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The prevalence of cannabis use among tobacco smokers: A systematic review protocol

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Title

The prevalence of cannabis use among tobacco smokers: A systematic review protocol

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Abstract

Introduction: Understanding the prevalence of cannabis use among tobacco smokers has important implications for research in terms of intervention effectiveness and measurement in smoking cessation trials. The co-use of these substances also has important implications for health service planning, specifically ensuring appropriate and adequate clinical treatment. To date there have been no synthesis of the literature on the prevalence of tobacco and cannabis co-use in adult clinical populations. Improved understanding of the current prevalence, route of administration, and specific subpopulations with the highest rates of tobacco and cannabis co-use will support future intervention development. We aim to provide a pooled estimate of the percentage of smokers who report using cannabis and to examine the prevalence of co-use by socio-demographic characteristics.

Methods and Analysis: We will conduct a systematic review using six scientific databases (CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus). Peer-reviewed journal articles published in English that report on tobacco and cannabis use will be included. Rates of co-use (simultaneous or sequentially) and routes of administration will be assessed. Use in populations groups will be described. Quality assessments will be conducted for all included studies. Data will be synthesised using a narrative approach.

Ethics and Dissemination: This review is based upon previously published data and therefore ethical approval or written informed consent will not be required. It is the intention of the research team to disseminate the results of the systematic review as a peer reviewed publication and conference presentations.

Systematic review registration: CRD42020194051.

Keywords: Public Health, Epidemiology, Substance Misuse

Strengths and limitations:

- Utilising the gold standard or meta-analysis, the proposed review will collate multiple studies to provide the first pooled prevalence of tobacco and cannabis co-use.
- This review will also provide important information on the sub-groups that require targeted intervention.
- There are several limitations that need to be noted, the first, is publication bias and the second is that if the included studies measures are too heterogeneous, we will not be able to complete a meta-analysis.

Introduction

Tobacco smoking continues to be a leading cause of preventable disease and death. An estimated 1.1 billion people continue to smoke tobacco. Over the past three decades the prevalence of tobacco smoking has been increasing in low- and middle-income countries (LMIC) [1] where an inverse relationship is seen in high income countries (HIC) where significant declines are noted. For example, in LMIC, the adult smoking prevalence rate has increased from 12.4% to 22.8% in Rwanda, from 33.8% to 39.5% in Indonesia, and from 16% to 40.4% in Zambia[2]. While in HIC, the tobacco smoking prevalence has reduced from 30.1% to 13.7% in the US[3], from 31% to 14.0% in Australia[4], 30% to 14.2% in New Zealand[5], and 33% to 14.1% in the United Kingdom[6]. The decline in the prevalence of tobacco smoking appears to be less apparent among specific sub-populations in HIC[7]. People who have a substance use disorder or are in treatment for substance misuse[8], people with a severe mental illness[9], people who are homeless or at risk of homelessness[10] are found to have smoking rates 2-6 times higher than the general population.

Cannabis is another commonly utilised substance[11]. Global estimates suggest that the number of cannabis users has increased in many countries, as has the treatment for cannabis use disorder[12]. Changing regulatory environments and the legalisation of cannabis in some countries, and decreasing perceptions of risk associated with cannabis use[13, 14], have been viewed to contribute to this recently increase in use[15-17]. Other contributors to the increased use of cannabis include socio-demographic and environmental risk factors. These factors may differ in between LMIC compared to high-income countries yet no review to date has examine this relationship.

Co-use can refer to concurrent use of both tobacco and cannabis, individually (sequentially), and to co-administration, or the use of the two substances at the same time, eg cannabis and tobacco leaf mixed within roll-your-own cigarettes (concurrent)[18]. Patterns of

tobacco and cannabis co-use appear to differ by country. A 2018 International Tobacco Control Survey identified that Canada, followed by the US (29.1%), England (21.6%), and Australia (21.4%) had the highest rates of tobacco and cannabis co-use [19]. There are limited studies examining tobacco and cannabis co-use in LMIC. Tobacco and cannabis co-use is often missed in population prevalence surveys[13].

Previous reviews on tobacco and cannabis co-use have examined mechanisms of initiation [20, 21] toxicant exposure[22], and co-administered products (such as blunts or spliffs) [23]. While other reviews have focused specifically on certain populations such as adolescents and young adults [24]. One important gap in the growing literature is a comprehensive pooled prevalence estimate of tobacco and cannabis co-use. Synthesising the existing data is important to understand the extent to which tobacco and cannabis co-use is occurring.

There appears to be an increased physiological effect of both substance when used together. The mechanisms underlying the co-use of tobacco and cannabis have been identified as shared genetic factors, environmental factors (peer influences; availability; younger age), and economic factors (lower socio-economic factors)[20]. More recently, another possible factor influencing co-use of tobacco and cannabis is the common route of administration e.g. smoking/ inhalation of both substances[18]. To date, only one review has examined route of administration and only focused on combustible forms of tobacco and cannabis co-use [23]. A synthesis of the literature that includes all possible routes of administration would fill this gap in the literature.

Compared to other substances, cannabis use among tobacco smokers appears to be more common than the co-use of other substances that occur at a remarkably reduced rate such as alcohol (33.3-45.7%), cocaine (37.5%-42.9%), stimulants (30-51.7%) and hallucinogens (35.6-41.7%)[25-27]. The relationship between tobacco and cannabis use is

synergistic in that tobacco use increases cannabis dependence symptoms [18, 28] and precipitates cannabis relapse [29] and similarly cannabis use increases the likelihood of nicotine dependence [30] and decreases tobacco cessation [31]. Given this, people who co-use both tobacco and cannabis are at greater risk for serious for serious health and psychosocial problems [21]. Co-use is associated with increased risks of toxicant exposure, poorer physical and mental functioning [23].

Understanding and accounting for current cannabis use among participants involved in smoking cessation research is important as it may have an impact on the intervention effect but also the measurement effect. If smokers are recruited into a smoking cessation intervention but their cannabis use is not addressed, then relapse to tobacco smoking is likely if they regularly mixed their tobacco with cannabis. Similarly, since cannabis use is detected in carbon monoxide breath analysis, this method of biochemical verification of tobacco smoking status may be inaccurate. Therefore, an alternate biochemical method such as serum or salivary cotinine may be preferable for self-reported tobacco smokers who utilise cannabis [32].

