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# Differential Effects of Cannabis and Tobacco on Lung Function in Mid–Adult Life

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## Abstract

**Rationale:** Evidence suggests that the effects of smoking cannabis on lung function are different from tobacco. However, long-term follow-up data are scarce and mostly based on young adults.

**Objectives:** To assess the effects of cannabis and tobacco on lung function in mid–adult life.

**Methods:** Cannabis and tobacco use were reported at ages 18, 21, 26, 32, 38, and 45 years in a population-based cohort study of 1,037 participants. Spirometry, plethysmography, and carbon monoxide transfer factor were measured at age 45. Associations between lung function and cannabis use were adjusted for tobacco use.

**Measurements and Main Results:** Data were available from 881 (88%) of 997 surviving participants. Cumulative cannabis use was associated with lower $FEV_1$/FVC ratios, owing to a tendency toward higher FVCs. Cannabis use was also associated with higher TLC, FRC, residual volume, and $V_A$ along with lower midexpiratory flows, airway conductance, and transfer factor. Quitting regular cannabis use between assessments was not associated with changes in spirometry.

**Conclusions:** Cannabis use is associated with higher lung volumes, suggesting hyperinflation. There is evidence of increased large-airway resistance and lower midexpiratory airflow, but impairment of $FEV_1$/FVC ratio is because of higher FVC. This pattern of effects is different to those of tobacco. We provide the first evidence that lifetime cannabis use may be associated with impairment of gas transfer.

**Keywords:** cannabis; cohort study; marijuana; respiratory function; tobacco

## At a Glance Commentary

**Scientific Knowledge on the Subject:** The effects of long-term cannabis use of pulmonary function are uncertain and appear to be different from smoking tobacco.

**What This Study Adds to the Field:** Cumulative cannabis and tobacco use was studied up to age 45 in a large population-based cohort. Cannabis was associated with a range of pulmonary function measures indicating hyperinflation, large-airway resistance, and impaired gas transfer. The pattern of these associations was different from that observed for tobacco smoking.

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This article has a related editorial.

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The effects of smoking cannabis on lung function are controversial (1). Several studies indicate that smoking cannabis leads to changes in lung function, but the pattern of these changes appears to be different from those of tobacco, and their clinical significance is uncertain. Thus, although smoking cannabis is associated with airway inflammation and symptoms of bronchitis, the evidence that persistent cannabis use causes airflow obstruction and chronic obstructive pulmonary disease is unconvincing.

Although cannabis has been associated with lower $FEV_1$/FVC ratios in some studies, this mostly appears to be due to an increase in the FVC rather than a reduction in $FEV_1$ (1–4). Cannabis use has also been associated with greater static lung volumes, suggesting hyperinflation and gas trapping, but there is no evidence that it impairs gas transfer (2, 5–7). A consistent finding is that cannabis users have higher large airway resistance and lower conductance, which is compatible with the evidence that cannabis causes bronchitis (1, 2, 5–7). However, there is considerable uncertainty about the effects of long-term cannabis use on lung function.

Cannabis is still illegal in most countries, making it difficult to study. Few studies have long-term data on cannabis use and lung function. Most cannabis users also smoke tobacco, and it is difficult to separate the effects of the two substances in observational, particularly cross-sectional, studies (1). Furthermore, much of the existing research has been on young adult populations, whereas any effects on lung function may not become evident until middle-to-late adult life. There are also questions about what happens after quitting cannabis use. Symptoms of bronchitis tend to improve after stopping cannabis, but whether the effects of cannabis on lung function are reversible is unknown (8, 9). One study suggested that the $FEV_1$ of ex-users of cannabis continued to decline after quitting, but this was based on a very small number of heavy cannabis users, most of whom also smoked tobacco (10, 11).

We have previously reported associations between cannabis use and lung function in the Dunedin Multidisciplinary Health and Development Study (Dunedin study): a population-based cohort followed to age 32 years (2). We now have follow-up data at age 45 years, thereby adding a further 13 years of follow-up into mid–adult life. We report on the associations between long-term cannabis use and a comprehensive range of lung function tests at age 45.

We do not have ethical approval to share individual-level data. Summary data may be available on reasonable request.

## Methods

Full methods are in the online supplement. Briefly, the Dunedin study comprises a population-based cohort of 1,037 individuals born in 1972–1973 and followed to age 45 years, when 938 of 997 surviving participants (94%) were assessed (12). The appropriate ethics committee approved each assessment.

