

Cannabis – suicide, schizophrenia and other ill-effects

***A research paper on the consequences of acute and chronic
cannabis use***



A review prepared for Drug Free Australia
First Edition, March 2009

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Published by Drug Free Australia Ltd

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This work has been supported by funding from the Australian Government Department of Health and Ageing
Opinions expressed in this publication are those of the authors and not necessarily those of Drug Free Australia Ltd or the Australian Government.

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ACKNOWLEDGEMENTS

This review of cannabis in Australia was written to provide up-to-date evidence to key researchers including those at the National Drug and Alcohol Research Centre (NDARC) and others involved in compiling the National Cannabis Strategy 2006-2009. It is intended that this research paper will provide useful information for future updates of the National Cannabis Strategy in Australia.

Drug Free Australia would like to acknowledge the following people for their assistance with the content of this review.

Heather Ashton DM, FRCP is Emeritus Professor of Clinical Psychopharmacology at the University of Newcastle upon Tyne, UK. Prof Ashton has conducted laboratory research on the effects of smoking THC on the brain and performance, and has carried out surveys on the extent of cannabis use in UK university students, including separate surveys on medical students, dentists and junior doctors. She has written extensively in professional journals on the adverse effects of cannabis use.

Gary Christian – Secretary, Drug Free Australia. Mr Christian was co-author of the research publication ‘The Kings Cross Injecting Room – The Case for Closure’ and co-writer of the ‘Quit Now Stop Smoking Program, 1986-87’. In 1999 he was co-founder of the Cabramatta ADRAcare Centre for drug dependent and homeless people of the area and from 2000-2003, he was President of Hassela Australia’s Teen Drug Rehabilitation program.

Herschel Mills Baker – President of Australian Parents for Drug Free Youth. Mr Baker was author of ‘Suicide/Schizophrenia - Consequences of Acute and Chronic Cannabis Use’ (1988 and 1996). He was responsible for updating the ‘Drug Awareness’ booklet for Lions International District 201.Q5 Zone 2 of Queensland, Australia. He also developed a drug prevention resource for parents entitled ‘Drug Free Kids: A Parent’s Guide’ and developed a series of ‘Parent Drug Education Courses’ successfully used by Queensland TAFE and many organisations in Wide Bay Queensland such as the Lions Clubs, Quota Club and churches.

Craig Thompson, former Magistrate, NSW and Chair of Drug Free Australia. Mr Thompson was co-author of ‘Drug Precipice’, and produced a range of papers including ‘Marijuana – Effects, Decriminalisation and Policies’. President of PRYDE Australia Inc. (18 years) Board Member of the Ted Noffs Foundation (7 years) and Member of the Australian National Council on Drugs (ANCD).

Mary Brett BSc (Hons), Board Member of EURAD. Appreciation is expressed for her extensive international research in the areas of the impact of cannabis use and its damaging effects. Her contribution to this publication consists of substantial quotations especially in the sections on ‘Pregnancy and Newborns’, ‘Cardiovascular Effects’, ‘Dependence and Cancer’. These excerpts were previously published by EURAD (Europe Against Drugs) in ‘Cannabis - A General Survey of its Harmful Effects Submission to The Social Justice Policy Group’ 2008), available at <http://www.eurad.net/pdf/Cannabis%20combined%20document%20new.pdf>

Dr Ivan Van Damme MD (Belgium), Member International Task Force on Strategic Drug Policy. Appreciation is expressed for peer-review of this publication, including substantial quotations in the sections describing Cannabis, the history of Cannabis prohibition, the effects of Cannabis on Australian Indigenous communities, Chronic Obstructive Pulmonary Disease, Cannabis and the Cardiovascular System and Cannabis – Effects on the Brain.

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Thanks and grateful appreciation also to the following people who provided useful and specific advice on issues covered in this paper, related to their jurisdictions:

Dr Craig Raeside, Forensic Psychiatrist, SA, Hon. Chris Foley, MP, Member for Maryborough, Queensland and Member Travel Safe Committee, Mrs. Nan Ott, Mrs. Debbie Mason and Ms Sharon Baker.

FOREWORD

This research paper gives a concise, clear, accurate and logical account of the main mental and physical risks of cannabis consumption, particularly for young users. The aim is to provide information and advice to politicians, decision-makers and researchers in order to ensure that the level of cannabis use in Australia is markedly reduced. The report provides practical recommendations towards this end and makes a valuable contribution to public knowledge and to the framing of government policies.

It is right that the emphasis is on young people since the age of first cannabis use is declining, and children and adolescents are the most vulnerable to the adverse effects. These include severe psychiatric disorders, cognitive impairment, and progression to other illegal drugs. It may be noted that the age of continuing cannabis use is also increasing and contributing to public risks, such as traffic and other accidents. These issues underline the importance of the addictive nature of cannabis, particularly in its increasingly more potent forms – unfortunately nurtured by burgeoning trafficking in hydroponically grown cannabis.

The widespread use of this pervasive and addictive drug demands urgent attention to the problem of quitting in people already cannabis dependent. None of the present methods, which rely mainly on psychological approaches, is highly effective. Further research, perhaps including the judicious use of cannabinoid antagonists combined with psychological therapies, needs to be explored, instigated and financed.

The report is written in a style easily accessible to the layman but is firmly based on hard scientific evidence, carefully selected from the vast amount of literature on cannabis that has accrued over the years. Policy makers would do well to heed its messages and recommendations.

Heather Ashton DM, FRCP

EXECUTIVE SUMMARY

Cannabis is the most commonly used illicit drug in Australia¹, with one in three aged 14 years and older using the drug in their lifetime². With the age of first use declining and the potency and popularity of the drug increasing there is clear incentive to ensure we understand the ramifications of its use on our health and communities.

This paper seeks to provide an introduction to the available literature on cannabis and the issues arising from cannabis use today, including: a description of the drug and its use; the increased potency of cannabis in the market; cannabis as a “gateway” to harder drug use; the issues of dependence and withdrawal; the significant cannabis harms on mental health, brain function and development, and physical conditions such as cancer; and, the problems encountered when trying to quit cannabis and the generally poor outcomes today.

The paper also provides recommendations on how we can effectively answer the questions surrounding cannabis use in Australia.

Throughout, we return to the issue of age of first use. Overwhelming evidence exists to support the fact that the age of first cannabis use is an important predictor of progression to heavier drug use and need for treatment (for example, see Pope et al, 2003; Anthony et al, 1994; Warner et al, 1995; Kandel et al, 1997). Clearly, there is a significant problem when boys aged 9 and 10 are discovered with cannabis in Brisbane schools³.

¹ Department of Parliamentary Services Research Note, June 2007.

² 2004 National Drug Strategy Household Survey

³ “Children caught with pot”, Sunday Mail, October 26, 2003

SECTION ONE: CANNABIS USE

A DESCRIPTION OF THE DRUG

Cannabis is the term most frequently used to refer to the drug deriving from the plant *Cannabis sativa*, the most commonly used illicit drug in Australia.

Cannabis is generally found in three forms, all of which contain delta-9 tetrahydrocannabinol (“THC”) as the main psychoactive ingredient. The most common and least potent of these forms is marijuana, a mix of the plant’s dried leaves and flowers. Cannabis in the form of hashish, or dried cannabis resin, produces stronger effects through its higher concentration of THC. Hashish oil, a thick oily liquid, is the third and most powerful form of cannabis.

Of the active constituents of cannabis there have been over 60 cannabinoids identified; however, only a few, and primarily THC, have been studied intensely. The primary metabolite, 11-hydroxy-THC, is also psychoactive and even more potent and, as with all cannabinoids, acts on the endogenous receptors in the brain and body.

Cannabis is well absorbed through inhaling its smoke or its inclusion in cakes or cookies and is very slowly metabolised by the body as it becomes deeply absorbed and entrenched in the body’s fatty tissues, with the brain a primary target. The complete elimination of a single dose from a user’s system may take up to thirty days (Cabral, 1989) and its acute effects can last several hours. In the case of chronic and frequent use, cannabis concentrations accumulate and can cause a chronic intoxication and dependency.

Further, the endocannabinoid system moderates many of the body’s vital functions, including motor control, cognition and memory, cardiovascular and endocrine activity, appetite, mood and immune responses. The endocannabinoid system’s regulation of these functions is fundamental to the brain’s normal performance and as such is central to understanding the pervasive effects of cannabis. THC overwhelms this system with long-lasting and extensive effects on both cannabinoid receptor type 1 (CB₁), in the brain, spinal cord and peripheral nerves; and cannabinoid receptor 2 (CB₂), in the body’s immune tissues. Physically, this means a decrease in the release of neurotransmitters, decreased neural firing and transmission of nerve impulses. The body’s natural substances which interact with CB₁ and CB₂ receptors are called anandamides. These modulators are released locally in discrete brain areas, and in contrast to THC, are rapidly de-activated in minutes.

It has also been argued that 27% of the population carry a high risk genetic variant which produces a weaker Catechol-O-Methyl Transferase (COMT) enzyme which is responsible for the break down of dopamine in the brain. Henquet (2005) argues that the excessive amounts of dopamine released by cannabis use places those with the weaker COMT enzyme at 10 times greater risk of developing psychosis and, later in life, of developing schizophrenia (see Section 4: Cannabis Harms, Mental Health).

Over 1,500 toxic chemicals have been identified in the smoke of cannabis, including carbon monoxide, carcinogens and irritants. These all greatly affect the body's respiratory and cardiovascular systems in a similar manner to the known effects of smoking tobacco. Moir et al's 2007 study of marijuana smoke found ammonia at levels up to 20-fold greater than that found in tobacco, hydrogen cyanide at concentrations 3-5 times those in tobacco smoke, and confirmed the presence of known carcinogens and other chemicals implicated in respiratory diseases.

The Institute of Medicine of Washington DC⁴ produced the table opposite, which shows a comprehensive comparison of the chemicals in cannabis and tobacco:

⁴ Sources cited by the Institute of Medicine, Marijuana and Health, Washington DC: Hoffmann, D et al, 1975; Hoffman, D et al, 1976; Brunnemann, KD et al, 1976; Brunnemann KD et al, 1977.

Table 1 – Comparison of Chemicals – Cannabis and Tobacco

A. Cigarettes			
	Units	Marijuana	Tobacco
		(85mm)	(85mm)
Average Weight	(mg)	1115	1110
Moisture	(%)	10.3	11.1
Pressure Drop	cm	14.7	7.2
Static Burning rate	mg/s	0.88	0.80
Puff Number		10.7	11.1
B. Mainstream Smoke			
I. Gas Phase	Units	Marijuana	Tobacco
Carbon Monoxide	%	3.99	4.58
	mg	17.6	20.2
Carbon Dioxide	%	8.27	9.38
	mg	57.3	65.0
Ammonia	mcg	228	199
HCN	mcg	532	498
Cyanogen (CN) ₂	mcg	19	20
Isoprene	mcg	83	310
Acetaldehyde	mcg	1200	980
Acetone	mcg	443	578
Acrolein	mcg	92	85
Acetonitrilebenzene	mcg	132	123
Benzene	mcg	76	67
Toluene	mcg	112	108
Vinyl chloride	ng	5.4	12.4
Dimethylnitrosamine	ng	75	84
Methylethylnitrosamine	ng	27	30
pH, third puff		6.56	6.14
fifth puff		6.57	6.15
seventh puff		6.58	6.14
ninth puff		6.56	6.10
tenth puff		6.58	6.02
II. Particulate phase			
	Units	Marijuana	Tobacco
TI particulate - dry	mg	22.7	39.0
Phenol	mcg	76.8	138.5
o-Cresol	mcg	17.9	24
m- and p-Cresol	mcg	54.4	65
Dimethylphenol	mcg	6.8	14.4
Catechol	mcg	188	328
Cannbidol	mcg	190	
D9 THC	mcg	820	
Cannabinol	mcg	400	
Nicotine	mcg		2850
N-Nitrosomicotine	ng		390
Naphthalene	mcg	3.0	1.2
1-Methylnaphthalene	mcg	6.1	3.65
2-Methylnaphthalene	mcg	3.6	1.4
Benz(a)anthracene	ng	75	43
Benzo(a)pyrene	ng	31	21.1

INCREASED POTENCY

Of particular concern in recent years is the cultivation of high potency cannabis, often referred to as “skunk” or “super skunk”⁵. This increase in potency, which in real terms refers to increased THC concentrations, is in addition to the existing hybrid varieties of cannabis which are continuing to gain popularity in Australia. High potency cannabis, or cannabis containing high THC concentrations, is currently cultivated in all states of Australia, largely through the use of hydroponics cultivation, and is also brought into Australia from countries such as Papua New Guinea, India, Lebanon, Morocco, Holland, Afghanistan, Thailand and Canada.

The effects of THC in the cannabis user, including those which are negative, are dose-related – the higher the dose of THC, the greater the effects – hence, the significance of increased cannabis potency (Raemaekers, 2006).

It is important to note that some publications dated as recently as 2006, be treated with caution on this matter, as the evidence base has now substantially changed. For example, the Australian National Council on Drugs (ANCD’s) position, outlines in the papers “*Cannabis: answers to your questions*” (2006) and “*Evidence-based answers to cannabis questions: a review of the literature*” (2006), is that in the past few decades Australia has only seen small increases in THC levels.

Of interest is the fact that, more than a decade ago, the Australian Bureau of Criminal Intelligence (1993) reported a THC content in cannabis plants of up to 30%, a substantial increase from the early 60’s when the typical cannabis joint contained as little as 0.5%. One example of our concerns regarding the increase of potency of cannabis in Australia is that of ‘Drug Kingpin’, Alexander Malcolm Lane, who used drug mules, paying up to \$30,000 a trip to travel to Amsterdam and bring back thousands of high-potency cannabis seeds.

The Courier-Mail August 17 2007. <http://www.news.com.au/story/0.23599.22257426-2.00.html>

In both the United States (US) and United Kingdom (UK) public offices have acknowledged THC potency increases. A joint report of the US’s Office of National Drug Control Policy (ONDCP) and the National Institute on Drug Abuse recently found that levels of THC in cannabis have reached the highest-ever levels since analysis of the drug began in the late 1970’s. They found the average to have increased from just below 4% in 1983 to a new high of 9.6% in 2008, a doubling of potency. John Walters, former Director of ONDCP, states “Baby boomer parents who still think marijuana is a harmless substance need to look at the facts. Marijuana potency has grown steeply over the past decade, with serious implications in particular for young people”.

The UK’s Home Office “Cannabis Potency Study 2008”, while finding a lesser increase over time (from 13.98% to 15.0%), nevertheless presents a startling average percentage of THC content at 15% potency. These figures, while not based on Australian data, cannot be ignored. It would be imprudent to assume the increases in potency seen in overseas cannabis markets are not mirrored within Australia.

⁵ See Appendix A and Appendix B for media reports

When it is considered that there is a well-demonstrated dose-response relationship between cannabis and its related drug-induced psychosis, where the greater the amount of cannabis consumed correlates to a higher degree of risk of psychosis, any three to fourfold increase in potency is absolutely critical in any assessment of cannabis harms.

When it is further considered that changed usage patterns, whereby young users smoke only the multiple potent heads of the cannabis plant and also use a more concentrated mode of drug delivery via the use of 'bongs', the ANCD paper's approach to potency is of concern. By emphasising their assessment of a narrow understanding of the thirty-fold claim, which makes three to fourfold increases pale into insignificance, the very significant conjuncture of these real and significant three to fourfold increases in cannabis potency, along with new usage patterns which deliver significantly higher doses of cannabinoids, is downplayed for the Australian reader at the very time that the scientific community has expressed alarm at this very same conjuncture and its relationship to psychosis. Concluding their discussion in ANCD Research Paper (2006, p.11), the authors cite US figures which do in fact show increases in potency which have more than tripled:

"Between 1980 and 1997 THC content increased from 1.2 per cent to 4.2 per cent. Cannabis samples (excluding hash and hash oil) analysed between May and August 2003 had average THC levels of 6.37 per cent (see 1.2 for details on potency for different forms of cannabis). This finding suggests definite rises in cannabis THC content. However, over the last two decades, such increases are not consistent with claims of a thirty-fold increase. While Australia has not collected such comprehensive data, moderate changes as seen in the United States and New Zealand data are likely to be replicated in Australian trends given that, with isolated exceptions, the majority of THC levels in studies of cannabis seizures have remained under 5 per cent."

GATEWAY DRUG

The term “gateway drug” is used to illustrate the tendency of cannabis to introduce the user to other illicit drugs, and arguments for and against the hypothesis have a long history.

There are multiple studies that have reached a conclusion in support of the gateway hypothesis (see Kandel, 1992 and 1996; Clayton, 1992; Bailey, 1992; Poikolainen et al, 2001). Specifically, the Centre on Addiction and Substance Abuse (CASA) at Columbia University found that children who use drugs, including cannabis, are up to 266 times more likely to use cocaine than those who do not use any of the gateway drugs identified (cannabis, tobacco and alcohol).