Only limited research has described the demographic and clinical characteristics of people who use both tobacco and cannabis. These studies predominately focussed on young people who use these substances. Demographic characteristics such as older adolescents[33, 34] another found that people who co-use tobacco and cannabis were younger than tobacco-only users[24], of male gender, and ethnicity. A synthesis of the current literature is critical for the development of an evidence base foundation for developing future randomised controlled trials. This review will provide the first synthesis of the literature and provide pivotal information for specific countries to influence the development of socially and culturally appropriate interventions to further the evidence base.

There is a clear need for an improved understanding as to the co-use of tobacco and cannabis use as this will have practical implications in the design of smoking cessation studies. Our review will ask the following questions 1. What is the percentage of smokers who report also using cannabis; 2. What is the nature of co-use of tobacco and cannabis (e.g. mixing together or smoking at different times, including routes of administration); and 3. What is the prevalence of co-use tobacco and cannabis by socio-demographic characteristics (age; gender; country – low and high income; clinical characteristics such as mental health diagnosis and substance use disorder).

METHODS

Study design

We will complete a systematic review examining the prevalence of cannabis use among tobacco smokers generally and by specific socio-demographic and clinical characteristics as well as the nature of the use of these substances (whether concurrently or individually). This review will be conducted in line with the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines. This review has been registered with PROSPERO (insert ID number). Any variations to the originally registered protocol will be submitted as an amendment to PROSPERO and indicated in the review publication.

Study criteria

Study designs: we will include the following study designs: cohort, cross-sectional, observational, baseline assessments/ surveys of intervention studies, national reports. We will exclude published editorials, letters, or conference proceedings (including abstracts), qualitative studies, thesis dissertations, and studies quoting the incidence rate rather than prevalence. Further, we will not use genetic epidemiological studies that report prevalence estimates in family members of individuals who use tobacco and cannabis.

Study populations and participants: Person-level data will be included from any adult population (aged > 18 years and older) including but not limited to educational populations (for example university populations), forensic or correctional populations, treatment seeking populations (people receiving treatment for substance use disorders or mental health conditions, oncological conditions, and other chronic diseases). We will include all routes of administration of tobacco use including alternate nicotine devices such as vaporisers.

Outcomes: We will include studies that report primary data on the prevalence of tobacco and cannabis use (such as total number of participants and percentages or proportions). Given that there is no standard assessment tool of tobacco and cannabis co-use we will include all measures as documented in the literature. For example, separate items that measure cannabis and tobacco use: "Do you currently smoke any tobacco products?" with response options i) yes, at least once a week; ii) yes, less often than once week; iii) no, not at all"; "During the past 30 days, on how many days did you use cannabis?"; "How many times is cannabis used per day on using days". Co-use has been defined in several recent US studies as the use of both substances within the past 30 days.

Additional eligibility criteria: Only articles that are published in English and that have been published in peer reviewed journals will be included [9].

Search Strategy

The search will be conducted in six databases: CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus, using keywords consistent across all databases and Medical Subject Headings (MeSH) applicable to specific databases. The Medline search terms are outlined in Table 1. Each search term is related to an overarching theme that map largely to the review aims (tobacco use and

cannabis use). It should be noted that the search terms have been developed with guidance from the Cochrane Public Health and Tobacco Addiction Group search terms.

Table 1. Search themes and terms

Theme	Search Terms
Study design	Epidemiology
	Cohort stud* OR Cohort analysis
	Cross-sectional stud* OR Cross-section analysis OR Observational analysis OR Prevalence OR Longitudinal
Tobacco use	tobacco OR nicotine OR smok* OR vap* OR cigar*
Cannabis use	cannabis OR cannabinoid* OR marijuana OR weed OR hash*

Screening

Two research assistants (AD, AL) will screen all titles and abstracts using the previously described inclusion criteria overseen by the post-doctoral research academic (ES). Any disagreements will be discussed between the post-doctoral research academic (ES) and the two research assistants (AD, AL). If a resolution cannot be found, the senior review author (BB) will hold a discussion until a resolution is found. The two RAs (AD, AL) completing 50% each. Again, any disagreements will be discussed between the post-doctoral research academic (ES) and the research assistants. All title, abstract, and full-text data screening will be completed using the Covidence online software v1919 73d6c782.

Data extraction

The team will develop a data extraction form based on the aims of the study. The data extraction form will include: country, year of publication, author, sample size, gender,

tobacco use prevalence (lifetime, last 12 months, current), cannabis use prevalence (lifetime, last 12 months, current), co-use prevalence, and routes of administration will be extracted for each paper. The co-use prevalence and calculated 95% confidence intervals (CI) for each estimate will be extracted. For papers reporting intervention studies, or for paper reporting repeated measures over time, we will use the prevalence data from the baseline assessment. Two post-doctoral research academics (ES and JR) will extract data from all included publications. Any disagreements will be discussed between all the two review authors. If a resolution cannot be found, the senior review author (BB) will be consulted in order to determine a resolution. Data will be extracted using the Covidence software.

Quality assessment

All cohort, cross-sectional, and case-control studies will be appraised according to Newcastle-Ottawa Quality Assessment Scale for cohort and case-control studies (adapted for cross-sectional studies). Using the tool each study is judged on eight items, that can be categorised into three further groups: 1. The selection of the study groups, 2. The comparability of the groups, and 3. The ascertainment of either the exposure or outcome of interest for case-control or cross-sectional studies respectively. Articles will not be excluded based upon their score on the quality appraisal tool. Quality scores will guide judgement of the methodological quality of the trial and reliability of the findings.

The risk of bias (quality) of all studies meeting the inclusion criteria will be formally assessed by ES and JR. Disagreements will be resolved by discussion with the senior review author (BB). Ratings will be presented in a table and will be used to inform the narrative synthesis.

