Effects of Marijuana Smoking on Pulmonary Function and Respiratory Complications

A Systematic Review

Jeanette M. Tetrault, 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 predefined 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

Marijuana remains the most commonly used illicit drug in the United States, with 14.6 million people 12 years and older reporting current use. The prevalence of marijuana abuse and dependence continues to increase and occurs in 18% of past-year marijuana users. 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 adverse 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. 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.
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 patients, 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 instrument that assessed reporting, bias or confounding, and power; a score of 12 or higher was considered good study quality. 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 $\tau=0.85$; $P<.001$ 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 assessment 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), changes in pulmonary function secondary to long-term marijuana smoking, and respiratory complications secondary to long-term marijuana smoking. The studies reviewed had diverse study designs; 12 studies had a laboratory challenge study design, 15 were cross-sectional, and 3 were observational cohort studies. 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), forced expiratory volume in 1 second (FEV1), airway resistance, and change in methacholine- and exercise-induced bronchospasm.

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

References 18, 19, 21-23, 25, 27, 28, 30, 31, 34-38.
Among the 5 studies that used FEV1 to assess airway response to marijuana challenge, 3 studies9,10,15 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 study16 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 study17 showed immediate reversal of both methacholine-induced and exercise-induced bronchospasm in asthmatic patients, marijuana caused correction of bronchospasm and associated airway hyperinflation.

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 studies18,23) 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 studies16,20,22,24,20,20,29 reported data on the effect of marijuana smoking on FEV1, forced vital capacity (FVC), and FEV1/FVC. One observational cohort study20 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.

Abbreviations: FEV1, forced expiratory volume in 1 second; sGaw, specific airway conductance.
Table 2. Studies That Reported Effects of Long-term Marijuana Inhalation on Pulmonary Function

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Design</th>
<th>No. of Subjects</th>
<th>Results</th>
<th>Control for Confounding</th>
<th>Mean Generic Quality Score</th>
<th>Mean Exposure and Disease Specific Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloom et al, 1987</td>
<td>Cross-sectional</td>
<td>990</td>
<td>For spirometric data: no significant effect of nontobacco cigarette smoking on FEV1 or FVC. Current smokers of nontobacco cigarettes showed significant decreases in FEV1/FVC ratio at P&lt;.05 compared with nonsmokers and tobacco smokers.</td>
<td>Tobacco</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Cruickshank, 1976</td>
<td>Cross-sectional</td>
<td>60</td>
<td>No differences in pulmonary function between marijuana smokers and controls</td>
<td>None</td>
<td>6.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Henderson et al, 1981</td>
<td>Case series</td>
<td>200</td>
<td>Among patients presenting with complaints consistent with chronic bronchitis, vital capacity reduced 15%-40%</td>
<td>None</td>
<td>4.5</td>
<td>1</td>
</tr>
<tr>
<td>Hernandez et al, 2001</td>
<td>Cross-sectional</td>
<td>23</td>
<td>Spirometry results normal in marijuana users</td>
<td>None</td>
<td>9.5</td>
<td>3</td>
</tr>
<tr>
<td>Moore et al, 2005</td>
<td>Cross-sectional</td>
<td>6728</td>
<td>Compared with nonusers, marijuana and tobacco users had higher proportion of subjects with an FEV1/FVC ratio &lt;.70% predicted (OR, 2.66; 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 FEV1/FVC ratio.</td>
<td>Tobacco</td>
<td>17.5</td>
<td>3</td>
</tr>
<tr>
<td>Sherman et al, 1991</td>
<td>Cross-sectional</td>
<td>63</td>
<td>No significant difference in FEV1/FVC and DLco in marijuana users compared with nonsmokers</td>
<td>Tobacco</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Sherrill et al, 1991</td>
<td>Observational cohort</td>
<td>856</td>
<td>Indexes of pulmonary function were significantly reduced in subjects reporting nontobacco cigarette smoking longitudinally</td>
<td>Tobacco</td>
<td>13.5</td>
<td>3</td>
</tr>
<tr>
<td>Tashkin et al, 1980</td>
<td>Cross-sectional</td>
<td>189</td>
<td>Marijuana smokers had lower sGaw compared with controls (P&lt;.001)</td>
<td>Tobacco</td>
<td>8.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Tashkin et al, 1997</td>
<td>Observational cohort</td>
<td>394</td>
<td>No effect of long-term marijuana smoking on FEV1 decline</td>
<td>Tobacco</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Tashkin et al, 1993</td>
<td>Cross-sectional</td>
<td>542</td>
<td>Association between marijuana smoking and decline of FEV1, in response to low doses of methacholine, indicating airway hyperresponsiveness</td>
<td>Tobacco</td>
<td>10.5</td>
<td>3</td>
</tr>
<tr>
<td>Taylor et al, 2000</td>
<td>Cross-sectional</td>
<td>862</td>
<td>Greater proportion of marijuana-dependent individuals showed a reduced FEV1/FVC ratio compared with nonsmokers (P&lt;.007)</td>
<td>Tobacco</td>
<td>12.5</td>
<td>3</td>
</tr>
<tr>
<td>Taylor et al, 2002</td>
<td>Observational cohort</td>
<td>930</td>
<td>Linear relationship between number of times cannabis used and decreasing FEV1/FVC (P&lt;.05). However, once confounders of age, tobacco, and weight were adjusted for, relationship was no longer significant (P = .09).</td>
<td>Tobacco</td>
<td>13.5</td>
<td>3</td>
</tr>
<tr>
<td>Tilles et al, 1986</td>
<td>Cross-sectional</td>
<td>68</td>
<td>Marijuana smoking, with or without tobacco smoking, was associated with a reduction in single-breath DLco compared with nonsmoking controls (P&lt;.05)</td>
<td>Tobacco</td>
<td>10.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Tashkin et al, 1987</td>
<td>Cross-sectional</td>
<td>446</td>
<td>Male marijuana smokers had reduced sGaw compared with male tobacco smokers. No difference in DLco among marijuana smokers and nonsmokers.</td>
<td>Tobacco</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; DLco, 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.
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 studies18,23 reported no differences with respect to FEV1/FVC ratio.

