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ORIGINAL ARTICLE



Systematic Review of Cannabis Use and Risk of Occupational Injury

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ABSTRACT

Aim: A range of nations, including countries of the European Union, Australia, and the Americas have recently implemented or proposed reforms to how they control cannabis use, thereby departing from traditional approaches of criminal prohibition that have dominated throughout most of the twentieth century. Given these policy developments and the widespread global use of cannabis, it is critically important to understand the possible risks associated with cannabis use in relation to major societal harms. Methods: This systematic review investigates the potential link between cannabis use and occupational injury. Consequently, it appraises all available current literature from five databases, following Cochrane and PRISMA guidelines. Results: Seven of the 16 reviewed studies show evidence supporting a positive association between cannabis use and occupational injury. One study shows evidence supporting a negative association and the remaining eight studies show no evidence of a significant relation. None of the studies assessed cannabis-related impairment. Only three of the reviewed studies show clear evidence that cannabis use preceded the occupational-injury event. Conclusion: The current body of evidence does not provide sufficient evidence to support the position that cannabis users are at increased risk of occupational injury. Further, the study quality assessment suggests significant biases in the extant literature are present due to potential confounding variables, selection of participants, and measurement of exposures and outcomes. Future high-quality evidence will be needed to elucidate the relation between cannabis use and occupational injury.

KEYWORDS

Cannabis; marijuana; occupation; injury; THC; systematic review

Introduction

According to the 2018 World Drug Report, the global annual prevalence of cannabis use is estimated to be near 3.9% overall, with an increased prevalence of 5.6% among 15-16 year old adolescents (United Nations Office on Drugs and Crime (UNODC), 2018). A number of countries worldwide have recently implemented or proposed reforms to how they control cannabis use, thereby departing from traditional approaches of criminal prohibition that have dominated throughout most of the twentieth century (American Public Health Association, 2016; European Monitoring Centre for Drugs & Drug Addiction, 2017; Statutes of Canada 2018, 2018). Given these policy developments and the widespread global use of cannabis, it is critically important to understand the possible risks associated with cannabis use in relation to major societal harms.

Cannabis use has been increasing in Western societies over recent decades (Rotermann & Macdonald, 2018; Substance Abuse and Mental Health Services Administration (SAMHSA), 2018). In Canada, the latest country to legalize adult recreational cannabis use (Department of Justice, 2018), a recent analysis suggests that the prevalence of self-reported past-year cannabis use has more than doubled between 1985

and 2015 (Rotermann & Macdonald, 2018). Reports from Statistics Canada (2019) following legalization on October 17, 2018 indicate that 18% of people aged 15 years or older reported they had used cannabis in the past three months compared to 14% from the previous year. This most recent estimate reflects about 5.3 million individuals, of which the majority are working-aged adults.

The increasing prevalence of cannabis use among working-aged adults in Canada (Azofeifa et al., 2016; Rotermann & Macdonald, 2018) may have implications regarding workplace safety. Based on the National Cannabis Survey, Statistics Canada (2019) estimates that roughly 13% of employed, current cannabis users in Canada consume cannabis before or during work. Globally, a minimum of 312,000 fatal unintentional occupational injuries occur per year due to hazardous conditions in the workplace (Concha-Barrientos et al., 2005). Due to the cognitive and physical impairment associated with cannabis use (Broyd et al., 2016; Martín-Santos et al., 2010; Memedovich et al., 2018; Scott et al., 2018), it is biologically plausible that cannabis use may be a factor associated with injury and mortality in the workplace. However, it is critically important to understand the context and temporality of impairment in order to assess the causal relation between cannabis use and workplace injury. This is important for government officials, employers, insurance companies, and health care systems since occupational injuries represent a significant burden from both economic and public health standpoints (Concha-Barrientos et al., 2005; Takala et al., 2014).

Currently, the literature is mixed. A number of studies have attempted to evaluate the association between cannabis use and occupational injury: some studies have shown a positive association, while others have shown no relation. At this time, we are not aware of any systematic reviews which have investigated the possible association between cannabis use and occupational injury. However, we have identified three nonsystematic reviews assessing the cannabis-occupational injury relation (Macdonald et al., 2010; National Academies of Sciences, Engineering, and Medicine (NASEM), 2017; World Health Organization, 2016). Each of these reviews has significant limitations. First, Macdonald et al. (2010) focused on cannabis testing in the workplace. This review only included a brief description of the possible link between cannabis use and occupational injury. Second, in the "cannabis and the workplace" section of the WHO review (2016), the authors state that this association is a concern that has not been systematically reviewed. Rather, the majority of studies investigating the link between cannabis and safety have focused on traffic safety outcomes (Asbridge et al., 2012; National Academies of Sciences, Engineering, and Medicine (NASEM), 2017; Rogeberg & Elvik, 2016). Third, in 2017, the NASEM conducted an exhaustive review on the health effects of cannabis use. Although this review was thorough and informative for the general health effects of cannabis, the investigation of the association between cannabis use and occupational injury was a small subsection including only six studies. The NASEM reviewers concluded that at the time of review there was insufficient evidence to suggest that cannabis use is associated with an increased risk of occupational accidents and injuries (National Academies of Sciences, Engineering, and Medicine (NASEM), 2017). However, without published methods of the review or a PRISMA guideline flowchart (Moher et al., 2009), this study cannot be replicated and does not provide an exhaustive assessment of the evidence found in rigorous systematic reviews.

