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EXPERT REVIEWS

Effects of smoking cannabis on lung function

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Although cannabis (or marijuana) is the world's most widely-used illicit drug, there has been surprisingly little research into its effects on respiratory health. Part of the problem is the inherent difficulty of studying the long-term effects of an illegal habit. It has often been assumed that smoking cannabis will have similar long-term effects to smoking tobacco. Several recent observational studies suggest that this is not the case and that cannabis has quite different effects on the lung function. There are consistent findings that smoking cannabis is associated with large airway inflammation, symptoms of bronchitis, increased airway resistance and lung hyperinflation. The evidence that smoking cannabis leads to features of chronic obstructive pulmonary disease, such as airflow obstruction and emphysema is not convincing. However, there are numerous case reports of bullous emphysema among cannabis smokers. These findings have not been confirmed in systematic analytical studies and probably represent uncommon adverse effects in very heavy cannabis smokers. There is now additional controversial evidence that cannabis is at least an occasional cause of respiratory malignancies, but again the evidence is inconclusive.

Keywords: bronchitis • bullae • cannabis • cigarettes • emphysema • lung cancer • lung function • marijuana • respiratory • tobacco

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Cannabis is the most widely used illicit drug worldwide [1]. It has been hailed for its analgesic properties [2] and pilloried for both its psychoactive and addictive nature [3]. It is illegal in most countries but decriminalized in some. In our country, New Zealand, cannabis is the third most commonly used drug after tobacco and alcohol, and the most commonly used illegal drug. Approximately three-quarters of New Zealanders have tried cannabis by age 25 and 13.7% of New Zealanders have used cannabis in recent years [4]. It is most often smoked although it can also be taken orally [5].

The widespread use of cannabis has raised many concerns over its long-term effects. Often these have been about the effects of chronic cannabis use on mental health [6]. However, the frequent practice of smoking cannabis also raises concerns over its potential for adverse effects on the respiratory system. Unfortunately, the illegal status of cannabis makes it difficult to obtain reliable data on cannabis use and its effects. Self-reports of cannabis consumption are likely to be inaccurate owing to social desirability bias and the fear of legal consequences. Furthermore, as most cannabis users also smoke tobacco, the effects of cannabis on the respiratory system may be obscured by the effects of tobacco.

Even if cannabis use is honestly reported by users, quantifying cannabis consumption is inherently difficult because, as an illegal substance, there is no standardization of supply and significant variations in strengths and amounts of cannabis occur. In addition, cannabis can be smoked via various methods including bongs and bubble pipes, as well as directly from a cannabis cigarette. These different methods of smoking cannabis may have influenced the quantity and composition of smoke inhaled. Most studies quantify exposure to cannabis smoke as 'joint-years' whereby one joint-year is equivalent to one joint smoked daily for a year. This approach is pragmatic but focuses on the frequency of cannabis use and ignores differences in the quantity of cannabis leaf in each joint and in the methods of smoking it. An internet survey of cannabis users found that two measures of the quantity of cannabis consumed – the amount of cannabis purchased each month and the usual level of intoxication after using it – predicted respiratory symptoms independently of and in addition to the reported frequency of use [7]. Unfortunately, few studies have gathered such detailed information.

Taken together, the difficulties in obtaining accurate information about cannabis use, the problem of quantifying consumption and the difficulty of separating the effects of cannabis from those of tobacco have meant that the respiratory side effects of cannabis have not been well studied. The likelihood that smoking cannabis harms the respiratory systems has usually been extrapolated from the well-documented effects of smoking tobacco. At face value, it seems reasonable to assume that cannabis and tobacco would have similar effects, since, apart from the main psychoactive ingredients of tetrahydrocannibinol and nicotine, the substances contain a broadly similar mix of chemicals [8]. However, recent reports suggest that the effects of cannabis and tobacco on lung function may be quite different. The paucity of direct evidence on the respiratory effects of chronic cannabis use therefore leaves a major gap in our understanding of one of the world's most commonly inhaled substances. This article appraises recent evidence that cannabis is harmful to lungs.