There are critics of the gateway theory who argue that a clear link between cannabis use and other illicit drugs does not reflect a causal sequence, relying upon the presence of confounding factors such as a user’s socio-economic status and family history (see Johnson, 1973; Hays et al, 1987).

In contrast, the US Office of National Drug Control Policy’s “2008 Marijuana Sourcebook” clearly states that recent research supports the gateway hypothesis, specifically that “its use creates greater risk of abuse or dependency on other drugs, such as heroin and cocaine”.

Further, a study on 311 sets of same-sex twins, in which only one twin smoked cannabis before age 17, found that early cannabis smokers were up to five times more likely than their twin to move on to harder drugs (Lynskey, 2003). Also, Hurd (2006) concluded that findings supported the gateway hypothesis when she conducted a study on rats. Hurd found that rats trained to self-administer heroin would administer greater doses if they had previously been exposed to THC. A further study of 75,000 adolescents and young adults found teenage cannabis smokers had a 50% higher risk of developing an alcohol-use disorder and specifically stated “Addictive drugs all act on a part of the brain that is described as the central reward circuitry. Once this system is exposed to one drug, the brain may become more sensitive to the effects of other drugs, as demonstrated by a number of rodent studies” (Gruzca, 2006).

In summary, as Kandel states (1992), very few try illicit drugs other than cannabis without prior use of cannabis.

(Behrendt 2009) results revealed several interesting findings. First and foremost, early onset users were shown to have an elevated risk of substance use disorder, even if the transition to substance use disorders was not immediate. The transition from first cannabis use to cannabis dependence occurred more rapidly than transitions to alcohol disorders and nicotine dependence. Substance use onset later in adolescence was associated with a more rapid progression to substance use disorders for alcohol and nicotine. Overall early onset of substance use was not shown to lead to a rapid progression of substance use disorders. But delaying first substance use is still important.

DEPENDENCE

There is general consensus that cannabis is addictive and the addiction carries with it all the adverse affects of dependence, including symptoms of withdrawal (see Ramstrom, 2003, in *A Survey of Scientific Studies*).

In fact, in 1992 the World Health Organisation (WHO) identified cannabinoid dependence syndrome and described that dependence as existing where three or more of the following diagnostic guidelines were experienced or exhibited during a year:

- a) a strong desire or sense of compulsion to take cannabinoid;
- b) difficulties in controlling cannabinoid-taking behaviour in terms of its onset, termination or levels of use;
- c) a physiological withdrawal state when cannabinoid use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for cannabinoid; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
- d) evidence of tolerance, such that increased doses of cannabinoid are required in order to achieve effects originally produced by lower doses;
- e) progressive neglect of alternative pleasures or interests because of cannabinoid use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
- f) persisting with cannabinoid use despite clear evidence of overtly harmful consequences, such as depressive mood states consequent to periods of heavy substance abuse, or drug-related impairment of cognitive functioning; and
- g) efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

Haney et al (1999) demonstrated withdrawal symptoms from pure THC delivered under laboratory conditions in humans and those symptoms such as anxiety and insomnia lead to difficulty in stopping cannabis use.

Budney et al (2004) reviewed the validity of cannabis withdrawal syndrome and concluded that the evidence of laboratory and clinical studies indicates that withdrawal syndrome reliably follows discontinuation of chronic cannabis use and further noted that the severity of withdrawal symptoms appeared substantial.

Later, in 2006, Budney & Hughes found evidence of a withdrawal syndrome in cannabis use and noted “demand for treatment of cannabis dependence has grown dramatically (and) the majority of people who enter treatment have difficulty in achieving and maintaining abstinence from cannabis”. They found laboratory studies had established the reliability, validity and time course of a cannabis withdrawal syndrome and pointed to the discovery of an endogenous cannabinoid system, the identification of cannabinoid receptors and demonstrations of precipitated withdrawal with cannabinoid receptor antagonists as the neurological basis for cannabis withdrawal.

In a wide ranging appraisal of the literature, Gardner reviewed 224 scientific papers in 2003 and concluded “cannabinoids act on the brain reward processes and reward-related behaviours in strikingly similar fashion to other addictive drugs”.

Budney (2006) also asked if specific dependence criteria were necessary for different substances in a report for *Addiction* and found that “cannabis dependence is much more similar to, than different from, other types of substance dependence, even with regard to withdrawal”.

Vandrey (2008) more recently suggested withdrawal from cannabis use is similar to that experienced when quitting smoking tobacco, in a controlled comparison based on the self-reporting of twelve heavy users of both cannabis and tobacco. The participants’ abstinence was confirmed objectively, procedures were identical during each abstinence period and abstinence periods occurred in a random order. The strength of this study is in the same participants reporting on withdrawal symptoms for tobacco and marijuana, eliminating the likelihood that results reflect physiological differences between subjects.

Vandrey found that “since tobacco withdrawal symptoms are well documented and included in the DSM-IV⁶ and the ICD-10⁷, we can infer from the results of this comparison that marijuana withdrawal is also clinically significant and should be included in these reference materials”.

Also, Cambridge University Press recently published “Cannabis Dependence: Its Nature, Consequences and Treatment” (2006), a report on over 2,500 adult daily cannabis users where 1, 111 adults met the DSM-IV criteria for dependence and reported significant associated problems, such as depression and lower levels of motivation and satisfaction with life.

Coffey et al (2003) related dependence to a user’s starting age and reported that weekly use of cannabis marks the threshold for an increased risk of later cannabis dependency, specifically amongst young users. Coffey et al reported “30% of teenagers smoking more than once a week became addicted by their early twenties, those between 14 and 17 were twenty times more likely”.

Interestingly, dependent cannabis users reported compulsive and out-of-control use more frequently than dependent alcohol users, withdrawal to a similar extent and tolerance considerably less often.

Chambers’ study (2003) supported the increased vulnerability of adolescent brains to addiction compared to adults. He suggested that drug addiction should be thought of as a development disorder in the brains of teenagers, in that the adolescents’ changing brain circuitry leaves them especially vulnerable to the effects of addictive drugs.

⁶ Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

⁷ International Classification of Diseases, 10th Edition

Finally, *Science Threads of Addiction, Substance Use and Health* (STASH January 2007) looked at the transition from drug use to dependence in over 8,000 participants. They found the probability of drug initiation and developing dependence both peaked at 18. Interestingly, male users were found to be approximately twice as likely to develop dependence in the first two to five years as female users.

SECTION TWO: CANNABIS HARMS

INTRODUCTION TO THE ADVERSE HEALTH CONSEQUENCES OF CANNABIS

Sweden was the first country in the world to extensively research the evidence on the adverse health consequences of cannabis use and has since adopted a strategy of community wide information sharing regarding the health hazards posed by the drug. Renowned psychiatrist Jan Ramstrom has compiled extensive reviews for the Swedish National Board of Health Welfare (in 1998) and National Institute of Public Health (in 2003) on the health implications of cannabis use. A result of Ramstrom's reviews was the report "*Adverse Health Consequences of Cannabis Use*", which provides outlines of mental disorders, physical injury, psychological and psychosocial injury. More recently in the United Kingdom, Brett (2008) produced "*Cannabis – A General Survey of its Harmful Effects*" in a review of the ever-widening range of negative effects upon health caused by the substance, including childhood development, mental illness and cognitive functioning.

In this section we shall discuss only a limited portion of the available literature on adverse health consequences in three primary areas including mental health, brain function and physicality.

MENTAL HEALTH

The harms of cannabis use on the user's mental health have been well documented and include specific research into the onset of schizophrenia (see Boydell, 2006; Solowij, 2007; Fergusson, 2005; Ferdinand, 2005, Veling 2008) and other mood disorders including depression, bi-polar disorder and amotivational syndrome (see Bovasso, 2001; Hayatbakhsh, 2007; Corcoran 2008). Research has also explored the links to suicide, especially in young people (Dervaux, 2003; Greenblatt, 1998; Beautrais, 1999).

Firstly, severe mental disturbances, such as momentary short-term psychosis or the long-term illness of schizophrenia, have been linked to cannabis use and especially so when cannabis use begins in adolescence. As a stimulant of the dopamine system, cannabis offers the user a pleasurable 'high'; however, this 'high' can become dangerous when dopamine levels become excessive. Murray (2005) discusses the impact of early cannabis use on the developing adolescent brain and specifically dopamine receptors, indicating early cannabis use may damage these receptors permanently, leaving a young cannabis user at a much higher risk of developing schizophrenia or experiencing psychosis.

A significant study in Sweden (Andreasson, 1987) examined, over fifteen years, the link between heavy cannabis use and schizophrenia in 50,087 members of the Swedish Army and conclusively found schizophrenia occurred more frequently in heavy consumers of cannabis.

The results were re-analysed and replicated in additional studies (Zammit, 2002; Fergusson, 2003) with the British Medical Journal (BMJ) reporting in 2002 heavy consumers of cannabis at age 18 were over 600% more likely to be diagnosed with schizophrenia over the next fifteen years than those who did not use cannabis. The BMJ report also clarified that it was cannabis use and not other drugs that was associated with schizophrenia.

Moore et al concluded in 2007, that “there is now sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life”. In fact, Moore et al found, in a review of 35 longitudinal studies that cannabis use increased the risk of developing a psychotic illness, such as schizophrenia, by 40%. This figure was doubled for frequent or heavy users. Reports by Hollis et al (2008); Henquet (2005) and Konings (2008) have found a significant positive association between cannabis use and mental health disturbance in young people who are genetically predisposed to mental health problems, such as schizophrenia.

Interestingly, Ramstrom (2003) demonstrated the association between adolescent cannabis use and adult psychosis persists even after controlling for many potential confounding variables, such as low IQ and education levels, unemployment, social integration, gender, age, ethnic group, tobacco smoking and previous psychotic symptoms. This finding was supported by recent studies of Finnish adolescents (Jouku et al, 2008) which showed an association between cannabis use and psychosis symptoms not caused by other drug use, family background or behavioural problems.

Further, researchers in Spain recently found a strong and independent link between cannabis use and the onset of psychosis at a young age, reporting that compared with nonusers, the age of psychotic onset was lowered by 7, 8.5 and 12 years among users, abusers and dependents respectively. These results are supported by multiple studies (Fergusson, 2005; Ferdinand, 2005; Solowij, 2007) and all highlight the notion of the younger the user, the worse the effects.

A second mental health issue frequently associated with cannabis use is depression and numerous studies support the connection.

For example, an Australian study of 3,239 young adults, from their birth to the age of 21, found a relationship between early initiation to and frequent use of cannabis and depression (Hayatbakhsh, 2007); a 16-year study of individuals not initially suffering from depression, but who then frequently used cannabis, were found to be four times more likely to develop depression at follow up (Bovasso, 2001); and, Fergusson (2002) studied 1,265 children over a 21-year period and concluded that cannabis use, particularly heavy or regular use, was associated with a later increase in depression and suicide. Recent articles in *The Age* newspaper (September 29, 2008) discuss Australian statistics showing that cannabis' toll on mental health, expressly causing depression, is more prevalent than that caused by the well known impact of amphetamines.

Thirdly, cannabis use can induce amotivational syndrome, a mental state characterised by apathy, an inability to carry out plans, deal with frustration or concentrate for any length of time (Cohen, 1982). While equivocal, amotivational syndrome strikes a chord in that it aptly describes the 'personality' of a chronic cannabis smoker and is supported by numerous studies (Newcomb & Bentler, 1988; Tunving, 1987; Cohen, 1982). Musty & Kaback (1995) maintain that amotivational syndrome exists and is a manifestation of depression.

Finally, multiple studies have linked cannabis use with suicide⁸. A study by Beautrais et al (1999) examined and found a relationship between cannabis abuse and suicide. Greenblatt (1998) found that young people, aged 12 to 17, who smoke cannabis weekly are three times more likely than non-users to have thoughts about committing suicide, and this ratio was confirmed by Lynskey et al (2004). Dervaux (2003) examined the link between cannabis abuse and the suicide attempts of schizophrenics, finding a close correlation.

⁸ See Appendix B for media articles on this issue

It is undeniable that cannabis affects the brain, and affects the brain's functioning adversely. Conclusive evidence shows that heavy marijuana use for five years or more may impair memory and slow cognitive function (Lambros, 2006; Ashtari, 2005; Robbe, 2006; Karila, 2005; Lundqvist, 2005; Fisk 2008; Solowij, 2008), with specific research completed on impaired driving ability (Kurathaler, 1999; Menetry, 2005; Drummer, 1994, 1998, with Gerostamoulos, 1999).

The short-term effects of cannabis use on brain function can include things such as problems with memory and learning, difficulty in thinking and problem solving, loss of coordination. Long-term effects include permanent memory impairment and overall slower cognitive function.

Importantly, Chambers (2003) and Pistis (2004) found the adolescent brain, while still under development, was particularly vulnerable to the ill effects of substance abuse, including cannabis. Researchers have concluded that repeated exposure to cannabis as an adolescent was related to abnormalities in the development of the specific fibres associated with higher aspects of language auditory functions (Ashtari, 2005). Giedd et al (1999) also discusses the development of the adolescent brain which does not reach physical maturity until the mid-twenties, and warned drug abuse could alter the normal course of brain growth. He later specifically looked at regions of the brain that control impulse and risky behaviours, reconfirming his previous findings that cannabis use on a developing adolescent brain can negatively affect overall and specific brain functions. In a study of brain abnormalities in schizophrenics as compared to the brain abnormalities presenting in adolescents frequently using cannabis, Kumra (2007) concluded the deficiencies were the same and in that part of the brain which develops during adolescence – emotional associations and other higher cognitive functions such as language, perception, creativity and problem solving.

Most recently, Medini et al (2008) confirmed the adverse brain impact of adolescent cannabis use in a study presented to the American Academy of Pediatrics. The research team found that the chronic use of cannabis during adolescence – a critical period of ongoing brain development – slowed psychomotor speed, led to poorer complex attention, verbal memory and also planning ability. Perhaps, most startlingly, these impacts continued after one month's abstinence from cannabis use.

Recent evidence on cannabis and cognitive functioning also comes from Greece (Messinis et al, 2006) where they found that those who smoked at least four joints per week for several years performed significantly worse than non-users in several areas, particularly verbal learning (the ability to remember previously learned words) and executive functioning (organising and coordinating simple tasks). Further, Ranganathan (2006) reviewed the literature on the acute effects of cannabis on memory, concluding that cannabinoids impair all stages of memory (including encoding, consolidation and retrieval).

Solowij et al (2002) examined the effects of the duration of cannabis use on specific areas of cognitive functioning among users seeking treatment for cannabis dependence. Their results also confirmed that long-term heavy cannabis users show impairments in memory and attention, and in fact that endure beyond the period of intoxication and with increasing years of regular cannabis use. Bolla (2002) found a dose-response relationship in that the more cannabis used, the worse they performed in cognitive testing, especially memory. It is very clear that regular cannabis use is associated with impaired functioning – both by objective measures and by the admission of users themselves (Pope Jr, 2004).

Alternate studies (Niveau & Dang, 2003; Howard & Menkes, 2007) also looked at the effects of cannabis use upon neural mechanisms controlling impulse and found a connection with acts of violence and aggression. Additionally, the latest evidence of brain abnormalities in long-term, chronic cannabis users further confirms that heavy daily use exerts harmful effects on brain tissue (Yucel, 2008) and in similar ways to those seen after long-term abuse of other major drugs (de Fonseca, 1997).

Specific research on the impacts of cannabis on driving ability has increased of late. Drummer (1994; 1998; with Gerostamoulos, 1999) has done significant research on the issue and found road fatalities related to cannabis intoxication have steadily increased over the last ten years. Consistent with Drummer's findings, past research examining the effects of THC on driving ability indicate it impairs both car control (Moskowitz, 1985) and the driver's awareness of the vehicle's position in traffic (Ramaekers et al, 2000). Hansteen et al (1976) also found THC intoxication is more likely to result in collisions with obstacles on a driving course than when not intoxicated. Studies by Papfotiou (2001, 2005) found that driver errors occurred more frequently when the driver was under the influence of both cannabis and alcohol. Since the two are frequently taken together it is concerning to note that a 2005 study (Laumon et al) found the risk of accident when cannabis was combined with alcohol was 16 times higher than when using either drug alone.

These findings indicate that cannabis impairs driving ability and given the prevalence of cannabis use (upward of 300,000 Australians smoke it daily; 750,000 smoking it weekly⁹) this poses a significant risk on our roads.