Since the methods of the current available reviews are unclear and include relatively few primary studies, a more detailed, transparent systematic review is warranted. Considering the burden of occupational injury and the recent legalization of recreational cannabis in countries worldwide, such as Canada, studies that investigate occupational risk factors may help guide public policy in this area. Substance use research, including cannabis, highlights the complexities of studying employee substance use. This includes the consideration of temporal context as well as the mediating and moderating factors in the association of cannabis use and occupational injuries. In this area, Frone (2019, 2013, 2004) highlights the importance of a multidimensional approach to understanding workplace substance use. Also presented in the literature are three pertinent areas for future research, including improving prevalence data surrounding substance use, understanding workplace antecedents of workplace substance use, and understanding the consequences of workplace substance use. The current review investigates the third recommendation for future research with the focus on cannabis use in the workplace. This systematic review attempts to answer the following question: Are cannabis users at an increased risk of occupational injury?

Methods

The design and methods of this systematic review followed the framework set out by the Cochrane Review Group (Higgins & Green, 2011).

Search strategy

Criteria for considering studies for this review

Studies eligible for review were required to contain an assessment of cannabis use, an assessment of workplace injury, and a comparative statistical estimate of association between cannabis use and workplace injury in relation to a non-cannabis-using comparison group. Studies were ineligible for review if they were not primary empirical studies (i.e. reviews), gray literature (poster presentation, abstract, or oral presentation only), or if they did not meet the inclusion criteria.

Types of studies

Only primary studies were included in this review. There were no study design limitations in the selection process.

Types of participants

There were no limitations regarding desired participant demographics, occupation type, or hours worked.

Types of exposure

The primary exposure in the selected studies was cannabis use. There were no limitations regarding the measurement of cannabis use, such as frequency, duration, intensity, or route of administration.

Types of outcome measures

The primary outcome of interest in the selected studies was occupational injury. All forms of assessment of occupational injury were accepted, whether injury was self-reported or determined by medical records. Studies were not excluded based on the severity of the injury. Incidents such as errors in performance, near misses, missed workdays, or termination of employment were not sufficient for inclusion.

An assessment of cannabis use and its comparative statistical association with workplace injury was evident in the included studies. Studies that did not contain a comparative statistic (in relation to a comparison or control group) were excluded. Some of these studies that were excluded only reported statistical relations between "substance use" or "illicit drugs" and occupational injury without distinguishing cannabis use from other drug use.

Search methods

A total of five databases were searched on May 1, 2018. These databases included EMBASE (Ovid) 1974 to 2018, MEDLINE (Ovid) 1946 to 2018, PsycINFO (EBSCO) to 2018, CINAHL (EBSCO) Complete to 2018, and Web of Science (Clarivate) 1900 to 2018.

Categories and keywords relating to "occupation," and "injury" were chosen for the search strategy. A medical research librarian was consulted regarding the strategy. Boolean operators were used to combine the selected terms. For example, whenever possible, when searching EMBASE (Ovid) and MEDLINE (Ovid), search terms were "exploded." See Appendix, Section 1 for the application of the search strategy to each database. Only minor changes were present in searches of the different databases. For example, when searching "tetrahydrocannabinol," EMBASE (Ovid) would allow for the term to be exploded, but MEDLINE (Ovid) would not. To account for these differences, the reviewers used a large variety of related search terms and used the explode function when possible. These variations can be seen in Appendix, Section 1. The references of eligible articles and excluded reviews were hand-searched for additional studies.

Data collection and analysis

Selection of studies

Two researchers, WB and KL, carried out the initial database searches with the assistance of a medical librarian. The results from each database were exported to RefWorks (Proquest, 2016) in RIS format, apart from the results from Web of Science, which were exported in BIB format. After recording the initial results for each database, all references were exported to an online systematic review management program, Covidence (Cochrane, 2019), which screened for and removed duplicates. Independently, the researchers screened the references in two phases. Titles and abstracts were screened first, and any conflicts were reviewed until a consensus was reached between reviewers. The included references went on to independent full-text screening. Following full-text review, RC reviewed the selected articles. After discussion between researchers, a consensus decision was made to exclude two additional articles that did not satisfy the inclusion criteria. Any study that met the inclusion criteria proceeded to data extraction. Although quality of evidence and study design were assessed, they were not used as a basis of exclusion.

Data extraction and management

Study characteristics, including the following, were extracted: author(s), date, country of origin (country in which the study took place), and type/design (cross-sectional, case control, or longitudinal cohort) (Table 1).

Regarding study participants, occupation, age range, and sex were extracted when provided by the studies. A summary table of the selection criteria from the included studies can be found in the supplemental information (See Supplemental File, Appendix Section 6.2.1).

Cannabis use, defined as the recreational or medicinal consumption of cannabis via any route of administration, was reported in the included studies as a dichotomous variable ("yes or no"), or by frequency of use, or presence of cannabis metabolites in urine. A measure of cannabis-related impairment was not reported in any study. A summary table of the assessment of cannabis use in the included studies can be found in the supplemental information (See Supplemental File, Appendix Section 6.2.2).

Occupational injury, defined as any injury occurring at or during work, was reported in the included studies in various methods. Most relied on dichotomous "yes or no" variables such as injury while working, injury while working since last interview, past-year work-related accident requiring medical treatment, or past-year work related accident. Two studies used alternative models of measuring occupational injury such as workers' compensation benefits (Kaestner & Grossman, 1998) and an injury outcome measured in the form of lost workdays counted from the day of the accident to the day following measured in calendar days, weekdays, work shifts, or working days (Khashaba et al., 2018). The above data is included in the supplemental information (See Supplemental File, Appendix Section 6.2.3).

