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Review

Cannabis for Therapeutic Purposes and public health and safety: A systematic and critical review

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ABSTRACT

Background: The use of Cannabis for Therapeutic Purposes (CTP) has recently become legal in many places. These policy and legal modifications may be related to changes in cannabis perceptions, availability and use and in the way cannabis is grown and sold. This may in turn have effects on public health and safety. To better understand the potential effects of CTP legalization on public health and safety, the current paper synthesizes and critically discusses the relevant literature.
Methods: Twenty-eight studies were identified by a comprehensive search strategy, and their characteristics and main findings were systematically reviewed according to the following content themes: CTP and illegal cannabis use; CTP and other public health issues; CTP, crime and neighbourhood disadvantage.
Results: The research field is currently limited by a lack of theoretical and methodological rigorous studies. The review shows that the most prevalent theme of investigation so far has been the relation between CTP and illegal cannabis use. In addition, the literature review shows that there is an absence of evidence to support many common concerns related to detrimental public health and safety effects of CTP legalization.
Conclusion: Although lack of evidence provides some reassurance that CTP legalization may not have posed a substantial threat to public health and safety, this conclusion needs to be examined in light of the limitations of studies conducted so far. Furthermore, as CTP policy continues to evolve, including incorporation of greater commercialization, it is possible that the full effects of CTP legalization have yet to take place. Ensuring study quality will allow future research to better investigate the complex role that CTP plays in relation to society at large, and public health and safety in particular.

Introduction

Although Cannabis for Therapeutic Purposes (CTP) played a significant role in western medicine towards the end of the 19th century (Bostwick, 2012; Grinspoon, 2005; Mikuriya, 1969), around the turn of the century and onwards its use has gradually vanished. One major force in this development was that CTP use and research was made increasingly difficult by the 1961 UN Convention on Narcotic Drugs which classified cannabis as a Schedule I drug, meaning no accepted medical use and high potential for abuse (Ballotta, Bergeron, & Hughes, 2008; Bostwick, 2012; UN, 1961). Medical developments also contributed to the decline of CTP as new medicines that were deemed safer and more predictable were developed and took CTP out of favour (Grinspoon, 2005; Kalant, 2001; Zuardi, 2006). Furthermore, other social, economic and legal factors contributed to the decline of CTP. For instance, import to Europe and the U.S. of high quality Indian hemp became increasingly difficult due to constraints in India and the influence of the two world wars (Fankhauser, 2008).

Novel pharmacological developments of the past few decades have brought a new wave of interest into the structural and physiological properties of cannabis. Furthermore, recent clinical trials have improved the evidence-base for the medical benefits of CTP (Campbell et al., 2001; Gates, Albertella, & Copeland, 2014; Lynch & Campbell, 2011; Machado Rocha, Stéfano, De Cássia Haiek, Rosa Oliveira, & Da Silveira, 2008; Martín-Sánchez, Furukawa, Taylor, & Martin, 2009; Tramer et al., 2001), indicating that cannabis may be a promising therapeutic agent.

The increased clinical evidence-base for CTP has been accompanied with expanding social and political pressures in many places to change regulatory frameworks to enable legal use of CTP. Hitherto, 23 states in the U.S. have legalized CTP (NCSL, 2014), as well as other countries, including Israel, Canada and the Netherlands (Belle-Isle et al., 2014). Additional states and countries are currently

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considering CTP legalization, including New Zealand and Australia (NCSL, 2014; Shipton & Shipton, 2014). These legal changes have brought about scientific and political debates regarding the possible detrimental and positive effects of CTP legalization on society (Levinthal, 2008). Concerns have, for instance, been raised that legalizing CTP may increase illegal cannabis use and may harm adolescents in particular (Joffe & Yancy, 2004). Others have pointed out that CTP legalization may be related to a substitution effect, where people move from alcohol use to cannabis use, which in turn may reduce alcohol-related harm in society (Lucas et al., 2013). From a different perspective, concerns have also been raised that cannabis dispensaries may cause crime in already disadvantaged communities (City of La Puente, 2008; The Denver Post, 2011).

Clearly, aside from strictly pertaining to clinical and medical issues, CTP is essentially a social matter, as it integrates cultural, legal, economic and political concerns. Social sciences have the potential to play a substantial role in developing our understanding of CTP, particularly at this point in time when CTP legal frameworks are changing (Holland, 2010; NCSL, 2014). In particular, social science research is essential in order to reach an understanding of the ways in which CTP use and policies are associated with public health and safety. Furthermore, social CTP research may inform the development of evidence-based CTP policies.

The current paper is the first to critically synthesize studies related to CTP policy and public health and safety. The review was guided by the following objectives: (1) to describe the nature and characteristics of CTP research related to public health and safety and thereby to identify trends in the research area; (2) to highlight the significant contributions in the field of CTP/public health and safety research; and (3) to identify gaps in the literature in order to point out directions for future research.

