

Effects of Marijuana Smoking on Pulmonary Function and Respiratory Complications

A Systematic Review

Jeanette M. Tetraault, MD; Kristina Crothers, MD; Brent A. Moore, PhD;
Reena Mehra, MD, MS; John Concato, MD, MS, MPH; David A. Fiellin, MD

Background: The relationship between marijuana smoking and pulmonary function or respiratory complications is poorly understood; therefore, we conducted a systematic review of the impact of marijuana smoking on pulmonary function and respiratory complications.

Methods: Studies that evaluated the effect of marijuana smoking on pulmonary function and respiratory complications were selected from the MEDLINE, PsychINFO, and EMBASE databases according to pre-defined criteria from January 1, 1966, to October 28, 2005. Two independent reviewers extracted data and evaluated study quality based on established criteria. Study results were critically appraised for clinical applicability and research methods.

Results: Thirty-four publications met selection criteria. Reports were classified as challenge studies if they examined the association between short-term marijuana use and airway response; other reports were classified as studies of long-term marijuana smoking and pulmonary function or respiratory complications. Eleven of 12 challenge studies found an association between short-

term marijuana administration and bronchodilation (eg, increases of 0.15-0.25 L in forced expiratory volume in 1 second). No consistent association was found between long-term marijuana smoking and airflow obstruction measures. All 14 studies that assessed long-term marijuana smoking and respiratory complications noted an association with increased respiratory symptoms, including cough, phlegm, and wheeze (eg, odds ratio, 2.00; 95% confidence interval, 1.32-3.01, for the association between marijuana smoking and cough). Studies were variable in their overall quality (eg, controlling for confounders, including tobacco smoking).

Conclusions: Short-term exposure to marijuana is associated with bronchodilation. Physiologic data were inconclusive regarding an association between long-term marijuana smoking and airflow obstruction measures. Long-term marijuana smoking is associated with increased respiratory symptoms suggestive of obstructive lung disease.

Arch Intern Med. 2007;167:221-228

Author Affiliations: Clinical Epidemiology Research Center, Department of Veterans Affairs Connecticut Healthcare System, West Haven Veterans Affairs Medical Center, West Haven, Conn (Drs Tetraault and Concato); Departments of Medicine (Drs Tetraault, Crothers, Concato, and Fiellin) and Psychiatry (Dr Moore), Yale University School of Medicine, New Haven, Conn; and Department of Medicine, Case Western University School of Medicine, Cleveland, Ohio (Dr Mehra).

MARIJUANA REMAINS THE most commonly used illicit drug in the United States, with 14.6 million people 12 years and older reporting current use.¹ The prevalence of marijuana abuse and dependence continues to increase and occurs in 18% of past-year marijuana users.² Given the persistently high prevalence of marijuana use, abuse, and dependence in the community, it is important to understand the potential adverse health outcomes that result from both short-term and long-term marijuana smoking.

Marijuana and tobacco smoke share many of the same compounds. Tobacco smoking is associated with numerous ad-

verse pulmonary clinical outcomes, affecting both pulmonary function and respiratory complications. Some of the known tobacco smoking-related adverse effects include cough, chronic bronchitis, impairment of gas exchange, and airway obstruction that leads to chronic obstructive pulmonary disease.^{3,4} The adverse impact of marijuana smoking on pulmonary function and respiratory complications has not been systematically assessed. The purpose of the current review is to determine the association between short-term marijuana smoking and airway response and the association between long-term marijuana smoking and pulmonary function or respiratory complications.

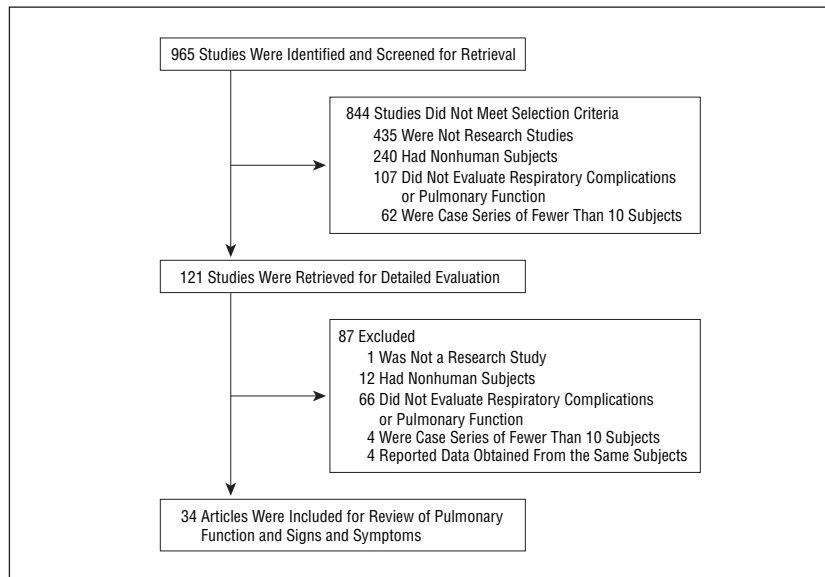


Figure. Literature search results.