The relation between cannabis use and occupational injury, defined as any positive or negative association or lack of association between cannabis use and occupational injury, was extracted from the included studies in the method that it was reported. The included studies reported this interaction using odds ratios, relative risks, percentages, and measures of cannabis metabolites. When available, pvalues and confidence intervals were also extracted. A summary table of the evidence is included (Table 1).

Quality assessment

The Newcastle-Ottawa Scale (NOS) (Wells et al., 2011) was used to assess the quality of the included studies. The scoring for each section of the NOS was discussed amongst the researchers until a consensus was reached, and then the score was reported. This was done for each study, one by one, section by section. No formal log of assessments by independent reviewers were recorded. The NOS included assessment of selection, comparability, and either exposure or outcome depending on the study type. For comparability, researchers reviewed appropriate literature in order to identify potentially important confounding variables (Table 4). Researchers used the NOS for cohort, case-control, and cross-sectional studies as seen in Appendix, Section 2.5. Results of the quality assessment are presented in Table 3. A table outlining the complete assessment of each study using the NOS is included in Appendix, Section 2.4.

In addition to using the NOS, the reviewers assessed the included studies for evidence of a temporal association between the exposure and outcome. Researchers evaluated

 Table 1. Summary of study results on the link between Cannabis use and Occupational Injury ("O" means no evidence of any association, "+" means evidence of positive association, "-" means evidence of negative association). CI = 95% confidence interval.

Study - Country	Type of Study & Reporting		Overview of study evidence		Comments and Conclusion
Barrio et al. (2012) – Spain	Cross-sectional Self-report	16-64 years old: Total use OR 1.3 (Cl 1.0-1.7) <weekly (cl="" 0.8-1.7)<="" 1.0-1.9)="" 1.2="" 1.4="" or="" td="" use="" weekly=""><td>16-34 years old: Total use OR 1.3 (Cl 0.9-1.8) <weekly (cl="" 0.8-1.9)="" 0.9-2.0)<="" 1.3="" or="" td="" use="" weekly=""><td>35-65 years old: Total use OR 1.2 (CI 0.7-1.9) < Weekly use OR 1.66 (CI 1.0-4.0) Weekly use OR 0.6 (CI 0.3-1.4)</td><td>n = 27,862 Any occupation Age groups overlap since study authors did total and subgroup analyses. Subgroups of 16-34 and 35-64 were chosen based off age strata used in reports of the European Monitoring Center for Drugs and Drug Addiction.</td></weekly></td></weekly>	16-34 years old: Total use OR 1.3 (Cl 0.9-1.8) <weekly (cl="" 0.8-1.9)="" 0.9-2.0)<="" 1.3="" or="" td="" use="" weekly=""><td>35-65 years old: Total use OR 1.2 (CI 0.7-1.9) < Weekly use OR 1.66 (CI 1.0-4.0) Weekly use OR 0.6 (CI 0.3-1.4)</td><td>n = 27,862 Any occupation Age groups overlap since study authors did total and subgroup analyses. Subgroups of 16-34 and 35-64 were chosen based off age strata used in reports of the European Monitoring Center for Drugs and Drug Addiction.</td></weekly>	35-65 years old: Total use OR 1.2 (CI 0.7-1.9) < Weekly use OR 1.66 (CI 1.0-4.0) Weekly use OR 0.6 (CI 0.3-1.4)	n = 27,862 Any occupation Age groups overlap since study authors did total and subgroup analyses. Subgroups of 16-34 and 35-64 were chosen based off age strata used in reports of the European Monitoring Center for Drugs and Drug Addiction.
Dong et al. (2015) – USA	Cross-sectional Self-report	With consideration of non-occupational factors Lifetime marijuana use on 11+ occasions OR 1.06 (Cl 0.96-1.18) 1-10 occasions OR 1.01 (Cl 0.91-1.12) With consideration of occupational and non-occupational factors Lifetime marijuana use on 11+ occasions OR 1.10 (Cl 0.99-1.21) 1-10 occasions OR 1.04 (Cl 0.99-1.21)	nal factors nd non-occupational factors		n = 12,686 Workers in the labor force only 0
Fransen et al. (2006) – New Zealand	Cross-Sectional Self-report	Unadjusted RR of work injury associated with past year cannabis use: RR: 1.29 (CI 1.11-1.50)	ted with past year cannabis use:		n = 15,687 Any occupation +
Hoffman and Larison (1999) – USA	Cross-sectional Self-report	No odds ratios achieved statistical significance. ¹ Never used cannabis (n = 4,925) OR 1.00 Used 3+ years ago (n = 2,556) OR 1.06 Used 1-3 years ago (n = 377) OR 1.03 Use 1-2 days in past year (n = 284) OR 1.51 Used 3-51 days in past year (n = 550) OR 0.98 Used at least weekly in past year (n = 405) OR OR	nl significance. ¹ OR 1.00 R 1.06 1.03 4) OR 1.51 550) OR 0.98 (n = 405) OR 1.01		n = 9,097 Any occupation O
Kaestner and Grossman (1998) – USA	Cross-sectional Self-report	Mean % of injured respondents in the last year who used cannabis: 1988 male (n = 2256): 36.9% 1992 male (n = 1727): 24.6%		1988 female (n = 2173): 27.4% 1992 female (n = 1559): 10.1%	n~7715 Any occupation Workers compensation as an indication of
		All groups except 1992 female had a significantly highe users in the injured vs non-injured groups ($\rho < 0.05$) Past year marijuana use was found to have a positive a estimated probability of having an accident in the p. The 1992 male estimates and all females estimates bas not staristically significant.	All groups except 1992 female had a significantly higher mean % of cannabis users in the injured vs non-injured groups (ρ < 0.05) Past year marijuana use was found to have a positive and significant effect on estimated probability of having an accident in the past year for 1988 males. The 1992 male estimates and all females estimates based of the data were generally not staristically significant.	ally	-+
Khashaba et al. (2018) – Egypt	Case-control Self-report and urine drug tests	Crude Or for non-fatal construction (n = 190, male on cannabis use based off self-reported cannabis use: OR 1.3 (Cl 0.5-3.3)	Crude OR for non-fatal construction (n = 190, male only) injuries associated with cannabis use based off self-reported cannabis use: OR 1.3 (Cl 0.5-3.3)		n = 190 Construction workers 0
Lasebikan and Jjomanta (2018) – Nigeria Macdonald (1995) – Canada	Cross-sectional Self-report Cross-sectional Self-report	Among injured group, those who had confirmed cannab tests did not have significantly different number of drange: 3-216 days, n = 24) than non-users (36 days, rilnjury in combat as a predictor of cannabis use: Lifetime use OR = 2.45 (Cl 1.39-7.41) Current use OR = 1.79 (Cl 1.04-5.21) Past year cannabis use associated with workplace injury: OR 2.5, probability value X²=0.00842	Among injured group, those who had confirmed cannabis use via urine drug tests did not have significantly different number of days lost from work (72 days, range: 3-216 days, $n = 24$) than non-users (36 days, range: 3-120 days, $n = 16$, $p = 0.1$). Injury in combat as a predictor of cannabis use: Lifetime use OR = 2.45 (Cl 1.39-7.41) Current use OR = 1.79 (Cl 1.04-5.21) Past year cannabis use associated with workplace injury: OR 2.5, probability value X^2 =0.00842	p = 0.1).	n = 223 Military workers + n = 882 Any occupation
Normand et al. (1990) – USA					+ n = 5465 Postal workers