Three studies2,3,30,31 examined changes in the diffusing capacity of the lung for carbon monoxide (DLCO) with long-term marijuana use. The DLCO 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 studies2,21 reported no difference in DLCO between long-term marijuana smokers and nonsmokers.

Four studies2,25,27,31 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,24 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,20,39 abnormal chest sounds,32 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-
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 their interactions) as time-dependent covariates, the authors

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

Abbreviation: OR, odds ratio.
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 FEV/FVC ratio, DLco, 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 reviews 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 review4 noted an association between bronchodilatation 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, MSed, of the University of Pennsylvania School of Medicine. Dr Tet- rault is supported by the Veterans Af-

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

REFERENCES

1. Substance Abuse and Mental Health Services Ad-


100.

4. Wolff AJ, O’Donnell AE. Pulmonary effects of il-


216.


6. Vachon L, Sulikowski A, Rich E. Marihuana ef-


7. Tashkin DP, Shapiro BJ, Frank IM. Acute effects of smoked marijuana and oral delta-9-
tetrahydrocannabinol on specific airway con-

8. Bernstein JG, Kuehlke JC, Mendelson JH. Medi-
cal implications of marijuana use. Am J Drug Al-


10. Renaud AM, Cormier Y. Acute effects of mari-


12. Tashkin DP, Shapiro BJ, Frank IM. Acute pulmo-


13. Tashkin DP, Shapiro BJ, Lee YE, Harper CE. Effects of smoked marijuana in experimentally in-
duced asthma. Am Rev Respir Dis. 1975;112:

377-386.


15. Tashkin DP, Reiss S, Shapiro BJ, Calvarese B, Ols-

en JL, Lodge JW. Bronchial effects of aerosol-


18. Bloom JW, Kaltenborn WT, Paoliotti P, Camilli A, Lebovitz MD. Respiratory effects of non-

295:1516-1518.


20. Henderson RL, Tennant FS, Guerry R. Respira-

21. Hernandez MJ, Martinez F, Blair HT, Miller WC. Airway response to inhaled histamine in asymp-


23. Sherman MP, Roth MD, Gong H Jr, Tashkin DP. Marihuana smoking, pulmonary function, and lung macrophage oxidative release. Pharmacol Bio-

chem Behav. 1991;40:663-669.

24. Sherrill DL, Krzyzanski M, Bloom JW, Lebo-

vitz MD. Respiratory effects of non-tobacco ciga-


25. Tashkin DP, Calvarese BM, Simmons MS, Sha-
pire BJ. Respiratory status of seventy-four habitual marijuana smokers. Chest. 1980;78:

699-706.

26. Tashkin DP, Simmons MS, Sherrill DL, Coulson AH. Heavy habitual marijuana smoking does not cause an accelerated decline in FEV1 with age. Am J Respir Crit Care Med. 1997;155:141-

148.

27. Tashkin DP, Simmons MS, Chang P, Liu H, Coul-


28. Taylor DR, Poulton R, Morfit TE, Ramakutty P, Sears MR. The respiratory effects of cannabis de-

pendence in young adults. Addiction. 2000;95:

1669-1677.

29. Taylor DR, Ferguson DM, Milne BJ, et al. A lon-
gitudinal study of the effects of tobacco and can-


30. Tilles DS, Goldenheid PD, Johnson DC, Mendel-

son JH, Melko NN, Hales CA. Marijuana smoking as cause of reduction in single-breath carbon mon-

oxide diffusing capacity. Am J Med. 1986;80:

601-606.

31. Tashkin DP, Coulson AH, Clark VA, et al. Respi-

135:209-216.


33. Tennant FS Jr. Histopathologic and clinical ab-

34. Boulougouris JC, Panayiotopoulos DP, Antypas E, Liakos A, Stefanis C. Effects of chronic hash-

ish use on medical status in 44 users compared with 38 controls. Ann N Y Acad Sci. 1976:282:

168-172.


37. Polen MR, Sidney S, Tekawa IS, Sadler M, Fried-
man GD. Health care use by frequent mariju-

38. Stern RG, Byard PJ, Tomasherski JF Jr, Doer-
shuk CF. Recreational use of psychoactive drugs by patients with cystic fibrosis. J Pediatr. 1987;

112:293-299.

39. Tennant FS Jr. Prendergast TJ. Medical manifesta-
tions associated with hashish. JAMA. 1971;


1308-1317.

42. Mehra R, Moore BA, Crothers K, Tetrault J, Fiel-
lin DA. The association between marijuana smok-
ing and lung cancer: a systematic review. Arch In-