4

Clearing the Smoke on Cannabis

Respiratory Effects of Cannabis Smoking – An Update

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This is the fourth in a series of reports that reviews the effects of cannabis use on various aspects of human functioning and development. This report on the respiratory effects of cannabis smoking provides an update of a previous report with new research findings that validate and extend our current understanding of this issue. Other reports in this series address the effects of chronic cannabis use on cognitive functioning and mental health, maternal cannabis use during pregnancy and cannabis use and driving. This series is intended for a broad audience, including health professionals, policy makers and researchers.

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Key Points

- Cannabis smoking has been consistently related to a greater incidence of cough, wheeze, aggravation of asthma, sore throat, chest tightness, shortness of breath and hoarse voice.
- There is emerging evidence that quitting cannabis smoking can reverse some of the negative respiratory symptoms associated with its use.
- Cannabis smoke contains many of the same chemicals as tobacco smoke, several of which are known carcinogens. Evidence for a link between cannabis smoking and serious conditions such as lung cancer is mixed. Further research is needed to clarify whether cannabis smoke is a causal factor for lung cancer.
- Many recent epidemiological studies suggest no causal relationship between cannabis and chronic obstructive pulmonary disease (COPD), at least in low to moderate cumulative doses.
- Further research is needed to clarify whether heavy cannabis smoking is a causal factor for COPD. Because of this uncertainty, caution should be exercised until the link between chronic regular use and COPD is better understood.
- It is essential for healthcare professionals to be aware of the impact of cannabis smoking on respiratory health so that they can inform and advise their patients, as well as develop strategies to promote further awareness and general respiratory health.

Background

After alcohol, cannabis (also referred to as marijuana) is the most widely used psychoactive substance in Canada. According to the 2013 Canadian Tobacco, Alcohol and Drugs Survey (CTADS), 10.6% of Canadians aged 15 years and older reported using cannabis at least once in the past year (Statistics Canada, 2015), virtually unchanged from 10.2% in 2012. The use of cannabis is generally more prevalent among young people, with 22.4% of youth aged 15 to 19 and 26.2% of young adults aged 20 to 24 reporting past-

year use. Approximately 28% of Canadians aged 15 and older who used cannabis in the past three months reported that they used this drug every day or almost every day.

A growing body of evidence suggests that cannabis use may negatively impact several aspects of people's lives, including mental and physical health, cognitive functioning, ability to drive a motor vehicle, and pre- and post-natal development among offspring. This report—the fourth in a series reviewing the effects of cannabis use on various aspects of human functioning and development (see Beirness & Porath-Waller, 2015; Porath-Waller, 2015; Porath-Waller, 2009)—provides an update on the topic of the respiratory effects of cannabis smoking. Following a review of the evidence, this report discusses implications for policy and practice.

Cannabis is a greenish or brownish material consisting of the dried flowering, fruiting tops and leaves of the cannabis plant, Cannabis sativa. Hashish or cannabis resin is the dried brown or black resinous secretion of the flowering tops of the cannabis plant. The acute effects of cannabis include euphoria and relaxation, changes in perception, time distortion, deficits in attention span and memory, body tremors, and impaired motor functioning. It is a controlled substance under the Controlled Drugs and Substances Act—meaning that the acts of growing, possessing, distributing and selling cannabis are illegal. There is an exception for those possessing cannabis for medical purposes as supported by a physician.

A Comparison and Contrast between Cannabis and Tobacco Smoke

Several reports have drawn comparisons between tobacco and cannabis smoke owing to the well-established respiratory harms of smoking tobacco, such as lung cancer, chronic obstructive pulmonary disease (COPD, a group of lung diseases that includes chronic bronchitis and emphysema) and respiratory infections. Smoke is usually inhaled from compacted and rolled leaves, analogous to a cigarette (a "joint"), or from a water pipe ("bong"), or by using a vaporizer. These reports have shown that both cannabis and tobacco smoke contain many of the same chemicals, several of which are also known carcinogens (Moir et al., 2007; Maerten et al., 2009). Some of these chemicals have been shown to be present in greater concentrations in cannabis smoke than in tobacco smoke (Moir et al., 2007; Singh et al., 2009), while others appear in greater concentrations in tobacco smoke (Moir et al., 2007). In addition, both cannabis and tobacco smoking have the potential to pass unhealthy levels of aluminum into the body through the lungs, which might contribute to respiratory as well as other health problems (e.g., neurological conditions) (Exley, Begum, Woolley, & Bloor, 2006).