No statistical analysis provided for injuries and accidents, only data. O n = 315 Coal miners	n = 3795 Multiple industries, including coal mining 0	n = 4159 Multiple industries, including coal mining 0	n = 2537 Postal workers +	n = 2226 or greater Any occupation High school students +	n=4424 Any occupation $oldot$		n = 2537 Postal workers +
				Adj for grade, sex, ethnicity, hours worked OR (Cl) 1.45 (1.10-1.90) 1.46 (1.01-2.12) 1.87 (1.38-5.34) 1.26 (1.01-1.56)	1.24 (0.76-2.03) 2.23 (1.34-3.71)		
No statistically significant relationship between drug-test results (including cannabis) and number of company-recorded workplace injuries or accidents among post-office workers. ¹ Marijuana metabolites: Random (n = 215) vs Post-accident (n = 100) Post-accident group In(Creatinine normalized marijuana metabolite concentration)=1.705 (Cl: 1.551-1.858) Random group In(Creatinine normalized marijuana metabolite concentration)=2.777 (Cl: 2.723-2.830) Mann-Whitney U test demonstrated significant difference between marijuana metabolites in nost-acrident groun and random groun (n = 0.000)		Compared urine metabolites in post-accident and randomly tested groups did not find statistically significantly difference ($p=0.413$).	This is a follow-up study of the same cohort in Zwerling et al. (1990). After 2 years of follow up, time to first injury analysis showed statistically significant increase in risk of injury among the cannabis positive group. The elevated relative risk was decreased compared to the previous study. RR 151 (CL 11-2-20) $n = 0.005$.	Occasions of Unadjusted data OR (Cl) Adj for grade, sex, ethnicity OR (Cl) cannabis use 1-9 (life) 1.41 (1.12-1.77) 1.42 (1.12-1.80) 10-39 (life) 2.17 (1.71-2.75) 1.94 (1.51-2.50) 1-9 (last 30d) 1.38 (1.08-1.77) 1.37 (1.06-1.77)	1.66 (1.15-2.40) 2.74 (1.87-4.01) etween cannabis use and minor injurier ing medical attention) at work with: ne: OR 1.17 (Cl 0.74-1.86) f other risks AND cannabis: 8.49 (Cl 5.3:	Statistically significant association only in group with high levels of other risks AND cannabis.	No statistical significance for cannabis use associated with workplace accidents (requiring medical attention). After 13 months of follow-up, time to first injury analysis showed statistically significant increase in risk of injury among the cannabis positive group. RR 1.85 (Cl 1.30-2.64, $p = 0.01$)
Longitudinal cohort study Urine drug tests Case-control Post-accident urine drug tests	Case-control Post-accident urine drug tests	Case-control Post-accident urine drug tests	Longitudinal Cohort study Urine drug tests	Cross-sectional Self-report	Cross-sectional Self-report		No statisti Zwerling et al. Longitudinal Cohort After 13 n (1990) – USA Urine drug tests analysis risk of RR 1.85 (C
Price (2012) – USA	Price (2014) – USA	Price (2016) – USA	Ryan et al. (1992)	Shipp et al. (2005) – USA	Wadsworth et al. (2006) – United Kingdom		Zwerling et al. (1990) – USA ¹ Study did not provid



Table 2. Temporal relation of assessed cannabis use and assessed occupational injury in the reviewed studies.

