

Response to Medical Innovation Bill (Part II): Health/Medical viewpoint

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South African Medical Research Council

BUILDING A HEALTHY NATION THROUGH RESEARCH



Outline

Building a healthy nation through research

1. Background
2. What is medical cannabis?
3. Legality of medical use of cannabis
4. Should we consider use of cannabis for medical purposes?
 1. Effectiveness
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 4. Supply & regulation
 5. Route of administration
5. Conclusions

Who I am

- Director of Alcohol Tobacco & Other Drug Research Unit at MRC (since 2001)
- Registered Clinical & Research Psychologist
- June 2014 *SAMJ* article on medical cannabis – updated since then

First exposure to Medical Cannabis

- Meeting Dr Raphael Mechoulam in 2000 in Hanover (Germany) @ Medicine Meets Millennium Conference
- Israeli scientist who isolated $\Delta(9)$ -tetrahydrocannabinol (THC - main psychoactive constituent of cannabis plant), in its pure form
- He spoke about benefits of cannabinoids in reducing brain swelling in trauma patients

OPINION

Legalising medical use of cannabis in South Africa: Is the empirical evidence sufficient to support policy shifts in this direction?

CD H Parry, BJ Myers

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Inkatha Freedom Party MP Mario Ortens-Ambrosini's impassioned plea to legalise the medical use of cannabis must be understood in the context of his own condition as well as legislative changes in at least ten countries. This article argues that any decisions to shift policy must be based on a consideration of the evidence on the risks and benefits associated with the medical use of cannabis for the individual and broader society. It concludes that there are important gaps in the evidence base, particularly in human trials supporting the efficacy of cannabis use for treating and preventing medical conditions and alleviating negative symptoms associated with these conditions. South African researchers should be enabled actively to support development of the necessary evidence base by conducting preclinical and clinical research in this area. Human trials to establish the efficacy of the use of cannabis/cannabinoids in addressing AIDS-related syndromes and other negative sequelae of HIV and AIDS are especially needed.

LAP 06/2014(046):398-400. DOI:10.7196/SAMJ0613



On 19 February 2014, Inkatha Freedom Party MP Mario Ortens-Ambrosini made an impassioned plea to President Zuma and the South African (SA) government to legalise the medical use of cannabis and informed Parliament that he was introducing a private member's bill, the Medical Innovation Bill, to move this agenda forward.¹⁰ The President responded by indicating that he had asked the Minister of Health to look into the matter.

Medical cannabis refers to the use of cannabis and its constituent cannabinoids, including $\Delta(9)$ -tetrahydrocannabinol (THC) and cannabidiol (CBD), as therapy to treat or alleviate symptoms of medical conditions. In some countries synthetic cannabinoids, such as rimonabant (Cannorex) and dronabinol (Marinol), are available for these purposes. Cannabinoids are delivered through various mechanisms, the most obvious being through smoking. However, smoking cannabis can be hazardous to health over the long term because toxic compounds are created in the combustion process. In addition, it is difficult to regulate the amount of cannabinoids being ingested. However, users report that smoking reduces symptoms quickly. Cannabinoids can also be ingested orally, inhaled through vapourisers (Nabiximols), and used transdermally and via suppositories. Synthetic cannabinoids are most often delivered in pill form. Obviously these delivery mechanisms vary in cost and ease of access. In SA, smoking is the cheapest and most easily accessible delivery mechanism as cannabis is widely available to purchase, though not without risk of arrest. Cannabis oil is also available on the black market, and there are recipes on the internet for people seeking to make their own.¹¹

Medical use of cannabis is now legal in Austria, Canada, Finland, Germany, Israel, Italy, the Netherlands, Portugal and Spain.

Furthermore, medical users of cannabis in 20 states and the District of Columbia in the USA are not prosecuted so long as they are in compliance with the state's marijuana sale regulations. In contrast, it is currently illegal to possess cannabis or trade in it in SA.¹² We also have no medications approved by the Medicines Control Council that contain THC, other cannabinoids or even synthetic cannabinoids.¹³ Cannabis has also not been approved for medical use by the US Federal Drug Administration, largely as a result of three shortcomings: (i) the lack of human clinical trials to show that the benefits outweigh the risks; (ii) inconsistencies in the main chemical compounds, particularly when smoked; and (iii) the negative health effects sometimes associated with cannabis use, particularly when smoked.¹⁴ Any decisions on legalising the medical use of cannabis must take into consideration the risk of possible harms that have been demonstrated among some people who regularly use cannabis, the possible effects that legalising medical use of cannabis may have on the non-medical use of the drug, possible impacts on communities and broader society, and the quality of the evidence supporting the medical use of cannabis.