In comparison with tobacco smokers, those who smoke cannabis tend to have a deeper and longer inhalation period, use unfiltered cannabis "joints," and smoke to a shorter butt length and at a greater combustion temperature (Mehra, Moore, & Crothers, 2006). These behaviours have been linked to four times the amount of tar inhaled and approximately one-third more tar deposits in the respiratory tract (Benson & Bentley 1995; Tashkin et al., 1991a; Tashkin et al., 1991b). Aldington and colleagues (2007) reported that cannabis smoking was linked to lower lung density and greater total lung capacity, associations that were not found with tobacco smoking (Aldington et al., 2007). In addition, the study results showed no significant change or decline in clinical measures of exhalation capacity in cannabis smokers.

Respiratory Symptoms and Serious Conditions Related to Cannabis Smoking

Prior to outlining the evidence related to the respiratory effects of cannabis, it is important to acknowledge that there have been a number of issues that have made it difficult to identify the consequences of smoking cannabis. For instance, many individuals who smoke cannabis also smoke tobacco, making it challenging to tease apart the effect of cannabis smoke alone (Rooke, Norberg, Copeland, & Swift, 2013). In addition, studies that rely on self-reported use might be subject to under-reporting (Hashibe et al., 2005). Also, many studies have comprised participants who are younger and have not had sufficient exposure to cannabis smoke for symptoms of illness to emerge (Mehra et al., 2006). As will be discussed, the risk of respiratory effects from cannabis smoke seems to be most prevalent among those who use cannabis daily or almost daily for many years and the sample size of individuals who fall within this category is often quite small (Hashibe et al., 2005).

Regular cannabis smoking can lead to respiratory bronchitis in a high proportion of users. It is puzzling that acutely, cannabis acts a bronchodilator, widening the air passages of the lung (Tashkin, Shapiro, & Frank, 1973; Vachon, Fitzgerald, & Solliday, Gould, & Gaensler 1973). However,

Errata: The following corrections have been made to this publication. Page 2, top of left-hand column: "Approximately 27% … every day in 2012" changed to "Approximately 28% … every day or almost every day"; reference removed.

those who smoke regularly are more likely to report a wide range of respiratory symptoms. Although not all cannabis users will suffer from the most serious conditions, there are common respiratory ailments that affect a relatively large number of users, with some symptoms affecting 40% of the user population (Moore, Augustson, Moser, & Budney, 2005). Several studies have indicated that compared to non-smokers, those who smoked cannabis with or without tobacco were more likely to experience chronic cough, wheeze, aggravation of asthma, sputum production, sore throat, chest tightness, shortness of breath and hoarse voice (Hancox, Shin, Gray, Poulton, & Sears, 2015; Moore et al., 2005; Taylor, Poulton, Moffit, Ramankutty, & Sears, 2000; Tetrault, et al., 2007). Moreover, a national survey in the United States indicated that cannabis users reported rates of respiratory symptoms similar to individuals who had smoked tobacco and were 10 years older, even when accounting for tobacco use, age, gender and current asthma (Moore et al., 2005). These respiratory symptoms likely stem from airway inflammation that can lead to chronic bronchitis (Tashkin et al., 2002).