METHODS

SEARCH STRATEGIES

English-language studies in persons 18 years or older were identified from the MEDLINE, PsychINFO, and EMBASE databases from January 1, 1966, to October 28, 2005, using medical subject headings and text words (see Appendix at http://www.tresearch.org/add_health/lit_reviews.htm). Only studies that involved marijuana smoking were considered for review.

SELECTION

Retrieval of studies was performed by 2 reviewers (B.A.M. and R.M.), who evaluated titles and abstracts from the initial electronic search of potentially relevant articles. Studies were excluded if they did not report primary data, did not include human subjects, did not report results of respiratory complications or pulmonary function tests, or reported on a case series with fewer than 10 subjects. For studies that presented data on similar or duplicate cohorts, we used data that represented the last follow-up for the cohort or findings from investigations that represented assessments of unique domains or variables. Articles that could not be categorized based on review of the abstract were evaluated in manuscript form. Studies with discordant categorizations by the 2 reviewers were resolved in collaboration with a third reviewer (D.A.F., K.C., or J.M.T.) to reach consensus.

VALIDITY ASSESSMENT

Study quality was evaluated by 2 reviewers (J.M.T. and K.C.) using an established generic instrument⁵ that assessed reporting, bias or confounding, and power; a score of 12 or higher was considered good study quality.⁵ We also applied exposure and disease-specific criteria to augment quality assessment using the generic instrument. For cross-sectional studies, these criteria were whether data were included on prior tobacco exposure and on dose and duration of marijuana exposure and whether a standardized method to assess the pulmonary outcome of interest was used. For observational cohort studies, an additional criterion was to screen patients at baseline and exclude those with the outcome of interest. Challenge studies needed to meet the criteria listed herein and also mask patients and study personnel to marijuana use. Differences between reviewers were resolved by consensus with input from a third reviewer (J.C. or D.A.F.). Interrater reliability was high ($r=0.79$ for the generic evaluation criteria; $r=0.89$, Kendall $\tau b=0.85$; $P<.001$ for the exposure and disease-specific criteria).

DATA SYNTHESIS

The heterogeneous nature of the studies and their outcomes precluded quantitative synthesis (ie, meta-analysis). Therefore, this review focuses on a qualitative synthesis of the data.

DATA ABSTRACTION

The initial literature search identified 965 citations. Inconsistencies regarding as-

essment of eligibility criteria were discussed by the whole team. Of the 965 abstracts initially reviewed, 931 were not relevant: 436 did not report primary data, 252 did not include human subjects, 173 lacked evaluation of respiratory complications or pulmonary function tests, 66 were case series of fewer than 10 patients, and 4 reported data obtained from the same patients. Ultimately, 34 unique articles were included in the review (Figure).

The outcomes of the 34 included studies were classified into 3 non-mutually exclusive categories: airway response to experimentally administered marijuana (challenge studies),⁶⁻¹⁷ changes in pulmonary function secondary to long-term marijuana smoking,¹⁸⁻³¹ and respiratory complications secondary to long-term marijuana smoking.^{18,20,22,24,28,31-39} The studies reviewed had diverse study designs; 12 studies had a laboratory challenge study design,⁶⁻¹⁷ 15 were cross-sectional,⁸ 3 were observational cohort studies,^{24,26,29} 3 were case series,^{20,33,39} and 1 was a case-control study.³²

RESULTS

REVIEW OF STUDIES CATEGORIZED BY STUDY OUTCOME

Short-term Marijuana Use and Airway Response

Twelve studies (Table 1) assessed the impact of short-term marijuana use on airway response. The studies used various measures to evaluate airway response: specific airway conductance (sGaw) (a measure that is inversely related to airway resistance),^{6,7,9,12,14-16} forced expiratory volume in 1 second (FEV₁),^{9-11,14,15} peak flow,⁸ airway resistance,¹⁷ and change in methacholine- and exercise-induced bronchospasm.¹³

Among the 7 studies that used sGaw to assess the airway response to marijuana challenge, 6 studies^{6,7,9,12,15,16} showed an increase in sGaw after marijuana challenge that ranged from 8% to 48%. Two of these studies^{6,12} showed that the increase in sGaw lasts up to 60 minutes after marijuana administration, and 1 study¹² demonstrated that peak sGaw occurred 15 minutes after smoking.