Harms associated with cannabis use

On the first issue, our own research has shown associations between cannabis use and road traffic injuries and other forms of trauma,¹⁵ crime, particularly property crime and murder,¹⁶ and sexual HIV risk behaviours,¹⁷ but the causal mechanisms were not clearly elucidated. Unpublished research conducted in SA using functional magnetic resonance imaging also showed cognitive deficits associated with cannabis use, even after participants had stopped using cannabis for several weeks (Cary 7, et al. - Functional magnetic resonance imaging (fMRI) of abstinent cannabis, cannabis/marijuana users, and normal controls,



Background-2

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- **19/2/14, IFP MP Mario Oriani-Ambrosini made an impassioned plea to President Zuma & parliament to legalise medical use of cannabis**
- **Informed parliament of intention to introducing a private member's bill (Medical Innovation Bill), to move agenda forward**
- **President Zuma indicated that he had asked Minister of Health to look into matter**





Purposes

2. The purposes of this Act are to—

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GENERAL NOTICE

NOTICE 100 OF 2014

MEDICAL INNOVATION BILL
PUBLICATION AND INVITATION FOR PUBLIC COMMENT

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No. 37349

GOVERNMENT GAZETTE, 18 FEBRUARY 2014

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- (1) codify existing best practices as to decisions by medical practitioners to innovate in cases where evidence-based treatment or management is not optimal or appropriate because the available evidence is insufficient or uncertain;
- (2) enhance certainty and clarity for medical practitioners and others regarding the criteria to be applied in determining whether to innovate in the cases referred to in subsection (1);
- (3) encourage responsible innovation in medical treatment and management by supporting reasonable and logical clinical decisions;
- (4) deter reckless, illogical and unreasonable departure from standard practice; and
- (5) legalise and regulate the use of cannabinoids for medical purposes and for beneficial commercial and industrial uses.

Application

3. Save for section 8 which shall apply throughout the Republic, this Act shall apply only with respect to one or more pilot health services, provided that—

- (1) within three months of the coming into force of this Act, the Minister shall identify and authorise at least one pilot health centre which shall have the capacity of treating a minimum of one hundred patients at any given time; and
- (2) any pilot health centre shall operate in terms of, and subject to, regulations, if any.

Background-3

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- **The Bill seeks to do more than just promote medical innovation - it has a subsidiary aim of promoting legalisation in general**
 - **Problematic: It should seek to do one or the other**
- **On a positive note it does seek to facilitate more medical research on medical cannabis**
 - **but it only seeks to promote a limited type of research – medical treatment for patients suffering from various conditions, rather than promoting a much broader array of research**

Background-4

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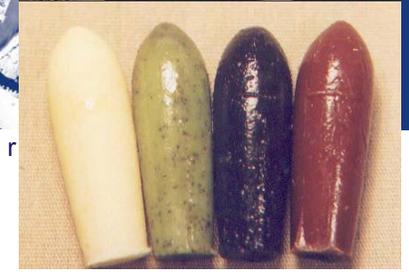
- **Medical cannabis refers to use of cannabis + constituent cannabinoids, incl. THC & cannabidiol (CBD), as therapy to treat or alleviate symptoms of medical conditions**
- **In some countries synthetic cannabinoids (e.g. nabilone (Cesamet ®) and dronabinol (Marinol ®), are available for these purposes**
- **Cannabinoids are delivered through various mechanisms, most obvious being through smoking**
 - **However, smoking cannabis can be hazardous to health over LT due to toxic compounds created in the combustion process**
 - **+ difficult to regulate the amount of cannabinoids being ingested (dosage)**
 - **However, users report that smoking is a fast-acting delivery mechanism**



Background-5

Building a healthy nation through

- **Cannabinoids can also be ingested orally, inhaled through vapourisers (Nabidiolex)® , used transdermally (patches) + via suppositories**
- **Synthetic cannabis most often delivered via pill**
- **Delivery mechanisms vary in cost + ease of access**
 - **In SA, smoking is cheapest + most easily accessible delivery mechanism as cannabis is widely available to purchase (risk of arrest)**
 - **Cannabis oil is also available on black market + recipes on internet for people seeking to make their own**



Legality of medical use of cannabis

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- **Medical use of cannabis is now legal in:**
 - Austria, Canada, Finland, Germany, Israel, Italy, Netherlands, Portugal, Spain
 - In USA, medical users of cannabis in 20 states + DC are not prosecuted as long as they are in compliance with state's MJ sale regulations
- **In SA currently illegal to possess cannabis or trade in it. We have no meds approved by MCC that contain THC, other cannabinoids, or even synthetic cannabinoids**
- **Cannabis has also not been approved for medical use by US-FDA**
 - lack of human clinical trials to showing benefits outweigh risks
 - inconsistencies in main chemical compound, esp. when smoked
 - negative health effects sometimes associated with cannabis use, esp. when smoked