Cannabis & bronchitis

Numerous studies confirm that smoking cannabis can lead to respiratory symptoms. These studies show that cough, increased sputum production and wheeze are present in approximately a fifth to a third of cannabis smokers [9–11]. Cannabis smoking is also associated with dyspnea, pharyngitis, hoarsening of voice and exacerbations of asthma [10]. These symptoms appear to result from the toxic effects of cannabis smoke on the bronchial mucosa. Bronchoscopic mucosal biopsies from 40 cannabis-only smokers and 31 tobacco-only smokers have demonstrated that both cannabis and tobacco smoking cause significant bronchial damage, with an increase in basal cell hyperplasia, goblet cell hyperplasia, cell disorganization, nuclear variation, and an increase in nuclear/cytoplasm ratio [12]. This study also

demonstrated an increase in squamous cell metaplasia in cannabis smokers, raising the possibility that smoking cannabis may be a risk factor for developing lung cancer.

Another report found that even asymptomatic cannabis smokers with normal physical examinations and spirometric function have central airway inflammation under direct bronchoscopic visualization, bronchial mucosal biopsies and bronchial lavage fluid [13]. Those who smoked both cannabis and tobacco also had distal airway inflammation. There was a high incidence of erythema, edema and airway secretions in both exclusive cannabis smokers and exclusive tobacco smokers. These findings demonstrate that routine physical examination and spirometry may be insensitive measures of lung injury caused by cannabis. While the finding that cannabis smoke causes mucosal damage is not surprising, the most striking result of this study was the fact that cannabis smokers of an average of a few joints a day had the same degree of airway damage as tobacco smokers of 20–30 cigarettes a day. Moreover, this damage was present in young and asymptomatic cannabis smokers.

Effect of cannabis on airflow obstruction

Acute effects

Cannabis has long been recognized as a bronchodilator. Indeed, newspapers in New Zealand (and presumably many other countries) carried advertisements for imported cannabis cigarettes as a treatment for asthma in the late 1800s [101]. Hence, inhaling cannabis appears to predate inhaled adrenergic bronchodilator therapy by at least half a century [14]. There appears to be no doubt that smoking cannabis does have acute bronchodilator effects: in a recent systematic review, 11 out of 12 studies demonstrated a bronchodilator effect of cannabis [10]. However, this acute bronchodilator effect is modest and does not appear to be sustained with continued use over 6–8 weeks [15]. It has been shown to be of slower onset than salbutamol, which has greater bronchodilator effects at 5 min compared to tetrahydrocannibinol [16]. The potential short-term therapeutic effects also need to be weighed against the adverse effects of increased bronchitis and exacerbations of asthma that have been associated with regular cannabis use. Consequently, cannabis is not currently considered to have a therapeutic role in acute bronchospasm (although this is occasionally claimed by cannabis users to justify their habit) and the acute effects will not be considered further in this article.

Long-term effects

Although it has often been assumed that chronic cannabis use will have similar effects on the airways to tobacco, objective evidence for this is lacking. Since the early 1970s, studies have looked for evidence of airway obstruction in cannabis smokers. Most of these have failed to show an association between chronic cannabis use and forced expiratory volume (FEV_1) values (Table 1). A systematic review by Tetrault *et al.* in 2007 found that the evidence that cannabis was associated with airflow obstruction was inconclusive [10]. Since then, at least three further studies have explored the association between cannabis smoking and airflow obstruction and/or chronic obstuctuve pulmonary disease (COPD).

Aldington *et al.* studied lung function in a convenience sample of 339 people in Wellington, New Zealand, who were either nonsmokers, smokers of either tobacco or cannabis only, or smokers of both substances [11]. This study found that unlike tobacco, cannabis smoking had no effect on FEV_1 values, although there was a borderline statistically significant trend to lower FEV_1/forced vital capacity (FVC) ratios in cannabis smokers which appeared to show a dose-dependant relationship. There were also statistically significant dose-dependent associations between a lifetime cumulative use of cannabis and specific airway conductance (sGaw) as well as an association between cannabis smoking and hyperinflation measured as total lung capacity by body plethysmography. Among those who smoked both substances, cannabis appeared to attenuate the effect of tobacco smoking on measures of airflow obstruction including FEV_1, FEV_1/FVC ratios and mid-expiratory flow values, although these effects were also of borderline statistical significance [8].

A Canadian population-based study of 878 individuals aged 40 years and over found no association between exclusive cannabis smoking and COPD. Only four COPD patients were exclusive current cannabis smokers, and this small number limits definite conclusions [17]. However, there was a statistically significant interaction with tobacco smoking: smokers of both cannabis and tobacco had an increased risk of developing airflow obstruction compared to nonsmokers, suggesting a synergistic effect of tobacco smoking and cannabis in the development of COPD. Smoking tobacco alone was also associated with an increased risk of COPD [17].