*References 18, 19, 21-23, 25, 27, 28, 30, 31, 34-38.

Table 1. Challenge Studies That Reported Effects of Short-term Marijuana Inhalation on Airway Response

Source	No. of Subjects	Results	Control for Confounding	Mean Generic Quality Score	Mean Exposure and Disease-Specific Quality Score
Vachon et al, ⁶ 1974	10	Marijuana smoking associated with increase in sGaw 1 h after smoking ($P<.001$)	None	8	1.5
Tashkin et al, ⁷ 1974	10	After smoking marijuana, average sGaw increased immediately ($P<.05$ compared with controls and placebo) in patients with asthma	Tobacco	11.5	3
Bernstein et al, ⁸ 1976	28	12 of 15 subjects showed increases in peak expiratory flow immediately after smoking a marijuana cigarette	None	7	2
Lavolette and Belanger, ⁹ 1986	11	Marijuana smoking produced increase in sGaw ($P<.01$) and FEV ₁ ($P<.05$)	Tobacco	10	2.5
Renaud and Cormier, ¹⁰ 1986	12	FEV ₁ increased immediately after marijuana smoking ($P<.01$)	None	12	3
Steward and Singh, ¹¹ 1975	20	No difference in FEV ₁ after smoking marijuana compared with baseline or placebo	None	15	2
Tashkin et al, ¹² 1973	32	After smoking marijuana, there was an immediate increase in sGaw, which peaked at 15 min after smoking and remained elevated at 60 min	Tobacco	16.5	3
Tashkin et al, ¹³ 1975	8	After both methacholine-induced and exercise-induced bronchospasm in asthmatic patients, marijuana caused correction of bronchospasm and associated airway hyperinflation	Tobacco	13	3
Tashkin et al, ¹⁴ 1976	28	After 47 to 59 d of heavy marijuana smoking, mean FEV ₁ decreased ($P<.01$) and mean sGaw decreased ($P<.001$). Modest but significant decrease in diffusing capacity also noted. Correlation between average quantity of daily marijuana smoked during the study and reduction of sGaw.	Tobacco	9	3
Tashkin et al, ¹⁵ 1977	11	FEV ₁ and sGaw increased after smoked marijuana ($P<.05$)	Tobacco	14.5	3
Vachon et al, ¹⁶ 1973	17	Increase in sGaw after marijuana inhalation	Tobacco	17	3
Wu et al, ¹⁷ 1992	23	After smoking marijuana, airway resistance decreased significantly at all levels of marijuana compared with placebo ($P<.05$)	Tobacco	17.5	3

Abbreviations: FEV₁, forced expiratory volume in 1 second; sGaw, specific airway conductance.

Among the 5 studies that used FEV₁ to assess airway response to marijuana challenge, 3 studies^{9,10,15} showed an increase in FEV₁ after smoking marijuana compared with baseline, ranging from 0.15 to 0.25 L. One study¹¹ showed no difference in FEV₁ after marijuana challenge compared with baseline or placebo.

One study⁸ used peak flow to assess marijuana effect on airway response and showed that 12 of 15 patients had an increase in peak flow immediately after marijuana inhalation, with a mean±SD prechallenge vs postchallenge peak flow of 509.2±76.1 vs 549.2±66.4 L/min×100, respectively ($P<.05$). Another study¹⁷ showed a mean±SD decrease in airway resistance after marijuana smoking compared with placebo (2.08±0.36 cm H₂O/L per second for low-dose marijuana smoking vs 1.49±0.26 cm H₂O/L per second for placebo and 1.97±0.35

cm H₂O/L per second for high-dose marijuana smoking vs 1.18±0.14 cm H₂O/L per second for placebo; $P<.05$ for both comparisons). Finally, a third study¹³ showed immediate reversal of both methacholine-induced and exercise-induced bronchospasm in patients with asthma after marijuana challenge.