⁹ Australian Institute of Health and Welfare 2005. Statistics on drug use in Australia 2004. AIHW Cat. No. PHE 62. Canberra: AIHW (Drug Statistics Series No. 15). p 22

PHYSICAL HARMS

Cannabis smoke contains many of the same known carcinogens as tobacco smoke. In fact, studies have found the tar from cannabis contains 50% more of some of the carcinogens found in tobacco, notably benzopyrene, a potent carcinogen and key factor in the development of lung cancer (Hoffman et al, 1997; Tashkin et al, 1997; Novotny et al, 1976; Leuchtenberger et al, 1983), and so it should not be surprising to see cannabis use as a factor in a wide range of adverse physical conditions, including lung cancer, chronic obstructive pulmonary disease, increased risk of heart or stroke due to adverse impacts on the cardiovascular system, weakened immune system and birth defects. Cannabis cigarettes also have a higher combustion temperature than tobacco cigarettes.

There is research to support the connection between cannabis use and cancer of the digestive and respiratory tracts (Hall, 2002), lung cancer (Berthiller 2008), lung (Sridar, 1994) and breast (McKallip, 2005). Aldington (2007; et al, 2008) found that long term cannabis use specifically increased the risk of lung cancer in young adults, particularly in those who started smoking cannabis at a young age. Tashkin (2006) explains that cannabis smokers typically hold their breath four times longer than tobacco smokers, allowing more time for particles to be deposited in the lungs. In addition, cannabis is usually smoked without an adequate filter.

Researchers have interviewed lung cancer patients in seeking to identify the main risk for the disease, such as smoking habits, family history and occupation (Tetrault et al, 2007). The patients were questioned about cannabis consumption and results showed lung cancer risk rose by 5.7 times for patients who had smoked a joint a day for 10 years, or two joints a day for five years, and after adjusting for cigarette smoking.

A study in 2006 (Terris et al) reported that, of 52 men with transitional cell bladder cancer, 88.5% had a history of smoking cannabis and almost 31% were still using the drug. Terris et al found that cannabis metabolites have a half-life in urine about 5 times greater than tobacco metabolites, and warned smoking cannabis may be a more potent stimulant than tobacco smoking of malignant cell transformation, a hallmark of cancer.

In relation to chronic obstructive pulmonary disease (COPD), the period of cannabis use seems to play an important role, particularly in regard to lung emphysema and various other respiratory complications such as asthma, dyspnea, pharyngitis and chronic cough (Tetrault et al, 2007). Beshay (2007) researched emphysema in young adults and agreed the period of cannabis use was influential. A further study Tan (2007) on people aged 40 and over found that smokers were two and a half times as likely as non-smokers to develop COPD and that adding cannabis to tobacco increased the risk again by one-third.

With regard to the body's cardiovascular system, the harms of cannabis use are again significant. At first, the intoxication produced by cannabis causes an increase in heart rate of between 20% and 50% (Huber et al, 1988; Jones, 1984) as THC increases the production of chemicals which stimulate the heart.

The increase in heart rate caused by cannabis is additive with the increased heart rate caused by nicotine in tobacco. THC is also found to have analgesic properties, lessening chest pain which Jones (1982, 1984) argues may delay the seeking of treatment, decrease the supply of oxygen to the heart and place it under greater strain. Maykut (1984) also found a rise in blood pressure if the person is sitting or lying, but upon standing drops drastically, in some cases causing the person to faint.

It must be added that tolerance can develop quickly to the acute cardiovascular effects of cannabis, with people receiving daily doses by mouth developing tolerance within 7 to 10 days, in a possible explanation of why effects can sometimes be missed (Benowitz & Jones, 1975; Nowlen & Cohen, 1977; Jones, 1984).

Supporting research as to the cardiovascular harms of cannabis use are found in Herring et al (2001), who used sound waves to measure cerebral artery blood flow resistance and found that prolonged cannabis use in 18 to 30 year olds increased the resistance in arteries and restricted blood flow to the brain; in Geller et al (2004) who detail an incident in which three teenagers, aged 15 to 17, “binge smoked” cannabis and suffered strokes from which two later died; and, in Mittleman (2001) who interviewed 3,882 patients of heart attacks and found the risk of myocardial infarction rose almost 5 times in the hour following the smoking of a joint.

We still do not know the long term effects of exposure to cannabis smoke on the cardiovascular system over extended periods, but experience with the problems of tobacco smoke should urge caution. Jones (1984) suggests “after years of repeated exposure, there may be lasting, perhaps even permanent alterations of the cardiovascular system function. There are enough similarities between THC and nicotine’s cardiovascular effects to make the possibility plausible” and this is supported by a multitude of research (Mukamal et al, 2008; Lindsay, 2005; Fisher et al, 2005; Korantzopoulos, 2008).

There is also significant supporting research on the effects of cannabis use during pregnancy on newborns, with THC readily crossing the placenta (Bada, 2006; Cornelius, 1995; Bailey, 1987) – Bluhm (2006) discusses an increased risk of neuroblastoma; Robinson et al (1989) identified an eleven-fold increase in leukaemia; and, there are multiple abnormalities in physical appearance, size, weight and hormonal functions discussed by Fried, 1980 and 1984; Zimmerman, 1991; Zuckerman, 1989; Barnett, 1983; El Marroun 2008; Mendelson, 1985 and 1986).

A paper by Klonoff-Cohen et al (2006) studied the effects of cannabis use on the outcomes of IVF and GIFT fertility treatments and concluded cannabis use lowered the prospects of successful treatments. They found females produced fewer eggs and the child once successfully conceived had a significantly lower birth weight.

The risk of miscarriage of ectopic pregnancy of women smoking cannabis in the early stages of pregnancy was highlighted in recent research by Day (2006). THC was found to mimic anandamide and its control over embryo development, disrupting the process and creating cell abnormalities in mice. Day also concluded that, “Prenatal exposure to marijuana, in addition to other factors, is a significant predictor of marijuana use at age 14”.

This study's findings warrant further attention to puberty as a sensitive period in an individual's development. With regards to prevention, there is a need to understand more about the pathways between pubertal development, child behaviour and substance and cannabis use. (Hayatbakhsh, 2009).

A review by Huizink & Mulder (2006) came to the conclusion that pre-natal exposure to cannabis use is related to some common neuro-behavioural and cognitive outcomes, including symptoms of ADHD such as inattention and impulsivity, decreased general cognitive functioning and deficits in learning and memory tasks.

Barros and colleagues, writing in *The Journal of Paediatrics* in January 2007, found that marijuana-exposed infants born to adolescent mothers scored differently on measures of arousal, regulation and excitability compared to non-exposed infants, where they displayed subtle behaviour changes in the first few days of life, i.e. they cried more, startled more easily and were more jittery. The authors said this may also interfere with mother-child bonding.

Harkany et al. (2007) found that endocannabinoid signalling modulates central nervous system patterning, so that "pharmacological interference with endocannabinoid signals during foetal development leads to long-lasting modifications of synaptic structure and functioning. Marijuana abuse during pregnancy can impair social behaviours, cognition and motor functions in the offspring with the impact lasting into adulthood".

Another paper in May 2007 had similar findings. Endocannabinoids in the human body play a vital role in the development of a baby's brain in that they are responsible for controlling how the complex system of nerves develop in the embryonic brain. Dr Ann Rajnicek states "Smoking cannabis could interfere with the signals that are being used in the brain to wire it up correctly in the first place. As the brain develops further, there will be functional problems – potential brain damage" (Berghuis et al. 2007).

The reason for the late appearance of this damage is assumed to be that the functions involved are "executive" cognitive functions that are not taken into use until the child is four to six years old. Another long-term study shows similar associations between exposure during the foetal stage and relatively late (at age 6 and 10 respectively) behavioural disturbances (Ramstrom, 2003).

SECTION THREE: QUITTING CANNABIS

It is not only important to have strategies to help people quit cannabis but prevention must be the aim of the policy makers. Student drug testing is intended as prevention and as a deterrent. It offers young people a tool to refuse drugs among their peers. Student drug testing, which include anonymity, privacy, non-coercion, also encourages families to seek help for their children in need. (McKinney 2005, DuPont 2002, Ticker 1997, Goldberg 2007).

While it is acknowledged that it is far easier and less expensive to adopt preventative measures than invest in treatment, for those who are addicted to cannabis, it is important to provide the means to be able to stop – just as we have seen implemented with other common drugs such as tobacco and alcohol. This section discusses symptoms, the need for treatment, effective treatment techniques and the high incidence of relapse.

Contributors to “*Cannabis Dependence, Its Nature, Consequences and Treatment*” state the symptoms of cannabis withdrawal are “irritability, anger, nervousness, sleep difficulty, change in appetite, physical discomfort” (2006) and Kouri (1999) found previous reports of an abstinence syndrome associated with chronic marijuana use were confirmed and also suggested aggressive behaviour as a component. There is also research to suggest staying clean for cannabis addicts is as hard as for heroin addicts (Roffman, Stephens, Marlatt, 2006).

Extensive research has found a connection between early cannabis use and the likelihood of need for treatment (Kandel & Yamaguchi, 1985; Robins & Przybeck, 1985; Adams & Gfroerer, 1988; Glantz & Pickens, 1992; Anthony & Petronis, 1995).

There is a need for effective treatment of cannabis misuse. Psychological therapies have been developed based on principles of motivational interviewing, cognitive-behavioural therapy and relapse prevention. The evidence base for these therapies is explored in a review by Maddock & Babbs (2006), and studies targeting both adult users and young people are considered. They also discuss new pharmacological treatments.

Increased recognition that marijuana can cause addiction and significant negative consequences in a subset of users has prompted the development of marijuana-specific interventions and treatment materials paralleling those for other substance use disorders. These advances have increased users’ and caregivers’ perceptions that it is acceptable to seek and provide treatment for cannabis use and have contributed to an increase in the number of individuals requesting help (Budney, 2007). In light of the recognition that people smoke cannabis mainly for pleasure (euphoria/“high”) it is noted that none of the available treatments are highly effective.

The Substance Abuse and Mental Health Services Administration (SAMHSA) released a treatment manual titled “Brief Counselling for Marijuana Dependence – a Manual for Treating Adults” and outlined procedures for individuals who use cannabis as their primary drug. The manual suggested chronic cannabis users tended not to seek treatment in traditional drug treatment settings, but that when given the opportunity would respond positively.

Increasing evidence suggests that counselling for cannabis dependence is effective (Steinberg et al, 2002; SAMHSA, 2005).

Clients in treatment require a sense of hope and positive expectations are especially critical when facing a protracted period of withdrawal (Zweben & O'Connell, 1992). Programs designed to aid cessation should focus on the negative effects of marijuana and should offer alternative ways to relieve negative physical and psychological conditions such as stress (Weiner, 1999).

Professionals working with cannabis dependent people often see them relapse repeatedly. Relapse may involve the length of detoxification; ease of access to the substance; social pressures in schools, work, entertainment, social and family settings; persistent denial; or the high level of functioning many addicts have when they enter recovery. Marijuana addicts who have not previously shown extensive drinking histories often believe they can consume alcohol and this can lead to a cannabis relapse (Chacin, 1996). Budney et al (2002) found clinical trials evaluating treatment for cannabis dependence suggest that the withdrawal syndrome, like other substance dependence disorders, is responsive to intervention but the majority have difficulty achieving and maintaining abstinence.

In recent years, multiple sources have released suggested treatment programs, ranging from counselling treatments for adults (SAMHSA, 2005), intervention programs (Maddock & Babbs, 2006) and specific treatment programs developed for women (Chacin, 2006). The work of Roffman & Stephens (2006) and Budney et al (2007) also discuss treatment options and are recommended reading on the topic.

SECTION FOUR: RECOMMENDATIONS

The evidence is clear that the younger the age of initiation to cannabis use, the greater the risk of harmful effects to the individual. The following recommendations aim to provide advice and strategies to politicians, decision-makers and researchers to ensure that the level of cannabis use in Australia is markedly reduced, within the next few years.

Drug Free Australia's research recommends:

1. That all Australian Governments urgently implement effective preventative drug education in all States and Territories, focusing on education, in both primary and secondary schools that includes the latest scientific research into the harmful effects of cannabis on the developing brain, together with information on issues related to the risk of suicide, drug-induced psychosis, schizophrenia and depression.
2. That the Federal Government urgently implements a national media campaign, similar to the "Bloody Idiot" alcohol campaign, in order to inform the community of the harmful effects of cannabis use on all community members. This would be an appropriate response to the concerns of the Australian community, as measured in the Pfizer/NDARC report of 2007, in which 77% of Australians expected the government to run a public health campaign alerting the public to the harms of cannabis.
3. That clear cannabis prevention policies be issued by the Commonwealth Department of Health and Ageing, to be implemented in all schools and further, that these be regularly updated and reinforced.
4. That Federal, State and Territory police are resourced to implement NOAH (Narcotics, Opiates, Amphetamines, Hashish 1992) blitzes every three months for a two year period. This should target users and potential users; it should deal with plantation and hydroponically grown cannabis, trafficking, financing, and/or selling drugs to children. Further, that the Proceeds of Crime funds be used to continue a NOAH cannabis campaign after the two-year period.
5. That all professionals working in drug and alcohol fields be required to strongly discourage any cannabis use by those whom they counsel or to whom they provide treatment for drug related problems.
6. That the Federal and all States and Territory Governments resource and conduct a long-term cannabis QUIT campaign, to be organised and implemented along lines similar to the successful "QUIT Tobacco" campaign. Further, that the Cancer Council of Australia be encouraged to promote the message that cannabis has carcinogenic properties that cause the same adverse health consequences as tobacco.

7. That greater penalties be introduced to prosecute suppliers and traffickers of drugs to children while young offenders be directed toward compulsory treatment rather than jail.
8. That clear messages about the harmful effects of cannabis on the young body should be issued by the Commonwealth Department of Health and Ageing with the cooperation of the State and Territory Governments be used in all schools and be constantly reinforced.
9. That recommendation Number 70 of the report to the *Ampe Akelyernemane Meke Mekarle* "Little Children are Sacred" Inquiry be fully implemented. This recommends that government develop and implement a multi-faceted approach to address the abuse of illicit substances in Aboriginal communities, in particular cannabis. This approach to include strategies for prevention, intervention and enforcement strategies which:
 - a) Recognise the geographic context of substance abuse, which occurs in both urban and remote locations, and its implications; and
 - b) Are population-based, youth-focused and integrate substance abuse, mental health and other health and welfare concerns into youth programs.
10. That drug testing in schools be encouraged, giving a clear message that drug use including cannabis, is not permitted. Many youngsters do not see cannabis as a drug or that it will harm them.
11. That roadside testing be implemented to identify drug-driving and related safety issues, in all States and Territories.