Assessment of study heterogeneity. Heterogeneity will be examined using visual inspection of box plots, forest plots and using the I2 statistic. Where there is evidence of high heterogeneity (I2>75%), heterogeneity will be explored via subgroup analyses according to

trial intervention and population characteristics. Funnel plots will be generated by statistical software to enable the assessment of publication bias.

Grading the strength of evidence. As recommended by the Cochrane Handbook for Systematic Reviews of Interventions, the overall quality of evidence of the outcomes (tobacco and cannabis co-use prevalence) will be presented using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. This involves a within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence will be rated at four levels: high, moderate, low and very low.

ES and JR will assess the quality of evidence using the GRADE tool and will present the findings to the investigator team. The team will discuss the assessment and modify the reported strength of recommendations.

Data synthesis

Depending on the outcome measure employed by studies, pooled estimates by lifetime use, 12-months, and current use will be calculated. If studies have used similar definitions and measures, cannabis prevalence plots including the associated confidence intervals for each study will be presented. If there are national prevalence estimates for cannabis use, we will examine the difference between the study and the national prevalence.

In order to obtain the national smoking prevalence rates, official country statistics websites and the World Health Organisation Health Observatory Data Repository[35] will be consulted and the prevalence data extracted. If the national cannabis prevalence estimates are not available for all included countries for all years in which included studies were completed, we will report this information descriptively in the results section.

Included studies will be examined by socio-demographic and clinical characteristics to provide individual prevalence estimates and distributions. These will include socio-

demographic characteristics such as age, gender, country, nationality and Indigeneity. These will also include clinical characteristics such as mental health diagnosis as per the clinical diagnostic handbooks and tools (such as the Diagnostic and Statistical Manual of mental disorders (DSM)[36] or the International Classification of Disease (ICD)[37]) including substance use disorders and clinical populations such as individuals receiving treatment from addiction treatment or mental health services, as well as those with cardiovascular disease, diabetes, or cancer.

Patient and Public Involvement

No patients involved.

Study Status

At the time of submission of this protocol, the authors had completed screening of titles, abstracts, and full-texts, and were beginning data extraction and quality assessment.

DISCUSSION

The co-use of tobacco and cannabis and the sub-population who are most likely to co-use these substances are important considerations for intervention planning. This systematic review will provide pooled prevalence estimates of cannabis use among tobacco smokers. This study will report on tobacco and cannabis co-use by specific socio-demographics and clinical characteristics to provide a more in-depth examination and synthesis of the available data. This study will also provide the routes of administration of tobacco and cannabis co-use as this is an important aspect when developing behavioural interventions for cessation.

Abbreviations

DSM, Diagnostic and Statistical Manual of mental disorders

ICD, International Classification of Disease

GRADE, Grading of Recommendations Assessment, Development, and Evaluation

MeSH, Medical Subject Headings

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RA, Research Assistant

Declarations

Ethics approval and consent to participate: Ethics approval was not required for this systematic review.

Consent for publication: Consent was not required for this systematic review

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

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Author contributions: ES prepared the systematic review protocol and drafted the manuscript. All authors provided feedback on the protocol and manuscript, and read and approved the final manuscript.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			1
Identification	1a	Identify the report as a protocol of a systematic review	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1 &14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6-7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-8
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	9
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	11
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (site when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Abstract

Introduction: Understanding the prevalence of cannabis use among tobacco smokers has important implications for research in terms of intervention effectiveness and measurement in smoking cessation trials. The co-use of these substances also has important implications for health service planning, specifically ensuring appropriate and adequate clinical treatment. To date there have been no synthesis of the literature on the prevalence of tobacco and cannabis co-use in adult clinical populations. Improved understanding of the current prevalence, route of administration, and specific subpopulations with the highest rates of tobacco and cannabis co-use will support future intervention development. We aim to provide a pooled estimate of the percentage of smokers who report using cannabis and to examine the prevalence of co-use by socio-demographic characteristics.

Methods and Analysis: We will conduct a systematic review using six scientific databases (CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus). Peer-reviewed journal articles published in English that report on tobacco and cannabis use will be included. Rates of co-use (simultaneous or sequentially) and routes of administration will be assessed. Use in populations groups will be described. Quality assessments will be conducted for all included studies. Data will be synthesised using a narrative approach.

Ethics and Dissemination: This review is based upon previously published data and therefore ethical approval or written informed consent will not be required. It is the intention of the research team to disseminate the results of the systematic review as a peer reviewed publication and conference presentations.

Systematic review registration: CRD42020194051.

Keywords: Public Health, Epidemiology, Substance Misuse

Strengths and limitations:

- Utilising the gold standard or meta-analysis, the proposed review will collate multiple studies to provide the first pooled prevalence of tobacco and cannabis co-use.
- This review will also provide important information on the sub-groups that require targeted intervention.
- There are several limitations that need to be noted, the first, is publication bias and the second is that if the included studies measures are too heterogeneous, we will not be able to complete a meta-analysis.

Introduction

Tobacco smoking continues to be a leading cause of preventable disease and death. An estimated 1.1 billion people continue to smoke tobacco. Over the past three decades the prevalence of tobacco smoking has been increasing in low- and middle-income countries (LMIC) [1] where an inverse relationship is seen in high income countries (HIC) where significant declines are noted. For example, in LMIC, the adult smoking prevalence rate has increased from 12.4% to 22.8% in Rwanda, from 33.8% to 39.5% in Indonesia, and from 16% to 40.4% in Zambia[2]. While in HIC, the tobacco smoking prevalence has reduced from 30.1% to 13.7% in the US[3], from 31% to 14.0% in Australia[4], 30% to 14.2% in New Zealand[5], and 33% to 14.1% in the United Kingdom[6]. The decline in the prevalence of tobacco smoking appears to be less apparent among specific sub-populations in HIC[7]. People who have a substance use disorder or are in treatment for substance misuse[8], people with a severe mental illness[9], people who are homeless or at risk of homelessness[10] are found to have smoking rates 2-6 times higher than the general population.