One study¹⁴ examined the impact of a more prolonged exposure to marijuana on airway response, in which subjects smoked marijuana ad libitum for 47 to 59 days in a sequestered environment. In contrast to the short-term exposure studies, this study demonstrated a decrease in sGaw compared with baseline (change of 16%±2%; $P<.001$) after the more prolonged exposure to marijuana, as well as a decrease in FEV₁ compared with baseline. This study also demonstrated a correlation between average daily quantity of marijuana smoked and decrease in sGaw.

Long-term Marijuana Smoking and Changes in Pulmonary Function

Fourteen studies (**Table 2**) addressed the impact of long-term marijuana smoking (described as nontobacco cigarette smoking in 2 studies^{18,24}) on abnormalities in pulmonary function, including 10 cross-sectional studies,[†] 3 observational cohort studies,^{24,26,29} and 1 case series.²⁰

Of these, 9 studies^{18-20,22-24,26,28,29} reported data on the effect of marijuana smoking on FEV₁, forced vital capacity (FVC), and FEV₁/FVC. One observational cohort study²⁶ reported no change in FEV₁ among marijuana smokers for a mean±SD follow-up of 4.9±2.0 years. Another observational cohort study²⁴ showed a 142-mL decrease in FEV₁ among patients who had previously smoked

†References 18, 19, 21-23, 25, 27, 28, 30, 31.

Table 2. Studies That Reported Effects of Long-term Marijuana Inhalation on Pulmonary Function

Source	Study Design	No. of Subjects	Results	Control for Confounding	Mean Generic Quality Score	Mean Exposure and Disease Specific Quality Score
Bloom et al, ¹⁸ 1987	Cross-sectional	990	For spirometric data: no significant effect of nontobacco cigarette smoking on FEV ₁ or FVC. Current smokers of nontobacco cigarettes showed significant decreases in FEV ₁ /FVC ratio at <i>P</i> <.05 compared with nonsmokers and tobacco smokers.	Tobacco	14	3
Cruickshank, ¹⁹ 1976	Cross-sectional	60	No differences in pulmonary function between marijuana smokers and controls	None	6.5	1.5
Henderson et al, ²⁰ 1972	Case series	200	Among patients presenting with complaints consistent with chronic bronchitis, vital capacity reduced 15%-40%	None	4.5	1
Hernandez et al, ²¹ 1981	Cross-sectional	23	Spirometry results normal in marijuana users	None	9.5	3
Moore et al, ²² 2005	Cross-sectional	6728	Compared with nonusers, marijuana and tobacco users had higher proportion of subjects with an FEV ₁ /FVC ratio <70% predicted (OR, 2.56; 95% CI, 1.54-4.35; and OR, 6.25; 95% CI, 4.76-8.33, respectively). Controlling for tobacco, marijuana use was not associated with a decreased FEV ₁ /FVC ratio.	Tobacco	17.5	3
Sherman et al, ²³ 1991	Cross-sectional	63	No significant difference in FEV ₁ /FVC and DL _{CO} in marijuana smokers compared with nonsmokers	Tobacco	10	3
Sherrill et al, ²⁴ 1991	Observational cohort	856	Indexes of pulmonary function were significantly reduced in subjects reporting nontobacco cigarette smoking longitudinally	Tobacco	13.5	3
Tashkin et al, ²⁵ 1980	Cross-sectional	189	Marijuana smokers had lower sGaw compared with controls (<i>P</i> <.001)	Tobacco	8.5	2.5
Tashkin et al, ²⁶ 1997	Observational cohort	394	No effect of long-term marijuana smoking on FEV ₁ decline	Tobacco	12	3
Tashkin et al, ²⁷ 1993	Cross-sectional	542	Association between marijuana smoking and decline of FEV ₁ in response to low doses of methacholine, indicating airway hyperresponsiveness	Tobacco	10.5	3
Taylor et al, ²⁸ 2000	Cross-sectional	862	Greater proportion of marijuana-dependent individuals showed a reduced FEV ₁ /FVC ratio compared with nonsmokers (<i>P</i> <.007)	Tobacco	12.5	3
Taylor et al, ²⁹ 2002	Observational cohort	930	Linear relationship between number of times cannabis used and decreasing FEV ₁ /FVC (<i>P</i> <.05). However, once confounders of age, tobacco, and weight were adjusted for, relationship was no longer significant (<i>P</i> = .09).	Tobacco	13.5	3
Tilles et al, ³⁰ 1986	Cross-sectional	68	Marijuana smoking, with or without tobacco smoking, was associated with a reduction in single-breath DL _{CO} compared with nonsmoking controls (<i>P</i> <.05)	Tobacco	10.5	2.5
Tashkin et al, ³¹ 1987	Cross-sectional	446	Male marijuana smokers had reduced sGaw compared with male tobacco smokers. No difference in DL _{CO} among marijuana smokers and nonsmokers.	Tobacco	12	3