At ages 18, 21, 26, 32, 38, and 45 years, participants were asked how many times they had used marijuana (cannabis) in the previous year (2, 13). Cumulative exposure to cannabis was calculated as the number of "joint-years" since age 17 (using cannabis once a day for a year equals 1 joint-year), assuming that cannabis use in the previous year was representative of the years between assessments. The maximum use was censored at 1 joint-year each year. Cumulative tobacco exposure was calculated from the reported number of pack-years (20 cigarettes a day for 1 year equals 1 pack-year) up to 18 years and between each assessment.

At age 45, $FEV_1$, FVC, forced expiratory flow between 25% and 75% of the vital capacity ($FEF_{25–75}$), TLC, FRC, residual volume (RV), specific airway conductance adjusted for thoracic gas volume (sGaw), $D_{LCO}$, and $V_A$ by methane dilution were measured using a body plethysmograph (Care Fusion) (14–16). Spirometry was repeated 10–15 minutes following inhalation of 200 μg salbutamol. Exhaled carbon monoxide was measured just before $D_{LCO}$. Hemoglobin, height, and weight were measured.

### Statistical Analysis

Associations between lifetime cannabis and tobacco exposure and lung function were assessed by linear regression using estimates of both joint-years and pack-years as independent variables. Analyses adjusted for height, sex, and weight. Analyses of $D_{LCO}$ also adjusted for exhaled carbon monoxide, hemoglobin, and whether the participant had smoked on the day of assessment. We tested whether sex or any tobacco smoking modified the association of lung function with cannabis use by fitting interaction terms and conducting separate analyses for men and women and for never and current or former tobacco smokers. Models were checked by diagnostic plots of the residuals.

Sex-specific spirometry prediction equations for each age were derived from never-tobacco-smoking participants without asthma. We compared percent-predicted spirometry before and after the first occasion of quitting regular cannabis use. Because residuals were not normally distributed, we used quantile regression of median joint-years to assess whether spirometry at age 15 or childhood asthma predicted subsequent cannabis use.

We further analyzed repeated measures of percent-predicted spirometry at ages 18, 21, 26, 32, 38, and 45 using mixed models with recent cannabis and tobacco use as the main predictors. These adjusted for spirometry at age 15, sex, weight, and age.

To visually compare trajectories between cannabis users and nonusers for tobacco smokers and nonsmokers, linear mixed models with a random participant effect, estimated using restricted maximum likelihood, were constructed including assessment age as a factor along with linear and quadratic joint-years and linear and quadratic pack-years at age 45, and the four interactions between these variables and assessment age.

Analyses used Stata version 17. Two-sided $P < 0.05$ was considered statistically significant.

## Results

Descriptive statistics of the cohort according to cannabis use by age 45 are summarized in Table 1. Women were less likely to have ever used cannabis than men and tended to use less of it (median [25th–75th percentile] joint-years, 0.03 [0–0.27] and 0.22 [0.01–3.30], respectively; $P < 0.001$ by quantile regression). There was no significant association between asthma at age 45 and joint-years cannabis or pack-years tobacco (Table 1 and Table E1 in the online supplement). Childhood asthma (by age 15) did not predict subsequent cannabis or tobacco use (data not shown). Cannabis smokers were more likely to smoke tobacco, and cumulative pack-years of tobacco smoking by age 45 correlated with joint-years of cannabis (Spearman's rho = 0.51; $P < 0.001$). The mean percent-predicted

**Table 1.** Age 45 Descriptive Variables

| | Cumulative Cannabis Use by Age 45 | | | |
|---|---|---|---|---|
| | None (*n* = 242) | ⩽5 Joint-Years (*n* = 510) | >5 Joint-Years (*n* = 129) | *P* Value |
| Sex, *n* (%) | | | | |
| Women | 150 (34) | 250 (57) | 40 (9) | <0.001*†‡§ |
| Men | 92 (21) | 260 (59) | 89 (20) | |
| Cumulative tobacco use, *n* (%) | | | | |
| None | 193 (45) | 218 (51) | 14 (3) | <0.001*†‡§ |
| ⩽5 pack-years | 17 (13) | 96 (78) | 10 (8) | |
| >5 pack-years | 32 (10) | 196 (59) | 105 (32) | |
| Current asthma, *n* (%) | | | | |
| No | 194 (27) | 421 (59) | 96 (14) | 0.109* |
| Yes | 48 (28) | 89 (52) | 33 (19) | |
| BMI, kg/m$^2$, mean (SD) | 29.1 (6.1) | 28.3 (5.6) | 27.2 (5.3) | 0.008†‖ |