Cannabis is another commonly utilised substance[11]. Global estimates suggest that the number of cannabis users has increased in many countries, as has the treatment for cannabis use disorder[12]. Changing regulatory environments and the legalisation of cannabis in some countries, and decreasing perceptions of risk associated with cannabis use[13, 14], have been viewed to contribute to this recently increase in use[15-17]. Other contributors to the increased use of cannabis include socio-demographic and environmental risk factors [18] including the COVID-19 pandemic [19]. These factors may differ in between LMIC compared to high-income countries yet no review to date has examine this relationship.

Co-use can refer to concurrent use of both tobacco and cannabis, individually (sequentially), and to co-administration, or the use of the two substances at the same time, eg cannabis and tobacco leaf mixed within roll-your-own cigarettes (concurrent)[20]. Patterns of

tobacco and cannabis co-use appear to differ by country. A 2018 International Tobacco Control Survey identified that Canada, followed by the US (29.1%), England (21.6%), and Australia (21.4%) had the highest rates of tobacco and cannabis co-use [21]. There are limited studies examining tobacco and cannabis co-use in LMIC. Tobacco and cannabis co-use is often missed in population prevalence surveys[13].

Previous reviews on tobacco and cannabis co-use have examined mechanisms of initiation [22, 23] toxicant exposure[24], and co-administered products (such as blunts or spliffs) [25]. While other reviews have focused specifically on certain populations such as adolescents and young adults [26]. Lemrye and co [27] in their review, detail the motivation and drivers of co-use including gateway theory and reverse gateway which may have implications in understanding co-use and interventions for cessation.

A recent review did explore treatment implications for those that co-use tobacco and cannabis [28], highlighting the challenges of single substance cessation and noting that interventions to address co-use cessation are lacking. Another, important gap in the growing literature is a comprehensive pooled prevalence estimate of tobacco and cannabis co-use. Synthesising existing data including correlates of use [29] is important to understand the extent to which tobacco and cannabis co-use is occurring.

There appears to be an increased physiological effect of both substance when used together. The mechanisms underlying the co-use of tobacco and cannabis have been identified as shared genetic factors, environmental factors (peer influences; availability; younger age), and economic factors (lower socio-economic factors)[22]. More recently, another possible factor influencing co-use of tobacco and cannabis is the common route of administration e.g. smoking/ inhalation of both substances[20]. To date, only one review has examined route of administration and only focused on combustible forms of tobacco and

cannabis co-use [25]. A synthesis of the literature that includes all possible routes of administration would fill this gap in the literature.

Compared to other substances, cannabis use among tobacco smokers appears to be more common than the co-use of other substances that occur at a remarkably reduced rate such as alcohol (33.3-45.7%), cocaine (37.5%-42.9%), stimulants (30-51.7%) and hallucinogens (35.6-41.7%)[30-32]. The relationship between tobacco and cannabis use is synergistic in that tobacco use increases cannabis dependence symptoms [20, 33] and precipitates cannabis relapse [34] and similarly cannabis use increases the likelihood of nicotine dependence [35] and decreases tobacco cessation [36]. Given this, people who co-use both tobacco and cannabis are at greater risk for serious for serious health and psychosocial problems [23]. Co-use is associated with increased risks of toxicant exposure, poorer physical and mental functioning [25].

Understanding and accounting for current cannabis use among participants involved in smoking cessation research is important as it may have an impact on the intervention effect but also the measurement effect. If smokers are recruited into a smoking cessation intervention but their cannabis use is not addressed, then relapse to tobacco smoking is likely if they regularly mixed their tobacco with cannabis. Similarly, since cannabis use is detected in carbon monoxide breath analysis, this method of biochemical verification of tobacco smoking status may be inaccurate. Therefore, an alternate biochemical method such as serum or salivary cotinine may be preferable for self-reported tobacco smokers who utilise cannabis [37].

Only limited research has described the demographic and clinical characteristics of people who use both tobacco and cannabis. These studies predominately focussed on young people who use these substances. Demographic characteristics such as older adolescents[38, 39] another found that people who co-use tobacco and cannabis were younger than tobacco-

only users[26], of male gender, and ethnicity. A synthesis of the current literature is critical for the development of an evidence base foundation for developing future randomised controlled trials. This review will provide the first synthesis of the literature and provide pivotal information for specific countries to influence the development of socially and culturally appropriate interventions to further the evidence base.

There is a clear need for an improved understanding as to the co-use of tobacco and cannabis use as this will have practical implications in the design of smoking cessation studies. The tiered approach of assessing co-use as explained by Hindocha and Mclure [40] suggests that consideration of individual-use data as well as co-use data be explored as often there is a lack of nuance in the current methods of collection and analysis. Our review will ask the following questions 1. What is the percentage of smokers who report also using cannabis; 2. What is the nature of co-use of tobacco and cannabis (e.g. mixing together or smoking at different times, including routes of administration); and 3. What is the prevalence of co-use tobacco and cannabis by socio-demographic characteristics (age; gender; country – low and high income; clinical characteristics such as mental health diagnosis and substance use disorder).

METHODS

Study design

We will complete a systematic review examining the prevalence of cannabis use among tobacco smokers generally and by specific socio-demographic and clinical characteristics as well as the nature of the use of these substances (whether concurrently or individually). This review will be conducted in line with the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines with data managed using Stata Statistical Software [41]. This review has been registered with PROSPERO (insert ID

number). Any variations to the originally registered protocol will be submitted as an amendment to PROSPERO and indicated in the review publication.

Study criteria

Study designs: we will include the following study designs: cohort, cross-sectional, observational, baseline studies, national reports. We will exclude published editorials, letters, or conference proceedings (including abstracts), qualitative studies, thesis dissertations, and studies quoting the incidence rate rather than prevalence. Further, we will not use genetic epidemiological studies that report prevalence estimates in family members of individuals who use tobacco and cannabis.

Study populations and participants: Person-level data will be included from any adult population (aged > 18 years and older) including but not limited to educational populations (for example university populations), forensic or correctional populations, treatment seeking populations (people receiving treatment for substance use disorders or mental health conditions, oncological conditions, and other chronic diseases). We will include all routes of administration of tobacco use including alternate nicotine devices such as vaporisers.