Abbreviations: CI, confidence interval; DL_{CO}, diffusing capacity of the lung for carbon monoxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; OR, odds ratio; sGaw, specific airway conductance.

nontobacco cigarettes (*P*<.01). One case series²⁰ noted that long-term hashish smokers who presented with respiratory complaints had a 15% to 40% decreased FVC compared with controls. One large cross-sectional study¹⁸ showed that male nontobacco cigarette smokers had a decrease in FEV₁/FVC ratio compared with both nonsmokers (90% predicted vs 98.4% predicted; *P*<.05)

and tobacco smokers (90% predicted vs 95.2% predicted; *P*<.05). Two other cross-sectional studies^{22,28} reported a decrease in the FEV₁/FVC ratio among marijuana smokers when compared with nonsmokers, but after adjusting for tobacco use, 1 of these studies²² demonstrated no difference between marijuana smokers and nonsmokers. One observational cohort study²⁴ reported that

FEV₁/FVC was reduced 1 year or more after nontobacco cigarette smoking compared with nonsmoking (decreased 1.9%±0.7%; *P*<.01), but no dose-response relationship was noted. Another large observational cohort study,²⁹ which followed up a birth cohort into adolescence, found that individuals using cannabis more than 900 times had mean FEV₁/FVC values that were decreased 7.2%

at the age of 18 years, 2.5% at the age of 21 years, and 5.0% at the age of 26 years compared with nonsmokers ($P < .05$ for all comparisons), but when adjusted for age, tobacco smoking, and weight, the association was no longer statistically significant. Two cross-sectional studies^{19,23} reported no differences with respect to FEV₁/FVC ratio.

Three studies^{23,30,31} examined changes in the diffusing capacity of the lung for carbon monoxide (DL_{CO}) with long-term marijuana use. The DL_{CO} was reduced in long-term marijuana smokers (74% ± 20% predicted) compared with nonsmoking controls (92% ± 11% predicted; $P < .05$) in 1 cross-sectional study,³⁰ although 2 studies^{23,31} reported no difference in DL_{CO} between long-term marijuana smokers and nonsmokers.

Four studies^{21,25,27,31} examined the impact of long-term marijuana smoking on airway resistance and airway hyperresponsiveness. Long-term marijuana smoking was associated with a decrease in sGaw in 2 cross-sectional studies; one²⁵ showed a decrease compared with control subjects (0.17 ± 0.00 L/s per centimeter H₂O for marijuana smokers and 0.24 ± 0.01 L/s per centimeter H₂O for controls; $P < .001$), and the other³¹ showed that, among men only, sGaw was decreased in marijuana smokers compared with tobacco smokers (0.19 L/s per centimeter H₂O for marijuana smokers and 0.21 L/s per centimeter H₂O for tobacco smokers; $P < .03$). Another cross-sectional study²¹ reported no change in airway resistance in response to inhaled histamine in marijuana users compared with nonsmoking controls. Finally, another cross-sectional study²⁷ reported an association between long-term marijuana smoking and a decrease in FEV₁ to lower doses of methacholine compared with nonsmoking controls, suggesting nonspecific airway hyperresponsiveness.

Long-term Marijuana Smoking and Respiratory Complications

We reviewed 14 studies (**Table 3**) that assessed the impact of long-term marijuana smoking on respiratory complications; 9 were cross-

sectional,^{18,22,28,31,34-38} 3 were case series,^{20,33,39} 1 was a case-control study,³² and 1 was an observational cohort.²⁴ All 14 studies showed an association between marijuana smoking (or nontobacco cigarette smoking) and an increased risk of various respiratory complications.