*Definition of abbreviation*: BMI = body mass index.
Only participants with spirometry data from age 45 are included.
*$P$ values from $\chi^2$ tests.
†$P < 0.05$ for no cannabis group compared to ⩽5 joint-year group,
‡$P < 0.05$ for no cannabis group compared to >5 joint-year group,
§$P < 0.05$ for ⩽5 joint-year cannabis group compared to >5 joint-year group.
‖$P$ values from Wald test from one-way ANOVA.

$FEV_1$, FVC, and $FEV_1$/FVC measures at age 15 were not associated with subsequent cannabis use (Table E2) and were not associated with median joint-years by age 45 ($P$ values > 0.76 in sex-adjusted quantile regression analyses).

Of the 143 participants who reported using cannabis at least six times in the previous year at age 45, 137 reported on how they usually used it, with multiple responses permitted. Most reported smoking joints or cones (61%), a pipe or bong (42%), "spots" (a method of heating cannabis to inhale the smoke [9%]), or a combination of these methods. Only three did not report inhaling cannabis smoke at age 45 (two oral and one vaping).

Overall, cannabis use was associated with higher lung volumes as measured by TLC, FRC, RV, and $V_A$, with a nonsignificant association with higher FVC values (Table 2). Cannabis was also associated with lower $FEV_1$/FVC ratios, lower $FEF_{25–75}$, and lower sGaw, but there was no significant association with $FEV_1$. There was also an association with lower gas transfer, both with and without adjustment for lung volume ($D_{LCO}$ and $D_{LCO}/V_A$) (Table 2). By contrast, tobacco smoking was associated with lower $FEV_1$ as well as higher static lung volumes (but not FVC or $V_A$) and lower gas transfer. Adjusting the analyses for childhood-onset asthma made no material difference to the findings. Excluding the three cannabis users at age 45 who did not report smoking it also made no material difference to the results.

Joint-years cannabis exposure was also associated with a similar pattern of differences in post-bronchodilator

**Table 2.** Association of Cannabis and Tobacco Use with Lung Function at Age 45

| | | Cannabis | | | Tobacco | | |
|---|---|---|---|---|---|---|---|
| | *n* | Coefficient | 95% CI | *P* Value | Coefficient | 95% CI | *P* Value |
| $FEV_1$, ml | 881 | −2.7 | −9.0 to 3.6 | 0.404 | −7.8 | −11.1 to −4.4 | **<0.001** |
| FVC, ml | 881 | 6.6 | −0.1 to 13.9 | 0.079 | −2.8 | −6.6 to 1.1 | 0.160 |
| $FEV_1$/FVC, % | 881 | −0.13 | −0.22 to −0.04 | **0.004** | −0.13 | −0.18 to −0.08 | **<0.001** |
| $FEF_{25–75}$, ml/s | 881 | −14.4 | −26.2 to −2.5 | **0.018** | −17.5 | −23.7 to −11.2 | **<0.001** |
| TLC, ml | 866 | 18.1 | 8.5 to 27.8 | **<0.001** | 6.8 | 1.7 to 12.0 | **0.009** |
| FRC, ml | 869 | 11.3 | 3.7 to 18.9 | **0.004** | 10.8 | 6.8 to 14.8 | **<0.001** |
| RV, ml | 866 | 10.7 | 5.6 to 15.8 | **<0.001** | 9.4 | 6.7 to 12.1 | **<0.001** |
| sGaw, ml/s/cm $H_2O$/L | 865 | −1.15 | −1.75 to −0.54 | **<0.001** | −0.65 | −0.97 to −0.34 | **<0.001** |
| $D_{LCO}$, ml/min/mm Hg | 839 | −0.051 | −0.100 to −0.001 | **0.045** | −0.073 | −0.105 to −0.042 | **<0.001** |
| $D_{LCO}/V_A$, ml/min/mm Hg/L | 839 | −0.016 | −0.024 to −0.008 | **<0.001** | −0.012 | −0.017 to −0.007 | **<0.001** |
| $V_A$, ml | 839 | 11.2 | 1.7 to 20.7 | **0.021** | 0.0 | −6.1 to 6.1 | 0.999 |