REFERENCES AND SUGGESTED ADDITIONAL READING

- Adams IB, Martin BR: "Cannabis: pharmacology and toxicology in animals and humans". *Addiction* **91** (11):1585-1614, 1996.
- Agrawal, A., Lynskey, M.T., Pergadia, M.L., Bucholz, K.K., Heath, A.C., Martin, N.G., & Madden, P.A. (2008). "Early cannabis use and DSM-IV nicotine dependence: A twin study". *Addiction* **103**, 1896-1904.
- Agrawal A, Madden PA, Bucholz KK, Heath AC, Lynskey MT "Transitions to regular smoking and to nicotine dependence in women using cannabis" *Drug Alcohol Depend* 2008 **1;95**(1-2):107-14
- Alan H. Jobe. MD. PhD "Marijuana effects on neurobehavior of newborns" *The Journal of Pediatrics* **149: 6:** 781-787, 2006.
- Aldington, S. 2007. "Cannabis linked to lung cancer risk" Thoracic Society conference Auckland Medical Research Institute in Wellington.
- Aldington, S., Harwood M., Cox B., Weatherall M., Beckert L., Robinson G., Beasley R. "Cannabis use and risk of lung cancer: A case-control study" *European Respiratory Journal* issue:**31**(2) 280-86 2008.
- Aldington S, Williams M, Nowitz M, Weatherall M, Pritchard A, Mc Naughton A, Robinson G, Beasley R, "The effects of cannabis on pulmonary structure, function and symptoms." *Thorax* **62:** 1058-1063, 2007.
- Alex Perkonig, Roselind Lied, Michael Hofer, Peter Schuster, Holger Sonntag & Hans-Ulrich Wittchen "Patterns of cannabis use, abuse and dependence over time: incidence, progression and stability in a sample of 1228 adolescents " *Addiction* (1999) **94**(11), 1663-1678.
- ANCD Hamilton M "Cape York Indigenous Issues" Australian National Council on Drugs 2002.
- ANCD Copeland J "Cannabis answers to your questions" Australian National Council on Drugs 2006.
http://www.ancd.org.au/publications/pdf/cannabis_qa.pdf
- ANCD Copeland J "evidence-based answers to Cannabis Questions a review of the literature" Australian National Council on Drugs 2006.
http://www.ancd.org.au/publications/pdf/rp11_cannabis_questions.pdf
- Andréasson, S., Allebeck, P., Engstrom, A., Rydberg, U., "Cannabis and Schizophrenia: a longitudinal study of Swedish conscripts", *The Lancet*, December 26, 1987, **2**(8574): 1483-1486.
- Andréasson, S., Allebeck, P., Rydberg, U., "Schizophrenia in users and nonusers of cannabis", *Acta Psychiatrica Scandinavica*, **79**, 1989, pp. 505-510.
- Anthony, J.C. Petronis, K.R., 1995. "Early-onset drug use and risk of later drug problems". *Drug Alcohol Depend.* **40**, 9-15.
- Anthony, J.C. Warner, L.A. & Kessler, R.C. (1994) "Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants:" basic findings from the National Comorbidity Survey, *Experimental and Clinical Psychopharmacology*, **2**, 244-268.
- Andrew J. "Psychiatric effects of cannabis". *British Journal of Psychiatry* **178**, 116-122 2001.
- Arendt M, Rosenberg R, Foldager L, Perto G, Munk-Jorgensen P., "Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases. *Br J Psychiatry* 2005; **187**; 510-5.
- Arseneault L Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. "Cannabis use in adolescence and risk for adult psychosis: Longitudinal prospective study" *BMJ*: **325**:1212-3 2002.
- Arseneault, L., Cannon, M., Witton, J Murray Robin M., et al "Causal association between cannabis and psychosis: examination of the evidence" *British Journal of Psychiatry.* **184**, 110-117 2004.
- Ashtari M, Kumra S "Brain Imaging-Cannabis and Schizophrenia look similar" presentation to the 91st scientific assembly radiological society of North America (RSNA) 2005.
<http://www.schizophrenia.com/sznews/archives/002708.html>
- Ashton, C.H. (7) "Adverse effects of cannabis and cannabinoids", *British Journal of Anaesthesia* **83** (4) 1999. pp 637-649. 1999.
- Australian Bureau of Criminal Intelligence, 1993 Australian Drug Intelligence Assessment, "Suicide/Schizophrenia Consequences of acute and chronic cannabis use" 1996 p. 22.
- Australian Crime Commission (Illicit Drug Data Report 2005/6 Cannabis
http://www.crimecommission.gov.au/content/publications/iddr_2005_06/Cannabis.pdf
- Australian Federal Police: http://www.afp.gov.au/site_search? Cannabis.
- Bada HS, Reynolds EW, Hansen WF. "Marijuana use, adolescent pregnancy, and alteration in newborn behavior: how complex can it get?" *J Pediatr* 2006 Dec;**149**(6):742-5.

- Bailey S L, Flewelling R L, and Rachal J V. "Predicting continued use of marijuana among adolescents: the relative influence of drug-specific and social context factors." *Journal of Health and Social Behavior*. 1992; **33**:51-66.
- Bailey EL, Swallow BL. "The relationship between cannabis use and schizotypal symptoms" *Eur Psychiatry*. (2):113-4 2004.
- Bangalore S.S, Prasad K M.R., Montrose D.M, Goradia D.D, Diwadkar V.A, Keshavan M.S "Cannabis use and brain structural alterations in first episode schizophrenia-A region of interest, voxel based morphometric study" *chizophrenia Research* 99 1-6 2008.
- BBC News: "Under 10s treated for drug abuse". Mike Linnell Oldham Lifeline Project and Jamelia Rashid Alcohol Substance Intervention Service (Oasis) 31st July 2007. <http://news.bbc.co.uk/1/hi/england/manchester/6924860.stm>
- Beautrais A.L., Joyce P. R. and Mulder R. T. "Cannabis abuse and serious suicide attempts" *Addiction* **94**(8), 1155-1164 (10) 1999.
- Benson MK, Bentley AM "Lung disease induced by drug addiction" *Thorax* **50**(11):1125-1127 1995.
- Berghuis P, Rajnicsek AM, Morozov YM, Ross R, Mulder J, Urban GM et al Hardwiring the Brain: Endocannabinoids Shape Neuronal Connectivity. *Science* 2007 May 25; **316**(5828):1212-6.
- Berthiller, J., Straif, K., Boniol, M., Voirin, N., Benhaïm-Luzon, V., Ayoub, W.B., Dari, I., Laouamri, S., Hamdi-Cherif, M., Bartal, M., Ayed, F.B., & Sasco, A.J. (2008). "Cannabis smoking and risk of lung cancer in men: A pooled analysis of three studies in Maghreb". *Journal of Thoracic Oncology* **3**, 1398-1403.
- Beshay M., Kaiser H., Niedhart D., Reymond M., Schmid R., "Emphysema and secondary pneumothorax in young adults smoking cannabis" *European Journal of Cardio-thoracic Surgery* 2007 Dec;**32**(6):834-8. Epub 2007 Oct 10..
- Bluhm EC; Daniels J; Pollock BH; Olshan AF; "Maternal use of recreational drugs and neuroblastoma in offspring: a report from the Children's Oncology Group (United States). *Cancer Causes Control*. 2006; **17**(5):663-9 (ISSN: 0957-5243).
- Bolla, K.I., et al. "Dose-related neurocognitive effects of marijuana use" *Neurology* **59** (9) 1337-1343 2002.
- Bovasso, GB. "Cannabis abuse as a risk factor for depressive symptoms". *The American Journal of Psychiatry*, **158**:2033-2037, 2001.
- Boydell J, Van Os J, Caspi A, Kennedy N, Giouroukou E, Fearon P, Farrell M, Murray RM "Trends in cannabis use prior to first presentation with schizophrenia, in South-East London between 1965 and 1999" *Psychol Med*. **36**(10):1441-6. 2006. Epub 2006 Jul 20.
- Brambilla C. Colonna M. "Cannabis: the next villain on the lung cancer battlefield?" *European Respiratory Journal* Editorial **31**: 227-228 2008.
- Brett M. "CANNABIS" A general survey of its Harmful Effects Submission to The Social Justice Policy Group 2008. <http://www.eurad.net/pdf/Cannabis%20combined%20document%20new.pdf>
- Bridget F. Grant, Roger Pickering "The relationship between cannabis use and DSM-IV cannabis abuse and dependence: Results from the National Longitudinal Alcohol Epidemiologic Survey" *Journal of Substance Abuse*, **10** Issue 3: 255-264 1999.
- British Lung Foundation "A Smoking Gun?" 2002.
- Brook, DW et al. "Drug use and the risk of major depressive disorder, alcohol dependence, and substance use disorders". *Archives of General Psychiatry*, **59**(11):1039-1044, 2002.
- Brook JS, Balka EB, BA, Whiteman B "The Risks for Late Adolescence of Early Adolescent Marijuana Use" *American Journal of Public Health* 1999; **89**(10):1549-1554.
- Budney AJ "Are specific dependence criteria necessary for different substances: how can research on cannabis inform this issue?" *Addiction* **101** (suppl. 1): 125-133 2006.
- Budney AJ, Brent A, Moore. "Development and Consequences of Cannabis Dependence" *J. Clin Pharmacol* **42**:28S-33S 2002.
- Budney AJ, Hughes JR, Moore BA, Vandrey R *Review of the validity and significance of cannabis withdrawal syndrome* *American J of Psychiatry* Nov. 2004; **161**(11):1967-77.
- Budney AJ, Hughes JR "The Cannabis Withdrawal Syndrome" *Curr. Opin. Psychiatry* **19**: 233-238 2006.
- Budney A.J., Rooffman R., Stephens R.S., Walker D "Marijuana Dependence and its Treatment" *Addiction Science & Clinical Practice* December 2007 pp 4-16. e-mail: ajbudney@uams.edu
- Budney, A., & Stanger, C. (2007). Contingency management for Marijuana (Cannabis) Abuse and Dependence. In S. Higgins, K. Silverman, & S. Heil (Eds). *Contingency Management in the treatment of Substance Use Disorders: A science-based treatment innovation*. New York: Guilford. Chapter 4 Marijuana pp 61-79.
- Budney AJ, Vandrey RG, Hughes JR, Moore BA, Bahrenburg B "Oral delta-9-tetrahydrocannabinol suppresses cannabis withdrawal symptoms" *Drug and Alcohol Dependence*; 2007 Jan **5**; **86** (1):22-9

- Busch FW Seid DA Wei EJ "Mutagenic activity of marijuana smoke condensates Cancer" *lett.* **6(6)**: 319-324 1979.
- Cabral G.A. Dove Pettit DA "Drugs and immunity: cannabinoids and their role in decreased resistance to infectious disease." *J Neuroimmunol* **83(1-2)**: 116-23 1998.
- Cambridge University Press: *Cannabis Dependence: Its Nature Consequences and Treatment* Eds. Roger Roffman and Robert Stephens *Addiction* **101(11)**:1589-1597 2006. <http://www.nida.nih.gov/pdf/ascp/vol4no1/marijuana.pdf>
- Cantwell R, Brwein J, Glazebrook C, et al. "Prevalence of substance misuse in first-episode psychosis". *British Journal of Psychiatry.*; **174**:150-153 1999.
- Carriot F; Sasco AJ "Cannabis and Cancer" *Rev Epidemiol Sante Publique* 2000; **48(5)**:473-83 ISSN: 0398-7620.
- Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, Harrington H, and others. "Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene x environment interaction". *Biol Psychiatry* 2005 **57(10)**:1117-27.
- Cassidy F, Ahearn EP, Carroll BJ. "Substance abuse in bipolar disorder" *Bipolar Disord* **3(4)**: 181-8 2001.
- Centre on Addiction and Substance Abuse at Columbia University (CASA) "Addiction / Gateway / Drug" Oct. 27, 1994. <http://www.samia.com/GROUPS/ANTIDRUG/mjcnct/addctn.htm>
- Chacin S., "Women's Marijuana Problems: An Overview with Implications for Outreach, Intervention, Treatment, and Research" *Journal of Chemical Dependency Treatment* Vol. **6**, No. $\frac{1}{2}$, pp, 129-167 1996.
- Chacko JA, Heiner JG, Siu W, Macy M, Terris MK "Association between marijuana use and transitional cell carcinoma." *Urology* **67**:100-104 2006.
- Chambers RA, Taylor JR, Potenza MN *Developmental Neurocircuitry of Motivation in Adolescence: A Critical Period of Addiction Vulnerability* *Am. J. Psychiatry* 2003; **160**:1041-1052.
- Chang L., C. Clock, Yakupov R., Ernst T. "Combined and Independent Effects of Chronic Marijuana Use and HIV on Brain Metabolites" *Neuroimmune Pharmacol* **1**: 65-76 2006.
- Charbonney E., Sztajzel J., Polletti P., Rutschmann O. "Paroxysmal atrial fibrillation after recreational marijuana smoking: another "holiday heart?" *Swiss Med Wkly* **135**: 412-414 2005.
- Christine N Vidal, PhD; Judith L. Rapoport, MD; Kiralee M. Hayashi, BS; Jennifer A. Geaga, BS; Yihong Sui, BS; Lauren E. Mclemore, BS; and others: "Dynamically Spreading Frontal and Cingulate Deficits Mapped in Adolescents with Schizophrenia" *Arch Gen Psychiatry.* 2006; **63**: 25-34.
- Clough AR, Burns CB, Guyula T, Yunupingu M. "Diversity of substance use in eastern Arnhem Land (Australia): patterns and recent changes." *Drug Alcohol Rev* 2002; **21(4)**:349-56.
- Clough AR, Cairney S, Maruff P, Parker R. "Rising cannabis use in remote Indigenous communities." *Med J Aust* 2002; **177(7)**:395-6.
- Clough AR, D'Abbs P, Cairney S, Gray D, Maruff P, Parker R, O'Reilly B "Emerging patterns of cannabis and other substance use in Aboriginal communities in Arnhem Land, Northern territory: a study of two communities" *Drug Alcohol Rev* **23(4)**:381-90 2004.
- Clough AR, Kylie Lee KS, Jaragba MKJ, Conigrave KM, Patton GC "Heavy cannabis use and depressive symptoms in three Aboriginal communities in Arnhem Land, Northern Territory" *MJA* Volume **188** Number 10 605-607 2008.
- Coffey C, Lynskey M, Wolfe R, Patton GC "Initiation and Progression of cannabis use in a population-based Australian adolescent longitudinal study" *Addiction* 2000; **95** No 11:1679-1690.
(A large cohort study of 2032 students from 44 secondary schools following the outcome and predictors of escalation to harmful daily cannabis use).
- Coffey C, Carlin J, Lynskey M, Ning Li, Patton GC "Adolescent Precursors of Cannabis Dependence: Findings from the Victorian Adolescent Health Cohort Stud" *Br. J. Psychiatry* 2003; **182**: 330-336.
- Coffman K. "The debate about marijuana usage in transplant candidates: recent medical evidence on marijuana health effects" *Organ Transplantation* **13(2)**:189-195 2008.
- Cohen S. "Cannabis: Effects upon Adolescent Motivation. In: *Marijuana and Youth: Clinical Observations on Motivation and Learning.*" Report. Rockville, MD: National Institute of Drug Abuse; 1982.
- Cornelius MD, Taylor PM, Geva D, Day NL. "Prenatal tobacco and marijuana use among adolescents: effects on offspring gestational age, growth, and morphology". *Pediatrics* 1995; **95**: 738-43.

- Copeland J Swift W, Hall W "Characteristics of Long-Term Cannabis Users in Sydney, Australia" *Eur Addict Res* 1998;4:190-197 (DOI: 10.1159/000018952).
[http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/publishing.nsf/Content/4FDE76ABD582C84ECA257314000BB6EB/\\$File/mono-57.pdf](http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/publishing.nsf/Content/4FDE76ABD582C84ECA257314000BB6EB/$File/mono-57.pdf)
- Copeland, Underwood and Van Wyck "The health and psychological consequences of cannabis use – chapter.6.5"
<http://www.healthconnect.gov.au/internet/wcms/publishing.nsf/Content/health-pubs-drug-cannab2-ch65.htm> (1980).
- Corcoran, C.M., Kimhy, D., Stanford, A., Khan, S., Walsh, J., Thompson, J., Schobel, S., Harkavy-Friedman, J., Goetz, R., Colibazzi, T., Cressman, V., & Malaspina, D. (2008). "Temporal association of cannabis use with symptoms in individuals at clinical high risk for psychosis" *Schizophrenia Research* 106, 286-293.
- Daaka Y, Zhu W, Friedman H, Klein T W. "Induction of Interleukin-2 alpha gene by delta-9-THC is mediated by nuclear factor kB and CBa cannabinoid receptor." *DNA and Cell Biology* 1997;16:301-309 (THC might augment AIDS development because of an increase in NK-kB which is known to activate the HIV genome and increase retro viral replication.).
- Day NL et al "Effect of Prenatal Marijuana Exposure on the Cognitive Development of Offspring at Age Three" *Neurotoxicology and Teratology* 1994; 16(2): 169-75.
- Day NL, Goldschmidt, Lidush, Thomas, Carrie "Prenatal marijuana exposure contributes to the prediction of marijuana use at age 14." *Addiction* Sept 2006; 101(9): 1313-22.
- Dean, B et al. "Studies on [³H]CP-55940 binding in the human central nervous system: regional specific changes in density of cannabinoid-1 receptors associated with schizophrenia and cannabis use". *Neuroscience*, 103:9-15, 2001.
- Degenhardt L, Coffey C, Moran P, Carlin JB, Patton GC (2007) "The predictors and consequences of adolescent amphetamine use: findings from the Victoria Adolescent Health Cohort Study" Volume 102 Issue 7 Page 1076-1084.
- Degenhardt, L and Hall W *Is cannabis use a contributory cause of psychosis?* *Canadian Journal of Psychiatry-revue Canadienne De Psychiatrie*, 51 9: 556-565 2006.
- Degenhardt L, Hall W, Lynskey M. "The relationship between cannabis use, depression and anxiety among Australian adults": findings from the National Survey of Mental Health and Wellbeing. *Soc Psychiatry Psychiatr Epidemiol* 2001; 36 (5): 219-227.
- Degenhardt LD, Hall W M, Teesson "Does cannabis use lead to mental-health problems? Parliamentary Library No. 21 Research Note 2007. <http://www.aph.gov.au/library/pubs/rn/2006-07/07rm21.pdf>
- Delahunty B, Putt J. "The policing implications of cannabis, amphetamine and other illicit drug use in Aboriginal and Torres Strait Islander communities" Australian Institute of Criminology 2006.
<http://www.aic.gov.au/publications/tandi2/tandi322t.html>
- Department of Parliamentary Services Research Note. 'Does cannabis use lead to mental-health problems?: findings from the research'. June 2007, no. 21 <http://www.aph.gov.au/library/pubs/rn/Index.htm>
- Dervaux A, Laqueille X, Bourdel MC, Leborgne MH, Olie JP, Loo H, Krebs MO. "Cannabis and schizophrenia: demographic and clinical correlates" *Encephale* 2003 29(1):11-7.
- Diana M, Melis M, Muntoni AL et al. "Mesolimbic dopaminergic decline after cannabinoid withdrawal". *Proc Natl Acad Sci* 95(17):10269-10273, 1998.
- Di Forti M, Murray RM. Cannabis consumption and risk of developing schizophrenia: myth or reality? *Epidemiol Psychiatr Soc*. 2005;14 (4):184-187.
- Drewe J "Desired effects and adverse effects of cannabis use" *Ther Umsch*. 2003; 60(6):313-6.
- Drummer, O.H. "Drugs in drivers killed in Victorian road traffic accidents". Melbourne: Victorian Institute of Forensic Medicine; May 1998. Report No. 0298.
- Drummer, O.H. & Gerostamoulos, J. "The involvement of drugs in car drivers killed in Victorian road traffic accidents." Melbourne: Vivtorian Institute of Forensic Medicine and Monash University Department of Forensic Medicine; July 1999. Report No. 0499.
- Drummer, O.H., Gerostamoulos, J., Batziris, H., Chu, M., Caplehorn, J., Robertson, M.D. & Swann, P. (2004), "The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes" *Accident Analysis and Prevention*, vol. 36, pp. 239-248.
- Drummer OH., Gerostamoulos et al *Incidence of drugs in drivers killed in Australian Road Traffic Accidents Forensic Sci. Inst.* 2003 July 8 134(2-3 154-162.
- D'Souza DC, Abi-Saab W, Madonick S, Forselius-Bielen K, Doersch A, Braley G, Gueorguieva R, Cooper T, Krystal J "Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction" *Biol Psychiatry* 15;57(6):594-608 2005.