Should we consider use of cannabis for medical purposes - 1

- **Use of cannabis for medical or other purposes was prohibited in SA 60+ years ago, at a time when scientific knowledge about it was scarce**
 - **Now clear that cannabis has medicinal utility, but this has been largely overlooked, with research & society's attention being directed to hazards of its recreational use rather than its medicinal benefit**
 - **Consideration of policy for medicinal cannabis should be kept separate from consideration of recreational cannabis, except in so far as increasing medical cannabis might increase recreational use**
- **Critical ? for approval of any medicine are evidence of:**
 - **effectiveness, safety, cost-effectiveness, supply, regulation, route of administration (Mather et al., 2013)**

1. Effectiveness (most of the data is focussed on symptom management rather than curing conditions) -- evidence is mixed (1)

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- Oriani-Ambrisoni referred to studies from Harvard cited in a Cannabis Position Paper presented to CDA in November 2013
- Highlights various studies, mainly pre-clinical* but some involving human subjects, that showed positive effects on a variety of conditions:
 - **Alzheimer's disease, amyotrophic lateral sclerosis, chronic pain, multiple sclerosis, diabetes mellitus, dystonia, fibromyalgia, incontinence, gastrointestinal disorders and various cancers (incl. lung cancer)**

Cannabis Position Paper 2013

As presented by the South African National Cannabis Working Group to the Central Drug Authority at the Department of Social Development

20 November 2013

André du Plessis
Imiël Visser
Alwyn Smit

*Test tube, cell culture, animal studies



Effectiveness of medical cannabis (2)

- Cannabinoids are used for symptom management (*palliative care*) in cancer
 - WRT pain relief in cancer patients
 - in experimental models of acute pain, inhaled cannabis resulted in dose-dependent pain relief
 - in patients with chronic pain both cannabis & cannabinoids outperformed placebo treatment
 - However, few studies have compared cannabis or cannabinoids with conventional meds
(Machado Rocha et al., 2008)
 - WRT effects of cannabis or cannabis extracts on AIDS wasting syndrome
 - A Cochrane Review found that 7 studies included in the review “suffered from bias & small sample size & lacked longitudinal data, limiting the extent to which conclusions could be drawn”
(Lutge et al., 2013)



Effectiveness of medical cannabis (3)

- Evidence is stronger regarding the positive effect of cannabinoids in treating chemotherapy-induced nausea + vomiting in cancer patients
 - Human studies suggest efficacy of cannabinoids in management of chemically induced nausea and vomiting
 - But further research aimed at developing new endocannabinoid-based anti-nausea and anti-emetic therapies is still warranted

(Sharkey et al., 2014)

- A German review found 82 favourable & only 9 unfavourable controlled studies assessing the potential for cannabis/cannabinoids for addressing about 1/2 a dozen conditions

(Grotenhermen & Müller-Vahl, 2012)



REVIEW ARTICLE

The Therapeutic Potential of Cannabis and Cannabinoids

Franjo Grotenhermen, Kirsten Müller-Vahl

SUMMARY

Background: Cannabis-based medications have been a topic of intense study since the endogenous cannabinoid system was discovered two decades ago. In 2011, for the first time, a cannabis extract was approved for clinical use in Germany.

Methods:

Objective: Selective literature review
Results: Cannabis-based medications exert their effects mainly through the activation of cannabinoid receptors (CB1 and CB2). More than 100 controlled clinical trials of cannabis-based or whole-plant preparations for various indications have been conducted since 1975. The findings of these trials have led to the approval of cannabis-based medicines (presonal, nabiximol, and a cannabis extract [THC:CBD=1:1]) in several countries. In Germany, a cannabis extract was approved in 2011 for the treatment of moderate to severe refractory spasticity in multiple sclerosis. It is commonly used off-label for the treatment of anorexia, nausea, and neuropathic pain. Patients can also apply for government permission to buy medicinal cannabis flowers for self-treatment under medical supervision. The most common side effects of cannabinoids are tiredness and dizziness (in more than 10% of patients), psychological effects, and dry mouth. Tolerance to these side effects usually develops within a short time. Withdrawal symptoms are hardly ever a problem in the therapeutic setting.
Conclusion: There is now clear evidence that cannabinoids are useful for the treatment of various medical conditions.