*Definition of abbreviations*: CI = confidence interval; $FEF_{25–75}$ = forced expiratory flow, midexpiratory phase; RV = residual volume; sGaw = specific airway conductance.
Linear regression analyses of lung function at age 45 using cumulative cannabis and tobacco as the exposures of interest. Analyses are adjusted for sex, height, weight, and use of the other substance. Analyses of $D_{LCO}$ also adjust for exhaled carbon monoxide, blood hemoglobin, and reported smoking on the day of assessment. Coefficients represent the difference in lung function associated with each joint-year of cannabis or pack-year of tobacco up to age 45. *P* values <0.05 are highlighted in bold.

**Table 3.** Association of Cannabis and Tobacco Use with Post-bronchodilator Spirometry at Age 45

| | | Cannabis | | | Tobacco | | |
|---|---|---|---|---|---|---|---|
| | *n* | Coefficient | 95% CI | *P* Value | Coefficient | 95% CI | *P* Value |
| $FEV_1$, ml | 871 | −0.8 | −7.2 to 5.6 | 0.810 | −7.9 | −11.2 to −4.6 | **<0.001** |
| FVC, ml | 871 | 10.1 | 2.6 to 17.6 | **0.008** | −1.9 | −5.7 to 2.0 | 0.340 |
| $FEV_1$/FVC, % | 871 | −0.16 | −0.25 to −0.08 | **<0.001** | −0.15 | −0.19 to −0.10 | **<0.001** |
| $FEF_{25–75}$, ml/s | 871 | −17.4 | −30.5 to −4.3 | **0.009** | −21.2 | −28.0 to −14.5 | **<0.001** |

*Definition of abbreviations*: CI = confidence interval; $FEF_{25–75}$ = forced expiratory flow, midexpiratory phase.
Linear regression analyses of post-bronchodilator spirometry lung function at age 45 using cumulative cannabis and tobacco as the exposures of interest. Analyses are adjusted for sex, height, weight, and use of the other substance. Coefficients represent the difference in lung function associated with each joint-year of cannabis or pack-year of tobacco up to age 45. *P* values <0.05 are highlighted in bold.

spirometry, except that in this instance the association with higher FVC values was statistically significant (Table 3).

The interaction tests between sex and joint-years were mostly not statistically significant, providing little evidence that the associations between cannabis use and lung function differed by sex (Table E3). The only statistically significant sex interaction with cannabis exposure was for RV, for which there was a stronger association with cannabis in women, although the association was in the same direction and also statistically significant in men. However, when analyzed separately, the associations between cannabis and higher FVC and $V_A$ and lower $FEV_1$/FVC and $FEF_{27–75}$ were only significant in men, whereas the associations with higher FRC and lower $D_{LCO}$ were only significant in women. Cannabis was associated with higher TLC and lower sGaw and $D_{LCO}/V_A$ in both sexes.

There was also little statistical evidence that tobacco smoking modified the association between cannabis and spirometry (most interaction *P* values are >0.05). Both subgroups of ever- and never-smokers of tobacco had statistically significant associations with lower $FEV_1$/FVC ratios and higher TLC values, but the association between cannabis use and FVC was only significant in those who had never smoked tobacco (Table 4). However, the other static lung volumes, FRC and RV, were only significantly associated with cannabis among tobacco smokers, with a statistically significant interaction between cannabis and tobacco for FRC. Associations between cannabis and lower sGaw, $D_{LCO}/V_A$, and higher $V_A$ were also only statistically significant among tobacco smokers, although the associations were of similar magnitude and direction among never tobacco smokers.

In total, 158 participants cut down or quit using cannabis from weekly or more to less than weekly during follow-up. This change in cannabis use was not associated with clinically or statistically significant changes in spirometry: $FEV_1$ improved by 0.1% predicted (95% CI, −1.0 to 1.3; *P* = 0.803), FVC decreased by 0.3% predicted (95% CI, −1.4 to 0.8; *P* = 0.561), and the $FEV_1$/FVC ratio increased by 0.5% predicted (95% CI, −0.3 to 1.3; *P* = 0.181).