Methods

Search strategy

A search on PubMed, Sociological Abstracts, Social Citation Index, and PsychINFO, was conducted to identify relevant keywords in titles, abstracts and subject descriptors. Searches included combinations of the following terms: “medical cannabis”, “medical marijuana”, “cannabis dispensaries”, “medical cannabis legalization”, “medical marijuana legislation”, “Cannabis for Therapeutic Purposes”. Searches included all literature that was published before June 2014 and the total number of papers found through all search combinations was 5667.

Selection of papers identified through the initial database search was conducted by independent review of all identified papers by the two authors based on titles and abstracts of the papers and the inclusion and exclusion criteria outlined in Table 1. The process resulted in the exclusion of 5643 papers, and the inclusion of 24 papers. Next, backward and forward searches were performed to identify any studies that the initial search might have missed (Greenhalgh, 2005). For backward searching, bibliographies of identified studies were checked, while for forward searching, Science Citation Index was used to identify subsequent citations of the identified studies. The five journals with the highest yield of references were additionally hand searched for further relevant references. Four additional papers were included through these search strategies, leading to 28 studies being finally included in this review.

Table 1
Exclusion and inclusion criteria.

Exclusion criteria	Inclusion criteria
Study design based on commentaries of the literature	Focus on association between CTP and public health and safety
Abstracts, dissertations, government or other non-peer reviewed reports, conference proceedings	Scholarly literature (peer reviewed journal articles)
Main focus on medical/pharmaceutical properties of CTP, patients or physicians	Presentation of empirical analysis
Published in language other than English	

Data extraction

Identified papers were organized into content areas and coded according to seven different variables. Firstly, studies were coded for type of study population (children/adolescents, adults or other) and type of data (primary or secondary data). Studies were also coded for data collection period and CTP policy change focus. In the U.S. (which is the location of all studies reviewed but one), individual states have legalized CTP at various time points since 1996. However, these states were acting under federal prohibitionist policy until 2009 when the federal government released a memo stating that federal resources should not focus on prosecuting CTP patients or caregivers who act according to state laws (Ogden, 2009). This shift sparked commercialization of CTP at the state level, including large scale retail sale and increasing levels of promotion (Salomonsen-Sautel, Min, Sakai, Thurstone, & Hopfer, 2014; Schuermeyer et al., 2014). Effectively, studies using data prior to 2009 examine state CTP legalization under enforced federal prohibition, whilst studies that use data after 2009 have the opportunity to examine state legalization in an environment where these changes would likely have much more of an effect. In order to incorporate these nuances in the literature review, all articles reviewed were coded for data collection period and whether or not the analyses took the state and/or federal CTP policy changes into account in their analyses.

Studies were also coded according to research design quality. Lower quality studies are defined as studies using cross sectional (one time point) observations only, whereas higher quality studies are defined as those that used pre-post design (using observations from before and after a policy change). Another quality indicator is whether some form of comparison group was used; studies with no comparison groups are of lower quality. Lastly, studies were coded for whether analysis was guided by specific theoretical frameworks or not.

Results

Details of the studies reviewed are summarized in Table 2. During the literature search, three content areas were identified: (1) CTP and illegal cannabis use, (2) CTP and other public health issues, and (3) CTP, crime and neighbourhood disadvantage. The majority of studies were published in the last 4 years (86%, $n = 24$), and all studies but one were conducted in the U.S. (96%, $n = 27$). The area of research that has received most attention by researchers is CTP and illegal cannabis use, representing 57% of all studies reviewed.

Although 10 studies (36%) used data before and after 2009, only three studies focused specifically on the 2009 federal policy change towards relaxed prohibition of CTP. All other studies focused on state CTP legalization only. As shown in Table 2, the vast majority of studies used secondary data (75%, $n = 21$). Many studies (61%, $n = 17$) included control groups by utilizing the opportunity to compare data across states or locations with different CTP policies. Fewer studies used pre-post CTP policy change designs (39%, $n = 11$). Furthermore, very few studies were guided by a specific theoretical framework (21%, $n = 6$).