Outcomes: We will include studies that report primary data on the prevalence of tobacco and cannabis use (such as total number of participants and percentages or proportions). Given that there is no standard assessment tool of tobacco and cannabis co-use we will include all measures as documented in the literature. For example, separate items that measure cannabis and tobacco use: “Do you currently smoke any tobacco products?” with response options i) yes, at least once a week; ii) yes, less often than once week; iii) no, not at all”; “During the past 30 days, on how many days did you use cannabis?”; “How many times is cannabis used per day on using days”. Co-use has been defined in several recent US studies as the use of both substances within the past 30 days.

Additional eligibility criteria: Only articles that are published in English and that have been published in peer reviewed journals will be included [9].

Search Strategy

The search will be conducted in six databases: CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus, using keywords consistent across all databases and Medical Subject Headings (MeSH) applicable to specific databases. The Medline search terms are outlined in Table 1. Each search term is related to an overarching theme that map largely to the review aims (tobacco use and cannabis use). It should be noted that the search terms have been developed with guidance from the Cochrane Public Health and Tobacco Addiction Group search terms.

Table 1. Search themes and terms

Theme	Search Terms
Study design	Epidemiology Cohort stud* OR Cohort analysis Cross-sectional stud* OR Cross-section analysis OR Observational analysis OR Prevalence OR Longitudinal
Tobacco use	tobacco OR nicotine OR smok* OR vap* OR cigar*
Cannabis use	cannabis OR cannabinoid* OR marijuana OR weed OR hash*

Screening

Two research assistants (AD, AL) will screen all titles and abstracts using the previously described inclusion criteria overseen by the research academics (ES, JR, TH). Any disagreements will be discussed. If a resolution cannot be found, the senior review author

(BB) will hold a discussion until a resolution is found. The two RAs (AD, AL) completing 50% each. Again, any disagreements will be discussed between the authors and the research assistants. All title, abstract, and full-text data screening will be completed using the Covidence online software v1919 73d6c782.

Data extraction

The team will develop a data extraction form based on the aims of the study. The data extraction form will include: country, year of publication, author, sample size, gender, tobacco use prevalence (lifetime, last 12 months, current), cannabis use prevalence (lifetime, last 12 months, current), co-use prevalence, and routes of administration will be extracted for each paper. The co-use prevalence and calculated 95% confidence intervals (CI) for each estimate will be extracted. For papers reporting measures over time, we will use the prevalence data from the baseline assessment. Two post-doctoral research academics (ES and JR) will extract data from all included publications. Any disagreements will be discussed between all authors. If a resolution cannot be found, the senior review author (BB) will be consulted in order to determine a resolution. Data will be extracted using the Covidence software.

Quality assessment

All cohort, cross-sectional, and case-control studies will be appraised according to Newcastle-Ottawa Quality Assessment Scale for cohort and case-control studies (adapted for cross-sectional studies). Using the tool each study is judged on eight items, that can be categorised into three further groups: 1. The selection of the study groups, 2. The comparability of the groups, and 3. The ascertainment of either the exposure or outcome of interest for case-control or cross-sectional studies respectively. Articles will not be excluded based upon their score on the quality appraisal tool. Quality scores will guide judgement of the methodological quality of the trial and reliability of the findings.

The risk of bias (quality) of all studies meeting the inclusion criteria will be formally assessed by ES, JR, TH. Disagreements will be resolved by discussion with the senior review author (BB). Ratings will be presented in a table and will be used to inform the narrative synthesis.

Assessment of study heterogeneity. Heterogeneity will be examined using visual inspection of box plots, forest plots and using the I2 statistic, Egger's test will be applied [42]. Where there is evidence of high heterogeneity (I2>75%), heterogeneity will be explored via subgroup analyses according to population characteristics. If the heterogeneity among the studies is large, a random-effects model will be used to calculate the pooled OR. Otherwise, a fixed-effects model will be applied. We will use a Generalised Linear Model approach, due to methodological concerns with the Freeman–Tukey double-arcsine transformation method [43, 44]. Funnel plots will be generated by statistical software to enable the assessment of publication bias. If publication bias is detected the approximate number of missing studies using the trim-and-fill method [45] will be conducted to provide insight into degree of bias.

Grading the strength of evidence. As recommended by the Cochrane Handbook for Systematic Reviews of Interventions, the overall quality of evidence of the outcomes (tobacco and cannabis co-use prevalence) will be presented using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. This involves a within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence will be rated at four levels: high, moderate, low and very low. If feasible, the analysis could include individual participant-level meta-analysis.

ES and JR will assess the quality of evidence using the GRADE tool and will present the findings to the fellow authors. The team will discuss the assessment and modify the reported strength of recommendations.

Data synthesis

Depending on the outcome measure employed by studies, pooled estimates by lifetime use, 12-months, and current use will be calculated. If studies have used similar definitions and measures, cannabis prevalence plots including the associated confidence intervals for each study will be presented. If there are national prevalence estimates for cannabis use, we will examine the difference between the study and the national prevalence.

In order to obtain the national smoking prevalence rates, official country statistics websites and the World Health Organisation Health Observatory Data Repository[46] will be consulted and the prevalence data extracted. If the national cannabis prevalence estimates are not available for all included countries for all years in which included studies were completed, we will report this information descriptively in the results section.

Included studies will be examined by socio-demographic and clinical characteristics to provide individual prevalence estimates and distributions. These will include socio-demographic characteristics such as age, gender, country, nationality and Indigeneity. These will also include clinical characteristics such as mental health diagnosis as per the clinical diagnostic handbooks and tools (such as the Diagnostic and Statistical Manual of mental disorders (DSM)[47] or the International Classification of Disease (ICD)[48]) including substance use disorders and clinical populations such as individuals receiving treatment from addiction treatment or mental health services, as well as those with cardiovascular disease, diabetes, or cancer.

Patient and Public Involvement

No patients involved.

Study Status

At the time of submission of this protocol, the authors had completed screening of titles, abstracts, and full-texts, and were beginning data extraction and quality assessment.