Longitudinal analyses of the life-course spirometry data from ages 18 to 45 with adjustment for baseline measurements at age 15 are shown in Table E4. These found statistically significant associations between recent cannabis use with higher percent-predicted FVC and lower $FEV_1$/FVC ratios. Tobacco was associated with lower $FEV_1$ and $FEV_1$/FVC ratios.

Estimated trajectories of $FEV_1$, FVC, and the $FEV_1$/FVC ratio from the mixed

**Table 4.** Associations of Cannabis Use with Lung Function at Age 45 in Tobacco Smokers and Nonsmokers

| | Never–Tobacco Smokers | | | | Current or Ex–Tobacco Smokers | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *n* | Coefficient | 95% CI | *P* Value | *n* | Coefficient | 95% CI | *P* Value | *P* Int Value* |
| $FEV_1$, ml | 425 | 0.8 | −14.8 to 16.3 | 0.924 | 456 | −3.1 | −10.3 to 4.0 | 0.391 | 0.220 |
| FVC, ml | 425 | 19.8 | 1.3 to 38.2 | **0.035** | 456 | 4.0 | −4.0 to 12.1 | 0.326 | 0.054 |
| $FEV_1$/FVC, % | 425 | −0.25 | −0.46 to -0.05 | **0.015** | 456 | −0.11 | −0.22 to 0.00 | **0.042** | 0.611 |
| $FEF_{25–75}$, ml/s | 425 | −25.2 | −55.3 to 4.9 | 0.101 | 456 | −12.4 | −25.5 to 0.6 | 0.062 | 0.989 |
| TLC, ml | 419 | 25.0 | 1.6 to 48.3 | **0.036** | 447 | 17.4 | 6.3 to 28.4 | **0.002** | 0.709 |
| FRC, ml | 421 | −1.3 | −19.0 to 16.4 | 0.888 | 448 | 13.7 | 4.9 to 22.6 | **0.002** | **0.034** |
| RV, ml | 419 | 5.7 | −5.2 to 16.7 | 0.302 | 447 | 11.9 | 5.6 to 18.2 | **<0.001** | 0.066 |
| sGaw, ml/s/cm $H_2O$/L | 417 | −1.23 | −2.88 to 0.42 | 0.145 | 448 | −1.13 | −1.76 to −0.49 | **0.001** | 0.679 |
| $D_{LCO}$, ml/min/mm Hg | 410 | −0.011 | −0.135 to 0.114 | 0.868 | 429 | −0.053 | −0.108 to −0.002 | 0.057 | 0.261 |
| $D_{LCO}/V_A$, ml/min/mm Hg/L | 410 | −0.012 | −0.032 to 0.008 | 0.238 | 429 | −0.016 | −0.025 to −0.008 | **<0.001** | 0.575 |

*Definition of abbreviations*: CI = confidence interval; $FEF_{25–75}$ = forced expiratory flow, midexpiratory phase; Int = interaction; RV = residual volume; sGaw = specific airway conductance.
Linear regression analyses of lung function at age 45 using joint-years cannabis exposure as the exposure of interest. All analyses adjust for sex, weight, and height. Analyses among ever-smokers also adjust for pack-years tobacco exposure, and analyses of $D_{LCO}$ also adjust for exhaled carbon monoxide and blood hemoglobin and reported smoking on the day of the test. Coefficients represent the difference in lung function associated with each joint-year of cannabis up to age 45.
**P* Int values are the *P* values for the interaction between ever-smoking and joint-years. *P* values <0.05 are highlighted in bold.

models are shown in Figure 1 for participants who were non–tobacco smokers or had accumulated 15 pack-years by age 45 according to whether they had not used cannabis or had accumulated 5 joint-years.

## Discussion

Findings from this longitudinal investigation of cannabis and tobacco use up to mid–adult life indicate that cannabis is associated with changes in lung function that are independent of the effects of tobacco smoke and appear to be of a different pattern. Both cannabis and tobacco were associated with lower values for the $FEV_1$/FVC ratio. However, this was mostly owing to higher values for FVC among cannabis users with little difference in $FEV_1$, whereas tobacco smokers had lower $FEV_1$ values.