- Duffy A, Milin R (1996). "Case study: withdrawal syndrome in adolescent chronic cannabis users", *Journal of the American Academy of Child and Adolescent Psychiatry*, **35** (12) 1618-1621.
- DuPont R.L., Campbell T.G. and Mazza J.J. "Elements of a Successful School-Based Student Drug Testing Program" 2002. http://www.randomstudentdrugtesting.org/pdf/elements_sdt_program.pdf
- Eisenstein K Toby, Joseph J Meissler, Qiana Wilson, John P Gaughan, Martin W. Adler "Anandamide and Delta9-tetrahydrocannabinol directly inhibit cells of the immune system via CB2 receptors" *Journal of Neuroimmunology* Vol. 189 Issue 1-2 pp 17-22 2007.
- Eldreth DA, Matochink JA, Cadet JL, Bolla KI. "Abnormal brain activity in prefrontal brain regions in abstinent marijuana users". *Neuroimage* 2004;**23**(3):914-20.
- Ellgren M, (Karolinska Institutet) "Neurobiological effects of early life cannabis exposure in relation to the gateway hypothesis" <http://diss.kib.ki.se/2007/978-91-7357-064-0/> 2007.
- El Marroun, H., Tiemeier, H., Jaddoe, V.W., Hofman, A., Mackenbach, J.P., Steegers, E.A., Verhulst, F.C., van den Brink, W., & Huizink, A.C. (2008). "Demographic, emotional and social determinants of cannabis use in early pregnancy: The Generation R study". *Drug and Alcohol Dependence* **98**, 218-226.
- Ernst T, Chang L, Arnold S (2003) "Increased glial markers predict increased working memory network activation in HIV patients". *Neuroimage* **19** Issue 4: 1686-1693.
- Ferdinand. RF et al. "Cannabis—psychosis pathway independent of other types of psychopathology". *Schizophrenia Research*, **79**(2-3):289-95, 2005.
- Fergusson, DM et al. "Cannabis use and psychosocial adjustment in adolescence and young adulthood". *Addiction* **97**:1123-1135, 2002.
- Fergusson, DM et al. "Cannabis dependence and psychotic symptoms in young people". *Psychological Medicine*, **33**:15-21, 2003.
- Fergusson DM, Boden JM "Cannabis use and adult ADHD symptoms" *Drug Alcohol Depend* **1;95**(1-2):90-6 2008.
- Fergusson DM, Boden JM (2008) "Cannabis use and later life outcomes" *Addiction* Volume 103 Issue 6 Page 969-976.
- Fergusson DM, Boden JM, Horwood LJ *Cannabis use and other illicit drug use: testing the cannabis gateway hypothesis* *Addiction* **101**(4):556-69 2006.
- Fergusson DM, Boden JM, Horwood LJ "The developmental antecedents of illicit drug use: Evidence from a 25-year longitudinal study" *Drug and Alcohol Dependence* 2008 Jul 1;**96**(1-2):165-77. Epub 2008 Apr 21.
- Ferguson, D., Horwood, L. J. "Early onset cannabis use and psychosocial adjustment in young adults." *Addiction* **92**; 279-296. 1997.
- Ferguson, D., Horwood, L.J, Ridder EM. "Test of causal linkages between cannabis use and psychotic symptoms" *Addiction* **100**; 354-66. 2005.
- Fergusson DM Horwood LJ "Does cannabis use encourage other forms of illicit drug use?" *Addiction* **95**(4), 505-520 2000.
- Fergusson DM, Horwood LJ "Cannabis use and dependence in a New Zealand birth cohort". *New Zealand Medical Journal*; **113**:56-58. 2000.
- Fergusson DM, Horwood LJ, Swain-Campbell NR. "Cannabis dependence and psychotic symptoms in young people" *Psychol Med* ;**33**:5-21 2003.
- Fergusson D.H., Horwood L.J., Swain-Campbell N. "Cannabis use and psychosocial adjustment in adolescence and young adulthood". *Addiction* **97**; 1123-35 2002. <http://www.jiacam.org/0202/CANNABIS.pdf>
- Fergusson D.M., Richie Poulton., Paul F Smith., Joseph M Boden. "Cannabis and Psychosis" *BMJ* Volume **332**(7534)172-175 2006.
- Fisher et al "Dangers of Cannabis" *Emergency Medicine Journal* **22**:612a 2005. <http://emj.bmj.com/cgi/content/full/22/9/612a>
- Fisk, J. & Montgomery, C. (2008). Real-world memory and executive processes in cannabis users and non-users. *Journal of Psychopharmacology* **22**, 727-736.
- Fried P A., " Adolescents Prenatally Exposed to Marijuana: Examination of Facts of Complex Behaviors and Comparisons with the Influence of In Utero Cigarettes" *J Clin Pharmacol* **42**:97S-102S 2002.
- Fried P A., "Marijuana use by pregnant women: Neurobehavioral effects in neonates" *Drug and Alcohol Dependence*. 1980 **6**:415-424.
- Fried P A., Watkinson B, and Willan. "Marijuana use during pregnancy and decreased length of Gestation." *American Journal of Obstet. Gynecol.* 1984;**150**(1):23-27.

- Friedman H, Newton C, Klein TW. "Microbial infections, immunomodulation, and drugs of abuse". Clin Microbiol Rev **16**(2):209-219, 2003.
- Garavan H, Nestor L, Roberts G, Hester R. "Deficits in learning and memory: Parahippocampal hyperactivity and frontocortical hypoactivity in cannabis users" Neuroimage 2008 Jan 12: 18296071 (P,S,E,B,D). <http://lib.bioinfo.pl/pmid:18296071>
- Gardner EL, *Addictive Potential of Cannabinoids: The underlying neurobiology* CPL Chemistry and Physics of Lipids 2002 **121**; 267-297.
- Gaziano J "Marijuana use among those at risk for cardiovascular events" American Heart Journal 2008; **155**:395-6.
- Geller T, Loftis L, Brink D, 2004 "Cerebellar Infarction in Adolescent Males Associated with Acute Marijuana Use" Pediatrics; Vol. **113** No 4: 365-70.
- Gfroerer J, Epstein J "Marijuana initiates and their impact on future drug treatment need" Drug and Alcohol Dependence **54** 1999 229-237.
- Ghosh S, Preet A, Groopman J, Ganju R "Cannabinoid receptor CB2 modulates the CXCL12/CXCR4-mediated chemotaxis of T lymphocytes" Volume **43**, Issue 14 July 2006, Pages 2169-2179
- Giedd Jay "The Structural Development of the Human Brain as measured Longitudinally with measured resonance Imaging" Chapter 3 pp50-73
http://books.google.com.au/books?hl=en&lr=&id=2xpvp4ie_8MC&oi=fnd&pg=PA50&dq=Giedd+Jay++Current+Direction+in+Psychological+Science+2007.+&ots=Vd2ZrIbRbE&sig=WZi3OkOj4LcnM54JXJNDznOnXVs#PPA50.M1
- Goldberg L, Elliot DL, MacKinnon DP, Moe EL, Kuehl KS, Yoon M, Taylor A, Williams J "Outcomes of a prospective trial of student-athlete drug testing: the Student Athlete Testing Using Random Notification" (SATURN) study." J Adolesc Health. 2007 Nov;**41**(5):421-9
http://www.ncbi.nlm.nih.gov/pubmed/17950161?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum
- Golub A, Johnson BD, "The Shifting Importance of Alcohol and Marijuana as Gateway Substances among Serious Drug Abusers" J. Stud Alcohol 1994;**55**:607-614.
- Goncharov I, Weiner L, Vogel Z (2005) "Delta 9-tetrahydrocannabinol increases C6 glioma cell death produced by oxidative stress". Neuroscience **134**: Issue 2: 567-574.
- Gray D, Morfitt B, Williams S, Ryan K, Coyne L. "Drug Use and Related Issues among young aboriginal people in Albany" National Centre for Research into the Prevention of Drug Abuse Curtin University of Technology 1996.
- Greenblatt, J. "Adolescent self-reported behaviours and their association with marijuana use". Based on data from the National Household Survey on Drug Abuse, 1994-1996, SAMSHA, 1998.
http://eric.ed.gov/ERICWebPortal/custom/portlets/recordDetails/detailmini.jsp?_nfpb=true&_ERICExtSearch_SearchValue_0=ED424526&_ERICExtSearch_SearchType_0=no&accno=ED424526
- Griggs W, Caldicott, Pfeiffer J, Edwards N, Pearce A, Davey M "The impact of drugs on road crashes, assaults and other trauma-a prospective trauma toxicology study" National Drug Law Enforcement Research Fund 65pp an initiative of the National Drug Strategy Trauma Service, Royal Adelaide Hospital and Emergency Department, Royal Adelaide Hospital 2007.
http://casr.adelaide.edu.au/library/newadditions/WhatsNew_May2007_CV.pdf
- Groopman Jerome E. M.D. "Marijuana component opens the door for virus that causes kaposi's sarcoma" American Association for Cancer Research 2007.
<http://www.sciencedaily.com/releases/2007/08/070801112156.htm>
- Grucza RA, Bierut LJ "Cigarette Smoking and the Risk for Alcohol Use Disorders Among Adolescent Drinkers" Alcohol Clin Exp Res. 2006 Dec;**30**(12):2046-54.
- Hall W. 'Cannabis policy challenges' in "Matters of Substance" Nov/Dec 2007 produced by the New Zealand Drug Foundation.
www.drugfoundation.org.nz.
- Hall, W., Degenhardt L. "Cannabis use and psychosis" Curr Psychiatry Rep. 2002 Jun;**4**(3):191-6.
- Hall, W., Degenhardt L. "What are the policy Implications of the evidence on cannabis and Psychosis? Can J Psychiatry, Vol **51**, No 9, 566-74 2006.
- Hall W., Macphee D. "Cannabis use and cancer" Addiction **97**,243-247 2002.
- Haney, M; Ward, A.S.; Comer, S.D.; Foltin, R.W.; and Fischman, M.W.; "Abstinence symptoms following smoked marijuana in humans" Psychopharmacology, 141:395-404, 1999.
- Harkany T, Guzman M, Galve-Roperh I, Berghuis P, Devi LA, Mackie K "The emerging functions of endocannabinoid signaling during CNS development" Trends Pharmacol Sci 2007; **28**(2): 88-92.
- Harrison G. Pope Jr., M.D. "Cognitive Effects of Long-Term Cannabis Use: The Devil is in the confounding variables" McaLean Hospital/Harvard Medical School 2004. <http://www.nida.nih.gov/whatsnew/meetings/apa/ppt/pope.ppt>

Hashibe M; Straif K; Tashkin DP; Morgenstern H; Greenland S; Zhang ZF "Epidemiologic review of marijuana and cancer risk" Alcohol 35(3):265-75 2005.

Hayatbakhsh, MR et al. "Cannabis and anxiety and depression in young adults: a large prospective study." Journal of the American Academy of Child and Adolescent Psychiatry, 46(3):408-17, 2007.

Hayatbakhsh, M.R., Mamun, A.A., Najman, J.M., O'Callaghan, M.J., Bor, W., & Alati, R. (2008). "Early childhood predictors of early substance use and substance use disorders: Prospective study." Australian and New Zealand Journal of Psychiatry 42, 720-731.

Hayatbakhsh, M.R., O'Callaghan, M.J., Jamrozik, K., Najman, J.M., Mamun, A.A., Alati, R., & Bor, W. (2008). "The association between school performance at 14 years and young adults' use of cannabis." An Australian birth cohort study". Journal of Drug Issues 38, 401-418.

Henquet C. COMT "Val158Met moderation of cannabis-induced effects on psychosis and cognition." Presented at the 13th Association of European Psychiatrists (AEP) Symposium by the Section on Epidemiology and Social Psychiatry; June 15-17, 2006; Bordeaux, France.

Henquet C. 'The Effects of COMT VAL¹⁵⁸Met Egnotype and Cannabis Use on Psychosis and Cognition'. Presented at the 13th Association of European Psychiatrists (AEP) Symposium by the Section on Epidemiology and Social Psychiatry held June 14-17, 2006.

Henquet C, Corcoran C. "Cannabis and psychosis: from genetics and biology to functional outcome and treatment." Program of the 5th International Conference on Early Psychosis; October 4-6, 2006; Birmingham, United Kingdom. Symposium 12. http://www.medscape.com/viewarticle/556097_6

Henquet, C., Di Forti, M., Morrison, P., Kuepper, R., & Murray, R.M. (2008). "Gene-environment interplay between cannabis and psychosis." Schizophrenia Bulletin 34, 1111-1121.

Henquet C, Krabbendam L, Spauwen J, et al. "Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people." BMJ. 2005;330:11-15.

Henquet C, Murray R, Linszen D, van Os J. "The environment and schizophrenia: the role of cannabis use". Schizophr Bull. 2005;31(3): 608-612 2005.

Henquet C, Rosa A, van Os J, Myin-Germeys I. COMT VAL₁₅₈MET moderation of cannabis induced psychosis: an experience sampling study (ESM). Program and abstracts of the 5th International Conference on Early Psychosis; Psychol Med. 2007 20:1-6. <http://lib.bioinfo.pl/auth:Henquet,C>

Hill S.W., Tam JDC, Thompson B.R. Naughton M.T. "Bullous lung disease due to marijuana" Respirology 13 issue 1: 122-127 2008.

Hiller C.F., Wilson F.J., Mazumder M.K., Wilson J.D., Bone R.C. Concentration and Particle Size Distribution in smoke from Marijuana Cigarettes with Different Delta9-Tetrahydrocannabinol Content Oxford University Press Vol 4 Number 3 page 451-454 1984.

Hillman SD, Silburn SR, Green A, Zubrick R. "Youth suicide in Western Australia involving cannabis and other drugs: a literature review and research report. Perth": TVW Telethon Institute for Child Health Research, WA Youth Suicide Advisory Committee (WA Strategy Against Drug Abuse); 2000. Occasional Paper Number 2. <http://www.dao.health.wa.gov.au/>

Hoffmann D Brunnemann KD Gori GB Wynder EL "On the carcinogenicity of marijuana smoke."Recent Advances Phytochem. 9:63-81 1975.

Howard, C. (2008). Application of new DNA markers for forensic examination of cannabis sativa seizures: Developmental validation of protocols and a genetic database. NDLERF Monograph Series No. 29. Hobart: National Drug Law Enforcement Research Fund.

Howard Richard C, Menkes David B, "Changes in brain function during acute cannabis intoxication: preliminary findings suggest a mechanism for cannabis-induced violence" Criminal Behaviour and Mental Health 17 Issue 2: 113-117 2007.

Huas, C., Hassler, C. & Choquet, M. (2008). "Has occasional cannabis use among adolescents also to be considered as a risk marker?" European Journal of Public Health 18, 626-629.

Huizink AC, Mulder EJ "Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioural and cognitive functioning in human offspring" Neurosci Biobehav Rev 2006 30(1) 24-41.

Hurd Y "Ongoing research into neurotransmitter levels in animals to mimic adolescent drug exposure, especially cannabis, seen in humans" Neurotoxicology and Teratology Vol. 28 Issue 3 pp 386-402 2006. e-mail yasmin.hurd@mssm.edu.