The lack of association between cannabis use and airflow obstruction was confirmed in a recent report from the Dunedin Multidisciplinary Health and Development Study, which tracked a population-based birth cohort of 1037 individuals with information on cannabis and tobacco use and lung function at 18, 21, 26 and 32 years of age [18]. Unlike tobacco, cannabis was not associated with lower FEV_1 values or with the FEV_1/FVC ratios once tobacco use had been adjusted for. Nor was there evidence of airflow obstruction among cannabis smokers who did not smoke tobacco. However, there was evidence of increased resistance to flow in the central airways with significant associations between cannabis use, lower sGaw and increased airway resistance. These effects were much stronger for cannabis than for tobacco. There was also a significant association between cannabis use and hyperinflation as measured by the FVC on spirometry (12 ml per joint-year [95% CI: 3.0–21.0]), total lung capacity (TLC; 25 ml per joint-year [95% CI: 13.9–36.0]), functional residual capacity (15.1 ml per joint-year [95% CI: 4.8–25.4] and residual volume (12.6 ml per joint-year [95% CI: 7.0–18.3]) by plethysmography, and alveolar volume (17.8 ml per joint-year [95% CI: 6.8–28.9]) by gas dilution. This association with hyperinflation was stronger for cannabis than tobacco.

Like the Aldington study, earlier reports from the Dunedin study had documented a borderline-significant association between cannabis use and lower FEV_1/FVC ratios [8,19]. It is now apparent that this trend to lower FEV_1/FVC ratios was owing to

increases in the FVC rather than cannabis-induced decreases in the absolute value of the FEV_1 [18]. Taken together, the pattern of findings from the studies by Aldington *et al.* and the Dunedin study suggests that cannabis causes central airways resistance to airflow (lower sGaw), associated with prominent symptoms of bronchitis [8,10,18,19] and hyperinflation, but that there is little or no effect on the FEV_1 and airflow obstruction. Of note, the practice of mixing cannabis and tobacco in the same joint is uncommon in New Zealand, enabling the researchers to study the effects of tobacco and cannabis separately.

Table 1. Epidemiological associations between cannabis use and lung function.

Study (year)	Study design	Subjects (n)	Results	Ref.
Hancox *et al.* (2010)	Observational cohort	919	Increased lung capacity and airway resistance in marijuana smokers. No evidence of airway obstruction, gas trapping or impaired gas transfer	[18]
Tan *et al.* (2009)	Observational cohort	878	Marijuana smoking not associated with increased bronchitic symptoms and COPD	[17]
Sherrill *et al.* (1991)	Observational cohort	856	Pulmonary function was reduced in subjects reporting marijuana smoking	[50]
Tashkin *et al.* (1997)	Observational cohort	394	No effect of marijuana smoking on FEV_1 decline	[51]
Aldington *et al.* (2007)	Cross-sectional	339	Marijuana associated with airflow obstruction, hyperinflation and large airways impairment	[11]
Bloom *et al.* (1987)	Cross-sectional	990	No effect of marijuana on FEV_1 or FVC	[45]
Cruickshank (1976)	Cross-sectional	60	No difference between marijuana smokers and controls	[46]
Hernandez *et al.* (1981)	Cross-sectional	23	Normal spirometry in marijuana smokers	[47]
Moore *et al.* (2005)	Cross-sectional	6728	marijuana use not associated with decreased FEV_1/FVC ratio	[48]
Sherman *et al.* (1991)	Cross-sectional	63	No significant difference in FEV_1/FVC and DL_{co} in marijuana smokers and nonsmokers	[49]
Tashkin *et al.* (1980)	Cross-sectional	189	Marijuana smokers had lower sGaw compared with controls ($p < 0.001$)	[21]
Tashkin *et al.* (1993)	Cross-sectional	542	Marijuana smoking associated with airway hyper-responsiveness with lose-dose methacholine	[52]
Tilles *et al.* (1986)	Cross-sectional	68	Marijuana smoking regardless of tobacco smoking, resulted in reduction of single breath DL_{co} compared with nonsmokers	[53]
Tashkin *et al.* (1987)	Cross-sectional	446	Male marijuana smokers had reduced sGaw compared with male tobacco smokers. No difference in DL_{co}	[20]
Total:		12,613		

Taylor *et al.* performed two studies (2000 [8] and 2002 [19]) on the same cohort that have been superseded by Hancox *et al.* [18].
COPD: Chronic obstructive pulmonary diease; DL_{co}: Diffusing capacity for carbon monoxide; FEV_1: Forced expiratory volume after 1 s; FVC: Forced vital capacity; sGaw: Specific airway conductance.