Study	Is it possible that the assessed occupational injury occurred before assessed cannabis use?	Explanation
Barrio et al. (2012)	Yes	Overlap between frequency of cannabis use and past-year occupational injury. Although some participants report use of cannabis as weekly, occupational injury may have preceded use.
Dong et al. (2015)	Yes	Lifetime use may occur prior to injury in some cases (i.e. if cannabis use noted at first interview and injury occurred following this), however, unclear in presented data.
Fransen et al. (2006)	Yes	Overlap between frequency of cannabis use and past-year occupational injury.
Hoffman and Larison (1999)	Yes	Overlap between frequency of cannabis use and past-year occupational injury.
Kaestner and Grossman (1998)	Yes	Overlap between past-year cannabis use and past-year occupational injury.
Khashaba et al. (2018)	Yes	Overlap between lifetime cannabis use and past-year occupational injury.
Lasebikan and Ijomanta (2018)	Yes	Overlap between lifetime or past-year cannabis use and lifetime occupational injury.
Macdonald (1995)	Yes	Overlap between past-year cannabis use and past-year occupational injury.
Normand et al. (1990)	No	Documented cannabis metabolites in urine prior to occupational injury since urine was assessed upon hiring of applicants.
Price (2012)	Yes	Post-accident urine samples were collected according to a strict chain of custody algorithm set by the US Department of Transportation. However, unclear if samples were taken at the time of the accident.
Price (2014)	Yes	Post-accident urine samples were collected according to a strict chain of custody algorithm set by the US Department of Transportation. However, unclear if samples were taken at the time of the accident.
Price (2016)	Yes	Post-accident urine samples were collected according to a strict chain of custody algorithm set by the US Department of Transportation. However, unclear if samples were taken at the time of the accident.
Ryan et al. (1992)	No	Documented cannabis metabolites in urine prior to occupational injury since urine was assessed upon hiring of applicants.
Shipp et al. (2005)	Yes	Overlap between lifetime or past-month cannabis use and lifetime occupational injury.
Wadsworth et al. (2006)	Yes	Overlap between past-year cannabis and past-month cannabis use with past-year occupational injury.
Zwerling et al. (1990)	No	Documented cannabis metabolites in urine prior to occupational injury since urine was assessed upon hiring of applicants.

the possibility that assessed occupational injury occurred prior to assessed cannabis use by reviewing the methodologies and data of each study. When insufficient, researchers emailed the authors of the studies for more information. A summary table of the assessment is included (Table 2).

Measure of treatment effect

The studies identified in this review report the risk of occupational injury using several different statistical measures (Table 1). There were no limits regarding the desired measurement of exposure effect.

Assessment of heterogeneity

Clinical heterogeneity and methodological heterogeneity, as described in the Cochrane Handbook for Systematic Reviews (Higgins & Green, 2011), were assessed by researchers during the quality assessment. According to Higgins and Green (2011), clinical heterogeneity is defined as "variability in the participants, interventions and outcomes studied," while methodological heterogeneity is the "variability in study design and risk of bias." Combined, these two forms

of heterogeneity result in statistical heterogeneity—the "variability in the intervention effects being evaluated in the different studies" (Higgins & Green, 2011).

Regarding clinical heterogeneity, the studies included in this review were diverse in participants. Some studies included specific samples of participants including postal workers, coal workers, construction workers, military workers, or labor force workers. The remaining studies included large samples of participants from any occupation (Table 1). For further details, review the supplemental information (Appendix, Section 2.1). This range was acceptable since target participants, as identified by our inclusion criteria, are those in the workforce. The interventions and outcomes were similar among all included studies since the intervention and outcome were specified as part of our inclusion cri-See the supplemental information for more information (Appendix, Section 2.2-2.3).

Regarding methodological heterogeneity, the studies included in this review were varied. Of the studies that met the inclusion criteria for this review, the research designs are as follows: nine are cross sectional studies, three are longitudinal cohort studies, and the remaining four are case-control studies (Table 1). All

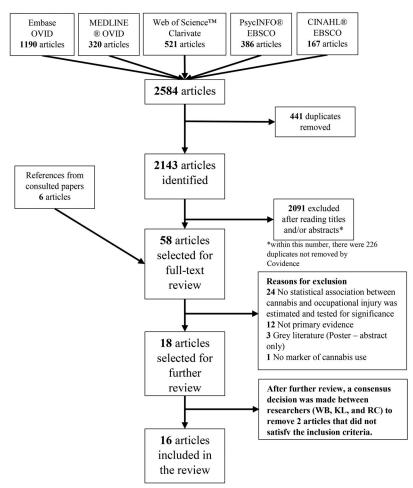


Figure 1. PRISMA flow chart (Moher et al., 2009) detailing the article selection process.

of the cross-sectional studies used self-reporting surveys to assess cannabis use and occupational injury. The three longitudinal cohort studies used urine drug screening and company injury records. Of the case-control studies, one study used interviews with urine drug screening and the remaining three studies used post-accident urine drug screening.

It is apparent that the above clinical and methodological heterogeneity may result in statistical heterogeneity among the studies included in this review. However, statistical heterogeneity was not formally assessed in this review.

Results

Summary of results

The literature search resulted in 2584 articles which were imported from multiple databases. The process is presented in a PRISMA flow chart as per Moher et al. (2009) (see Figure 1). After screening titles, abstracts, full text, and additional references from consulted papers, 16 articles met the criteria to be included in the review.

Studies supporting an increased risk of occupational injury with cannabis use

Seven of the 16 reviewed studies demonstrated a significant positive relation between cannabis use

occupational injury (Fransen et al., 2006; Kaestner & Grossman, 1998; Lasebikan & Ijomanta, 2018; Macdonald, 1995; Ryan et al., 1992; Shipp et al., 2005; Zwerling et al., 1990) (Table 1). Wadsworth et al. (2006) also presented data that supports a link between cannabis use and occupational injury when other risk factors are present. However, there is no evidence of any relation between cannabis use and occupational injury in the absence of these risk factors.