Both tobacco and cannabis use were also associated with higher values for static lung volumes (TLC, FRC, and RV) by plethysmography, indicating a tendency toward hyperinflation and gas trapping, but only cannabis was associated with increased $V_A$ by gas dilution. Both cannabis and tobacco were also associated with lower sGaw and lower $FEF_{25–75}$.

Unlike our earlier assessment of this cohort at age 32 (2), we found that by age 45, cannabis was now associated with lower values for $D_{LCO}$. The $D_{LCO}/V_A$ was even more strongly associated with cannabis use, but this is partly explained by higher volumes of gas distribution ($V_A$). As far as we are aware, this is the first time that a reduction in gas transfer has been reported in association with cannabis use, with previous cross-sectional studies finding no association (5–7). It is likely that our earlier report and other studies did not follow cannabis users for long enough to demonstrate an impairment of gas transfer. This finding could indicate that long-term cannabis use may lead to emphysematous changes. Although emphysema does not appear to be common among cannabis users unless they also smoke tobacco (7), there are numerous reports of giant bullous emphysema among heavy cannabis users, suggesting that long-term cannabis may lead to alveolar destruction (1). Our finding of an association between cannabis use and gas transfer should be interpreted with some caution, however, given the *P* value of 0.045. We only found an association between cannabis use and lower gas transfer factor among those who also smoked tobacco, although the lack of association among non–tobacco users could also be explained by their much lower exposure to cannabis.

Except for the new finding of a lower gas transfer, the pattern of lung function associations with cannabis use is consistent with the findings from the same cohort 13 years earlier (age 32). At that age, cannabis use was associated with greater dynamic and static lung volumes and lower airway conductance, but an association with lower $FEV_1$/FVC ratio was due to higher FVC values with no evidence of a reduction in $FEV_1$. These findings are also consistent with other reports that cannabis is associated with greater VC but little difference in $FEV_1$ (1–4). The finding of a pattern of the associations with higher values for TLC, FRC, RV, and $V_A$ as well as FVC support the inference that cannabis use leads to greater lung volumes. An association between