Increased cough, sputum production, and wheeze were reported in 4 of these studies.^{18,22,24,31} One cross-sectional study³¹ reported increased prevalence of chronic cough (18%-24%), sputum production (20%-26%), and wheeze (25%-37%) among marijuana and/or tobacco smokers compared with nonsmokers ($P < .05$ for all comparisons) but not between marijuana and tobacco smokers. A large cross-sectional study¹⁸ suggested a dose response between intensity and duration of nontobacco cigarette smoking and cough. Another large cross-sectional study²² showed that after controlling for sex, age, current asthma, and number of tobacco cigarettes smoked per day, marijuana smoking was associated with increased odds of cough (odds ratio [OR], 2.00; 95% confidence interval [CI], 1.32-3.01), phlegm (OR, 1.89; 95% CI, 1.35-2.66), and wheeze (OR, 2.98; 95% CI, 2.05-4.34) compared with controls ($P < .01$ for all comparisons). A large observational cohort study²⁴ showed an increased odds of cough (OR, 1.73; 95% CI, 1.21-2.47), phlegm (OR, 1.53; 95% CI, 1.08-2.18), and wheeze (OR, 2.01; 95% CI, 1.50-2.70) in current nontobacco smokers compared with nonsmokers after adjusting for age, tobacco smoking, and occurrence of symptoms reported previously.

The remainder of the studies showed an association between marijuana smoking and various respiratory complications: bronchitis,^{20,22,31,35,39} dyspnea,^{28,33,35,36} pharyngitis,^{20,35,37} hoarse voice,^{34,35} worsening asthma symptoms,^{20,35} abnormal chest sounds,²² worsening cystic fibrosis symptoms,³⁸ acute exacerbations of bronchial asthma,³² and chest tightness.²⁸

STUDY QUALITY

On the basis of study design, the studies reported were of variable quality using the standardized scale.⁵

The mean quality score was 12.6 (range, 6-18) for the 12 challenge studies, 5.2 (range, 4-7) for the 3 case series, 10.5 (range, 3-19) for the 15 cross-sectional studies, 12 for the 1 case-control study, and 13 (range, 10-14) for the 3 observational cohort studies.

Study quality was also evaluated based on study outcome. The mean quality score for the airway response in studies of short-term marijuana use was 12.6 (range, 6-18). For studies that evaluated changes in pulmonary function secondary to long-term marijuana smoking, the mean quality score was 11.1 (range, 4-19). For the studies categorized as respiratory complications secondary to long-term marijuana smoking, the mean quality score was 10.3 (range, 4-18).

When also scoring publications based on disease-specific criteria, the studies that met the highest level of study quality using both scales were the 3 observational cohort studies.^{24,26,29} Therefore, a discussion of these 3 studies in greater detail is warranted. The most recent observational cohort study²⁹ followed up a birth cohort of 930 participants in New Zealand to the age of 26 years. At 18, 21, and 26 years of age, marijuana and tobacco smoking were assessed with a standardized questionnaire, and pulmonary function was measured by spirometry. Confounding factors (age, tobacco smoking measured as cigarettes per day, and weight) were accounted for using a fixed-effects regression model. The authors report that during 8 years of follow-up, the dose-dependent relationship seen between cumulative marijuana smoking and decreasing FEV₁/FVC was reduced to nonsignificant once the confounding factors were controlled for. The authors suggest that longer follow-up time is necessary for the dose-dependent relationship to persist in the context of confounding factors.

Another observational cohort study²⁶ followed up a convenience sample of 394 white adults for 8 years. Among the study participants, 131 were heavy and habitual smokers of marijuana, 112 smoked marijuana and tobacco, 65 smoked only tobacco, and 86 were nonsmok-

Table 3. Studies That Reported Effects of Long-term Marijuana Inhalation on Respiratory Complications