DISCUSSION

The co-use of tobacco and cannabis and the sub-population who are most likely to co-use these substances are important considerations for intervention planning. This systematic review will provide pooled prevalence estimates of cannabis use among tobacco smokers. This study will report on tobacco and cannabis co-use by specific socio-demographics and clinical characteristics to provide a more in-depth examination and synthesis of the available data. This study will also provide the routes of administration of tobacco and cannabis co-use as this is an important aspect when developing behavioural interventions for cessation.

Abbreviations

DSM, Diagnostic and Statistical Manual of mental disorders

ICD, International Classification of Disease

GRADE, Grading of Recommendations Assessment, Development, and Evaluation

MeSH, Medical Subject Headings

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RA, Research Assistant

Declarations

Ethics approval and consent to participate: Ethics approval was not required for this systematic review.

Consent for publication: Consent was not required for this systematic review

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: None to report.

Author contributions: ES, JR, TH developed the protocol and drafted the manuscript. BB reviewed drafts and provided methodological feedback. All authors approved the final manuscript.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			1
Identification	1a	Identify the report as a protocol of a systematic review	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1 &14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6-7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-8
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	9
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	11
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (site when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Title

The prevalence of cannabis use among tobacco smokers: A systematic review protocol

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Abstract

Introduction: Understanding the prevalence of cannabis use among tobacco smokers has important implications for research in terms of intervention effectiveness and measurement in smoking cessation trials. The co-use of these substances also has important implications for health service planning, specifically ensuring appropriate and adequate clinical treatment. To date there have been no synthesis of the literature on the prevalence of tobacco and cannabis co-use in adult clinical populations. Improved understanding of the current prevalence, route of administration, and specific subpopulations with the highest rates of tobacco and cannabis co-use will support future intervention development. We aim to provide a pooled estimate of the percentage of smokers who report using cannabis and to examine the prevalence of co-use by socio-demographic characteristics.

Methods and Analysis: We will conduct a systematic review using six scientific databases with published articles from 2000 -2022 inclusive (CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus). Peer-reviewed journal articles published in English that report on tobacco and cannabis use will be included. Rates of co-use (simultaneous or sequentially) and routes of administration will be assessed. Use in populations groups will be described. Quality assessments will be conducted for all included studies. Data will be synthesised using a narrative approach. This study will be conducted from June 2022 until the end of August 2022.

Ethics and Dissemination: This review is based upon previously published data and therefore ethical approval or written informed consent will not be required. It is the intention of the research team to disseminate the results of the systematic review as a peer reviewed publication and conference presentations.

Systematic review registration: CRD42020194051.

Keywords: Public Health, Epidemiology, Substance Misuse

Strengths and limitations:

- Utilising the gold standard or meta-analysis, the proposed review will collate multiple studies to provide the first pooled prevalence of tobacco and cannabis co-use.
- This review will also provide important information on the sub-groups that require targeted intervention.
- There are several limitations that need to be noted, the first, is publication bias and the second is that if the included studies measures are too heterogeneous, we will not be able to complete a meta-analysis.

Introduction

Tobacco smoking continues to be a leading cause of preventable disease and death. An estimated 1.1 billion people continue to smoke tobacco. Over the past three decades the prevalence of tobacco smoking has been increasing in low- and middle-income countries (LMIC) [1] where an inverse relationship is seen in high income countries (HIC) where significant declines are noted. For example, in LMIC, the adult smoking prevalence rate has increased from 12.4% to 22.8% in Rwanda, from 33.8% to 39.5% in Indonesia, and from 16% to 40.4% in Zambia[2]. While in HIC, the tobacco smoking prevalence has reduced from 30.1% to 13.7% in the US[3], from 31% to 14.0% in Australia[4], 30% to 14.2% in New Zealand[5], and 33% to 14.1% in the United Kingdom[6]. The decline in the prevalence of tobacco smoking appears to be less apparent among specific sub-populations in HIC[7]. People who have a substance use disorder or are in treatment for substance misuse[8], people with a severe mental illness[9], people who are homeless or at risk of homelessness[10] are found to have smoking rates 2-6 times higher than the general population.

Cannabis is another commonly utilised substance[11]. Global estimates suggest that the number of cannabis users has increased in many countries, as has the treatment for cannabis use disorder[12]. Changing regulatory environments and the legalisation of cannabis in some countries, and decreasing perceptions of risk associated with cannabis use[13, 14], have been viewed to contribute to this recently increase in use[15-17]. Other contributors to the increased use of cannabis include socio-demographic and environmental risk factors [18] including the COVID-19 pandemic [19]. These factors may differ in between LMIC compared to high-income countries yet no review to date has examine this relationship.

Co-use can refer to concurrent use of both tobacco and cannabis, individually (sequentially), and to co-administration, or the use of the two substances at the same time, eg cannabis and tobacco leaf mixed within roll-your-own cigarettes (concurrent)[20]. Patterns of

tobacco and cannabis co-use appear to differ by country. A 2018 International Tobacco Control Survey identified that Canada, followed by the US (29.1%), England (21.6%), and Australia (21.4%) had the highest rates of tobacco and cannabis co-use [21]. There are limited studies examining tobacco and cannabis co-use in LMIC. Tobacco and cannabis co-use is often missed in population prevalence surveys[13].

Previous reviews on tobacco and cannabis co-use have examined mechanisms of initiation [22, 23] toxicant exposure[24], and co-administered products (such as blunts or spliffs) [25]. While other reviews have focused specifically on certain populations such as adolescents and young adults [26]. Lemrye and co [27] in their review, detail the motivation and drivers of co-use including gateway theory and reverse gateway which may have implications in understanding co-use and interventions for cessation.

A recent review did explore treatment implications for those that co-use tobacco and cannabis [28], highlighting the challenges of single substance cessation and noting that interventions to address co-use cessation are lacking. Another, important gap in the growing literature is a comprehensive pooled prevalence estimate of tobacco and cannabis co-use. Synthesising existing data including correlates of use [29] is important to understand the extent to which tobacco and cannabis co-use is occurring.

There appears to be an increased physiological effect of both substance when used together. The mechanisms underlying the co-use of tobacco and cannabis have been identified as shared genetic factors, environmental factors (peer influences; availability; younger age), and economic factors (lower socio-economic factors)[22]. More recently, another possible factor influencing co-use of tobacco and cannabis is the common route of administration e.g. smoking/ inhalation of both substances[20]. To date, only one review has examined route of administration and only focused on combustible forms of tobacco and

cannabis co-use [25]. A synthesis of the literature that includes all possible routes of administration would fill this gap in the literature.