Studies supporting a decreased risk of occupational injury with cannabis use

Price (2012) found that the presence of cannabis metabolites reduced the risk of occupational injury (Table 1).

Studies providing no evidence of any association between cannabis use and occupational injury

The remaining eight studies that were reviewed showed no evidence of any link between occupational injury and cannabis use (Barrio et al., 2012; Dong et al., 2015; Hoffman & Larison, 1999; Khashaba et al., 2018; Normand et al., 1990; Price, 2016, 2014) (Table 1).

Table 3. Summary of the study quality assessments for all cross-sectional, case-control, and cohort studies included in this systematic review.

Cross-sectional studies	Year	Selection (5 max)	Comparability (2 max)	Outcome (3 max)	Total (10 max)
Barrio et al.	2012	**	**	*	5
Dong et al.	2015	**	**	**	6
Fransen et al.	2006	*		**	3
Hoffman and Larison	1999	**	**	*	5
Kaestner and Grossman	1998	**	**	**	6
Lasebikan and Ijomanta	2018	**	*	**	5
Macdonald	1995	**		*	3
Shipp et al.	2005	**	*	**	5
Wadsworth et al.	2006	**	*	**	5
Cohort studies	Year	Selection (4 max)	Comparability (2 max)	Outcome (3 max)	Total (9 max)
Normand et al.	1990	***	**	*	6
Ryan et al.	1992	***	**	*	6
Zwerling et al.	1990	***	**	*	6
Case-control studies	Year	Selection (4 max)	Comparability (2 max)	Exposure (3 max)	Total (9 max)
Khashaba et al.	2018	**	• • • • • • • • • • • • • • • • • • • •	**	4
Price	2012	**		***	5
Price	2014	**		***	5
Price	2016	**		***	5

Studies providing evidence of a temporal relation between cannabis use and occupational injury

In order to determine causality in an epidemiological framework, the "causal" exposure variable must precede the outcome. The reviewed studies were analyzed for the temporal association between assessed cannabis use and assessed occupational injury (Table 2). There is clear evidence in only three of these studies that show exposure precedes the outcome (Normand et al., 1990; Ryan et al., 1992; Zwerling et al., 1990).

Quality of the included studies

Using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2011), all reviewed studies were assessed for quality (Table 3). The nine cross-sectional studies were evaluated to have an average total score of 4.78/10 (range: 3-6). The three cohort studies averaged 6.00/9 (range: 6-6) and the four case-control studies averaged 4.75/9 (range: 4-5).

Discussion

This systematic review focuses on examining all currently accessible cannabis literature estimating a possible association between cannabis use and occupational injury. Seven of the 16 included studies suggest an association between cannabis use and increased occupational injury, while one study suggested a negative association between cannabis use and occupational injury. The remaining eight studies showed no evidence of a relation between cannabis use and occupational injury. This review identifies numerous concerns in the area of cannabis research which are primarily focused on important epidemiological considerations for ascertaining causation. Most strikingly, only three of the 16 studies showed a temporal relation whereby cannabis use was known to be used before occupational injury. Similarly, although cannabis use is a variable in every study, lack of research and methods regarding assessment of cannabis impairment are such that none of the included studies can ensure impairment during time of injury. Additionally, lack

of control and analysis of important potential confounding variables (Table 4) consistently put studies at serious risk of bias. Finally, future researchers may benefit by paying close attention to the research concerns highlighted in this study.

In the epidemiological literature on the potential relation between substance use and occupational injury, there appear to be two general research approaches (Macdonald, 1995). The first approach aims to investigate if substance users are at an increased risk of occupational injuries. The second approach is to analyze the association between injuries and impairment from substance use. Although the second approach tends to be more scientifically rigorous, it is a difficult approach to take in cannabis research as there is no universally accepted methods of measuring cannabis-related impairment (Macdonald, 2019). Evidence of impairment at the time of injury would be preferable but is currently not feasible for cannabis research. The current three methods of assessing impairment are observational or behavioral testing, biological testing with blood samples, and biological testing with oral fluid samples (Capler et al., 2017); however, quantitative tetrahydrocannabinol (THC) levels may not necessarily reflect level of impairment (Capler et al., 2017; Logan et al., 2016; Reisfield et al., 2012), have low sensitivity and specificity (Logan et al., 2016), and are highly complicated by variables such as tolerance (Capler et al., 2017). Likely due to these barriers, the first epidemiological approach is used by all of the studies assessed in this review. It is important to understand this approach as it places heavy weight on the biological plausibility of cannabis impairment (Broyd et al., 2016; Martín-Santos et al., 2010; Memedovich et al., 2018; Scott et al., 2018) in the association of use and occupational injury, instead of more concrete measurements of impairment which are preferable in inferring causality. This is an important distinction to make, since research surrounding health consequences of drug use may influence political, public, and policy-makers' opinions.

