

Global Burden of Disease

**Mental Disorders and
Illicit Drug Use Expert Group**



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**Overview of injuries/diseases to be
included in the comparative risk
assessment for regular cannabis use**

Illicit Drugs Discussion Paper No. 5

OVERVIEW OF INJURIES/DISEASES TO BE INCLUDED IN THE COMPARATIVE RISK ASSESSMENT FOR REGULAR CANNABIS USE

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1 Introduction

One component of the Global Burden of Disease (GBD) study involves investigation of risk factors for disease and injury. The GBD defines “risks” according to the following considerations:

- Risk factors should be potentially modifiable;
- Risks should be assessed irrespective of place in a causal chain or scientific discipline that has traditionally analysed the risk factor, as long as evidence of causal effect can be established;
- Risks are defined to be not too broad (e.g. diet or environment as a whole) or too narrow (e.g. every single fruit and vegetable or every toxicant in tobacco smoke) with a relatively specific definition of risk factor exposure;
- Protective as well as hazardous factors are considered. However, the absence of a specific intervention should not be assessed as a risk factor, but rather in measurement of intervention coverage and effectiveness; and
- There exist sufficient data on risk factor exposure and risk-factor disease relationships.

In this paper we summarise briefly the decisions that have been made with respect to the conduct of comparative risk assessment (CRA) exercises for cannabis¹. The evidence upon which these have been based is reviewed in detail in two previous discussion papers^{1 2}. The interested reader is encouraged to read those papers, which may be accessed through our website: www.gbd.unsw.edu.au. The evidence and resulting decisions made for injecting drug use, and for opioids, cocaine and ATS use, are outlined in separate papers.

Estimates of the contribution that cannabis use might make to the burden of disease need to be made because cannabis use is the most widely used illicit drug in almost every country worldwide; the United Nations Office on Drugs and Crime estimates that

¹ Cannabis: a generic term for preparations (e.g. marijuana, hashish and hash oil) derived from the *cannabis sativa* plant.

Cannabis is the most widely used illicit drug globally, and its use has increased over the past decade. In 2005, around 160 million adults (4% of the global adult population) were estimated to have used cannabis in the previous year, 10% higher than estimated use in the mid 1990s³; and both regular and dependent cannabis use increase risks for adverse consequences⁴. The major risks considered in the GBD for inclusion in the CRA component of the project are summarised below.

2 Cannabis dependence

Regular cannabis use will be considered as the risk factor for cannabis dependence. In other words, the burden of disease attributable to cannabis dependence will be entirely attributed to use of the drug.

3 Cancer

There is inconsistent evidence provided by case-control and cohort studies for an association between cannabis use and cancer⁵⁻⁹. "Heavy" and sustained use has been associated with increased risk of brain tumour (use at least once a month)⁵ and lung cancer (>10 joint years of use)¹⁰. Although light use has been associated with cancer, this relationship is non-existent when confounding factors are controlled for⁵⁻⁹.

The effects of long term cannabis smoking on respiratory function are less clear.^{11 12} A longitudinal study^{13 14} of respiratory function in 1037 New Zealand youths followed from birth until the age of 21¹³ and 26¹⁴ found impaired respiratory function in cannabis dependent users but this finding was not replicated in longer term follow up studies in Los Angeles.¹¹ Chronic cannabis smoking has not so far been found to increase the risk of emphysema¹⁵ with follow up over 8 years failing to find increased rates of emphysema in cannabis only smokers in the USA¹⁵ or New Zealand.¹⁶

The lack of consistency and limited data available has led to the decision **not** to consider regular cannabis use as a risk factor for cancers in this iteration of the GBD.

Future research examining this issue in other samples and with statistical control for co-occurring tobacco use would be of considerable importance.

4 Motor vehicle accidents

Epidemiological studies of motor vehicle accidents have produced equivocal results because most drivers who have cannabinoids in their blood also have high blood alcohol levels^{17 18}. Two studies with reasonable numbers of persons who have *only* used cannabis have not found clear evidence of increased culpability in these drivers¹⁹. Modest associations have been found by three case-control studies comparing detection of THC with drug and alcohol free drivers²⁰, when focusing on drivers who had higher levels of THC detected ($\geq 5\text{ng/ml}$), the risk of culpable driving was increased^{21 22}.

It has been decided, in light of the evidence, that risk for **motor vehicle accidents (both fatal and non-fatal) will be included** in the CRA exercise for regular cannabis use.

5 Depression

Cross-sectional and longitudinal studies have provided mixed evidence on the nature of the association between cannabis use and depression. Cross-sectional studies have suggested that the relationship can be explained by other factors such as the use of other drugs. There have been only a limited number of studies that have controlled for potential confounding variables in the association between heavy cannabis use and depression. These have found that the risk is much reduced by statistical control; a modest relationship remains but in previous reviews both groups concluded that more evidence using comprehensive statistical control for confounders needed to be conducted to provide more convincing evidence that associations cannot be explained by other factors^{23 24}.

The decision taken for this exercise is therefore to **refrain from examining cannabis use as a risk factor for depression**, in line with the criteria defined for the CRA exercise above.

6 Schizophrenia and other psychotic disorders

Based upon previous reviews of the evidence, and discussed in some length in an earlier discussion paper, we feel it is reasonable to conclude that regular cannabis use predicts an increased risk of schizophrenia or psychotic disorders. The evidence suggests that this risk is particularly for those who have a pre-existing vulnerability to the disorder (through a personal or family history of schizophrenia or psychotic disorders). A contributory causal relationship is biologically plausible, and also consistent with the stress-diathesis model of schizophrenia^{25 26} and evidence that a genetic vulnerability to psychosis increases the risk that cannabis users will develop psychosis²⁷⁻³⁰. A vulnerability hypothesis is also consistent with the fact that the *treated* incidence of schizophrenia has not obviously increased during the 1970s and 1980s^{31 32} when there have been substantial increases in cannabis use among young adults in Australia and North America³³.

It is proposed that the **pooled odds ratios and 95% confidence intervals from recent meta-analytic reviews^{24 34} be used to estimate the burden of disease related to regular cannabis use as a risk factor for schizophrenia and other psychotic disorders**. These represent the summaries of existing general population cohort studies examining the magnitude of risk. Details are provided in a separate GBD Discussion Paper¹.

We propose to undertake a nuanced approach to the estimates in this instance given the remaining debates occurring around this issue: 1) a model that will assume **greater severity of schizophrenia** among those using cannabis regularly who have developed the disorder; 2) a model that will assume the association reflects **earlier onset** of the disorder among those who would have developed it anyway; 3) a model that will assume **reduced remission** from schizophrenia once it has developed; and a model that assumed **increased incidence** of schizophrenia. The resulting estimates of burden will be compared and contrasted with further expert consultation.

7 Suicide

Although there has been concern about the association between cannabis use and suicide attempts and fatalities, the literature on this topic is far from convincing². Studies that have been conducted have either failed to find an association, or have not controlled for confounding variables.

It is proposed that **no estimate of suicide attributable to regular cannabis use be made.**

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