Compared to other substances, cannabis use among tobacco smokers appears to be more common than the co-use of other substances that occur at a remarkably reduced rate such as alcohol (33.3-45.7%), cocaine (37.5%-42.9%), stimulants (30-51.7%) and hallucinogens (35.6-41.7%)[30-32]. The relationship between tobacco and cannabis use is synergistic in that tobacco use increases cannabis dependence symptoms [20, 33] and precipitates cannabis relapse [34] and similarly cannabis use increases the likelihood of nicotine dependence [35] and decreases tobacco cessation [36]. Given this, people who co-use both tobacco and cannabis are at greater risk for serious for serious health and psychosocial problems [23]. Co-use is associated with increased risks of toxicant exposure, poorer physical and mental functioning [25].

Understanding and accounting for current cannabis use among participants involved in smoking cessation research is important as it may have an impact on the intervention effect but also the measurement effect. If smokers are recruited into a smoking cessation intervention but their cannabis use is not addressed, then relapse to tobacco smoking is likely if they regularly mixed their tobacco with cannabis. Similarly, since cannabis use is detected in carbon monoxide breath analysis, this method of biochemical verification of tobacco smoking status may be inaccurate. Therefore, an alternate biochemical method such as serum or salivary cotinine may be preferable for self-reported tobacco smokers who utilise cannabis [37].

Only limited research has described the demographic and clinical characteristics of people who use both tobacco and cannabis. These studies predominately focussed on young people who use these substances. Demographic characteristics such as older adolescents[38, 39] another found that people who co-use tobacco and cannabis were younger than tobacco-

only users[26], of male gender, and ethnicity. A synthesis of the current literature is critical for the development of an evidence base foundation for developing future randomised controlled trials. This review will provide the first synthesis of the literature and provide pivotal information for specific countries to influence the development of socially and culturally appropriate interventions to further the evidence base.

There is a clear need for an improved understanding as to the co-use of tobacco and cannabis use as this will have practical implications in the design of smoking cessation studies. The tiered approach of assessing co-use as explained by Hindocha and Mclure [40] suggests that consideration of individual-use data as well as co-use data be explored as often there is a lack of nuance in the current methods of collection and analysis. Our review will ask the following questions 1. What is the percentage of smokers who report also using cannabis; 2. What is the nature of co-use of tobacco and cannabis (e.g. mixing together or smoking at different times, including routes of administration); and 3. What is the prevalence of co-use tobacco and cannabis by socio-demographic characteristics (age; gender; country – low and high income; clinical characteristics such as mental health diagnosis and substance use disorder).

METHODS

Study design

We will complete a systematic review examining the prevalence of cannabis use among tobacco smokers generally and by specific socio-demographic and clinical characteristics as well as the nature of the use of these substances (whether concurrently or individually). This review will be conducted in line with the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines with data managed using Stata Statistical Software [41]. This review has been registered with PROSPERO (insert ID

number). Any variations to the originally registered protocol will be submitted as an amendment to PROSPERO and indicated in the review publication.

Study criteria

Study designs: we will include the following study designs: cohort, cross-sectional, observational, baseline studies, national reports. We will exclude published editorials, letters, or conference proceedings (including abstracts), qualitative studies, thesis dissertations, and studies quoting the incidence rate rather than prevalence. Further, we will not use genetic epidemiological studies that report prevalence estimates in family members of individuals who use tobacco and cannabis. This study will be conducted from June 2022 until the end of August 2022.

Study populations and participants: Person-level data will be included from any adult population (aged > 18 years and older) including but not limited to educational populations (for example university populations), forensic or correctional populations, treatment seeking populations (people receiving treatment for substance use disorders or mental health conditions, oncological conditions, and other chronic diseases). We will include all routes of administration of tobacco use including alternate nicotine devices such as vaporisers.

Outcomes: We will include studies that report primary data on the prevalence of tobacco and cannabis use (such as total number of participants and percentages or proportions). Given that there is no standard assessment tool of tobacco and cannabis co-use we will include all measures as documented in the literature. For example, separate items that measure cannabis and tobacco use: “Do you currently smoke any tobacco products?” with response options i) yes, at least once a week; ii) yes, less often than once week; iii) no, not at all”; “During the past 30 days, on how many days did you use cannabis?”; “How many times

is cannabis used per day on using days". Co-use has been defined in several recent US studies as the use of both substances within the past 30 days.

Additional eligibility criteria: Only articles that are published in English and that have been published in peer reviewed journals will be included [9].

Ethics and Dissemination: This review is based upon previously published data and therefore ethical approval or written informed consent will not be required. It is the intention of the research team to disseminate the results of the systematic review as a peer reviewed publication and conference presentations.

Search Strategy

The search will be conducted in six databases with published articles from 2000 -2022 inclusive: CENTRAL, CINAHL, EMBASE, Medline, PsycINFO, Psychology and Behavioural Sciences Collection, Scopus, using keywords consistent across all databases and Medical Subject Headings (MeSH) applicable to specific databases. The Medline search terms are outlined in Table 1. Each search term is related to an overarching theme that map largely to the review aims (tobacco use and cannabis use). It should be noted that the search terms have been developed with guidance from the Cochrane Public Health and Tobacco Addiction Group search terms.

Table 1. Search themes and terms

Theme	**Search Terms**	**Limitations**
Study design	Epidemiology Cohort stud* OR Cohort analysis	2000-2022

	Cross-sectional stud* OR Cross-section analysis OR Observational analysis OR Prevalence OR Longitudinal	
Tobacco use	tobacco OR nicotine OR smok* OR vap* OR cigar*	Exclude clinical trials
Cannabis use	cannabis OR cannabinoid* OR marijuana OR weed OR hash*	

Screening

Two research assistants (AD, AL) will screen all titles and abstracts using the previously described inclusion criteria overseen by the research academics (ES, JR, TH). Any disagreements will be discussed. If a resolution cannot be found, the senior review author (BB) will hold a discussion until a resolution is found. The two RAs (AD, AL) completing 50% each. Again, any disagreements will be discussed between the authors and the research assistants. All title, abstract, and full-text data screening will be completed using the Covidence online software v1919 73d6c782.