Table 2

Author(s), year	Study population	Data type	Data collection period	CTP policy change focus	Study design	Comparison group	Theory driven	Main findings
CTP and illegal cannabis use								
Anderson et al. (2013)	Adolescents (15–19 year-olds) and adults	Secondary	1990–2010	State	Pre-post	√	√	CTP legalization was associated with a reduction in traffic fatalities not involving alcohol and associated with decreases in the price of cannabis and alcohol consumption, especially in young adults.
Cerdá et al. (2012)	Adults	Secondary	2004–2005	State	Cross-sectional	√	×	Residents of states with CTP laws had higher odds of cannabis use and cannabis abuse/dependence.
Choo et al. (2014)	Adolescents (grades 9–12)	Secondary	1991–2011	State	Pre-post	√	×	There were no significant differences in adolescent cannabis use before and after CTP legalization. In two states there was a reduction in adolescent cannabis use after CTP legalization.
Friese and Grube (2013)	Adolescents (13–19 year-olds)	Secondary	2010	State	Cross-sectional	×	×	Counties with relatively high levels of CTP licenses were unrelated to lifetime or 30 day cannabis use. Voter approval of CTP was positively related to lifetime and 30 day cannabis use.
Gorman and Huber (2007)	Others – arrestees and ER patients	Secondary	1994–2002; 1987–2003	State	Pre-post	×	×	No statistically significant pre-law versus post-law differences were found in cannabis urine analysis among arrestees or in the proportion of emergency department visits in which cannabis was mentioned
Harper et al. (2012)	Adolescents and adults (12 year-olds and older)	Secondary	2002–2009	State	Pre-post	√	×	CTP legalization decreased past-month use among adolescents and had no discernible effect on the perceived riskiness of monthly use.
Jaffe and Klein (2010)	Child and adolescent psychiatrists	Primary	Not stated	State	Cross-sectional	×	×	According to child and adolescent psychiatrist, adolescent patients have been influenced by the advent of CTP legalization in that they perceive cannabis to be more beneficial and more available.
Khatapoush and Hallfors (2004)	Adolescents and young adults (16–25 year-olds)	Secondary	1995, 1997 and 1999	State	Pre-post	√	×	Although some cannabis-related attitudes changed after CTP legalization in California, use did not increase.
Lynne-Landsman et al. (2013)	Adolescents (12–18 year-olds)	Secondary	2003–2011	State	Pre-post	√	×	No association was found between CTP legalization and adolescent illegal cannabis use
Masten and Guenzburger (2014)	Fatal-crash-involved drivers	Secondary	1992–2009	State	Pre-post	√	×	The implementation of CTP laws was found to be reliably associated with increased cannabinoid prevalence in fatal-crash involved drivers in only three out of 12 states examined.
Pacula et al. (2010)	Arrestees	Secondary	2000–2003	State	Pre-post	√	√	CTP legalization was associated with a reduction in the price of illegal cannabis.
Salomonsen-Sautel et al. (2012)	Adolescents in substance abuse treatment (14–18 year-olds)	Primary	2010–2011	State	Cross-sectional	×	×	Approximately 74% of the adolescents in substance abuse treatment had used diverted CTP.
Salomonsen-Sautel et al. (2014)	Fatal-crash-involved drivers	Secondary	1994–2011	State and Federal	Pre-post	√	×	CTP commercialization after 2009 federal policy change was associated with increasing numbers of cannabis positive drivers involved in fatal motor vehicle crashes. No such trends were found in states without CTP laws.
Schuermeyer et al. (2014)	Adolescents and adults (12 year-olds and older)	Secondary	2003–2011	State and Federal	Pre-post	√	×	Commercialization of CTP after 2009 federal policy change was associated with lower cannabis risk perception. Evidence was also found for increase in cannabis use/abuse after CTP commercialization.

Schwartz et al. (2003)	Parents and their adolescent children (13–19 year-olds)	Primary	1999	State	Cross-sectional	×	×	Twenty-eight percent of the parent group and 55% of the teenagers believed that passage of CTP legalization would make it easier for teens to smoke CTP.
Thurstone et al. (2011)	Adolescents (15–19 year-olds) in substance use treatment	Primary	2010–2011	State	Cross-sectional	√	×	49% of adolescent in substance use treatment reported obtaining cannabis from someone with a CTP license.
Wall et al. (2011)	Adolescents (12–17 year-olds)	Secondary	2002–2008	State	Pre-post	√	×	States that legalized CTP had higher average adolescent cannabis use and lower perception of cannabis riskiness than states that did not legalize CTP, even prior to CTP legal changes.
Wall et al. (2012)	Adolescents and adults (12 year-olds and older)	Secondary	2002–2008	State	Pre-post	√	×	CTP legalization was unrelated to past-month use among adolescents
CTP and other public health issues								
Anderson et al. (2014)	Adolescents and adults (15 years and older)	Secondary	1990–2007	State	Cross-sectional	√	×	CTP legalization was associated with a reduction in male suicide rates aged 20–39.
Hazekamp (2006)	CTP	Primary	Not stated	NA	Cross-sectional	√	×	Compared to samples obtained from coffeeshops, cannabis obtained from pharmacies was less contaminated with bacteria and fungi. No difference in potency was found.
Sevigny et al. (2014)	Cannabis seized by law enforcement	Secondary	1990–2010	State	Pre-post	√	×	No significant difference in THC levels before and after CTP legalization was found.
Wang et al. (2013)	Children (0–12 year-olds)	Secondary	2005–2011	State and Federal	Pre-post	×	×	An increase in unintentional cannabis ingestions by young children was found after 2009, following new federal and state regulations.
Wang et al. (2014)	Children (0–9 year-olds)	Secondary	2005–2011	State	Pre-post	√	×	Although the number of pediatric exposures to cannabis was low, the rate of exposure increased from 2005 to 2011 in states that had legalized CTP.
CTP, crime and neighbourhood disadvantage								
Boggess et al. (2014)	CTP centers	Secondary	2000, 2004 and 2006–2010	State	Pre-post	√	√	CTP centers are likely to be situated in neighbourhoods with higher crime rates and more retail employment. CTP center establishment was not associated with ethnic/racial neighbourhood composition or neighbourhood poverty.
Freisthler et al. (2013)	CTP dispensaries	Primary	2010–2011	State	Cross-sectional	×	√	Dispensaries with security cameras and signs requiring an identification prescription card had significantly lower levels of violence within 100 and 250 feet.
Kepple and Freisthler (2012)	Census tracts in Sacramento	Secondary	2009	State	Cross-sectional	×	√	No association was found between density of CTP dispensaries and crime
Morris et al. (2014)	Crime rates	Secondary	1990–2006	State	Pre-post	√	×	No indication found that CTP legalization increases Part I offenses. Results showed that CTP legalization was associated with a decrease in homicide and assault rates.
Morrison et al. (2014)	Adult population in California	Primary	2009	State	Cross-sectional	×	√	Cannabis dispensaries were located in areas of more cannabis demand, poverty and alcohol outlets