In summary, there is currently no convincing evidence that smoking cannabis causes airflow obstruction. This may be surprising and appears to conflict with the consistent evidence for increased resistance to airflow in the large airways. In addition to the studies reported previously, four other studies have found that cannabis smokers have increased levels of airway Raw and/or lower levels of SGaw than nonusers or tobacco smokers [11,18,20,21]. These findings suggest that cannabis has significant effects on large airway function associated with bronchitis and mucous production, which are greater than those found for tobacco, but has little or no effect on airway obstruction and the risk of COPD.

Emphysema & bullous disease

There are now at least 36 case reports of bullous lung disease attributable to heavy cannabis smoking in English literature. These cases consistently report upper lobe predominance with relatively preserved lower lung parenchyma (Table 2). Despite the presence of bullae on high resolution CT scans, lung function tests and chest x-ray appearances have largely been unremarkable in these patients. Most of these cases have been reported in young adults under the age of 45 years. This age distribution may reflect the fact that older generations may not have smoked much cannabis or may be owing to a reporting bias. How cannabis might cause such severe lung damage is not clear. It has been postulated that the methods of inhalation of cannabis smoke may cause significant barotrauma. Cannabis smokers tend to hold their breath for up to four-times longer than cigarette smokers, with a nearly 70% increase in inspiratory volume [22]. This high lung volume and breath holding results in the prolonged exposure to inhaled particulates at very high temperatures, which in turn may be responsible for epithelial injury and inflammation.

Currently, the evidence that smoking cannabis causes emphysema and bullae is limited to these case reports and therefore

remains anecdotal. Although Tashkin *et al.* demonstrated modest short-term decreases in gas transfer (DL_{co}) among 30 men allowed to smoke cannabis *ad libitum* for 94 days [15], none of the population-based studies have been able to confirm that cannabis consumption is associated with persistent impairment of DL_{co} [11,15,16]. This is in stark contrast to tobacco smoking, for which a reduction in DL_{co} is probably the most sensitive indicator of parenchymal lung damage. In Aldington's cross-sectional study, exclusive smokers of cannabis were much less likely to show evidence of emphysema on high-resolution CT scans than tobacco smokers, suggesting that macroscopic emphysema is not a common consequence of cannabis use [11].

Even though cannabis smoking is infrequently associated with emphysema in population-based studies, two studies have found a trend towards increased static lung volumes among cannabis users. Both the cohort study by Hancox *et al.* [18] and the cross-sectional study by Aldington *et al.* [11] found greater total lung capacities among cannabis users, while Aldington also found evidence that cannabis was associated with hyperinflation on high-resolution CT scans. This is consistent with other studies demonstrating that cannabis is associated with statistically significant increases in FVC on spirometry [17]. It is difficult to interpret the significance of these increases in static and dynamic lung volumes: whereas hyperinflation is usually a feature of emphysema, this seems to be unlikely without evidence that cannabis causes either airflow obstruction (measured by FEV_1/FVC ratios), impaired gas transfer (DL_{co}), or parenchymal destruction on high-resolution CT scans.

There are at least two reasons why these observational studies conflict with numerous case reports of severe emphysematous bullae among cannabis smokers. Perhaps the most likely explanation relates to the dose of cannabis smoked. Most of the reported cases of bullous emphysema have been in very heavy cannabis smokers. For example, in the largest series of patients (n = 17) the mean lifetime consumption of cannabis was 54 joint-years [23]. Although cannabis use is very common, such prolonged heavy use is not. Even in large population-based studies there may only be a small number of heavy cannabis users. Indeed, in the cohort study by Hancox *et al.*, none of the participants had accumulated more than a 30 joint-year history by the age of 32 [Hancox RJ; Unpublished data]. Purposeful samples, such as that used by Aldington, may be more likely to identify such heavy users, but it is important to note that Aldington *et al.* applied very strict exclusion criteria to their sample to exclude the possibility of respiratory effects owing to other illicit drugs. This may have also excluded the heaviest users of cannabis. The only exclusive cannabis smoker with macroscopic emphysema on high-resolution CT scanning in their study had a 437 joint-year history [11].