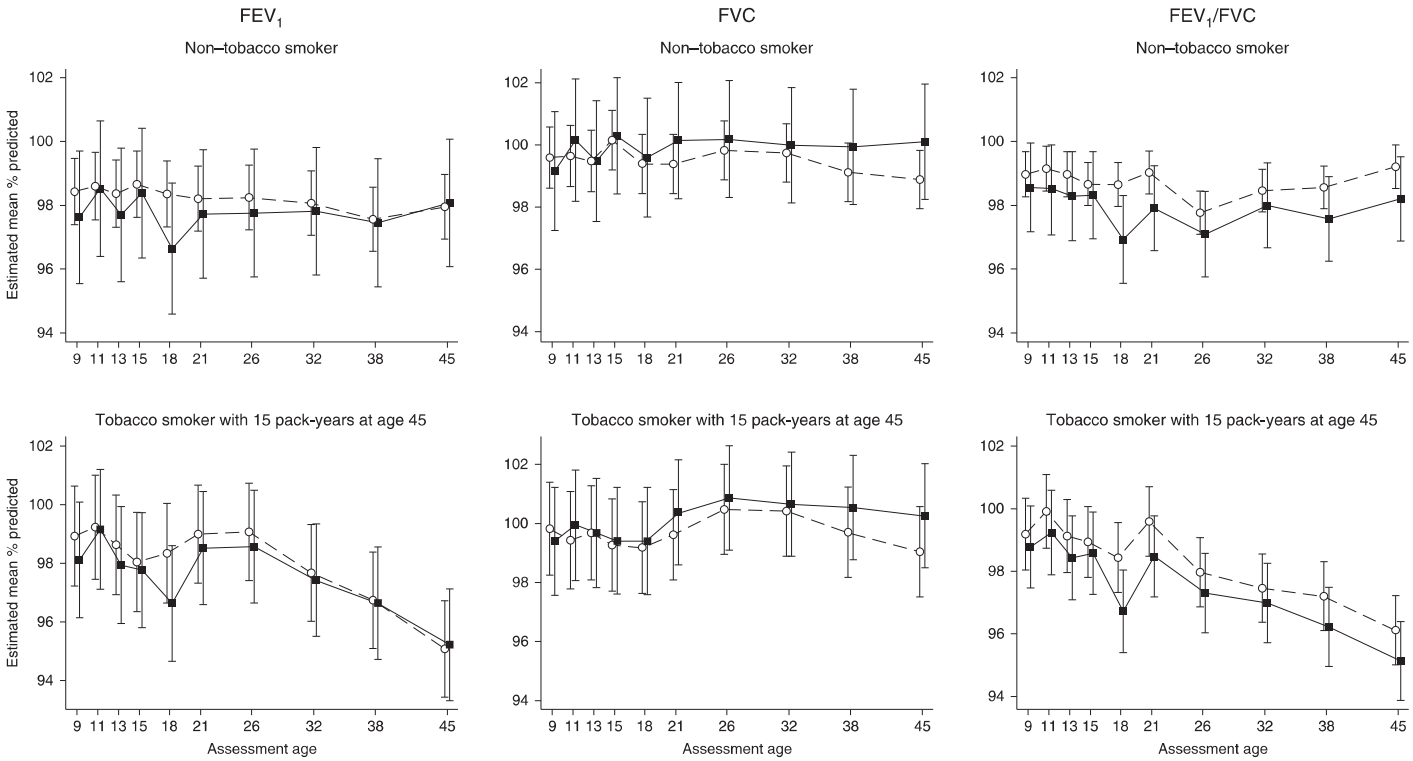


**Figure 1.** Estimated mean percent-predicted (95% confidence interval) spirometry function at each assessment for non–tobacco smokers (top row) and tobacco smokers of 15 pack-years by age 45 (bottom row). The open circles and dashed lines are the estimated values for non–cannabis users. The squares and solid lines show the estimates for a person who has accumulated 5 joint-years by age 45. Estimates are from linear mixed models of lung function using joint-years cannabis (linear and quadratic terms), pack-years tobacco (linear and quadratic terms), age, and the four interactions between age and the continuous variables as the independent variables alongside a random participant effect.

cannabis and lower sGaw has been a consistent finding, suggesting that cannabis impacts on large airway function despite having little effect on $FEV_1$ (2, 5–7). This observation is compatible with the high prevalence of bronchitis symptoms and evidence of bronchial epithelial injury among cannabis smokers (19–22). In support of this, we also found an association between cannabis use and lower $FEF_{25–75}$.

Women were less likely to use cannabis than men in this cohort, and if they did, they tended to use less. However, for some of the lung function measures, the associations with cannabis use were equally strong or stronger among women (Table E3). Although mostly not supported by statistically significant tests for sex interactions, there were several apparent differences between men and women when analyzed separately. The associations of cannabis with spirometry (FVC, $FEV_1$/FVC, and $FEF_{25–75}$) and $V_A$ were stronger in men, but the associations with higher FRC and RV and lower $D_{LCO}$ were stronger in women. Whether there are biological mechanisms underlying these apparent differences in susceptibility, whether they reflect differences in cannabis use, or whether these are chance findings is not clear, and these observations require confirmation in other cohorts.

The main difficulty in assessing the effects of cannabis on lung function is distinguishing these from tobacco. Most cannabis users also smoked tobacco, and there was a strong correlation between reported joint-years and pack-years (rho = 0.51). We adjusted for pack-years of tobacco use in all analyses, but any errors in reported tobacco use may mean that the regression analyses do not adequately adjust for the confounding influence of tobacco smoking. We therefore analyzed the associations between cannabis use and lung function in those who had never used tobacco (Table 4). It is important to note that most heavy cannabis users were also tobacco smokers, reducing the power to detect associations among never–tobacco users. Nevertheless, the pattern of associations was similar to those among tobacco smokers: both ever– and never–tobacco users had associations between cannabis and the $FEV_1$/FVC ratio and TLC, whereas there were also tendencies to lower values for $FEF_{25–75}$, sGaw, and $D_{LCO}/V_A$ and higher-value $V_A$ among never–tobacco users. There was only one statistically significant interaction between ever–tobacco smoking and cannabis use, and that was for FRC, which was only associated with cannabis among tobacco users.

Although our primary aim was to assess the impact of cumulative cannabis and tobacco exposure on lung function in mid–adult life, we also undertook supplementary longitudinal analyses of the repeated spirometry measures throughout adult life. These adjusted for percent-predicted spirometry at age 15 and used recent use of cannabis and tobacco as the main predictors. These analyses provided consistent findings: cannabis use was associated with higher percent predicted FVC values, but not with $FEV_1$, whereas tobacco was associated with lower $FEV_1$ values, but not with FVC (Table E4). Hence, both were associated with lower $FEV_1$/FVC ratios but owing to different mechanisms.