CTP and illegal cannabis use

A main concern regarding CTP legalization is that it may increase illegal cannabis use in the general population and among adolescents in particular (Gorman & Huber, 2007; Joy, Watson, & Benson, 1999). There are various hypothetical mechanisms through which this may occur. CTP legalization may: (1) reduce the perceived legal risk of illegal cannabis use, (2) reduce the perceived harm associated with illegal cannabis use, and (3) increase the availability of cannabis primarily through greater commercial promotion and availability of the substance, or through diversion of CTP to the black market (Joffe & Yancy, 2004; Pacula, Kilmer, Grossman, & Chaloupka, 2010). All these factors are known to increase illegal cannabis use (Botvin, Griffin, Diaz, & Ifill-Williams, 2001; Elek, Miller-Day, & Hecht, 2006). However, it is also plausible that legalizing CTP for severely ill patients could reduce the perception of cannabis as a recreational drug, thus resulting in reduced illegal cannabis use.

Two cross-sectional studies have examined the *perceived* likelihood that CTP legalization would increase illegal use of cannabis, one in a sample of child and adolescent psychiatrists (Jaffe & Klein, 2010) and one in adolescents (Schwartz, Cooper, Oria, & Sheridan, 2003). Respondents in both studies deemed it possible that CTP legalization would increase cannabis availability and prevalence. Still, these indirect measures of perceived effects may not reflect reality, and studies that examine the link between CTP legalization and actual illegal cannabis use have not reached coherent conclusions.

Three studies have examined this link in high risk groups (Gorman & Huber, 2007; Salomonsen-Sautel, Sakai, Thurstone, Corley, & Hopfer, 2012; Thurstone, Lieberman, & Schmiege, 2011). This approach is important, as it is reasonably assumed that as a drug becomes more available, those who are most "at-risk" will be the first to initiate use (Gorman & Huber, 2007). Gorman and Huber (2007) examined trends in cannabis use among two high risk groups (arrestees and emergency department patients) from the mid-1990s through 2002 in states that had passed CTP laws at some point during this time period. Results showed that the introduction of CTP laws was not associated with an increase in cannabis use among either arrestees or emergency department patients.

Two other studies, of relatively poorer quality (see Table 2 for details), have examined diversion of CTP in adolescents treated for substance use problems in states where CTP is legal (Salomonsen-Sautel et al., 2012; Thurstone et al., 2011). Both the studies used data after the 2009 federal CTP policy change and effectively they examine state legalization under federal policy not to enforce cannabis laws. Both studies found evidence of diversion in the sense that a substantial proportion of participants reported obtaining cannabis from someone with a CTP license; 49% in the study by Thurstone et al. (2011) and 75% in the study by Salomonsen-Sautel et al. (2012).

Of all studies that have examined the link between CTP and illegal cannabis use, the majority (66%, $n = 12$) have examined this link in the general (non-risk) population, and among these studies, the majority has included adolescents (83%, $n = 10$). Using fairly weak research designs (see Table 2 for details), one study has found that states with CTP legalization have relatively high cannabis use level (Cerdá, Wall, Keyes, Galea, & Hasin, 2012), and another study has found voter approval of CTP legalization to be positively associated with adolescent cannabis use (Friese & Grube, 2013). Both these studies were based on cross-sectional designs and thus cannot be used to infer that CTP legalization is causally related to relative high levels of illegal cannabis use. Using a pre-post CTP legal change research design, Wall et al. (2011) found that states that legalized CTP had higher average adolescent cannabis use and lower perception of cannabis riskiness than states that did not legalize CTP, even prior to CTP legal changes. As such, evidence suggests that social norms at the state level contribute to both legalization of CTP and high levels of illegal cannabis use.