Hurd Y, Professor of Psychiatry, Pharmacology and Biological Chemistry Ongoing research into neurotransmitter levels in animals to mimic adolescent drug exposure, especially cannabis, seen in humans. Paper now available: Neuropsychopharmacology advance online publication 5th July 2006 doi:10.1038/sj.nnp.1301127 32: 607-615 2006 Correspondence to yasmin.hurd@mssm.edu.

Ilse Kurzthaler, Martina Hummer, Carl Miller, Barbara Sperner-Unterweger, Verena Gunther, Heinrich Wechdom, M.S.; Hans-Jurgen Battista, Wolfgang Fleischhacker, "Effects of Cannabis Use on Cognitive Functions and Driving Ability" J Clin Psychiatry 1999;60:395-399.

- Ishida J, Peters M, Jin C, Louie K, Tan V, Bacchetti P and Terrault N "Influence of Cannabis Use on Severity of Hepatitis C Disease" *Clinical Gastroenterology and Hepatology* **6** 69-75 2008
http://www.janis7hepc.com/drugs_that_cause_liver_damage.htm#da
- Jan Ramstrom "Adverse Health Consequences of Cannabis Use" ISBN 91-7201-289-7 National Institute of Public Health Sweden 1998.
- Järbe, T. U. C., Hiltunen, A. J., Mechoulam, R. "Stereospecificity of the discriminate stimulus functions of the dimethylheptyl homologs of 11-hydroxy- Δ^9 -tetrahydrocannabinol in rats and pigeons". *Journal of Pharmacol. Exp. Ther.*, **250**, 1989, pp. 1000-1005.
- Jay N. Giedd "Adolescent Brain Development: Vulnerabilities and Opportunities" *Ann. N.Y. Acad Sci* **1021**: 61-63 2004.
- Jay N Giedd (2004) "Structural Magnetic Resonance Imaging of the Adolescent Brain" *Annals of the New York Academy of Science* Vol 1021 (1), 77-85.
- Jay N. Giedd, MD, Liv S Clasen, PhD, Gregory L. Wallace, MA, Rhoshel K. Lenroot, MD, Jason P. Lerch, PhD, Elizabert Molloy Wells, MD, Joathan D. Blumenthal, MA, Jean E. Nelson, MHS, Julia W. Tossell MD, Catherine Stayer, MD, PhD, Alan C. Evans PhD and Carole A. Samango-Sproue, EdD. "XXY (Klinefelter Syndrome: A Pediatric Quantitative Brain Magnetic Resonance Imaging Case-Control Study" *Pediatrics* Vol **119** No. 1 January, pp. e232-e240 2007.
- Jayanthi S, Buie S, Moore S, Heming RI, Better W, Wilson NM, Contoreggi C, Cadet JL "Heavy marijuana users show increased serum apolipoprotein C3 levels: evidence from proteomic analyses" *Molecular Psychiatry* 2008; DOI: 10.1038/mp.2008.50
<http://www.nature.com/mp>
- Jones RT, *Cardiovascular System Effects of Marijuana* *Journal of Clinical Pharmacology* 2002 **42** (11 Suppl):58S-63S.
- Kandel DB, Yamaguchi K, Chen K "Stages of Progression in Drug Involvement from Adolescence to Adulthood: Further Evidence for the Gateway Theory" *J Study Alcohol* **53**(5):447-457 1992.
- Kraft, B.; Frickey, N.; Kaufmann, R.; Reif, M.; Frey, R.; Gustorff, B; Kress, H. "Lack of Analgesia by oral Standardized Cannabis Extract on Acute Inflammatory Pain and Hyperalgesia in Volunteers" *Anesthesiology*. 109(1):101-110, July 2008. doi: 10.1097/ALN.0b013e31817881e1
- Kari Poikolainen, Annamari Tuulio-Henriksson, Terhi Aalto-Setälä, Mauri Marttunen, Tuula Anttila, Jouko Lonnqvist "Correlates of initiation to cannabis use: a 5-year follow-up of 15-19 year-old adolescents" *Drug and Alcohol Dependence* **62** (2001) 175-180.
- Karila L, Vignau J, Alter C, Reynaud M. "Acute and chronic cognitive disorders caused by cannabis use" *Rev Prat* 15;**55**(1):23-26 discussion 27-29 2005.
- Kelley R. Mark Ph.D., Denny George, Ph.D., Young Michael, Ph.D. "Modified stages of acquisition of gateway drug use: A primary prevention application of the stages of change model" *J. Drug Education*, **29**(3) 189-203, 1999.
- Kelly E, Darke S, Ross J "A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions" *Drug and Alcohol Review* **23**, 319-344 2004.
- Klonoff-Cohen HS, Natarajan L, Chen RV "A prospective study of the effects of female and male marijuana use on in vitro fertilization (IVF) and gamete intrafallopian transfer (GIFT) outcomes" *Amer J Obst Gynecol* 2006; **194**(2):369-76.
- Kokkevi A, Gabhainn S.N, Spyropoulou M, and the Risk Behaviour Focus Group of the HBSC "Early Initiation of Cannabis Use: A Cross-national European Perspective" *Journal of Adolescent Health* 712-719 2006.
- Konings, M., Henquet, C., Maharajh, H.D., Hutchinson, G., & Van Os, J. (2008). "Early exposure to cannabis and risk for psychosis in young adolescents in Trinidad." *Acta Psychiatrica Scandinavica* **118**, 209-213
- Korantzopoulos P, Liu T, Papaioannides D, Li G, Goudevenos J. A "Atrial fibrillation and Marijuana Smoking" *Int J Clin Pract*. **62** (2):308-313 2008.
- Kouri E.M, Pope Jr H.G, Lukas S.E. "Changes in aggressive behavior during withdrawal for long-term marijuana use" *Psychopharmacology* **143**:302-308 1999.
- Kumra, S. "Schizophrenia and cannabis use". *Minnesota Medicine*, **90**(1):36-8, 2007.
- Lambros Messinis, Ph. D., "Neuropsychological deficits in long-term frequent cannabis users" *Neurology* **66**:737-739 2006.
- Lancet "Cannabis smokers risk psychosis" paper published in *The Lancet* written by seven British psychiatrists, psychologists July 27 2007.
http://www.timesonline.co.uk/tol/life_and_style/health/article2148315.ece
- Lane Malcolm Alexander "Australia's cannabis king put away for 13 years" *The Courier-Mail* August 17 2007.
<http://www.news.com.au/story/0,23599,22257426-2,00.html>

- Laumon B, Gadegbeku B, Martin, J, Biecheler M. "Cannabis intoxication and fatal road crashes in France: population based case-control study" *BMJ* ;**331**:1371 2005.
- Lehrmann E. "Chronic Abuse of Different Drugs Causes Similar Brain Changes"
<http://www.nida.nih.gov/pdf/newsscan/newsscan51.pdf>
- Lindsay A.C., Foale R.A., Warren O., Henry J.A. "Cannabis as a precipitant of cardiovascular emergencies" *Emergency Medicine Journal* **22**: 679-680 2005. [Int J Cardiol.](#) 2005 **104**(2):230-2.
- L. Lu, C. Leonard, P. Thompson, E Kan, J Jolley, S. Welcome, A. Toga, and E. Sowell. "Normal Developmental Changes in Inferior Frontal Gray Matter Are Associated with Improvement in Phonological Processing: A Longitudinal MRI Analysis." *Cereb Cortex*, May 1, 2007; **17** (5): 1092-1099.
- Looby A, Earleywine M "Negative consequences associated with dependence in daily cannabis users" *Substance Abuse Treatment, Prevention and Policy* January 2007; **2**:3
- Note: M Earleywine is on the board of the MPP (Marijuana Policy Project). Among their aims are the legalisation of medical marijuana and the reform of marijuana policy.
- Lundqvist T. "Cognitive consequences of cannabis use: Comparison with abuse of stimulants and heroin with regards to attention, memory and executive functions." *Pharmacology, Biochemistry and Behavior* **81**(2) (2005) 319-330.
- Lundqvist T. "Recent scientific data on the consequences of cannabis use" Drug Addiction Treatment Centre, Lund University Hospital, Kioskgatan 17, S-221 85 Lund Sweden. Email thomas.lundqvist@med.lu.se (2003) http://www.droginfo.com/pdf/publicerade_artiklar/Recent_scientific_data.pdf.
- Lynskey M., "Escalation of Drug Use in Early-Onset Cannabis Users vs. Co-Twin Controls" *JAMA* **289** No.4 427-433 2003.
- Lynskey M.T. Editorial "Life-time cannabis use and late onset mood and anxiety disorders" *Addiction*. **102**(8):1181-1182 2007.
- Lynskey, M et al. "Major depressive disorder, suicidal ideation, and suicide attempt in twins discordant for cannabis dependence and early-onset cannabis use". *Archives of General Psychiatry*, **61**:1026-1032, 2004.
- Lynskey M., Hall W. "The effects of adolescent cannabis use on educational attainment." *Addiction* 2000; **95**(11): 1621-30.
- Mach F, Steffens S et al 2005 Low dose oral cannabinoid therapy reduces progression of atherosclerosis in mice. *Nature* **434**:782-6. <http://www.nature.com/nature/journal/v434/n7034/full/nature03389.html>
- Macleod, J., Oakes, R., Copello, A., et al "Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies" *Lancet* **363**(9421):1579-1588 2004.
- Maddock Clementine & Babbs Michelle "Intervention for cannabis misuse" *Advances in Psychiatric* Vol. **12**, 432-439 2006.
- Maharajh, HD et al. "Cannabis and suicidal behaviour among adolescents: a pilot study from Trinidad". *The Scientific World Journal* Vol.5:576-85, 2005.
- Marina Carvalho de Moraes Barros, MD, PhD, Ruth Guinsburg, MD, PhD, Clovis de Araujo Peres, PhD, Sandro Mitsuhiro, MD, Elisa Chalem, Ronaldo Ramos Laranjeira, MD, PhD. "Exposure to marijuana during pregnancy alters neurobehavior in the early neonatal period" *The Journal of Pediatrics* Vol. 149: Issue **6**, 781-787 2006.
- Marios Marselos & Petros Karamanakos "Mutagenicity, developmental toxicity and carcinogenicity of cannabis." *Addiction Biology* (1999) **4** (1) 5-12.
- Massi P; Vaccani A; Parolaro D "Cannabinoids, immune system and cytokine network" *Curr Pharm Des.* 2006; Vol. **12** Number 24:3135-46(12).
- McGhee R, Williams S, Poulton R, Moffitt T "A longitudinal study of cannabis use and mental health from adolescence to early adulthood" *Addiction* **95**(4), 491-503 2000.
- McHale S; Hunt N "Executive function deficits in short-term abstinent cannabis users" *Human Psychopharmacology: Clinical and Experimental* Volume 23 Issue 5, page 409-415 2008.
- McKallip RJ; Nagarkatti PS, "Delta-9-tetrahydrocannabinol enhances breast cancer growth and metastasis by suppression of the antitumor response" *J Immunol*, 2005; **174**(6):3281-9.
- McKay DR, Tennant CC "Is the grass greener? The link between cannabis and psychosis" *Med J Aust* **172**:284-286 2000.
- McKinney J.R. "The effectiveness and legality of random student drug testing programs revisited" 2005 http://www.randomstudentdrugtesting.org/pdf/el_random_student_drug_testing.pdf
- McLaren J. & Mattick R.P. "Cannabis in Australia Use, supply, harms, and responses" NDARC Monograph No. 57 National Drug and Alcohol Research Centre 2007.

McLean J. & Swift J "Cannabis potency and contamination: a review of the literature" *Addiction*, Volume 103, Number 7, pp. 1100-1109(10) 2008.

Medina, Hanson, Schweinsburg, Cohen-Zion, Nagel, Tapert "Neuropsychological functioning in adolescent marijuana users: Subtle deficits detectable after a month of abstinence" *Journal of the International Neuropsychological Society* (2007), **13**: 807-820.
<http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=1296240>

Medina K L et al presented at the 2008 meeting of the American Academy of Pediatrics in Boston. (ANI) "Neuroimaging Marijuana Use and its Effects on Cognitive Functions" University of Cincinnati.

Mehra R, Moore BA, Crothers K, Tetrault J, Fiellin DA (2006). "The association between marijuana smoking and lung cancer. A systematic review". *Arch Inter Med* **166**(13): 1359-1367.

Mendelson J H, et al. "Marijuana smoking suppresses leuteinizing hormone in women." *Journal of Pharm. Exp. Therapeutics*. 1986;**237**:862-866.

Mendelson J H, Mello N K, and Ellingvoe J. "Acute effects of marijuana smoking on prolactin levels in human females." *The Journal of Pharm. and Exp. Therap.* 1985;**232**::220-222.

Menetrey A, Augsburger M, Favrat B, Pin MA, Rothuizen LE, Appenzeller M, Buclin T, Mangin P, Giroud C. "Assessment of Driving Capability through the use of Clinical and Psychomotor Tests in Relation to Blood Cannabinoids Level Following Oral Administration of 20 mg Dronabinol or of a cannabis Decoction Made with 20 or 60 mg Delta9-THC". *JAnal Toxicol*. 2005 Vol **29** Number(5):327-38(12).

Mental Health Council of Australia, "Where there's smoke..." Cannabis and Mental Health. MHCA, 2006.
<http://www.mhca.org.au/documents/MHCACannabisfinalLR.pdf>

Messinis L et al *Neuropsychological deficits in long-term frequent cannabis users* *Neurology* 2006; **66**: 737-9.

Mikkel Arendt, Raben Rosenberg, Leslie Foldager, Gurli Perto and Povl Munk-Jorgensen. "Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases." *British Journal of Psychiatry* **187**, 510-515 2005.

Mirken B, Earleywine M. "The cannabis and psychosis connection questioned: a comment on Fergusson et al". *Addiction* 2005 Vol. Issue 5 **100**:715-6.

Moiche BP, Atxa de la Presa MA, Guesta A (2001). " Transitional cell carcinoma in a young heavy marijuana smoker." *Arch Esp Urol* **54**:165-167.

Moir, David et al. "A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions" *Toxicol.*; 2007; **21**(2); 494-502.

Moore BA, Augustson EM, Moser RP, Budney AJ *Respiratory Effects of Marijuana and Tobacco Use in a US Sample* *J Gen Intern Med* 2005; **20**: 33-37.

Moore BA, Budney AJ "Relapse in outpatient treatment for marijuana dependence" *Journal of Substance Abuse Treatment*. 2003 **25**(2):85-89.

Moore, T et al. "Cannabis use and risk of psychotic or affective mental health outcomes: a systemic review". *The Lancet*, Vol. **370**(9584): 319-328, 2007.

Morgenstern J, Langenbucher J, Labouvie EW *The generalizability of the dependence syndrome across substances: an examination of some properties of the proposed DSM-IV dependence criteria* *Addiction* 1994; **89** (9):1105-1113.

Moussouttas M, "Cannabis Use and Cerebrovascular Disease" *Neurologist* 2004 **10**(1): 47-53.

Mukamal K J, Maclure M, Muller J E, Mittleman M A. *An exploratory prospective study of marijuana use and mortality following acute myocardial infarction*" *American Heart Journal* **155**: (3) 465-70 2008.

Musty RE, Kaback L. Relationships between Motivation and Depression in Chronic Marijuana Users. *Life Sciences* 1995; **56**, issue 23-24, 2151-8.

National Campaign Against Drug Abuse "Department of Health, Housing and Community Services. *National Campaign Against Drug Abuse Social Issues Survey, 1991 (Computer file)*. Canberra: Social Science Data Archives, The Australian National University, 1997.

National Drug & Alcohol Research Centre Ross J. "Illicit drug use in Australia: Epidemiology, use patterns and associated harm. 2007.
<http://www.springerlink.com/content/xq64343767454374/>

National Drug Intelligence Centre Marijuana October 2006.
<http://www.aic.gov.au/publications/tandi2/tandi308.pdf>

Narang S, Gibson D, Wasan A D, Ross E L, Michna E, Nedeljkovic S S, Jamison R N "Efficacy of Dronabinol as an Adjuvant Treatment for Chronic Pain Patient on Opioid Therapy" *The Journal of Pain*, Vol 9, 254-264 2008.