The other reason why systematic studies have failed to identify the lung function changes reported in individual case reports may be that bullous lung disease is a rare complication. The number of cases reported in the literature is small in relation to the widespread use of cannabis. It is possible that, when compared to tobacco, only a relatively small proportion of people are susceptible to developing parenchymal lung damage from cannabis smoke and even then, only if they smoke a very large amount. Hence, impairment of gas transfer and macroscopic evidence of emphysema are unlikely to be detected among general population samples. This explanation would require parenchymal lung damage to be caused by a process distinct from the central inflammation that is observed in most regular cannabis users.

In summary, the existing data are unable to confirm a definite link between cannabis and bullous emphysema. However, the case reports support the likelihood that at least occasional heavy cannabis smokers are susceptible to this disease. Further evidence from systematic observational studies is required to confirm this.

Different to tobacco?

The findings previously summarized suggest that smoking cannabis does have adverse effects on respiratory function, but contrary to what is often assumed, the pattern of damage in cannabis smokers is different from that associated with tobacco. There is now clear evidence that smoking cannabis causes inflammatory changes in the central bronchi and a consistent trend to increased airway resistance (or reduced conductance). Surprisingly, this does not appear to have a great impact on the FEV_1. Trends to lower FEV_1/FVC ratios have also been observed in several studies, but this seems to be due to an increase in the FVC, rather than a reduction in FEV_1. The higher FVC observed among cannabis users is consistent with evidence of hyperinflation seen on plethysmography and on CT scans. The patterns of effects associated with tobacco and cannabis smoking in a cohort of 32 year olds are compared in Table 3.

Table 2. Reports of bullous lung disease in cannabis users.

Study (year)	Pateints (n)	Mean age (years)	Mean joint-years	Results	Ref.
Beshay *et al.* (2007)	17	27	53	Upper lobe predominance with bullae ranging from 0.3 to 12 cm	[23]
Johnson *et al.* (2000)	4	38	NS	All had upper lobe bullae and normal lower lobes	[40]
Gao *et al.* (2010)	1	23	NS	Bilateral upper lobe bullae, more prominent on the right	[41]
Hii *et al.* (2008)	10	41	74	Upper and mid-zone emphysematous bullae	[42]
Phan *et al.* (2005)	1	26	>10	Extensive cystic and bullous lung changes primarily affecting lower lobes	[43]
Thompson *et al.* (2002)	3	39	NS	Large apical lung bullae	[44]

NS: Not stated.

Why cannabis and tobacco should have different effects on the lungs is not clear. As noted, other than nicotine and cannabinoids, smoke from the two substances contains a similar mix of chemicals. It is possible that tetrahydrocannibinol, a known short-term bronchodilator [10], has long-lasting effects on lung function (although the short-term bronchodilator effect seen in single-dose studies does not persist during continued use [15]). It is also possible that differences in the concentration of some unidentified substance in the smoke results in these differences. However, it seems more likely that the different methods of smoking cannabis compared to smoking tobacco are responsible for the different effects on lung function. Cannabis is usually smoked unfiltered and the smoke from cannabis is hotter compared to filtered tobacco smoking [22]. Cannabis smokers also tend to take much deeper breaths and employ breath-holding techniques to increase the absorption of tetrahydrocannabinol as bioavailability ranges from 18 to 50%, depending on the volume of air inhaled, the depth of inhalation and the duration of retention of smoke in the alveoli [24,25]. It is possible that by using Valsalva maneuvres to increase the uptake of tetrahydrocannabinol, smokers also subject themselves to hyperexpansion of the chest and the potential for barotrauma. Interestingly, although prolonged breath-holding and Valsalva maneuvres appear to be widely used by cannabis smokers, studies indicate that is not necessary to perform these maneuvres because the psychoactive effects of cannabis are similar if it is smoked normally [26,27].

Cannabis can also be taken in a variety of ways: either rolled and smoked like cigarettes, inhaled through specialized devices that use water filtration, bongs or such as vaporizers, and can also be consumed in cakes, beverages and oils. To date, we are not aware of any research looking specifically at the methods of cannabis delivery to the lungs and their long-term impact on lung function.