Of the eight studies that used a pre-post design and have looked at the relation between CTP and illegal cannabis use in the general non-risk population, five studies have found CTP legalization to be unrelated to a subsequent increase in illegal cannabis use (Choo et al., 2014; Harper, Strumpf, and Kaufman, 2012; Khatapoush & Hallfors, 2004; Lynne-Landsman, Livingston, & Wagenaar, 2013; Masten & Guenzburger, 2014). One study has also found that CTP legalization is unrelated to changes in perceived risk of cannabis use (Harper et al., 2012).

In contrast, two studies have found evidence that CTP legalization is associated with a reduction in illegal cannabis use (Choo et al., 2014; Harper et al., 2012). Although both these studies used relatively strong research designs (pre-post CTP legalization and control groups), a sensitivity analysis of the Harper et al. (2012) study showed that when two states with exceptional high cannabis use (Montana and Vermont) were dropped from analysis, no significant decrease in cannabis use after CTP legalization remained (Wall et al., 2012).

In addition to these studies, and in somewhat contrast to their findings, two studies with strong research designs (including both pre-post CTP policy change observations and control groups) have found an increase in cannabis use in Colorado after the 2009 federal change which sparked a growth in CTP commercialization including large scale retail. Furthermore, the studies show that these increases in cannabis use differed from trends in states without CTP legalization (Salomonsen-Sautel et al., 2014; Schuermeyer et al., 2014).

While all of the above-mentioned studies used self-reported survey or surveillance data in order to examine the effects of CTP legalization on illegal cannabis use, an alternative method is to examine the effect of CTP legalization on the price of cannabis. This line of research relies on economic theory, which suggests that a cannabis price increase is an indicator of increased demand. Following this logic, a potential cannabis price increase subsequent to CTP legalization is indicative of increased use. Two studies have used this approach focusing on state legalization only. Results are inconsistent in that Pacula et al. (2010) found evidence that the price of street cannabis increased after passing CTP legalization, whereas Anderson, Hansen, and Rees (2013), using different data and methods, found that CTP legalization was associated with a reduction in the price of cannabis.

In sum, while inconsistencies in findings are prevalent, quite a few studies that have examined the passage of CTP legalization have concluded that CTP legalization is unrelated to subsequent changes in cannabis use in the general population (Choo et al., 2014; Harper et al., 2012; Khatapoush & Hallfors, 2004; Lynne-Landsman et al., 2013; Masten & Guenzburger, 2014). This is in contrast to two studies that have found a negative relation (Choo et al., 2014; Harper et al., 2012) and two studies that have found a positive relation (Salomonsen-Sautel et al., 2014; Schuermeyer et al., 2014). Some evidence also points towards the possibility that CTP may get diverted to high risk adolescents who are in substance abuse treatment (Salomonsen-Sautel et al., 2012; Thurstone et al., 2011).

Noticeably, the two studies that have found a positive relation in the general population (Salomonsen-Sautel et al., 2014; Schuermeyer et al., 2014) are the only studies reviewed that focus on the 2009 federal change and subsequent CTP commercialization, as opposed to CTP state legalization per se. Both these studies are from Colorado and it is unclear whether results can be extrapolated to other places. Nevertheless, both the studies make the important point that although CTP was officially legalized in 2000, commercialization and large scale retail CTP dispensaries were only established in 2009, after the federal policy shift and after the

Colorado Board of Health cancelled the limit of numbers of patients and caregivers CTP distributes could serve (Ingold, 2009; Sensible Colorado, 2013). The fact that a relation between CTP policy and increased illegal cannabis use has so far only been found in these two studies and not in studies that look only at CTP state legalization, suggests that while state-wide CTP legalization may not encourage cannabis use in the general population, federal policy and subsequent commercialization may in fact do.

CTP and other public health issues

We located five studies that assessed the relation between CTP legalization and diverse public health implications other than the issue of illicit cannabis use. Studies were generally of high quality, with four studies using both a pre-post CTP policy change design and control groups.

Anderson et al. (2013) focused on state CTP legalization and showed it was associated with a reduction in alcohol consumption in adults. The authors suggest that the observed relation could be explained by a substitution effect; CTP legalization increases the use of cannabis, which in turn substitutes the use of alcohol. However, since studies that similarly focus on state CTP legalization have failed to find evidence that it increases cannabis use in the general population (see above section), the underlying mechanisms through which CTP legalization may reduce alcohol use remain unclear.

In a different study, Anderson, Rees, and Sabia (2014) showed that CTP state legalization was associated with a reduction in suicide rates among young males (but not among females). The authors noted that the results are consistent with the hypothesis that legalizing CTP leads to increased cannabis use, which in turn helps more individuals to cope with stressful life events. However, this is not strongly supported by the literature reviewed in the above section where quite a few studies focusing on state CTP legalization failed to find support for the hypothesis that legalization increases use of cannabis (Choo et al., 2014; Harper et al., 2012; Khatapoush & Hallfors, 2004; Lynne-Landsman et al., 2013; Masten & Guenzburger, 2014). However, if increased cannabis use after CTP legalization is confined to a small proportion of people with mental health problems, it is possible that previous studies that examine the general population lack sensitivity to capture this effect (see Table 2 for an overview of populations included in studies).