Negrete, Juan C., "Editorial: "cannabis and schizophrenia", *British Journal of Addiction* Vol. **84** Issue 4 1989, pp. 349-351

- Negrete, J. C., et. al., "Cannabis effects the severity of schizophrenic symptoms: results of a clinical survey", Psych. Med., **16**, 1986, pp. 515-520
- Nieder AM, Lipke MC, Madjar S (2006). "Transitional cell carcinoma associated with marijuana: Case report and review of literature." Urology Vol. **67**, Issue 1, 200.e5-200.e6.
- Niveau G, Dang C (2003). "Cannabis and violent crime" Medicine, Science and the Law **43**(2):115-121.
- Northern Territory Police, Fire and Emergency Services. 2007 annual report. Darwin: NTPFES, 2007. http://www.nt.gov.au/pfes/documents/File/police/publications/annrep/Annual_Report_2007_FINAL.pdf (accessed Apr 2008).
- Pacifici R., Roset P.N., Segura J., Segura J. "Modulation of the Immune System in Cannabis Users" JAMA Vol **289**, No. 15 1929-1931 2003.
- Pacula R, Ringel J, Dobkin C, Truong K "The incremental inpatient costs associated with marijuana comorbidity" Drug and Alcohol Dependence **92** 248-257 2008.
- Papafotiou Katherine "An evaluation of the efficiency of sobriety testing to detect blood levels of cannabis and impaired driving ability Swinburne University of Technology 2001.
<http://adt.lib.swin.edu.au/uploads/approved/adt-VSWT20050323.083420/public/02whole.pdf>
- Papathanasopoulos P, Messinis L, Lyros E, Kastellakis A, Panagis G "Multiple sclerosis, cannabinoids, and cognition" J Neuropsychiatry Clin Neurosci. 2008 Winter;**20**(1):36-51.
- Patton G "Cannabis Linked to use of amphetamines" Addiction **8**, 2007
- Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. "Cannabis use and mental health in young people:" cohort study. BMJ.**325** (7374):1195-1198 2002.
- Patton GC, Coffey C, Lynskey MT, Reid S, Hemphill S, Carlin JB and Hall W "Trajectories of adolescent alcohol and cannabis use into young adulthood" Addiction **102**:607-615 2007.
- Pedersen CB, Mortensen PB. Are the cause(s) responsible for urban-rural difference in schizophrenia risk rooted in families or in individuals? Am J Epidemiol. 2006;**163**: (11): 971-978.
- Pistis M, Perra S, Pillolla G, Melis M, Muntoni AL, Gessa GL, "Adolescent exposure to cannabinoids induces long-lasting changes in the response to drugs of abuse of rat midbrain dopamine neurons" Biol Psychiatry **56**:86-94 2004.
- Pope Jr HG, Gruber AJ, Hudson JI, Huestis MA, Yurgelun-Todd D "Neuropsychological performance in long-term cannabis users." Arch Gen Psychiatry 2001;**58**(10):909-15.
- Pope HG, Gruber AJ, Yurgelun-Todd D. "The residual neuropsychological effects of cannabis: the current status of research". Drug and Alcohol Dependence. **38**, Number 1 pp. 25-34 (10) 1995.
- Poulton RG, Brooks M, Moffitt TE, et al "Prevalence and correlates of cannabis use and dependence in young New Zealanders" New Zealand Medical Journal **110**:(1039):68-70 1997.
- Putt J. Delahunty B "Illicit drug use in rural and remote Indigenous communities" No. 322 Trends & Issues in crime and criminal justice Australian Institute of Criminology 2006.
- Rais M, Cahn W, Van Haren N, Schnack H, Caspers E, M.S. Pol HH, Kahn R. "Excessive Brain Volume Loss Over Time in Cannabis-Using First-Episode Schizophrenia Patients" Am J Psychiatry 2008; **165**:490-496.
- Ranga K., Krishnan R "Psychiatric and Medical Comorbidities of Bipolar Disorder" Psychosomatic Medicine **67**:1-8 2005.
- Ranganathan, Mohini D'Souza, Deepak Cyril. "The acute effects of cannabinoids on memory in humans: a review" Psychopharmacology **188** (4) 2006 pp. 425-444 (20) 2006.
- Ramaekers JG, Kauert G, Van Ruitenbeek P, Theunissen EL, Schneider E, Moeller MR. "High-potency marijuana impairs executive function and inhibitory motor control" Neuropsychopharmacology **31**: 2296-2303 2006.
- Ramaekers, J.G, Lamers, C.T. J., Robbe, H. W. J. & O'Hanlon, J. F. "Low doses of marijuana and alcohol severely impair driving when taken together." In Alcohol, drugs and Traffic Safety Stockholm, Sweden, Eds. Hans Laurell and Frans Schlyter. May 21-26, 2000.
- Ramstrom, J. "Adverse Health Consequences of Cannabis Use: a survey of scientific studies published up to and including the autumn of 2003". National Institute of Public Health, Sweden, 2004.
- Raphael, B et al. "Comorbidity: cannabis and complexity. Journal of Psychiatric Practice". **11**(3):161-76, 2005.
- Rey, J. "Does marijuana contribute to psychotic illness?" Current Psychiatry, Vol. **6**, No. 2, 2007.

- Rey J, Sawyer MG, Raphael B, Patton GC, Lynskey MT, "The mental health of teenagers who use marijuana" Br J Psychiatry **180**:222-6 2002.
- Rey J, Tennant C "Cannabis and Mental health" BMJ **325** 1183-1184 2002
- Robbe D. "Marijuana wreaks havoc on brain's memory cells" 2006; nature Neuroscience (DOI: 10.1038/nn1801).
- Robison,L.L., BuckleyJ.D., Daigle A.E. (1989) "Maternal drug use and risk of childhood nnonlymphoblastic leukemia among offspring. An epidemiologic investigation implicating marijuana (a report from the Children's Cancer Study Group)". Cancer, 63, 1904-1911. <http://mutage.oxfordjournals.org/cgi/reprint/13/6/557>
- Rodriguez de Fonseca F, et al "Activation of corticotropin-releasing factor in the limbic system during cannabinoid withdrawal" Science **276** (5321): 2050-2054, 1997.
- Roffman R, Stephens R, Marlatt A "Cannabis Dependence Its Nature, Consequences and Treatment" Cambridge, UK: Cambridge University Press ISBN#0-521-81447-2. http://assets.cambridge.org/97805218/14478/frontmatter/9780521814478_frontmatter.pdf
- Rosenblatt KA, Daling JR, Chen C, Sherman KJ, Schwartz SM (2004). "Marijuana Use and Risk of Oral Squamous Cell Carcinoma." Cancer Research **64**(11):4049-4054.
- Roth MD Kleerup EC Arora A Barsky S Taskin DP "Airway inflammation in young marijuana and tobacco smokers" Am. Rev. Respir. Crit. Care. Med **157**: (3) 928-937 1998.
- Roth MD Zhu L Sharma S Stolina M Chen K Park A Tashkin DP Dubinett SM "D-9-tetrahydrocannabinol inhibits antigen presentation in vitro and anti-tumor immunity in vivo" Symposium International Cannabinoid Research Society Stone Mountain GA June 1997. <http://www.eurad.net/mari/References%20for%20Cannabis%20and%20Cancer%20sorted.pdf>
- Sahaa S, Chant D, Welham J, McGrath J. "A systematic review of the prevalence of schizophrenia". PloS Med 2005;**2**(5):e141.
- SAMHSA's "Brief Counselling for Marijuana Dependence A Manual for Treating Adults"166 pages Substance Abuse and Mental Health Services Administration 2005. www.ncadi.samhsa.gov
- Sarafian T, Habib N, Mao JT, Tsu IH, Yamamoto ML, Hsu E, Tashkin DP, Roth MD "Gene expression changes in human small airway epithelial cells exposed to Delta-9-tetrahydrocannabinol." Toxicol Lett. August 14th 2005; **158**(2): 95-107.
- Schiffman J, Nakamura B, Earleywine M, LaBrie J. "Symptoms of schizotypy precede cannabis use" Psychiatry Res. **30**; 134(1):37-42 2005.
- Schneider M., Koch M." Chronic pubertal, but not adult chronic cannabinoid treatment impairs sensorimotor gating, recognition memory, and the performance in progressive ratio task in adult rats" Neuropsychopharmacology 2003; **28**:(10) 1760-9.
- Schramm-Sapota N.L., Cha Y M., Chaudhry S., Wilson W. A., Awartzwelder H.S. Kuhn C. M. "Differential anxiogenic, aversive, and locomotor effects of THC in adolescent and adult rats" Psychopharmacology (Berl) 2007; **191**: (4) 867-77.
- Schwartz R. "Marijuana: A decade and a half later, still a crude drug with Underappreciated Toxicity" Pediatrics Vol. 109 pp. 284- 289 2002.
- Semple D, McIntosh A, Lawrie S. "Cannabis as a risk factor for psychosis: systematic review" J Psychopharmacol **19**(2):187-194 2005.
- Selten JP, Zeyl C, Dwarkasing R, Lumsden V, Kahn RS, Van Harten PN. "First-contact incidence of schizophrenia in Surinam." Br J Psychiatry. 2005;186:74-75.
- Shen D, Liu D, Liu H, Clasen L, Giedd J, Davatzikos C. "Automated morphometric study of brain variation in XXY males." Neuroimage. 2004; **23** : 648-653
- Sidney S, 2002 "Cardiovascular Consequences of Marijuana Use" Journal of Clinical Pharmacology **42**: 64-70.
- Sixty-minutes "Out of Control" Reporter Liz Hayes 20.9.2007. <http://sixtyminutes.ninemsn.com.au/article.aspx?id=297623>
- Smesny S, Rosburg T, Baur K, Rudolph N, Sauer H, Cannabinoids influence Lipid-Arachidonic Acid Pathways in Schizophrenia Neuropsychopharmacology 2007; **32**: 2067-2073.
- Smit F, Boiler L, Cuijpers P. Cannabis use and the risk of later schizophrenia: a review. Addiction. 2004;**99**:425-430.
- Soderstorm CA, Dischinger PC, Kerns TJ, et al. "Marijuana and other drug use among automobile and motorcycle drivers treated at a trauma centre". Accid Anal Prev 1995;**27**:131-135
- Solowij, N et al. "Cannabis and cognitive dysfunction: parallels with endophenotypes of schizophrenia?" Journal of Psychiatry & Neuroscience, **32**(1):30-52, 2007.
- Solowij N, 1,2,3 and Battisti R. 1 "The Chronic Effects of Cannabis on Memory in Humans: A Review Current Drug Abuse Reviews, 2008", 1, 81-98811874-4737/08

- Solowij N., Grenyer B.F. "Are the adverse consequences of cannabis use age-dependent?" *Addiction* **97**(9): 1083-6 2002.
- Solowij N, Stephens R et al, *Cognitive functioning of long-term heavy cannabis users seeking treatment* J Am Med Assoc; **287**(9): 1123-1131.2002.
- Solowij N, Stephens RS, Roffiman RA, Babor T, Kadden R, Miller M, et al. "Marijuana Treatment Project Research Group Cognitive functioning of long-term heavy cannabis users seeking treatment". *JAMA* ;**287**(1):54-61. 2002.
- South Australian Department of State Aboriginal Affairs "Aboriginal People and Drug Use" South Australian Drug Summit June 24-28 2002.
- Sporn AL, Greenstein DK, Gogtay N, Jeffries NO, Lenane M, Gochman P, Clasen LS, Blumenthal J, Giedd JN, Rapoport JL. "Progressive brain volume loss during adolescence in childhood-onset schizophrenia". *Am J Psychiatry*. 2003; **160**:2181-2189.
- Stacy AW, Newcomb MD, Bentler PM. "Cognitive motivation and drug use: a 9 year longitudinal study." *J Abnorm Psychol*. 1991; **100** (4):502-515.
- STASH (Science Threads on Addiction, Substance Use and Health) "The transition from drug use to drug dependence: The bridge to more troubled waters." STASH 2007; Vol. **3**(1). <http://www.basisonline.org/2007/01/index.html>
- Stefanis NC, Delespaul P, Henquet C, Bakoula C, Stefanis CN, Van Os J. "Early adolescent cannabis exposure and positive and negative dimensions of psychosis" *Addiction* Vol. **99**:1333-1341 2004.
- Steinberg, K.L.; Roffman, R.A.; Carroll, K.M.; Kabela, E.; Kadden, R.; Miller, M.; Duresky, D.; and The Marijuana Treatment Project Research Group. "Tailoring cannabis dependence treatment for a diverse population". *Addiction* Vol. **97**(Suppl. 1):135-142, 2002.
- Stirling, J., Barkus, E.J., Nabosi, L., Irshad, S., Roemer, G., Schreudergoidheijt, B., & Lewis, S. (2008). "Cannabis-induced psychotic-like experiences are predicted by high schizotypy. Confirmation of preliminary results in a large cohort." *Psychopathology* **41**, 371-378.
- Stirling J, Lewis S, Hopkins R, White C. "Cannabis use prior to first onset psychosis predicts spared neurocognition at 10-year follow-up" *Schizophr Res* Vol. **75**(1):135-137 2005.
- Takei N, Sham P, O'Callaghan E, Murray GK, Glover G, Murray RM. "Prenatal exposure to influenza and the development of schizophrenia: is the effect confined to females?" *Am J Psychiatry*. 1994;**151**:117-119.
- Tamminga CA, Holcomb HH. "Phenotype of schizophrenia: a review and formulation". *Mod Psychiatry* 2005;**10**-27-39.
- Tan W,. "The Impact of Cigarette and Marijuana Smoking in Chronic Obstructive Lung Disease Study in Vancouver, Canada" The American Thoracic Society International Conference on Disease Study in Vancouver Canada 2007. <http://www.medicalnewstoday.com/articles/72372.php>
- Tarter, Ralph E. PhD. "Predictors of Marijuana Use in Adolescents Before and After Licit Drug Use: Examination of Gateway Hypothesis" *The Am J Psychiatry* **163**:2134-2140 2006.
- Tashkin DP "Effects of marijuana smoking profile on respiratory deposition of tar and absorption of CO and D-9 tetrahydrocannabinol Pulmonary pathophysiology and immune consequences of smoked substance abuse" FESEB Summer Research Conference July 18-23 Copper Mountain CO 1999. <http://www.nida.nih.gov/PDF/MeetSum/faseb99/FASEB.pdf>.
- Tashkin DP "Is frequent marijuana smoking harmful to health?" *Western J Medicine* **158**:635-637 1993.
- Tashkin DP "Smoked marijuana as a cause of lung injury" *Monaldi Arch Chest Dis* **63**(2):93-100 2005.
- Tashkin DP "Study Finds Link No between Marijuana Use and Lung Cancer" American Thoracic Society 2006. <http://www.thoracic.org/sections/publications/press-releases/conference/articles/study-finds-no-link-between-marijuana-use-and-lung-cancer.html>
- Tashkin, D.P., Coulson, A.H., Clark, V.A., Simmons, M., Bourque, L.B., Duann, S., Spivey, G.H. & Gong, H. "Respiratory symptoms and lung function in habitual heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone, and nonsmokers." *American Review of Respiratory Diseases*, **135**, 209-216 1987.
- Tashkin DP, Simmons MS, Sherrill DL, Coulson AH. "Heavy habitual marijuana smoking does not cause an accelerated decline in FEVI with age." *American Journal of Respiratory and Critical Care Medicine* Vol **155**:141-148 1997.
- Terris M et al "Marijuana use linked to early bladder cancer" *Urology* January 2006. <http://www.eurad.net/pdf/Report.pdf>.
- Tetraut JM, Crothers K, Moore BA et al, *Effects of marijuana smoking on pulmonary function and respiratory complications: a systematic review*. *Arch Intern Med* 2007; **167**(3): 221-8.

Thomson W.M., Moffit, Poulton R., Welch D., Hancox R., "Heavy marijuana use has been found to contribute to gum disease, apart from the known effects that tobacco smoke was already known to have" JAMA vol. 299 5: 525-531 2008.

Ticker R, Connolly D "Drugs and the college athlete: an analysis of the attitudes of student athletes at risk" J Drug Educ.1997;27 (2):105-19
http://www.ncbi.nlm.nih.gov/pubmed/9270209?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Ujike H, Morita Y. "New perspectives in the studies on endocannabinoid and cannabis: cannabinoid receptors and schizophrenia". J Pharmacol Sci 2004;**96**:376-81.

Vandrey R.G., Budney A.J., Hughes J.R., Liguori A. "A within-subject comparison of withdrawal symptoms during abstinence from cannabis, tobacco, and both substances" Drug and Alcohol Dependence 2008 **92** (1-3)48-54.

Vandrey R., Budney A., Liguori A. "Marijuana withdrawal as bad as withdrawal from cigarettes" Drug and Alcohol Dependence January 2007 5; 86 (1) 22-9.

Vandrey R G, Budney A J, Moore B A, Hughes J R. "A cross-study Comparison of Cannabis and Tobacco withdrawal" The American Journal on Addiction. **14**:54-63, 2005.

Van Os, J et al. "Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people" British Medical Journal, **330**:11-,2005.

Van Os J, Bak M, Hansen M, Bijl RV, de Graaf R, Verdoux H. "Cannabis use and psychosis; a longitudinal population based study". Am J Epidemiol 2002;**156**(4)319-27.

