Effect of marijuana smoking on lung function change in older ever tobacco smokers

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To the Editor:

While the impact of marijuana use on symptoms of chronic bronchitis has been widely reported, the association with lung function change over time, especially in those at risk of or with COPD, has been less studied [1–6]. A recent longitudinal analysis of data of the CanCOLD study [2] reported that heavy current or former marijuana smoking defined by ⩾20 joint-years (average number of joints smoked per day multiplied by the number of years smoked) was associated with a significantly worse forced expiratory volume in 1 s (FEV_1) decline over a mean of 5.9 years compared to never smokers of marijuana and tobacco after adjustment for tobacco pack-years [3]. However, questions have been raised concerning the design of this study [4, 5]. To further address whether marijuana smoking impacts lung function change over time in mid-life and older persons, we performed a longitudinal analysis of the trajectory of lung function change in participants with a heavy tobacco smoking history with or without COPD from the Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS).

SPIROMICS is an ongoing prospective observational study of 2979 participants aged 40–80 years stratified into groups with no tobacco smoking history/normal spirometry and those with ⩾20 pack-years of tobacco smoking with or without COPD [6]. To allow for an adequate estimate of the trajectory of lung function change, the present analysis was restricted to the 1286 ever-tobacco smoking participants with non-missing marijuana use status at baseline (visit 1) and a total of ⩾3 visits at which spirometry was performed. They were classified as never-marijuana smokers (NMS; n=697), former marijuana smokers (FMS; n=498) or current marijuana smokers (CMS; n=91). The cumulative lifetime history of marijuana smoking in joint-years was not available for all FMS and CMS. The 336 self-reported ever-marijuana smokers who did provide this information were categorised by their cumulative lifetime amount of marijuana smoked in joint-years, as follows: >0 to <10 (n=204); 10 to <20 (n=45); and ⩾20 (n=87). The 697 NMS were classified as having 0 joint-years. Baseline demographic and clinical characteristics including smoking history (tobacco pack-years and marijuana joint-years) and smoking status were collected, and post-bronchodilator spirometry was measured following 2005 ATS/ERS criteria [7]. We used linear mixed effects models to assess annualised changes in post-bronchodilator FEV_1 and forced vital capacity (FVC). Linear mixed models were fit including the primary predictor, marijuana smoking status (NMS, FMS or CMS), and the following baseline covariates: age, sex, race, tobacco smoking status (current or former), tobacco pack-years and FEV_1 % predicted. To assess dose–response relationships, the same models were used with the primary predictor being categorical marijuana joint-years at baseline (0, >0 to <10, 10 to <20 and ⩾20). The SPIROMICS parent study was approved by the institutional review boards of each individual site prior to the enrolment of participants. All participants provided informed consent.

CMS, when compared with NMS, tended to be younger (60.9 *versus* 65.0 years) and more often current tobacco smokers (48.4% *versus* 30.0%), men (63.7% *versus* 49.1%), and black (25.3% *versus* 16.0%). They also had a better post-bronchodilator mean±SD FEV_1 % predicted (83.4±23.2 *versus* 72.6±23.9), but similar levels of respiratory symptoms compared with NMS. Directionally similar baseline findings were noted comparing FMS with NMS and those with ⩾20 marijuana joint-years *versus* those with 0 joint-years.

Among participants with ⩾3 spirometry visits at least 1 year apart (n=1286), the median (IQR) number of spirometry visits was 4 (2), 4 (1) and 4 (1), and the mean±SD follow-up time was 4.8±1.9, 5.2±1.7 and

Shareable abstract (@ERSpublications)
This cohort study of tobacco smokers with COPD failed to demonstrate any clinically significant association of current/former marijuana smoking of any cumulative lifetime amount with a worsening trajectory of FEV_1 over an average of approximately 5 years https://bit.ly/3ISoc2c

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5.1±1.6 years for NMS, FMS and CMS, respectively. Among 1033 participants with data allowing calculation of joint-year history (including the 697 NMS with 0 joint years and the 336 ever-marijuana smokers with >0 joint-years), the median (IQR) number of spirometry visits was 4 (2), 4 (1), 3 (1) and 4 (1) and the mean±SD number of follow-up years was 4.8±1.9, 4.9±1.7, 4.9±1.6 and 5.2±1.6 for those with 0, >0 to <10, 10 to <20 and ⩾20 joint-years, respectively.

While numerically higher annual rates of FEV_1 change (mL) were found comparing CMS with NMS, these differences were not statistically significant (table 1). Similar rates of change in FEV_1 and FVC were found comparing FMS with NMS. Estimated rates of change in FEV_1 and FVC between joint-year-based categories were very similar across all joint-year groups (table 1); *e.g.* the mean (95% CI) rates of change in FEV_1 (in mL per year) for those with ⩾20 *versus* 0 joint-years was 36 (95% CI 47–25) *versus* 34 (95% CI 38–30), with a nonsignificant between-group difference (−2, 95% CI −14–10; p=0.74).