It is possible that the lack of consistent effects in the field may be due to poor measurement of the exposure, especially given the biological plausibility linking cannabis use, cannabis impairment, and increased risk of occupational injury. Across all identified studies, the assessment of cannabis use

ship with occupational injury in at least one of the following studies: Wadsworth et al. (2006), Cui et al. (2015), Zwerling et al. (1996), Shipp et al. (2005), Hoffman and Larison (1999), Nkyekyer et al. (2018), Dong et al. (2015). Table 4. Summary of potentially confounding variables in the association between cannabis use and occupational injury and the adjustments made in the included studies. Each variable was investigated for a relation-

				Hoffman										
Confounding	Barrio	Dong	Fransen	and Larison,	Kaestner	Khashaba	Lasebikan	Macdonald Norman	Norman	Price Price Price	Ryan	Shipp	Wadsworth	Zwerling
domains* Study	et al., 2012	et al., 2012 et al., 2015 et al., 2006	t al., 2006	1999	and Grossman, 1998		et al., 2018 and Ijomanta, 2018	1995	et al. 1990	2012 2014 2016 et al., 1992	5 et al., 1992	et al., 2005	et al., 2006	et al., 1990
Age	×			×	×		×		×		×		×	×
Alcohol use or dependence	×	×		×	×								×	
Education level	×	×		×	×							×	×	
Experience (job, shiftwork)					×								×	
Gender/Sex (studies did not differentiate)	×	×		×	×		×		×		×	×	×	×
Hours (full time, part time, total weekly)		×		×	×							×		
Income				×	×								×	
Indicators of Mental health	×												×	
Job type (blue/white collar, manual/desk etc)	×	×		×					×		×		×	×
Opiate or benzodiazepine use	×													
Personality (Esp. Neuroticism, Introversion)													×	
Physical Health (e.g., BMI >30, disabled from		×			×								×	×
work, exercise status)														
Race-ethnicity		×		×					×		×	×		×
Region/location/rural/population	×	×		×										
Risk taking behavior													×	
Self-employed (protective)/union status/other					×									
Sleep status/fatigue													×	
Stimulant (cocaine, amphetamines, ecstasy) use	×	×		×										
Tobacco consumption	×	×									×		×	×

focused primarily on cannabis-use frequency: three studies incorporated lifetime use (yes/no); five studies assessed pastyear use (yes/no); one study assessed past-month use (yes/ no); six studies assessed current use (yes/no) depending on the presence of positive or negative cannabis metabolites; and five studies included graded frequencies, such as 1-11 times in lifetime, 11+ in lifetime, and so on. It is possible that the heterogeneity of findings across studies may be due to these crude measures of cannabis-use exposure. Prior reviews and critiques of cannabis-use assessment have urged the field to incorporate more detailed assessments of cannabis use, including patterns of recent use, quantity of use, potency of cannabis product type, route of administration, detailed frequency assessment, and cannabis-use setting (Asbridge et al., 2014; Casajuana et al., 2016; Temple et al., 2011).

A concerning concept surrounding cannabis research is that of inferring causality. In 1965, Sir Austin Bradford Hill proposed nine features of association for inferring a causal relationship (Hill, 1965) which have been further discussed for applications in scientific advancement (Fedak et al., 2015; Rothman & Greenland, 2005). This systematic review focuses primarily on investigating criteria 2: consistency. Researchers in this present study identified three primary concerns regarding causality in the context of cannabis use and occupational injury. Although not exhaustive to infer causality, they present opportunities for improvement in future research. The first is determining if there is in fact a relationship between two variables, which approximates Hill's criteria 1: strength of association, and criteria 5: biological gradient. The second is that the "causal" variable must precede the outcome variable, which corresponds to Hill's criteria 4: temporality. The third concern is quite complex and involves controlling for potential confounding variables in order to rule out a spurious association between cannabis use and occupational injuries due to common causes, as well as the modeling of moderator variables which can identify subgroups with weaker or stronger associations between cannabis use and occupational injuries. Much of the current literature surrounding cannabis research focuses on the first concern via statistical calculations based on dichotomous self-reported cannabis use (Macdonald et al., 2010; National Academies of Sciences, Engineering, and Medicine (NASEM), 2017; World Health Organization, 2016), but fall short on the latter two. Unfortunately, only three of the 16 studies assessed in this review can demonstrate a temporal relationship to satisfy our second concern of causality, whereby cannabis use precedes occupational injury (Table 2). In the remaining 13 studies, overlap in the reported timeframe of occupational injury and cannabis use results in the possibility of occupational injury occurring prior to cannabis use. The study carried out by Lasebikan and Ijomanta (2018) highlights this concern, showing a positive relationship between being injured in combat and cannabis use. In studies unable to demonstrate a temporal relationship, the direction of association cannot be deter-

mined. Therefore, we recommend that future researchers

pay close attention to the temporal relation between cannabis and occupational injury in the assessment.

The third concern regarding causality in epidemiological research is that the association between cannabis use and occupational injuries is not the result of common exogenous causes of both cannabis use and occupational injuries. A model initially proposed by Frone (2004), which was updated and presented in Frone (2013, 2019), expresses the complexities of analyzing psychoactive substance use and job-associated outcomes. These complexities include the temporal association and differentiation of substance use and impairment, as briefly discussed above. Further discussed in the model is the need to control for confounding variables, assess moderating processes, and the need for better methodology in substance use research. In the present study, we investigated risk factors for occupational injury and, from a brief search of relevant literature, we identified a list of evidence-based potential confounding domains referred to in the studies (Table 4) (Barrio et al., 2012; Cui et al., 2015; Dong et al., 2015; Hoffman & Larison, 1999; Nkyekyer et al., 2018; Wadsworth et al., 2006; Zwerling et al., 1996; Zwerling et al., 1990). Few studies investigated the domains in the same manner; the 19 listed domains were an attempt to combine the evidence but would greatly benefit from future research or a current systematic review on occupational risk factors. Additionally, the present study took a simplified approach compared to the multicausal model presented by Frone (2004, 2013, 2019), which includes confounding and moderating processes that future research should pursue. Further research would also benefit by considering these evidence-based risk factors associated with occupational injury. Overall, individual studies controlled for relatively few of these variables, with six studies not adjusting or accounting for any potential confounding variables.