Despite the evidence for a link between cannabis smoking and a wide range of respiratory symptoms, research on the relationship between cannabis and COPD is unclear. COPD is a progressive lung disease involving damage to the air sacs in the lungs and the narrowing and blocking of the airways. While a few older studies have observed a relation between regular cannabis smoking and higher airway obstruction compared to non-smokers (e.g., Sherrill, Krzyzanowski, Bloom, & Lebowitz, 1991; Taylor et al., 2000; Taylor et al., 2002), many newer reports have observed no relationship (e.g., Hancox et al., 2010; Moore et al., 2005; Tashkin, Suimmons, Sherrill, & Coulson, 1997). In a review of the literature it was suggested that the risk of developing COPD is negligible among occasional cannabis smokers, but the authors cautioned further research is needed to eliminate the possibility that chronic regular use can lead to its development (Joshi, Joshi, & Bartter, 2014). A systematic review of 14 studies indicated no dependable relationship between long-term cannabis smoking and airway obstruction (Tetrault et al., 2007). A cohort study that followed 5,115 participants for 20 years observed a non-linear relationship between cannabis smoking and airway obstruction. Essentially, among those with low levels of exposure there was no evidence of adverse effects, whereas among heavy users decreases in air function were found, although the sample size of heavy users was quite small (Pletcher et. al., 2012). The largest cross-sectional population study to date in the United States reported that cumulative lifetime cannabis use, up to 20 joint-years,[1] is not associated with COPD (Kempker, Honig, & Martin, 2015).

Within Canada, a cohort study of 878 individuals over the age of 40 observed that compared to smoking tobacco alone, the combined use of cannabis and tobacco was related to three times the risk of developing COPD. However, this effect was only observed among individuals who reported smoking more than 50 joints in their lifetime, and no association was found between cannabis use alone and COPD (Tan et al., 2009). These effects persisted even after adjustment for potential confounders such as age, sex, asthma and other comorbidities, and comparable tobacco exposure (in pack-years; i.e., the quantity of cigarette packs smoked daily multiplied by the number of years of smoking). Due to such conflicting findings, definitive conclusions about the relation between smoking cannabis and COPD cannot be determined based on the existing data.

Other respiratory conditions in relation to cannabis smoking have been examined to a lesser extent. For instance, Lee and Hancox (2011) reviewed 36 case reports of bullous lung disease that have been linked to heavy cannabis smoking. This disease, also referred to as bullous emphysema, is characterized by blisters on the lung that are filled with air from the deterioration of healthy airspace tissue. Among the 36 cases reviewed, the individuals were typically in young adulthood, but despite the abnormalities observed, the lung function of these individuals was largely unaffected (Lee & Hancox, 2011). Given that these cases are anecdotal in nature, larger scale research is required to clarify whether a clear link exists. Similarly, several cases of pneumothorax[2] have been documented in relation to cannabis smoking (e.g., Goodyear et al., 2004; Beshay et al., 2007). Together, these incidences of bullous lung disease and pneumothorax have been thought to arise from the deep inhalation and breath-holding techniques commonly performed by cannabis smokers.

Other conditions associated with cannabis smoking include pulmonary fibrosis,[3] byssinosis[4] and lung tumours (Phan, Lau, & Li, 2005). The state of research on cannabis smoking and respiratory conditions is too limited to provide estimates of the prevalence of these and other serious health threats.

[1] The article defined joint-years as the number of joints smoked per day multiplied by the number of years of smoking. For example, if an individual smoked two joints per day for 10 years, he or she would have a smoking history of 20 joint-years

[2] Pneumothorax refers to air leaks that put pressure on the space between the lung and chest resulting in a collapsed lung.

[3] Pulmonary fibrosis is a condition that involves the scarring of the lungs, where fibrotic tissue forms in the place of the alveoli, irreversibly limiting the ability to transfer oxygen into the bloodstream.

[4] Byssinosis is caused by the endotoxins of a bacteria, and results in the narrowing of the trachea and destruction of lung tissue. The disease is most commonly associated with exposure to cotton dust in poorly ventilated working conditions.

However, given the harms known to be associated with tobacco smoking and the existing evidence suggesting that cannabis smokers might demonstrate comparable respiratory symptoms with shorter smoking histories, there is valid concern that prolonged cannabis use could put users at risk of acquiring serious lung and airway diseases.