Van Os J, Hanssen M, Bak M, Bijl RV, Vollebergh W. "Do urbanicity and familial liability coparticipate in causing psychosis?" Am J Psychiatry. 2003;**160**:425-429.

Veen ND, Selten JP, van der Tweel I, Feller WG, Hoek Hw, Kahn RS. "Cannabis use and age at onset of Schizophrenia" Am J Psychiatry 2004 Mar;**161**(3):501-506.

Veling, W., Mackenbach, J.P., van Os, J., & Hoek, H.W. (2008). Cannabis use and genetic predisposition for schizophrenia: A case-control study. *Psychological Medicine* 38, 1251-1256.

Verdoux H, Gindre C, Sorbara F, Tournier M, Swendsen JD. "Effects of cannabis and psychosis vulnerability in daily life: an experience sampling test study". Psychol Med 2002; **33**:23-32 2003.

Victoria Police "Impaired Driver Enforcement Training Version 1.0 Testing for Drug Impaired Driving- An Instructional CD-Rom. Copyright Vic Roads 1999.

Victoria Police "Random roadside drug testing program expanded" 28 February 2006.

Watanabe K, Motoya E, Matsuzawa N, Funahashi T, Kimura T, Matsunaga T, Arizono K, Yamamoto I (2005). "Marijuana extracts possess the effects like the endocrine disrupting chemicals." Toxicol **206**:471-478.

Watson C, Fleming J, Alexander K. "A survey of drug use patterns in Northern Territory Aboriginal communities: 1986-1987. Darwin: Northern Territory Department of Health and Community Services, Drug and Alcohol Bureau; 1988".

Weinberg NZ, Glantz M "Child psychopathology risk factors for drug abuse: overview" J Clin Child Psychol. 1999 Sep;**28**(3):290-7

Weiner Michelle D., Sussman Steve, McCuller William J., Lichtman Kara "Factors in Marijuana Cessation among High-Risk Youth" J Drug Education Vol **29**(4) 337-357, 1999.

Werch CE, Anzalone D. "Stage Theory and Research on Tobacco, Alcohol, and Other Drug Use", Journal of Drug Education **25**:2, pp. 81-98, 1995.

WHO/ARF (Addiction Research Foundation) Report: "Adverse Health and Behavioural Consequences of Cannabis Use" Addiction Research Foundation <http://www.eurad.net/pdf/Report.pdf> 2006.

Wilson W., Mathew R., Turkington T., Hawk T., Coleman E., Provenzale J., "Brain Morphological Changes and Early Marijuana Use: A Magnetic Resonance and Position Emission Tomography Study" Journal of Addictive Diseases Volume 19 Number 1 2000.

Wu TC Tashkin DP Djahed B Rose JE "Pulmonary hazards of smoking marijuana as compared with Tobacco" New England Journal of Medicine **318**:347-351 1988.

Yücel M, Lubman D I, Harrison BJ, Fornito A, Allen NB et al, "A combined spectroscopy and functional MRI investigation of the dorsal anterior cingulate region in opiate addiction." Molecular psychiatry 2007; **12**: 691-702.

Yücel, M., Lubman, D.I., Harrison, B.J., Fornito, A., Wellard, R.M., Roffel, K., Allen, N.B., Clarke, K., Wood, S.J., Forman, S.D. & Pantelis, C. (2007). "Neuronal, physiological and brain-behavioural abnormalities in opiate-addicted individuals" Molecular Psychiatry. **12**, 611.

- Yücel, M., Lubman, D.I., Velakoulis, D., Wong, MTH., Wood, S.J., Condello, A., Brewer, W.J. & Pantelis, C (2006). "Structural brain correlates of alcohol and cannabis use in recreational users". *Acta Neuropsychiatrica*. 18(5), 226-229.
- Yücel, M., Solowij, N., Respondek, C., Whittle, S., Fornito, A., Pantelis, C., Lubman, D.I. (In Press; Accepted January 2008). "Regional brain abnormalities associated with heavy long-term cannabis use." *Arch Gen Psychiatry*. 2008;65(6):694-701.
- Yurgelun-Todd DA, Gruber SA, Hanson RA, Baird AA, Renshaw P, Pope HC." *Residual effects of marijuana use: a fMRI study. Proceedings of the 60th annual scientific meeting of the college on problems of drug dependence*". MDIDA Research Monograph, vol **179**;1999. P.78.
- Zammit, S et al. "Self-reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study". *British Medical Journal*, **325**:1199-1201, 2002.
- Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G. "Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969; historical cohort study." *BMJ* 2002;**325**:1199-1201.
- Zammit S., Bisaga A., M. D. "Pot and Psychosis: Possible Link?" *The Lancet* 370, 319-328 (2007).
- Zammit, S., Moore, T.H., Lingford-Hughes, A., Barnes, T.R., Jones, P.B., Burke, M., & Lewis, G. (2008). Effects of cannabis use on outcomes of psychotic disorders: Systematic review. *The British Journal of Psychiatry* 193, 357-363.
- Zhang X., Wang J.F., Kunos G., Groopman J.E. *Cannabinoid Modulation of Kaposi's Sarcoma-Associated Herpesvirus Infection and Transformation*". *Cancer Res* **67**: (15) 7230-7237, 2007.
- Zhang, ZF, Morgenstern, H, Spitz, MR, Tashkin, DP, Marshall, JR, Hsu, TC and Schantz, SP, "Marijuana use and increased risk of squamous cell carcinoma of the head and neck" *Cancer Epidemiol. Biomarkers Prev.* 8(12) 1071-8, 1999.
- Zhu LX, Sharma M, Stolina S, et al. "Delta-9-tetrahydrocannabinol inhibits antitumor immunity by a CB2 receptor-mediated, cytokine-dependent pathway". *J Immunology* **165**(1):373-380, 2000.
- Zimmer L., "Chapter One: The History of Cannabis Prohibition" "The Ascendancy and Decline of Worldwide Cannabis Prohibition" 1996. <http://www.hereinstead.com/Lynn-Zimmer-On-World-Wide-Cannabis-Prohibition.pdf>
- Zimmerman S, Zimmerman A M. "Genetic effects of marijuana". *The International Journal of Addictions*. 1990-1991;**25**:19-23.
- Zuckerman B et al. "Effects of maternal marijuana and cocaine use on fetal growth". *NEJM*. 1989;**320**:762-768.
- Zweben Joan Ellen Ph.D., O'Connell Kathleen "Strategies for Breaking Marijuana Dependence" *Journal of Psychoactive Drugs* Vol **24**(2) pp 165-171 1992. <http://members.optushome.com.au/~apdfy/Strategy.html>

APPENDIX A: UNITED KINGDOM

An article by David Wilkes in the Daily Mail dated 5 September 2007 see link:

http://www.dailymail.co.uk/pages/live/articles/news/news.html?in_article_id=480162&in_page_id=1770

“Mother blames cannabis for suicide of promising violinist daughter”

Talented, bubbly and pretty, Laura Bower-McKnight had it all to live for. A gifted musician, the 22-year-old studied at the prestigious Royal Welsh College of Music and seemed destined for a career in the performing arts. But her life once so full of promise was prematurely ended when she killed herself after cannabis turned her into a shambling wreck and left her an depressed recluse terrified of going outdoors. She was found dead at her family's home last week after hanging herself from the end of her bed. Her heartbroken mother told how smoking a single joint of the potent "skunk" variety of the drug triggered a psychotic episode in her violinist daughter and set her on the road to her death.

Mrs. McKnight said: "People think nothing of cannabis nowadays. They just don't realise this drug can tip you over the edge. "A lot of people try it". With the government downgrading it, I think young people assume it is completely harmless." But it can destroy your mind."

Having returned to the family home in North Hykeham, troubled Laura, who had previously smoked normal cannabis with friends, tried a joint of skunk - and the experience proved devastating. Mrs. McKnight said: "It wasn't the real Laura, the always-on-the-go, lovely young woman, the musician, the passionate writer, the artist." It tipped her into psychosis. We lost our wonderful girl for a while. Her behaviour became completely erratic. She was doing very odd things. Mrs. McKnight said she and her husband Malcolm, Laura's stepfather, now only hoped their daughter's death would serve as a warning to others.

She said: "Laura would have wanted us to highlight these issues. We were so close. It's just a massive, irreplaceable loss from our lives. "There are a lot of young, vulnerable people. Expectations of them are so high. Drug use, depression and suicide among them is a growing problem." Mr. McKnight, 44, an engineer, added: "Different people have different limits with drugs. For some even the tiniest amount can be too much."

An article by Paul Britton in the Manchester Evening News on 17 April 2006 see link:

http://www.manchestereveningnews.co.uk/news/s/210/210885_parents_blame_cannabis_for_sons_suicide.html

‘Parents blame cannabis for son's suicide’

A grieving family blames cannabis for causing the mental illness that drove their son to suicide. Lee Michael Wellock, 24, was found hanging from a tree with a note in his pocket indicating that he intended to kill himself. Lee had smoked the drug since he left Elton High school in Bury to work at a computer company. His parents, Michael and Denise, of Newington Drive in Bury, said it "took over and controlled" their son's life and ultimately led to his death. Lee, who did not drink alcohol, smoke cigarettes or take any other drugs, developed mental health problems at the age of 18 and was diagnosed with schizophrenia at 22, an inquest in Bury was told.

An article by Richards Edwards in the Telegraph Newspaper on the 25 September 2007 see link:

<http://www.telegraph.co.uk/news/main.jhtml?xml=/news/2007/09/25/nsuicide125.xml>

“Suicide girl jumped to death at hospital”

The daughter of an aristocratic couple jumped to her death following an eight-year descent into mental illness triggered by cannabis, it has emerged. Genevieve Butler, 28, the daughter of Lord and Lady Dunboyne, the Anglo-Irish family, threw herself from a balcony at a London hospital after breaking free from a nurse who was taking her for a cigarette break.

Her parents told of how their "clever, bright and quick-witted" daughter had been lost to them eight years ago when she was diagnosed with drug-induced -paranoia after using cannabis. *“Potent marijuana blamed for remote youth suicides”* reported in 'The Australian' on Wednesday 21 November 2007 highly potent marijuana is being blamed for youth suicides and psychotic episodes in a remote central Australian community, which is struggling to cope with increasing levels of drug use over the past 12 months. Susie Low the head of the Internationally-recognised substance abuse program at Mt Theo outstation said "In two out of the last three (suicides), the young men were under the influence of alcohol and marijuana". Ms Low's anecdotal concerns support the findings of two reports on marijuana use in the Territory, the most recent of which said 60 per cent of people in some Arnhem Land communities were cannabis users.

APPENDIX B: AUSTRALIA

Spencer Gear in a Letters to the Editor, Fraser Coast Chronicle Maryborough Queensland on the 15 March 2007 wrote. Sadly, I have conducted the funeral of a 27-year old who committed suicide. Her family told me that the doctor said that her psychosis was probably marijuana induced. Herschel Baker (FCC 31-3-07) is right in challenging Dr. Kees Nydam's incorrect statement that "finding a clear-cut association between marijuana and mental health was not easy." It is clear in the research literature.

"Potent marijuana blamed for remote youth suicides" reported in The Australian on Wednesday 21 November 2007 highly potent marijuana is being blamed for youth suicides and psychotic episodes in a remote central Australian community, which is struggling to cope with increasing levels of drug use over the past 12 months. Susie Low the head of the Internationally-recognised substance abuse program at Mt Theo outstation said "In two out of the last three (suicides), the young men were under the influence of alcohol and marijuana". Ms Low's anecdotal concerns support the findings of two reports on marijuana use in the Territory, the most recent of which said 60 per cent of people in some Arnhem land communities were cannabis users.

Cannabis may trigger psychosis: experts

The Sydney Morning Herald March 7, 2005 - 1:24AM www.SMH.com.au.

<http://www.smh.com.au/news/Health/Cannabis-may-trigger-psychosis-experts/2005/03/07/1110044267823.html>

Cannabis is not the harmless drug many people believe it to be, with new evidence showing today's genetically engineered crops are more potent and may trigger psychotic illnesses, Australian scientists say. One in five Australian teenagers smoke cannabis every week, some as young as 10, and 10 per cent of those become addicted. Psychologists, bioscientists and counsellors are seeing more young Australians developing psychoses, depression and anxiety disorders through cannabis use, the ABC's *Four Corners* program has been told. Professor Vaughan Carr, Scientific Director of the Neuroscience Institute, said he believed there were similarities between the effects of cannabis on the brain, and schizophrenia. "I think that the odds are better than 50-50 that cannabis use in sufficient quantities beginning early enough in life may produce some cases of schizophrenia in people who otherwise would not have developed it," he told *Four Corners*, which airs tonight. "But that's my gut feeling. Roughly one in five adolescents overall are cannabis users in reasonable quantities. "I would have to say that all of them are at risk, but the earlier the onset of cannabis use and the greater the frequency of use, the higher the risk."

Sydney psychologist Andrew Campbell said there was much debate about whether cannabis uncovered an existing psychosis, or caused it. "My view is that it is bringing on new cases of psychosis," he told the program. "I see a lot of people with long-standing psychosis and if I see one in 10 people in a day, seven of them will have used cannabis on a daily basis at the first time of onset of psychosis."

The experts also say new hydroponically grown crops have been engineered into a much more toxic drug than 30 years ago. Dr Campbell said the new variety grew only about a metre high with little leaf and a lot of heads. As a result, the main chemical, tetrahydrocannabinol, or THC, is much more concentrated. "So when you buy \$25 worth of cannabis these days you're mainly getting heads. You don't get the leaf which is much lower in concentration of cannabis," Dr Campbell told the program. The experts also say that because new research has shown the brain is not fully wired until a person is in their early to mid-20s, teenage users are most at risk of developing mental illness.

Melbourne's Early Psychosis Prevention and Intervention Centre (EPPIC) director, Pat McGorry, said at least 70 per cent of young people who attended the centre had used cannabis. "The proportion of patients using it that we see has gone up. I would say it's doubled since the early '80s when we started to look at this group of patients," Professor McGorry said.

Convicted of manslaughter after relying on cannabis psychosis re diminished responsibility.

Daily Telegraph by Michele Tydd 3rd September 1991

In the Supreme Court at Wollongong on the 3rd September, 1991, a Bega man pleaded guilty to slashing his neighbour's throat and stabbing him in the stomach and anus, on the spur of the moment, in the victim's caravan at Burragate on 3rd September, 1991. He was a long term user of marijuana and a friend of the deceased.

He raised diminished responsibility and was found to be suffering from a marijuana-induced psychosis. He was freed by the Judge after being held in custody for some two years.

“Skunk Sparks a stink” by Christopher Taylor The Sunday Mail 9 April 1994.

Drug Counsellors are concerned that skunk weed is 10 to 15 times more potent than normal cannabis strains and that is a conservative estimate. Experts say the strain has an almost hallucinogenic effect. Where marijuana gives the user a sense of euphoria, skunk can leave the user in a state that could easily be mistaken for mental imbalance.

The user can become intensely paranoid even exhibiting extreme schizophrenic traits. Experts said the strain can create “users with retarded motivation and responses.

“Video dream made me stab brother” Daily Telegraph 9 November 1988.

A 19 year old who cut his brother’s throat while he was asleep. He had seen the film Platoon and he believed he was an American soldier and his brother a member of the Vietcong. He had used 4 cones of marijuana and was said to be hallucinating, a psychiatrist gave evidence that he was suffering from a cannabis induced toxic psychosis. He was convicted of murder. The trial Justice, Justice Yeldham remarked “So much for those who would legalise marijuana”.

“Debbie’s alleged killer sobbed, say police” The Sydney Morning Herald September 15, 1987
www.SMH.com.au.

A 21-year-old man who is a heavy user of cannabis and lived with his family and nine-year old sister at Maitland in NSW, he was directed by voices (auditory hallucinations) to kill a member of his family and hence sexually assaulted and bashed his sister to death in their flat they both occupied. His plea of diminished responsibility as a result of cannabis induced psychosis was accepted. He was sentenced to three years imprisonment with a parole period of two years.

Innisfail Advocate of Saturday July 18, 1992.

“In the Townsville Bulletin newspaper on Thursday was the shocking story of two teenagers facing committal proceedings for murder, who, after smoking 20 cones of marijuana, allegedly battered a man to death with a shifting spanner and a large lump of wood. Police asked the youth (about the marijuana): “How effective was it?” to which the youth answered: “Well, I can’t remember much after it happened”. The youth also allegedly told police: “I wish I’d never had that first cone of marijuana”.

This horrifying, yet pathetic, story involving marijuana usage is not an isolated case of marijuana smoking leading to a shocking allegedly criminal act.

Need Help?

The following websites are recommended for additional information:



www.drugfree.org.au



<http://ncpic.org.au>



<http://www.theantidrug.com>



<http://www.nida.nih.gov>