Moving away from alcohol and mental health issues, two studies have examined whether the increasing number of licensed CTP users increases the risk that children will unintentionally digest cannabis. While both studies include 2009 data, only one focus explicitly on the 2009 federal change in CTP policy (Wang, Roosevelt, & Heard, 2013). Both studies do, however, find an increase in unintentional cannabis ingestions by young children after CTP legalization (Wang et al., 2013, 2014). Researchers have specified that unintentional cannabis exposure in children remained low even after CTP legalization (Wang et al., 2014), and that most pediatric unintentional ingestions were from CTP packaged in the form of food products, such as cakes (Wang et al., 2013).

While the observed increase in pediatric unintentional cannabis exposure may be caused by increased use and storage of cannabis in households, it is also possible that the observed increase is related to increased willingness to report unintentional CTP exposure in an atmosphere where CTP is legal. Indeed, a similar line of thought has been suggested in relation to data showing increases in mentions of cannabis use in emergency room records after cannabis depenalization (Model, 1993).

Concerns have also been raised that CTP legalization may be associated with a rise in cannabis potency, which in turn may have detrimental health effects in cannabis users (Crippa et al., 2009; Di Forti et al., 2009; Ramaekers, Berghaus, van Laar, & Drummer, 2004; Ramaekers et al., 2006). Sevigny, Pacula, and Heaton (2014) recently examined the association between CTP legalization and cannabis potency and found no significant difference in THC levels before and after CTP legalization in the U.S. However, when specific CTP regulatory frameworks were examined, results suggested that average potency increased more in states that permit dispensaries as compared to states that allow home cultivation. The authors suggest that this may be caused by relatively greater quality control and higher potency of CTP in cannabis dispensaries as compared to home cultivation by patients and caregivers who may lack the necessary amenities, resources, or skills to cultivate potent CTP.

In a different legal context, a study from the Netherlands examined whether CTP sold at pharmacies differed in potency to cannabis sold in coffee-shops (Hazekamp, 2006). No differences were found in potency of cannabis sold in these two different locations. However, the CTP sold in pharmacies was less likely to have potentially damaging and dangerous contaminants than the cannabis sold in coffee-shops.

In sum, researchers have examined diverse public health outcomes of CTP legalization. Collectively, findings suggest that CTP legalization may on one hand reduce alcohol use and suicide rates, while on the other hand increase unintentional digestion by children. In the U.S there is some evidence that CTP legalization may increase potency under certain conditions, while the same seems not to be true in the Netherlands. Within each topic there is, however, only one or two studies published. This limits the ability to compare results across studies and to evaluate the overall stability and the general trends in findings.

CTP, crime and neighbourhood disadvantage

CTP legalization has been accompanied with a growth of cannabis dispensaries in the U.S., and concerns have been raised that dispensaries are breeding grounds for criminal networks, as they have on-site stock of cannabis and are predominantly cash-based businesses (California Police Chiefs Association's Task Force on Marijuana Dispensaries, 2009). Five studies have explored whether the establishment of CTP dispensaries or CTP legalization is related to local crime rates, two of these studies (Boggess, Pérez, Cope, Root, & Stretesky, 2014; Morris, TenEyck, Barnes, & Kovandzic, 2014) used strong study designs (including pre-post CTP policy change designs and control groups, see Table 2 for details). None of the studies reviewed in this section focused on the 2009 federal CTP policy change.

In particular, one of the studies examined whether different levels of security measures influence crime in the area around CTP dispensaries. Results showed that dispensaries with security cameras and signs requiring an identification prescription card had significantly lower levels of violent crimes within 100 and 250 feet than dispensaries without these security measures (Freisthler, Kepple, Sims, & Martin, 2013).

Boggess et al. (2014) found that cannabis dispensaries tend to be disproportionately opened in areas with high crime rates. The researchers suggest that this may be caused by dispensaries being established in areas with retail concentrations, which in turn tend to be locations related to crime. In a different study, Kepple and Freisthler (2012) failed to find cross-sectional associations between the geographic density of CTP dispensaries and violence or property crime rates. Using a stronger research design, Morris et al. (2014) echo the Kepple and Freisthler (2012) finding in that they found no association between relatively high state crime rates and CTP legalization. Morris et al. (2014) further showed that CTP legalization was related to a reduction in homicides and assaults, and the authors suggest that this may be mediated by lower alcohol consumption following CTP legalization, although the study did not test this assumption directly. As previously noted, one study has found CTP legalization to be related to lower alcohol use (Anderson

et al., 2013), although the mechanism through which this occurs remains unclear.