Cannabis and the Lung's Immune System Defence

Apart from the respiratory conditions caused by the inhalation of cannabis smoke and combusted materials, risks might be worsened by the Δ9-tetrahydrocannabinol (THC) in cannabis smoke. Briefly, THC is the primary psychoactive component of the cannabis plant that is responsible for the "high." The presence of THC in human airways was found to cause cellular changes, especially to mitochondrial energetics, which are responsible, in part, for the health of cells and their energy production (Sarafian et al., 2006). In effect, the THC from cannabis smoke that enters the lungs and airways increases the risk of adverse pulmonary conditions (Sarafian et al., 2006). Indeed, data from outpatient medical clinics have revealed that cannabis-only smokers used healthcare services for respiratory illnesses more often than non-smokers over a two-year assessment (Polen, Sidney, Tekawa, Sadler, & Friedman, 1993).

Among those cells affected by THC are the alveolar macrophages, which are a main defence against infections in the lungs. It is thought that cannabis smoking might cause deficiencies in the immune system, based, in part, on findings that THC inhibits the ability of T-cells and alveolar macrophages to protect the body from foreign pathogens (Shay et al., 2003; Tashkin & Roth, 2006). A weakened immune response in the lungs predisposes cannabis smokers to affliction by viral, bacterial or fungal pathogens that would normally pose little threat to a healthy immune system (Shay et al., 2003). In fact, fungal contamination has been highlighted as a potential risk of cannabis smoking. In this regard, several case reports of lung infections stemming from a species of fungus that is present on cannabis plants (*Aspergillus fumigatus*) have been observed (Gargani, Bishop, & Denning, 2011; Tashkin, 2005).

Lung Cancer

The Canadian Cancer Society (2015) estimated that 20,900 Canadians would die of lung cancer in 2015, which underscores the importance of examining the carcinogenic effects of smoking cannabis. As described earlier, cannabis smoke contains many of the same carcinogens that exist in tobacco smoke, making the link between cannabis smoking and lung cancer worth exploring (Tashkin, 2005). There is consistent evidence to suggest that smoking cannabis is associated with premalignant cancerous changes in the lung (Hall & Degenhardt, 2014; Mehra et al., 2006). Despite this evidence, efforts to establish a relationship between cannabis smoking and lung cancer, while also accounting for tobacco smoking, have yielded weak if not non-existent relationships, especially among occasional or moderate users (Tashkin, 2013; Mehra et al., 2006)

A population-based cohort study of 49,321 Swedish male conscripts followed for 40 years observed that lifetime cannabis smoking of at least 50 times at the initial assessment point (i.e., at age 18 to 20 years old) was related to twice the risk of developing lung cancer even when controlling for baseline tobacco use and other confounds. This study had several strengths, including a large sample size and long follow-up period. However, this study relied only on the initial assessment of cannabis and tobacco smoking and so it cannot account for these behaviours across the 40-year follow-up. This gap is particularly problematic as 91% of the cannabis smokers in this study concurrently smoked tobacco (Callaghan, Allebeck, & Sidorchuk, 2014). Another study that pooled together three samples of male cannabis smokers in North Africa reported that the odds of developing lung cancer were over twofold greater among individuals who had ever smoked cannabis, although cannabis and tobacco are often mixed in this region (Berthiller et al., 2008). A study of lung cancer patients in New Zealand observed an 8% higher risk of lung cancer for every year an individual smoked one joint per day although once tobacco smoking was accounted for this relationship was only present for those who had more than 10 joint years (Aldington et al., 2008).

A systematic review of 19 studies spanning from 1996–2006 reported no significant relationship between cannabis smoking and lung cancer when controlling for tobacco use (Mehra et al., 2006). In line with these findings, a study of more than 1,200 individuals with lung cancer reported no relation between cannabis smoking and the presence of lung cancer (Berthiller et al., 2009). A retrospective study of health records across eight years from over 64,855 patients in California found no significant relationship between cannabis smoking and lung cancer when accounting for tobacco; however, an association was observed for prostate cancer (Sidney, Quesenberry, Friedman, & Tekawa, 1997). Further, a case-control study of 1,212 lung and upper aerodigestive tract cancers compared to 1,040 cancer-free cases did not find a significant relationship between cannabis smoking and cancer once age, gender, ethnicity, education, alcohol and

tobacco use were accounted for (Hashibe et al., 2006). The International Lung Cancer Consortium conducted a pooled analysis of 2,159 lung cancer cases and compared them to 2,985 controls. This research group observed little to no significant relation between smoking cannabis and lung cancer, although there was a weak increasing trend among regular and heavy cannabis smokers and lung cancer (however, this group was quite small) (Zhang et al., 2015).