Importantly, whether cannabis and tobacco have synergistic effects on lung function is a question that remains unanswered. Most cannabis smokers also smoke tobacco and it seems likely that they would be predisposed to a combination of effects. Tan *et al.* found that although cannabis smoking alone was not associated with an increased risk of COPD in their sample of older adults, it appeared to increase the risk among those who also smoked tobacco [17]. However, other studies have found little evidence that cannabis modifies the effects of tobacco on lung function. Rather, the pattern of abnormalities found in those who smoke both substances suggests an additive effect or a combination of the different tobacco and cannabis effects, rather than synergistic action [11,12,18,19].

Table 3. Differences in lung function associated with cannabis and tobacco use.

Measure	Cannabis	Tobacco
FEV_1	↔	↔/↓
FVC	↑	↔
FEV_1/FVC ratio	↔	↓
TLC	↑	↔/↑
RV	↑	↑
DL_{co}	↔	↓
sGaw	↓	↔/↓

↔: No association; ↑: Increase; ↓: Decrease.
DL_{co}: Diffusing capacity for carbon monoxide; FEV_1: Forced expiratory volume; FVC: Forced vital capacity; RV: Residual volume; sGaw: Specific airway conductance; TLC: Total lung capacity.
Data taken from [18].

The fact that there appears to be a difference in the pattern of lung function abnormalities associated with tobacco and cannabis does not necessarily mean that cannabis will not have a similar effect to tobacco for lung cancer and other health problems. However, conflicting reports published in recent years have also been unable to resolve the issue of whether cannabis smoking causes lung malignancies.

While it has been found that cannabis condensates are more cytotoxic, mutagenic and have a greater tendency to induce chromosomal damage and in a more erratic fashion compared with tobacco [28], a systematic review of the evidence by Mehra *et al.* in 2006 failed to demonstrate a clear increased risk of lung cancer among cannabis smokers after accounting for tobacco use. They cite methodological deficiencies in the observational studies that they reviewed and a lack of adjustment for tobacco smoking as the main reason they were unable to reach the conclusion that cannabis is a cause of lung cancer [29]. The evidence that cannabis smoking causes lung cancer remains elusive [30]. For example, a large American cohort study found no evidence of an increase in overall cancer risk, and no increased risk of lung cancer in particular among cannabis smokers [31].

Recently, a New Zealand case–control study of 79 cases of lung cancer showed a trend towards an increased risk of lung cancer of about 8% for each joint-year smoked (compared with a 7% increase in risk for each pack-year of cigarette smoking). This increase in risk was only evident for the heaviest tertile (>10.5 joint-years) of cannabis smokers who had a relative risk of 5.7 (95% CI: 1.5–21.6) after adjusting for cigarette smoking and other potential confounding variables [32]. By contrast, a larger case–control study of 2252 subjects in Los Angeles (CA, USA) did not find an increased risk of lung cancer nor for oropharyngeal cancers in cannabis smokers despite some subjects smoking very large amounts of cannabis (in excess of 60 joint-years) [33]. Possible reasons for the differences between these findings include differences in study design and the selection of controls, selection bias of the cases, difficulty in quantifying cannabis use, and the difficulty in separating the effects of tobacco from those of cannabis in people who smoke both [29,30,32]. Further data are urgently required to resolve this issue.

The continuing uncertainty about the risk of lung cancer associated with cannabis highlights the problems associated with studying the effects of an illegal and unstandardized substance such as cannabis. On the other hand, these conflicting epidemiological findings are matched by contradictory biological data from *in vitro* studies which have found that that cannabinoids have both antineoplastic effects [34] and can also stimulate growth of

lung cancer cells [35]. In fact, despite the similarities in chemical properties, the pharmacological effects of cannabis and tobacco smoke differ substantially and this may influence the carcinogenic potential of the smoke [36].

Expert commentary

For a substance that is so widely used, the paucity of evidence on the respiratory effects of smoking cannabis is surprising. The evidence that we have suggests that cannabis definitely does have respiratory effects, but that these are different to tobacco. The relationship between cannabis smoking and the common smoking-related problems associated with tobacco such as airway obstruction, emphysema and lung cancer is not clear. Notwithstanding the difficulties in conducting research on illegal substances and the problems of quantifying cannabis consumption, further studies with large population samples and long-term follow-up are needed.