Examining the relation between CTP dispensaries and neighbourhood disadvantage more broadly, Morrison, Gruenewald, Freisthler, Ponicki, and Remer (2014) found that cannabis dispensaries tend to be located in areas of low income and of relatively high presence of alcohol outlets. These results stand in contrast to results from a study with a stronger research design, that show, after controlling for a range of confounders, that the number of cannabis dispensaries was not associated with poor neighbourhoods, and that they distribute equally with respect to race and ethnicity (Boggess et al., 2014). The study also found that establishment of CTP dispensaries was unrelated to increases in neighbourhood poverty rates or racial/ethnic isolation over time.

In sum, some of the studies that have examined the CTP-crime link are of relatively poor quality, lacking pre-post designs and control groups. Furthermore, although there have been concerns that CTP legalization may increase crime and social disadvantage, the relevant research is inconclusive; only one study finds support that dispensaries are positively related to high crime rates (Boggess et al., 2014), and in this study it is suggested that dispensaries do not cause crime, but rather that they are disproportionately established in communities with existing high crime rates. Additionally, two studies find no or a negative relation between dispensaries and crime rates (Kepple & Freisthler, 2012; Morris et al., 2014) and while one study found dispensaries to be linked with neighbourhood disadvantage (Morrison et al., 2014), an additional study failed to confirm this finding (Boggess et al., 2014).

Discussion

CTP legalization is a controversial topic and a valid empirical foundation is needed to guide a rational discussion regarding the associated public health and safety risks and benefits. The current literature review is one step towards achieving this as it aims to synthesize and evaluate the social CTP research in order to reach a better understanding of the achievements and gaps in the current knowledge base, and to indicate future research avenues pertaining to CTP and public health and safety.

The literature review has strengths in that it includes the most up-to-date literature identified by a comprehensive search protocol. However, it is possible that some literature may have been missed during the searches. In particular, the review excludes non-English literature. Most peer-reviewed journals are, however, published in English, and it is thus unlikely that exclusion of non-English literature leads to substantial omissions.

The blurred boundaries between CTP and illegal cannabis use

So far, the area of investigation receiving most attention from researchers is the relation between CTP and illegal cannabis use. As such, the literature is largely rooted in the assumption that the boundaries between CTP and illegal cannabis use are blurred. Yet, this is not explicitly elaborated on in the literature. For instance, researchers have noted that CTP legalization may increase illegal cannabis use through CTP diversion (Joffe & Yancy, 2004; Pacula et al., 2010), yet it is not clear what the parameters and definition of CTP diversion are. In studies on prescription medicines, diversion typically involves the intentional channeling of medicines from legal sources (e.g. patients) to people who use them illegally (Inciardi, Surratt, Kurtz, & Burke, 2006; Inciardi, Surratt, Kurtz, & Cicero, 2007). However, this concept is in need of further refinement when applied to CTP diversion. One consideration is, for instance, whether diversion includes CTP users sharing illegally sourced cannabis with other CTP users. Another relevant consideration is whether any cannabis possessed by a licensed CTP user is in fact CTP.

The current literature review did not identify any study that directly examine the concept of CTP diversion and empirically test its extent and mechanisms. As such, the current review identifies a need for critical attention to the concept and empirical investigation of CTP diversion specifically and the blurred boundaries between CTP and illegal cannabis use more generally.

Absence of evidence and lessons learnt from other research fields

The current literature review shows that there is an absence of evidence to support the validity of some commonly held public concerns related to CTP legalization. For instance, a commonly held assumption is that CTP legalization increases crime rates (California Police Chiefs Association's Task Force on Marijuana Dispensaries, 2009; The New York Times, 2014), but there is no strong direct empirical evidence to support this (Freisthler et al., 2013; Kepple & Freisthler, 2012; Morris et al., 2014). Claims have also been raised that CTP legalization increases the prevalence of high potency cannabis (CNN, 2013; EMCDDA, 2004). However, only two studies have examined the validity of this claim; one study indicates that allowing dispensaries to sell CTP is associated with higher potency cannabis (Sevigny et al., 2014), while a study from the Netherlands found no potency differences between cannabis sold in pharmacies and cannabis sold in coffee shops (Hazekamp, 2006).

Another major concern, is that CTP legalization may increase illegal cannabis use in the general population (Gorman & Huber, 2007; Joy et al., 1999; NIDA, 2014; The Seattle Times, 2011); yet various studies fail to find evidence to support this (Choo et al., 2014; Harper et al., 2012; Khatapoush & Hallfors, 2004; Lynne-Landsman et al., 2013; Masten & Guenzburger, 2014). Two studies have, however, found an association between CTP legalization and subsequent increases in illegal cannabis use in the general population (Salomonsen-Sautel et al., 2014; Schuermeyer et al., 2014). These two studies differ from other studies reviewed in that they examine the 2009 federal change towards relaxed prohibition and subsequent CTP commercialization rather than state legalization per se. Taken together, the results of this review suggest that it is important to pay particular attention to federal policy and market forces rather than merely statewide legalization when examining CTP policy and its relation to public health and safety.