With the growing number of US states legalising marijuana for medicinal and/or recreational use along with increasing prevalence of marijuana smoking among adolescents and adults [8], we need to better understand marijuana's impact on lung health in adult tobacco smokers in mid- and older life. Our analysis of the SPIROMICS cohort of current and former tobacco smokers with or at high risk of developing COPD examined marijuana smoking's influence on lung function and represents an extension of a previously published cross-sectional analysis of the baseline findings in SPIROMICS [9]. Although we observed a trend toward higher rates of decline in post-bronchodilator FEV_1 and FVC among CMS (but not FMS) compared with NMS, none of these differences across the three marijuana use groups were statistically significant. Similarly, comparing different categories of lifetime cumulative amounts of marijuana smoking, no significant differences were noted in rates of change in lung function, comparing even the heaviest lifetime users of marijuana (⩾20 joint-years) with never marijuana smokers (0 joint-years).

Our findings contrast with the results of a study of TAN *et al.* [3], who reported a significantly greater rate of FEV_1 decline among only the heaviest marijuana-smoking participants (⩾20 joint-years) *versus* the never marijuana-smoking participants. Interestingly, the same study reported no difference in rates of FEV_1 decline between the heaviest current *versus* former marijuana smokers, possibly due to the impact of continuing tobacco smoking among the marijuana quitters rather than an enduring effect of marijuana among the quitters, since nearly all marijuana smokers in CanCOLD also smoked tobacco. Moreover, while the reference group in the study of TAN *et al.* [3] comprised never-smokers of either substance without COPD, the reference control group in our analysis comprised never marijuana smokers with ⩾20 pack-years of tobacco smoking, most of whom had COPD, providing more insight into a possible additive effect of marijuana on lung function decline among tobacco smokers.

Our study has several limitations. SPIROMICS was not specifically designed to examine the effects of marijuana smoking on lung function decline, and marijuana use was self-reported and thus prone to recall or reporting biases. The number of years to detect any demonstrable effect of exposure to marijuana is unknown, as is the magnitude of exposure and the possible exposure threshold, so that the power of our analysis to detect an effect on lung function of exposure to marijuana is unknown. Thus, our findings might be due to low statistical power due to the limitations of an inadequate sample size and/or a relatively short observation period and/or a true lack of association. The most common mode of inhalation of

TABLE 1 Estimated year change in post-bronchodilator forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) by baseline marijuana use status and joint-years (JYs) category[#]

Outcomes	Never (n=697) Coefficient (95% CI)	Former (n=498) Coefficient (95% CI)	Current (n=91) Coefficient (95% CI)		Current *versus* never Difference (95% CI)
FEV_1 (mL per year)	−34 (−39, −30)	−32 (−37, −27)	−44 (−56, −33)		−10 (−22, 2); p=0.117
FVC (mL per year)	−44 (−51, −38)	−42 (−49, −34)	−55 (−72, −37)		−10 (−29, 9); p=0.293
Outcomes	**0 JYs (n=697) Coefficient (95% CI)**	**>0–<10 JYs (n=204) Coefficient (95% CI)**	**10–<20 JYs (n=45) Coefficient (95% CI)**	**⩾20 JYs (n=87) Coefficient (95% CI)**	**⩾20 JYs *versus* 0 JYs Difference (95% CI)**
FEV_1 (mL per year)	−34 (−38, −30)	−31 (−39, −24)	−36 (−52, −20)	−36 (−47, −25)	−2 (−14, 10); p=0.737
FVC (mL per year)	−45 (−51, −38)	−35 (−47, −23)	−53 (−78, −27)	−50 (−68, −32)	−5 (−24, 14); p=0.586

[#]: at average age at visit 1, average tobacco smoking pack-years at visit 1, average FEV_1 % predicted at visit 1, and reference groups gender, white race, and not current tobacco smoker at visit 1. Models were fit using available case analysis.

marijuana is *via* smoking a joint [10], but the amount of marijuana actually delivered with each use is highly variable and difficult to quantify, so the metric used for quantitating cumulative lifetime amount of marijuana smoked (joint-year) is crude. In addition, marijuana is inhaled by various methods besides smoking a joint, including use of a pipe, bong, hookah, blunt, dabbing or vaping, or ingestion as edibles/tinctures [11], none of which information was collected at baseline. Using information collected at baseline, we did not take into account the fact that some CMS at baseline quit smoking marijuana during follow-up. Nevertheless, the two categorisations applied in this analysis, one based on marijuana smoking status and the other based on the life-time cumulative exposure, allowed for the adequate interpretation of the impact of marijuana smoking on those with ⩾20 joint-years category who were current smokers at baseline but subsequently quit smoking marijuana, as they would still remain in the same category independent of their current marijuana smoking status at the end of follow-up.

Our study has some important strengths. SPIROMICS is a large, multicentre, prospective, well-profiled cohort which adequately represented women and African-Americans, suggesting a measure of generalisability. A fairly large number of subjects had a history of current or former marijuana use with a moderate to heavy exposure (from 10 to >20 joint-years), thereby allowing for an assessment of dose–response relationships. Most importantly, this longitudinal analysis was limited to the participants with an average of ⩾3 spirometric datapoints, allowing for a reliable insight into the trajectory of lung function decline.

Among ever tobacco smokers of ⩾20 pack-years with established COPD or at risk of developing COPD followed for approximately 5 years, we were unable to demonstrate that current and/or former marijuana smoking was independently associated with a significantly deleterious impact on lung function change over time. This result might be due to low statistical power due to the limitations of an inadequate sample size and/or a relatively short observation period and/or to a true lack of association, underscoring the need for further studies with a larger number of participants and a longer exposure time for assessing any clinically relevant negative effect of marijuana on the lung.

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