Case reports of bullous emphysema among cannabis smokers are difficult to reconcile with systematic observational data. These cases are probably rare, although they may also be under-recognized because of under-reporting of cannabis use. They are likely to represent the extreme end of the spectrum of cannabis-related lung disease, occurring only in very heavy smokers. However, the evidence remains anecdotal and the development of bullae and emphysema as a consequence of smoking cannabis is not supported by the available systematic observational studies. Clearly, more needs to be done to confirm whether there is a genuine cause-and-effect relationship between smoking cannabis and lung bullae and, if such a relationship exists, a threshold at which irreversible damage occurs.

We also need research into the methods of inhaling cannabis and the influence that this may have on its respiratory effects. Whether breath-holding and Valsalva maneuvres can explain the association between cannabis use and lung hyperinflation is intriguing: nothing in our understanding of lung physiology appears to indicate that such simple maneuvres could make such a marked difference to lung function.

A relatively unexplored area is whether cannabis has therapeutic potential as an acute bronchodilator, either as an adjunct or an alternative to current drugs. As noted, cannabis has a long history as treatment for asthma [101]. It is unlikely that anyone would advocate smoking cannabis to treat obstructive airways disease, but there may be less harmful ways to deliver the drug. Early research investigated the effects of cannabis aerosols [15,37]. More recently, vaporizers have been proposed as a method of inhaling 'medical cannabis' in a smoke-free form. An internet survey suggested that users of vaporizers had fewer respiratory symptoms but we are not aware of any published long-term studies of their effects [38].

Despite the continuing uncertainty regarding the effects of cannabis on the lungs, we suggest that health practitioners routinely ask about cannabis use when taking a medical history. Although medical students are taught to ask about illicit drugs (particularly intravenous drugs), until recently, little attention has been given to quantifying cannabis use [39]. Given the widespread use of this substance in many countries, this should be carried out far more often. It is particularly important for patients with unexplained respiratory symptoms, apparently 'idiopathic' lung bullae or pneumothorax, lung, and head and neck cancers. While the relationship between cannabis and these diseases may still be unproven, by raising awareness of cannabis use, we are more likely to establish whether there is a causal relationship or not.

The research findings may also have implications for drug policy. We have strong evidence that cannabis causes bronchial inflammation, respiratory symptoms and affects lung function. While we do not yet understand the full significance of the pattern of lung function changes documented by the research, it is clear that smoking cannabis is not harmless to the lungs. Cannabis is also a controversial cause of lung cancer and emphysematous bullae in a small but uncertain number of users. It is beyond the scope of this article to consider whether these harms are best reduced by maintaining the illegal status of cannabis, decriminalization, or by legalising and regulating its use. What we can say is that cannabis is harmful to lungs and that drug policies should take this into consideration. We also recommend that future policies should encourage further research into the health effects of smoking cannabis.

In conclusion, cannabis has been shown to have a range of effects on lung function that are different to those found with tobacco. Acute inhalation of cannabis produces bronchodilation, but chronic use is associated with bronchitic symptoms, central airway inflammation, and increased large airway resistance to airflow. There is also evidence for lung hyperinflation, but no convincing evidence that cannabis smoking leads to airflow obstruction and COPD. Despite the case reports of emphysematous bullae among heavy cannabis users, it has not yet been proven that cannabis causes emphysema. Cannabis also contains many carcinogenic substances but it remains controversial whether it is a cause of lung malignancies.

Five-year view

We have a great deal to learn about the effects of cannabis on the lungs. Over the next 5 years we anticipate more studies examining the effect of smoking cannabis on lung function:

- Large population-based cohort studies with longer periods of follow-up. Hopefully these will include heavier cannabis smokers to clarify the effects of cannabis smoking on the risk of developing COPD;
- Case–control studies of lung cancer to assess the link between cannabis smoking and lung malignancies. The current evidence is conflicting and further studies are urgently needed;
- Case–control studies of cannabis use in patients with bullous emphysema and correlation to quantity of cannabis smoked. To date, we only have anecdotal evidence from case reports and case series linking cannabis to lung bullae. This contrasts with the failure to demonstrate a link between cannabis exposure and emphysema in population-based cohort studies. More case reports will not resolve this issue; we need analytical studies of cannabis exposure among people with bullous lung disease and control subjects;