The fact that relatively few studies have directly examined the impact of the 2009 federal policy change towards CTP and the subsequent CTP commercialization suggests that the full effect of CTP legalization remains unknown. To guide further policy debate and research it may be useful to draw upon experiences in other relevant fields. Studies from the U.S., the Netherlands and Australia have, for instance, shown that eliminating (or significantly reducing) criminal penalties for first time possession of small quantitative of cannabis has either no or very small effects on the prevalence of cannabis use (see MacCOUN & Reuter, 2001a, 2001b for review). However, it has been suggested that the Dutch move towards a broader *de facto* legalization which allowed for greater access and increasing levels of promotion in the mid-1980s was associated with an increase in cannabis use (MacCOUN & Reuter, 2001a).

These findings echoes those of the current literature review in that there is a lack of evidence that CTP legalization at the state level alone increased cannabis use, whereas federal policy towards relaxed prohibition and subsequent CTP commercialization seems to have had this effect. Researchers have pointed out similar experiences in terms of commercialization of tobacco and that lessons learnt in this area may be useful for understanding how to prevent

detrimental public health effects of CTP legalization and subsequent commercialization (Richter & Levy, 2014).

Limitations related to data and theory

The use of natural, quasi-experimental study designs to study the effects of CTP on public health and safety has recently become possible thanks to recent introductions of CTP legalization in the U.S. and elsewhere. To a large extent, researchers have utilized this opportunity by making use of secondary cross-sectional data. While of considerable value, these data are limited as they rarely allow researchers to examine causal relations and underlying mechanisms. This is, for instance, evident in studies that find an association between CTP legalization and changes in crime rates, alcohol use, and suicide. In these studies it remains unclear how CTP legalization may cause the observed changes, especially in light of previous studies that fail to find evidence that CTP legalization causes changes in cannabis use in the general population (Choo et al., 2014; Harper et al., 2012; Khatapoush & Hallfors, 2004; Lynne-Landsman et al., 2013; Masten & Guenzburger, 2014).

In light of these limitations, one way forward is to gather primary longitudinal data with information that enables examination of potential underlying mechanisms of CTP legalization effects. Another strategy is to add CTP survey items to existing surveys that monitor drug use trends and attitudes. This would enable investigations of how CTP relates to illegal use of cannabis, alcohol and mental health issues more directly than what has been possible so far.

The vast majority of the studies reviewed in this article stem from the U.S. Since countries differ widely in terms of cannabis use prevalence rates (Hibell, 2012; Sznitman et al., 2013) and CTP regulatory systems (Hoffmann & Weber, 2010), results from the U.S. may not be directly relevant to other geographic areas. In order to better understand how different CTP regulatory systems influence public health and safety there is a need for studies outside of the U.S.

It is also possible to learn more about the influence of diverse CTP regulatory systems by conducting comparisons across U.S. states. So far, only two studies have used this approach, and found that different regulatory CTP systems within the U.S. have distinct effects in terms of potency (Sevigny et al., 2014), but probably not in terms of prevalence of cannabinoid in drivers of fatal vehicle crashes (Masten & Guenzburger, 2014). Furthermore, just a few studies have specifically focused on federal CTP policy and CTP commercialization (Salomonsen-Sautel et al., 2014; Schuermeyer et al., 2014; Wang et al., 2013). Many of the studies do, however, utilize data that could, if revisited, be used to tease out the individual and combined effects of state and federal CTP policy. There is thus some opportunity to further develop the field of social CTP research with existing data.

Finally, the current social CTP research may be improved by a more systematic inclusion of theory. For instance, researchers may adopt the "rational choice" perspective of modern economics, which specifies three mechanisms through which CTP legalization may influence cannabis use, namely drug availability, drug prices and deterrent effect of punishment. Researchers may also rely on other theoretical perspectives such as reactance theory (Brehm & Brehm, 1981), which suggests that the illicit status of cannabis enhances its attractiveness and causes a "forbidden fruit effect". Following this line of thought researchers may start by examining whether the desirability of cannabis changes upon CTP legalization. Furthermore, labelling theory and social shaming (Braithwaite, 1989) may be applied for studying if and how CTP legalization effects the social control of cannabis use, which in turn play a major role in regulating substance use (Elliott, Huizinga, & Ageton, 1985; Paternoster, 1989). Previous research suggests that the effect of CTP legalization is difficult to determine (MacCOUN & Reuter, 2001a). Relying more heavily on theoretical frameworks may help researchers understand the effects better.

Conclusion

Parallel to the evolving trends in CTP legalization around the world, the effects of CTP policies on public health and safety are deserving of continued close attention by scientists. This review shows that while social CTP research is an emerging and rapidly growing field, the literature is still limited, both by number and by lack of rigorous theoretical and methodological basis. In order to direct and assess policy changes with scientific data, instead of plain beliefs or misconceptions, further research developments are needed and more involvement of social scientists is encouraged.

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Conflict of interest

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