Some evidence from cell culture systems and animal models shows that isolated THC and other cannabinoids directly infused into the tumours might inhibit their growth by regulating certain cell processes, leading to growth arrest and cell death, as well as by inhibiting tumour angiogenesis (growth) (for reviews, see Bifulco, Laezza, Pisanti, & Gazzerro, 2006; Hall, MacDonald, & Currow, 2005; Velasco, Sánchez, & Guzmán, 2012). It is important to keep in mind, however, that these inhibitory effects have been demonstrated using THC and other cannabinoids (not cannabis smoke) in preclinical and preliminary clinical testing, and do not necessarily imply that exposure to cannabis smoke can prevent cancer occurrence in humans (Velasco et al., 2012). Moreover, the concentrations required to reach such effects are much greater (e.g., 10 times) than the peak blood concentration that would arise from an individual smoking a high dose of cannabis (Sarfaraz, Afaq, Adhami, & Mukhtar, 2005).

Cannabis Vaporization

Due to the carcinogenic properties of combusted cannabis smoke, some researchers have examined whether the harms of cannabis smoking can be reduced by the use of vaporizers (Earlywine & Barnwell, 2007; Earleywine & Van Dam, 2010; Van Dam & Earlywine, 2010). Vaporizers heat cannabis to a temperature that still releases the active cannabinoids, but does so without causing the cannabis to combust. Smaller correlational studies provide some evidence that the use of vaporizers might limit some of the common respiratory symptoms experienced by cannabis smokers, particularly among those who also smoke tobacco (Earlywine & Barnwell, 2007; Earlywine & Van Dam, 2010). A small non-randomized trial of individuals who smoked cannabis regularly (n = 12) and who were assigned to switch to a vaporizing device for 30 days observed a significant reduction in self-reported respiratory symptoms and improved lung function (Van Dam & Earlywine, 2010). For those authorized to smoke dried cannabis for medical purposes, the use of an approved vaporizer device (e.g., the Volcano Medic®), which has been tested and shown to limit exposure to toxins such as carbon monoxide, is advisable (Abrams et al., 2007). Vaporizers, however, might not protect against any potential negative effects that might be caused by the consumption of active cannabinoids into the lungs or the rest of the body, regardless of the fact that smoke is not being inhaled using such devices. Although respiratory symptoms might be reduced by vaporizing cannabis, one report observed that vaporizing cannabis can yield substantial concentrations of the toxin ammonia (Bloor, Wang, Španěl, & Smith, 2008), a chemical that can cause neurological impairments (Kilburn, 2000).

Quitting Cannabis Smoking

Studies examining whether quitting cannabis smoking leads to an improvement in respiratory symptoms have produced promising results. In a longitudinal study conducted among 299 participants over a period of approximately 10 years, quitting smoking cannabis reduced the likelihood of having chronic bronchitis to that of people who had never smoked (Tashkin, Simmons, & Tseng, 2012). A larger longitudinal study that comprised 1,037 participants followed up at ages 26, 32 and 38 revealed that symptoms of coughing and sputum production were improved among individuals who stopped cannabis smoking regularly (i.e., greater than or equal to 52 times in the past year), whereas among participants who continued smoking symptoms were maintained or got worse (Hancox et al., 2015). Importantly, this study also observed that by the age of 38 years, morning cough and wheeze among regular users was persistent even after reducing or quitting cannabis, suggesting that earlier cessation might be most beneficial for improving respiratory symptoms.