Source	Study Design	No of Subjects	Results	Control for Confounding	Mean Generic Quality Score	Mean Exposure and Disease Specific Quality Score
Bloom et al, ¹⁸ 1987	Cross-sectional	990	Multivariable analysis shows association between intensity and duration of nontobacco cigarettes and cough, phlegm, and wheeze	Tobacco	14	3
Henderson et al, ²⁰ 1972	Case series	200	Cannabis smokers complained of pharyngitis (n = 150), rhinitis (n = 26), chronic bronchitis (n = 20), and asthma (n = 4)	None	4.5	0.5
Moore et al, ²² 2005	Cross-sectional	6728	Marijuana use associated with respiratory symptoms, chronic bronchitis, coughing on most days, phlegm, wheezing, and chest sounds without a cold	Tobacco	17.5	3
Sherrill et al, ²⁴ 1991	Observational cohort	1802	Marijuana smoking associated with cough, phlegm, and wheeze	Tobacco	13.5	3
Taylor et al, ²⁸ 2000	Cross-sectional	943	Marijuana use associated with wheezing apart from colds, exercise-related shortness of breath, nocturnal waking with chest tightness, and morning sputum production	Tobacco	12.5	3
Tashkin et al, ³¹ 1987	Cross-sectional	446	Marijuana smokers had increased rates of chronic cough, sputum production, wheeze, and more than 1 prolonged episode of bronchitis during the previous 3 y compared with the nonsmokers	Tobacco	11.5	3
Gaeta et al, ³² 1996	Case-control	200	44% of asthma group compared with 20% of control group admitted to or tested positive for recent substance use (OR, 3.14; <i>P</i> < .001). In acute bronchospasm group, 82% admitted to recently using inhaled substances compared with 55% of controls (OR, 3.68; <i>P</i> < .02). No difference in proportions of asthma and control groups that reported marijuana use.	None	12	1
Tennant, ³³ 1980	Case series	36	Marijuana smokers complained of increased amounts of dyspnea and excess sputum production	None	7	2
Boulougouris et al, ³⁴ 1976	Cross-sectional	82	Verbal hoarseness was detected in 4 of 44 hashish users and 2 of 38 controls. Two of 44 users and 1 of 38 controls had signs of emphysema.	None	8	1.5
Chopra, ³⁵ 1973	Cross-sectional	124	Laryngitis, pharyngitis, bronchitis, dyspnea, asthma, irritating cough, hoarse voice, and dryness of the throat were more common in those who smoked higher daily dose of marijuana.	None	3	1
Mehndiratta and Wig, ³⁶ 1975	Cross-sectional	75	Cannabis smokers complained of weight loss, cough, dyspnea, and poor sleep	None	8	1.5
Polen et al, ³⁷ 1993	Cross-sectional	902	Marijuana smokers reported more days ill with cold, flu, or sore throat in past year than nonsmokers	Tobacco	15	3
Stern et al, ³⁸ 1987	Cross-sectional	173	In patients with cystic fibrosis, 20% of marijuana users noted immediate and 5% noted long-term improvement in symptoms; 30% of users noted immediate and 40% noted long-term worsening of symptoms.	None	13	1
Tennant and Prendergast, ³⁹ 1971	Case series	31	39% of marijuana smokers complained of rhinopharyngitis and 29% complained of bronchitis	None	4	0.5

Abbreviation: OR, odds ratio.

ers; 255 participants had measurement of FEV₁ at least 6 times during an 8-year period. A random-effects model, including height, intensity of marijuana use (marijuana cigarettes per day), and intensity of tobacco use (cigarettes per day) was used and failed to show a significant relationship between

marijuana smoking and FEV₁ decline. Potential weaknesses of this study include lack of adjustment of duration of marijuana smoking and a low follow-up rate of 65%.

An additional observational cohort study²⁴ used data obtained from 3-year follow-up surveys conducted during a 6-year period in a

random stratified cluster sample of households in Tucson, Ariz, between 1981 and 1988. Using a 2-stage random-effects model with height and sex as constant covariates and nontobacco cigarette smoking and tobacco cigarette smoking (and their interactions) as time-dependent covariates, the authors

showed that among 856 subjects for whom longitudinal pulmonary function data were available, nontobacco cigarette smokers had a significant decrease in FEV₁/FVC ratio and previous nontobacco smokers had a decrease in FEV₁. Of the total study population (n=1802), current nontobacco cigarette smokers had an increase in chronic cough, phlegm, and wheeze after adjusting for age, tobacco smoking, and preexisting symptoms (from a prior assessment). The potential limitations of this study include the author's focus on subjects who smoked nontobacco cigarettes (which were assumed to contain marijuana), a relatively low number of respondents with current nontobacco cigarette smoking (range, 57-79 respondents), and different questions used to assess current nontobacco cigarette smoking in earlier surveys compared with later surveys.

COMMENT

We systematically reviewed 34 studies that assessed the impact of short-term marijuana use on airway response and long-term marijuana smoking on pulmonary function and respiratory complications. This literature supports a bronchodilating effect soon after marijuana inhalation, although the results of 1 study suggested a reversal of this effect after more prolonged marijuana smoking. Overall, these studies fail to report a consistent association between long-term marijuana smoking and FEV₁/FVC ratio, DL_{CO}, or airway hyperreactivity. Finally, the literature suggests that long-term marijuana smoking is associated with an increased risk of respiratory complications, including an increase in cough, sputum production, and wheeze, persisting after adjusting for tobacco smoking.

