 ^{ns}	98.4 ^{=.07}	98.9 ^{=.06}	96.4 ^{ref}	2.18, p=.09
Adjusted ⁺	97.6 ^{ns}	98.4 ^{=.07}	98.9 ^{=.06}	96.4 ^{ref}	2.14, p=.09
Adjusted ⁺⁺	96.5 ^{ns}	97.7 ^{ns}	99.5 ^{ns}	96.5 ^{ref}	0.75, p=ns
FEV ₁ (% of predicted – mean)					
Unadjusted	96.2 ^{ns}	96.6 ^{ns}	98.7 ^{ns}	96.4 ^{ref}	0.71, p=ns
Adjusted ⁺	96.2 ^{ns}	96.5 ^{ns}	98.7 ^{=.08}	96.4 ^{ref}	1.12, p=ns
Adjusted ⁺⁺	96.3 ^{ns}	96.7 ^{ns}	99.8 ^{ns}	96.7 ^{ref}	2.02, p=ns
FEV1/FVC					
(% of predicted – mean)		0			
Unadjusted	98.2 ^{ns}	97.6 ^{=.07}	99.3 ^{ns}	99.4 ^{ref}	1.39, p=ns
Adjusted ⁺	98.2 ^{ns}	97.5 ^{ns}	99.3 ^{ns}	99.4 ^{ref}	0.83, p=ns
Adjusted ⁺⁺	99.4 ^{ns}	98.3 ^{ns}	99.8 ^{ns}	99.6 ^{ref}	0.59, p=ns

Table 4: Cannabis Use at 21 and 30 Years and Lung Function at 30 Years(Analysis of Variance and Covariance)

+ adjusted for respondent tobacco use at 30 years

++ adjusted for the same measure of lung function at 21 years.

Figure 1: MUSP Study 21- and 30-Year Follow-ups.



Highlights

- Cigarette smoking and cannabis use and co-use are risk factors for impaired lung function.
- By 30 years of age, those who have smoked cigarettes since the adolescent period already show evidence of impairment of lung function.
- By 30 years of age, those who have used cannabis ever since the adolescent period do not appear to have evidence of impaired lung function.
- Co-use of tobacco and cannabis does not appear to predict lung function beyond the effects of tobacco use alone.

Journal Pre-proof

The authors declare no conflict of interest.

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