Data extraction

The team will develop a data extraction form based on the aims of the study. The data extraction form will include: country, year of publication, author, sample size, gender, tobacco use prevalence (lifetime, last 12 months, current), cannabis use prevalence (lifetime, last 12 months, current), co-use prevalence, and routes of administration will be extracted for each paper. The co-use prevalence and calculated 95% confidence intervals (CI) for each estimate will be extracted. For papers reporting measures over time, we will use the

prevalence data from the baseline assessment. Two post-doctoral research academics (ES and JR) will extract data from all included publications. Any disagreements will be discussed between all authors. If a resolution cannot be found, the senior review author (BB) will be consulted in order to determine a resolution. Data will be extracted using the Covidence software.

Quality assessment

All cohort, cross-sectional, and case-control studies will be appraised according to Newcastle-Ottawa Quality Assessment Scale for cohort and case-control studies (adapted for cross-sectional studies). Using the tool each study is judged on eight items, that can be categorised into three further groups: 1. The selection of the study groups, 2. The comparability of the groups, and 3. The ascertainment of either the exposure or outcome of interest for case-control or cross-sectional studies respectively. Articles will not be excluded based upon their score on the quality appraisal tool. Quality scores will guide judgement of the methodological quality of the trial and reliability of the findings.

The risk of bias (quality) of all studies meeting the inclusion criteria will be formally assessed by ES, JR, TH. Disagreements will be resolved by discussion with the senior review author (BB). Ratings will be presented in a table and will be used to inform the narrative synthesis.

Assessment of study heterogeneity. Heterogeneity will be examined using visual inspection of box plots, forest plots and using the I2 statistic, Egger's test will be applied [42]. Where there is evidence of high heterogeneity (I2>75%), heterogeneity will be explored via subgroup analyses according to population characteristics. If the heterogeneity among the studies is large, a random-effects model will be used to calculate the pooled OR. Otherwise, a fixed-effects model will be applied. We will use a Generalised Linear Model approach, due to methodological concerns with the Freeman–Tukey double-arcsine transformation method

[43, 44]. Funnel plots will be generated by statistical software to enable the assessment of publication bias. If publication bias is detected the approximate number of missing studies using the trim-and-fill method [45] will be conducted to provide insight into degree of bias.

Grading the strength of evidence. As recommended by the Cochrane Handbook for Systematic Reviews of Interventions, the overall quality of evidence of the outcomes (tobacco and cannabis co-use prevalence) will be presented using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. This involves a within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The overall quality of evidence will be rated at four levels: high, moderate, low and very low. If feasible, the analysis could include individual participant-level meta-analysis.

ES and JR will assess the quality of evidence using the GRADE tool and will present the findings to the fellow authors. The team will discuss the assessment and modify the reported strength of recommendations.

Data synthesis

Depending on the outcome measure employed by studies, pooled estimates by lifetime use, 12-months, and current use will be calculated. If studies have used similar definitions and measures, cannabis prevalence plots including the associated confidence intervals for each study will be presented. If there are national prevalence estimates for cannabis use, we will examine the difference between the study and the national prevalence.

In order to obtain the national smoking prevalence rates, official country statistics websites and the World Health Organisation Health Observatory Data Repository[46] will be consulted and the prevalence data extracted. If the national cannabis prevalence estimates are not available for all included countries for all years in which included studies were completed, we will report this information descriptively in the results section.

Included studies will be examined by socio-demographic and clinical characteristics to provide individual prevalence estimates and distributions. These will include socio-demographic characteristics such as age, gender, country, nationality and Indigeneity. These will also include clinical characteristics such as mental health diagnosis as per the clinical diagnostic handbooks and tools (such as the Diagnostic and Statistical Manual of mental disorders (DSM)[47] or the International Classification of Disease (ICD)[48]) including substance use disorders and clinical populations such as individuals receiving treatment from addiction treatment or mental health services, as well as those with cardiovascular disease, diabetes, or cancer.

Patient and Public Involvement

No patients involved.

Study Status

At the time of submission of this protocol, the authors had completed screening of titles, abstracts, and full-texts, and were beginning data extraction and quality assessment.

DISCUSSION

The co-use of tobacco and cannabis and the sub-population who are most likely to co-use these substances are important considerations for intervention planning. This systematic review will provide pooled prevalence estimates of cannabis use among tobacco smokers. This study will report on tobacco and cannabis co-use by specific socio-demographics and clinical characteristics to provide a more in-depth examination and synthesis of the available data. This study will also provide the routes of administration of tobacco and cannabis co-use as this is an important aspect when developing behavioural interventions for cessation. As with all research, naturally there are limitations to be considered. Firstly, is publication bias, it is likely that given the rigorous nature of predetermined search strategies some publications may be missed from this review. Secondly, is that if the included studies measures are too

heterogeneous, a complete a meta-analysis may not be feasible. However, in utilising the gold standard of meta-analysis, the proposed review will collate multiple studies to provide the first pooled prevalence of tobacco and cannabis co-use. This review will also provide important information on the sub-groups that require targeted intervention. As such, the benefits of this review will outweigh any such methodological limitations.

Abbreviations

DSM, Diagnostic and Statistical Manual of mental disorders

ICD, International Classification of Disease

GRADE, Grading of Recommendations Assessment, Development, and Evaluation

MeSH, Medical Subject Headings

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RA, Research Assistant

Declarations

Ethics approval and consent to participate: Ethics approval was not required for this systematic review.

Consent for publication: Consent was not required for this systematic review

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: None to report.

Author contributions: ES, JR, TH developed the protocol and drafted the manuscript. BB reviewed drafts and provided methodological feedback. All authors approved the final manuscript.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			1
Identification	1a	Identify the report as a protocol of a systematic review	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1 &14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6-7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-8
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	9
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9-10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9-10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	11
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (site when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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