The modeled trajectories of spirometry from ages 9 to 45 years are consistent with our other analyses (Figure 1). These show no material difference in early lung function among those who would subsequently smoke tobacco or cannabis (using cumulative use at age 45). Over adulthood, tobacco smoking was associated with a progressive decline in percent-predicted $FEV_1$, little change in FVC, and hence a decline in the $FEV_1$/FVC ratio. By contrast, cannabis use was not associated with a decline in $FEV_1$ but a tendency to higher FVC values, also resulting in lower $FEV_1$/FVC ratios.

It is unclear why cannabis has different associations with lung function from tobacco. Cannabis users tend to smoke far fewer times a day than tobacco smokers, and it is possible that the participants have not smoked enough cannabis for it to have a measurable effect on some aspects of lung function. However, this seems unlikely in view of the strong associations with higher lung volumes and lower airway conductance. Apart from the active ingredients of cannabinoids and nicotine, the inhaled combustion products in cannabis and tobacco smoke are qualitatively similar (23). The consistency of our findings with other studies indicates that there are likely to be real biological differences between the effects of cannabis and tobacco smoke, but we can only speculate about the reasons for this. Delta-9-tetrahydrocannibiol is a short-term bronchodilator, and it is possible that it has long-term effects (24). The commonly used technique of smoking cannabis, with deeper inhalations and breath holding, may be another reason (25).

This study has a number of limitations. Cannabis use was reported for the previous year at each assessment, and our estimate of use assumes that the consumption of cannabis was similar for the intervening years. At some assessments, the maximum amount of cannabis recorded was censored at once a day (365 days a year), and we will have underestimated consumption for those who used cannabis more often than this. We also do not know how much cannabis was used on each occasion. Hence, our measure of cannabis exposure will be less accurate than that of tobacco. Study members may have underreported cannabis use because it is an illegal substance, although our well-established record of confidentiality and nonintervention over 45 years of the lives of the study members tends to encourage honest reports. For most assessment ages, we do not know how the cannabis was used, although, when asked at age 45, nearly all users (98%) said that they usually smoked it using one or more of several techniques. By necessity, we have assumed that our measure of joint-years represents smoked cannabis. Excluding the three participants who took cannabis by other means at age 45 made no material difference to the findings. We have not collected data on vaping, either cannabis or tobacco, through the life course, although vaping has only recently become available and is unlikely to substantially influence the lifetime exposures in this cohort. We have undertaken a large number of statistical analyses and have not adjusted the *P* values for multiple testing. Hence, our interpretation is based on the overall pattern for findings and individual statistically significant findings should be interpreted cautiously.

The study also has a number of strengths. Both cannabis and tobacco smoking were assessed on a number of occasions throughout early-to-middle adult life in a population-based cohort with a high rate of follow-up. We have measurements of spirometry since childhood, which enabled us to test whether early lung function influenced the likelihood of smoking. We found no evidence that spirometric lung function at age 15 was associated with subsequent use of tobacco or cannabis, providing no evidence of a "healthy smoker" effect for cannabis.

The findings of this and other studies should inform the current debates around the world about the legalization and/or decriminalization of cannabis. In some

countries, there has been little discussion about the potential respiratory health consequences of increased cannabis consumption. Interpreting the evidence in the context of forming policies presents difficulties, however: It is increasingly clear that cannabis has different effects on lung function to tobacco, and the effects of widespread cannabis use will not necessarily mirror the harms caused by tobacco smoking. The long-term consequences of the hyperinflation, gas trapping, and lower sGaw observed in several studies are not yet known. Despite this, bronchitis with symptoms of cough and sputum production has been documented (1, 8). We have added the observation of impaired gas transfer to this list of concerns. There are also many reports of severe bullous lung disease in heavy cannabis users, but epidemiological data on this association are lacking. We also need research into the mechanisms of the effects of cannabis on lung function.

## Conclusions

Cannabis is associated with evidence of hyperinflation, increased large airway resistance, and impairment of gas transfer in midadulthood. The pattern of lung function changes is distinct from those of tobacco, suggesting that smoking cannabis and tobacco have different physiological consequences for the lungs. ■

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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