Many engage in polysubstance individuals Concurrent polysubstance use occurs when an individual uses two or more substances over some period but not on the same occasion of use, whereas simultaneous polysubstance use represents the use of two or more substances at the same time. Because few studies controlled for concurrent use of other psychoactive drugs (e.g. Ramchand et al., 2009; Simpson et al., 2005) and no studies assessed simultaneous drug use, future research should evaluate further the confounding influence of concurrent polysubstance use, as well as the synergistic influence of simultaneous polysubstance use on the risk of occupational injury due to using cannabis.

Another important factor to consider is baseline occupational risk, referred to by Frone (2004) as the "latent potential for injury and property damage accidents on a given job." If substance use compounds occupational risk (Dong et al., 2015; Frone, 2004; Wadsworth et al., 2006), it is plausible that an observable difference in occupational injury will only be seen among cannabis users in the context of higherrisk occupations, as seen in Wadsworth et al. (2006). Frone (2004) refers to this as a moderating process because cannabis may interact with the latent potential for injuries. The following example illustrates this issue: a laborer working at

heights will have a greater latent potential for physical injury from falling than an office worker. Although polysubstance use and baseline occupational risk are only two of many potential risk factors identified, they highlight the importance of considering variables as either confounding variables or as moderating variables. They also highlight the need for future research to be more rigorous in this context in order to aid in the ascertainment of inferring causality.

This review serves to highlight several concerns surrounding research focused on cannabis use and occupational injury. A pattern of three major concerns were identified throughout the 16 assessed research studies. First, the field focuses exclusively on estimating risk of occupational injury among cannabis users. Currently, we are not aware of any studies which assess impairment and injury. The absence of global standards surrounding cannabis impairment make this research challenging and stands as a prospective area of research on its own. In the meantime, researchers may focus on improving data surrounding cannabis use in research studies. One recommendation is to move away from simple dichotomous groups of substance use. Data collection and analysis should ideally attempt to classify impairment during work and consider frequency, intensity, duration, timing, and route of administration as these have been shown to impact cannabis-related impairment (Borodovsky et al., 2016; Casajuana et al., 2016; Frone, 2006, 1998; Russell et al., 2018; Temple et al., 2011).

Similarly, more rigorous data collection and analysis could address the second concern demonstrated in this area of research. To progress toward causality studies must show that cannabis use precedes occupational injury. More precise data collection surrounding the timing of cannabis use and injury (or directly asking study participants if cannabis use preceded injury) would help maintain the temporal relationship. For longitudinal studies, data analysis might analyze cannabis use from the previous years in association with current year injury. Simple changes in data collection and analysis can solve a critical concern in this research field.

Control and understanding of confounding variables represent additional weakness in the field. Wadsworth et al. (2006) alone identified 12 variables associated with injury and a further nine variables associated with cognition or accidents. We believe that concurrent drug use (including alcohol) and baseline occupational risk are two of many critical confounders to be considered. Additional variables are identified in other studies to provide our best estimate of 19 major confounding variables considered in this review (Table 4). Although likely not exhaustive, this list of potential confounding variables should be considered by future researchers in the data collection and analysis of cannabis use and injury. If these variables are not accounted for, the estimated independent risk of cannabis use may be biased. Future research may also benefit from analysis of the contribution of any of these risk factors. Although there are many areas of improvement which are noted in this review, we believe these three foci to be of critical importance in determining the risks of cannabis use, especially regarding occupational injury.



Recommendations arising from this systematic review primarily focus on research design. First, researchers should attempt to classify cannabis impairment prior to injury and consider not only frequency of use, but also intensity, duration, timing, route of administration, and potency of substance. Research providing methods for the quantitative assessment of cannabis-related impairment may be a key prospective field of research. Second, researchers need to pay close attention to the temporal relation between assessment of cannabis use and assessment of occupational injury. Third, they must also understand and adjust for potential confounding variables and explore moderating processes in cannabis research. Specifically, systematically analyzing the risk factors for occupational injury may provide excellent insight for this field. Finally, focusing on polysubstance use, both concurrent and/or simultaneous use, as well as consideration of latent injury potential in different occupations may be key for future areas of research.

Conclusion

The goal of this systematic review was to investigate whether cannabis users are at increased risk of occupational injury. After screening over 2500 articles, 16 articles met our inclusion criteria. Of these 16 articles, seven suggested that cannabis use may be associated with increased occupational injury, one study suggested a negative association, and the remaining eight studies showed a null relation between cannabis use and occupational injury. It is important to note the use of the word "association," as the included studies only investigated one component condition for establishing causality. Regrettably, only three of the 16 studies employed research designs that insured that cannabis use preceded the occupational-injury outcome. Of the 19 assessed confounding variables such as alcohol use and baseline job risk, only four studies assessed for more than half of the confounders, with most controlling for only a few, and six studies controlling for no confounding variables. Given these limitations, the current body of evidence is insufficient to support the position that cannabis users are at increased risk of occupational injury. However, this review does provide several recommendations to address these concerns to improve future research in this field.

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No potential conflict of interest was reported by the author(s).

Authors' contribution

WB and KL contributed equally to the production of this manuscript. Each researcher was involved in the search, screening, data extraction, and the quality assessment of the included articles. RC conceived the

research project and provided supervision. All authors have approved the final article.

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