Conclusions and Implications

Research indicates that smoking cannabis is not harmless to the lungs and airways. These harms are evident in the commonly reported symptoms of cannabis smokers. The respiratory effects of cannabis smoking can impair breathing, which could negatively affect athletic performance (Saugy et al., 2006) and possibly limit activities of daily living (Moore et al., 2005). Although the evidence is mixed as to whether cannabis smoking is linked with lung cancer, the fact that cannabis smoke contains many of the carcinogens found in tobacco smoke necessitates further research on this topic. THC exposure to the lungs is of concern, as it might compromise the immune system defences of the lungs—specifically the ability to defend against foreign pathogens.

The dissemination of information on respiratory harms—and indeed all potential harms—linked with cannabis use is intended to convey a clear message that it is not harmless and is associated with a risk of personal harm. The potential for harm to the lungs, airways and immune systems of cannabis smokers should be of concern to users, healthcare professionals and policy makers. Effective, evidence-

informed initiatives should be implemented to promote knowledge of the respiratory risks and harms of cannabis smoking, as well as the health benefits of cessation. The public health experience with tobacco smoking prevention, reduction and cessation provides a valuable source of evidence to inform these initiatives. The fact that some of the respiratory effects of cannabis are similar to tobacco smoking even with shorter smoking histories illustrates the need to achieve similar levels of success with public health campaigns (Moore et al., 2005).

The findings from this review have important implications for those individuals who use fresh (i.e., buds and leaves), dried, and oil forms of cannabis for medical purposes. For example, there is concern about the risk of contaminants as there can be severe lung harms from smoking contaminated dried cannabis by individuals with compromised immune systems (Denning et al., 1991; Hamadeh, Ardehali, Locksley & York, 1988). Fortunately, cannabis for medical purposes is regulated for quality in Canada; however, there have still been some instances of recalls due to contaminants. This report suggests that cannabis smoking can induce respiratory symptoms and it is advisable for individuals who have pre-existing respiratory issues to use alternative medicines, formats or methods of delivery. Indeed, in their Preliminary Guidance Document, the College of Family Physicians of Canada recommends that dried cannabis is not appropriate for individuals who have respiratory disease (College of Family Physicians of Canada, 2014).

Most of the studies in the current review examined self-reported cannabis use, so there remains a gap in our understanding of whether dried or oil forms of cannabis have differential effects on respiratory function. This question is particularly important since in July 2015 regulations were expanded to allow Canadian licensed producers to supply cannabis in fresh, dried and oil forms (Health Canada, 2015). Cannabis is not a single uniform product and the safety of one cannabis product does not guarantee the safety of another. Indeed, the respiratory effects of other cannabis formulations that are used recreationally, such as “dabs” or “shatter,” that are highly concentrated and produced by extracting THC and other cannabinoids using a solvent (e.g., butane or carbon dioxide), are unknown.

Further research is also required to examine the long-term safety of unregulated cannabis vaporization techniques, such as e-cigarettes. This research is important as individuals might perceive vaporization as a safer alternative despite a lack of research evidence to support this view. Research is also greatly needed to determine whether there are any respiratory effects due to second-hand cannabis smoke exposure.

As most individuals initiate cannabis use during adolescence, determining the effects of cannabis smoke on the developing lung is essential. The lung is still undergoing substantial development during adolescence and long-term functional impairments from air pollutant exposure during this time have been demonstrated (Gauderman et al., 2004). Findings such as these raise the question as to what impact cannabis smoke might have during this critical period. In addition, there have been reports that THC concentrations have been increasing (ElSohly et al., 2000; Mehmedic et al., 2010; Potter, Clark & Brown, 2008). Determining whether higher levels of THC result in different effects on the respiratory system remains a key area for exploration.

Continued regular cannabis smoking among youth and young adults has the potential to increase the burden on healthcare systems. Moreover, the negative effects of cannabis smoking are compounded when a user also regularly smokes tobacco (Taylor & Hall, 2003). More research is needed to better understand the impact of long-term regular use of cannabis. Healthcare professionals must inform users, whether potential, confirmed or suspected, and whether use is for recreational or therapeutic purposes, of the potential harms associated with smoking cannabis and develop strategies to promote further awareness and general respiratory health.

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