- In addition, we hope to see research into the different ways of inhaling cannabis, for example, comparing 'bongs' or water filtration devices with unfiltered 'joints' (direct cigarette smoking) and with other devices such as vaporizers. These methods of inhalation may have markedly different effects on the lung, but we are not aware of any systematic studies of this;
- A better understanding of the long-term pulmonary effects of repeated Valsalva maneuvres and deep breath holding commonly used by cannabis smokers is also needed. This is a difficult issue to study, but we hope that more imaginative researchers than ourselves will find a way;
- We hope that there will be research into cannabis users perspectives of the health risks of cannabis smoking. How do they decide which method to use for smoking it? What limits cannabis consumption – do users titrate the dose according to their level of intoxication? This would identify educational needs and the potential for harm reduction. This information may also inform future drug policies;
- We expect medical marijuana to become more widely used in the coming years and that more countries will legalise its use. We need to know more about the potential adverse effects of this and also of the potential effects of synthetic cannabinoids on the lung. An intriguing possibility is that cannabinoids have an unexploited potential as a bronchodilator. While the bronchodilator action of cannabis has been known for more than a century, we still do not know if this could be useful in practice;
- Finally, we anticipate that taking and quantifying an individuals cannabis smoking history will become as routine in clinical practice as recording tobacco exposure. Doctors should inform their patients about the known effects of cannabis smoke in causing bronchitis. It may be difficult to persuade users to stop smoking cannabis but they need to be advised of the possible risk of lung cancer.

Key issues

- Cannabis is widely used throughout the world and is currently the most common illegal drug.
- The pattern of lung function abnormalities among cannabis smokers is clearly different from those associated with tobacco smoking.
- Cannabis smoke has potent effects on the bronchial mucosa and is associated with large airway inflammation and symptoms of bronchitis.
- Systematic research into the long-term effects of smoking cannabis on lung function show increased large airways resistance and hyperinflation.
- By contrast there is no convincing evidence that smoking cannabis causes obstructive airways disease or emphysema.
- The numerous case reports of bullous emphysema in the literature have not been replicated in systematic studies. It is likely that these represent occasional complications among extremely heavy cannabis smokers.
- More data are needed on the controversial issue of whether smoking cannabis causes lung cancer.
- The advantages and disadvantages of the different methods of inhaling cannabis (joint, bong, pipe or vaporizer) are unknown.
- Cannabis has acute bronchodilator effects but there is no evidence that this is clinically useful.

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Activity Evaluation
Where 1 is strongly disagree and 5 is strongly agree

	1	2	3	4	5
1. The activity supported the learning objectives.					
2. The material was organized clearly for learning to occur.					
3. The content learned from this activity will impact my practice.					
4. The activity was presented objectively and free of commercial bias.					

1. 42-year-old man presents with coughing. He quit smoking cigarettes 20 years ago but has smoked cannabis several times per week over the last 15 years. He says that he is worried "that the pot is hurting my lungs." What should you consider in regard to the effects of cannabis on respiratory health?

- ☐ **A** Cannabis is a potent bronchoconstrictor
- ☐ **B** The acute airway effects of cannabis do not appear to be sustained after 8 weeks of regular use
- ☐ **C** Many respiratory abnormalities related to cannabis use may be detected on physical examination
- ☐ **D** Many respiratory abnormalities related to cannabis use may be detected on spirometry

2. Which of the following lung function values is most likely to be abnormal in this patient?

- ☐ **A** Forced expiratory volume in 1 second (FEV1)
- ☐ **B** Forced vital capacity (FVC)
- ☐ **C** Airway resistance (Raw)
- ☐ **D** FEV1/FVC

3. What can you tell this patient about the association between cannabis use and emphysema/bullous disease?

- ☐ **A** Most adults with chronic cannabis use have evidence of pulmonary bullae
- ☐ **B** Bullae associated with cannabis are invariably located in the lower lobes
- ☐ **C** Chronic cannabis use reduces diffusion lung capacity for carbon monoxide (DL_{CO})
- ☐ **D** Cannabis does not appear to promote emphysema

4. The patient is also concerned about the effects of cannabis on his risk for cancer. What can you tell him?

- ☐ **A** There is conflicting evidence as to whether cannabis can promote lung cancer
- ☐ **B** Cannabis condensates are less mutagenic than tobacco condensates
- ☐ **C** Cannabis appears to increase the risk for oropharyngeal cancer but not lung cancer
- ☐ **D** Bong smoking appears to confer a lower risk for lung cancer compared with smoking joints