This research may inform the debate regarding the increasing use of marijuana for medical purposes accompanying recent legislative changes.⁴⁰ Our findings, however, do not directly apply to pulmonary administration of tetrahydrocannabinol via specialized delivery systems.⁴¹

Our synthesis of the data is unique compared with other re-

views in the literature. A recent review⁴ reported that marijuana smoking was associated with airway inflammation, acute bronchospasm, airflow obstruction, diffusion impairment, and emphysema. Another recent review³ noted an association between bronchodilation and increased cough, sputum, and airway inflammation with long-term marijuana smoking. Our systematic review covers a broader range of studies than previously included and also considers study quality.

The studies we reviewed were variable in quality when evaluated with a standardized assessment tool and a disease-specific assessment tool. Therefore, many methodological limitations need to be considered when interpreting the data reviewed herein. For example, many of the studies failed to adjust for important confounding factors, including tobacco, other inhaled drugs, and occupational and environmental exposures. Although some studies controlled for tobacco smoking status (ie, past, present, or never smoking), most, including the 3 observational cohort studies, did not control for dose or duration (ie, pack-years) of tobacco use, the best available measure of tobacco exposure, which is most strongly correlated with the development of obstructive lung disease. In addition, among the studies that examined the effect of long-term marijuana smoking on respiratory complications and pulmonary function, no standardized measure of marijuana dose or duration was defined. Although some studies reported marijuana cigarette-years of marijuana exposure, other studies reported only if the number of times marijuana was used by an individual was greater than a certain threshold, which varied from at least once to more than 900 times. Also, outcome measurements were not standardized. These factors pose difficulties in comparing and/or combining the results of studies. Finally, our search strategies, although extensive, may not have identified all possible studies that examined these relationships.

Despite these limitations, this review should alert primary care physicians to the potential adverse

health outcomes associated with the widespread use and abuse of and dependence on marijuana. Large prospective studies should be designed that carefully account for potential confounding factors (including detailed assessments of tobacco, substance abuse, and occupational and environmental exposures) that can affect lung health. Such studies should use standard exposure and outcome criteria to accurately measure potential associations. The present findings should be considered in conjunction with a recent review⁴² that showed an association between marijuana smoking and premalignant changes in the lung. On the basis of currently available information, health care professionals should consider marijuana smoking in their patients who present with respiratory complications and advise their patients regarding the potential impact of this behavior on their health.

Accepted for Publication: October 5, 2006.

Correspondence: Jeanette M. Tetrault, MD, Clinical Epidemiology Research Center, West Haven VA Hospital, 950 Campbell Ave, Mail Code 151B, West Haven, CT 06516 (jeanette.tetrault@yale.edu).

Author Contributions: *Study concept and design:* Tetrault, Crothers, Moore, Mehra, and Fiellin. *Acquisition of data:* Tetrault, Crothers, Moore, and Fiellin. *Analysis and interpretation of data:* Tetrault, Crothers, Moore, Mehra, Concato, and Fiellin. *Drafting of the manuscript:* Tetrault, Concato, and Fiellin. *Critical revision of the manuscript for important intellectual content:* Crothers, Moore, Mehra, Concato, and Fiellin. *Statistical analysis:* Tetrault, Moore, and Concato. *Obtained funding:* Moore and Fiellin. *Administrative, technical, and material support:* Concato and Fiellin. *Study supervision:* Crothers, Concato, and Fiellin.

Financial Disclosure: None reported.

Funding/Support: This study was funded by the Program of Research Integrating Substance Use in Mainstream Healthcare (PRISM) with support from the Robert Wood Johnson Foundation, the National

Institute on Drug Abuse (NIDA), and the National Institute on Alcohol Abuse and Alcoholism. The codirectors of PRISM are A. T. McLellan, PhD, of the Treatment Research Institute and B. J. Turner, MD, MEd, of the University of Pennsylvania School of Medicine. Dr Tetraault is supported by the Veterans Affairs Office of Academic Affiliations. Dr Crothers is supported by the Yale Mentored Clinical Scholar Program (grant NIH/NCRR K12 RR0117594-01). Dr Moore is supported by NIDA grant R21 DA019246-02. Dr Mehra is supported by an American Heart Association award (grant 0530188N), an Association of Subspecialty Professors and CHEST Foundation of the American College of Chest Physicians T. Franklin Williams Geriatric Development Research Award, and a K23 Mentored Patient-Oriented Career Development Award (NIH/NHLBI HL079114). Dr Fiellin is a Robert Wood Johnson Foundation Generalist Physician Faculty Scholar.

Previous Presentation: This work was presented at the 29th annual conference of the Society of General Internal Medicine; April 27, 2006; Los Angeles, Calif.

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