► On this site:

Grotenhermen F, Müller-Vahl K. The therapeutic potential of cannabis and cannabinoids. *Deutsch Arztebl* 2012; 109(29-30): 495-501. DOI: 10.32388/2012.0495

Knowledge about the therapeutic potential of cannabis products has been greatly improved by a large number of clinical trials in recent years (1-5). In October 2008, the German Medical Association, the National Association of Statutory Health Insurance Physicians, and the Drug Commission of the German Medical Association issued the following statement at a hearing of the Health Committee of the German Federal Parliament (Bundestag): "The benefits of treatment with cannabinoids for a number of medical indications has been shown in controlled trials in which predominantly standardized and/or synthetic cannabinoid preparations were used. The use of such preparations may therefore be reasonable for patients in whom conventional treatment does not achieve adequate relief of symptoms such as spasticity, pain, nausea, vomiting, or loss of appetite" (6). The first cannabis-based medication was approved for use in Germany in 2011. In this article we present the current state of knowledge on the therapeutic application of cannabinoid medications.

Method

This review covers publications identified by a search of the medical database PubMed (January 2000 to December 2011) using the terms "cannabis" OR marijuana OR THC OR endocannabinoid". Reviews from standard references (1-5) and the study database of the International Association for Cannabis-based Medicines (IACBM) were also analyzed. With regard to therapeutic potential, exclusively data from randomized controlled trials were considered.

History

Medications based on cannabis have been used for therapeutic purposes in many cultures for centuries (7). In Europe, they were used at the end of the 19th century to treat pain, spasms, tetanus, sleep disorders, depression, and loss of appetite. In the first half of the 20th century cannabinoid medications fell into almost complete disuse, partly because scientists were unable to establish the chemical structure of the ingredients of the cannabis plant (*Cannabis sativa* L.). It was only in 1964 that (-)-trans-delta-9-tetrahydrocannabinol (THC, dronabinol), the principal active ingredient of cannabis, was microchemically defined (8). This, followed by the discovery of the body's own cannabinoid system with specific receptors and endogenous ligands, marked the

The Therapeutic Potential of Cannabis and Cannabinoids



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Franjo Grotenhermen, Kirsten Müller-Vahl

TABLE

Overview of controlled trials of cannabis medications for established indications*¹

Indication	Number of randomized controlled trials (some three-armed)	Positive studies	Negative studies
Spasticity	n = 12 (dronabinol: [e1, e2, e4–e6]; cannabis: [e1–e3, e6–e12]) in multiple sclerosis	n = 9 (e4–e12)	n = 3 (e1–e3)
	n = 3 (dronabinol: [e13–e14]; nabilone: [e15] in paraplegia)	n = 3 (e13–e15)	–
Nausea and vomiting due to cytostatics	n = 41 (dronabinol: [e16–e34]; cannabis cigarettes: [e25]; cannabis extract: [e35]; nabilone: [e36–e52]; levonantradol: [e53–e56])	n = 40	n = 1 (e18)
Loss of appetite/weight loss	n = 7 (dronabinol: [e59–e65]; cannabis cigarettes: [e63–e65]) in HIV/Aids	n = 7	–
	n = 4 (dronabinol: [e66–e68]; cannabis extract: [e69]) in various tumor diseases	n = 3	n = 1 (e69)
	n = 1 (dronabinol: [e70]) in Alzheimer's disease	n = 1	–
Chronic pain	n = 14 (dronabinol: [e71–e74]; nabilone: [e75, e76]; cannabis extract: [e73, e74, e77–e79]; cannabis cigarettes: [e80–e83]; CT3 (ajulemic acid): [e84]) in neuropathic pain or pain in MS	n = 12 (e71, e73–e75, e77–e84)	n = 2 (e72, e76)
	n = 12 (dronabinol: [e85–e87, e93]; NIB: [e88]; benzopyrano-peridine: [e89]; cannabis extract: [e87, e90, e94]; nabilone: [e91, e92, e96]; cannabis cigarettes: [e95]) in chronic pain (cancer, rheumatism, fibromyalgia)	n = 11 ([e85, e86, e87] cannabis extract, [e88, e90–e96])	n = 2 ([e87] dronabinol, [e89])

*¹ A complete list of clinical trials of cannabis medications can be found on the website of the IACM (24)

Effectiveness of medical cannabis (4)

- **Concerns re above study:**
 - Possible vested interest in showing a positive effect- they consult for pharma and have other links to cannabis related associations
 - No meta-analysis. We have no idea if there is actually a positive effect (taking all of these studies into account), how homogenous the findings are, etc.
 - No consideration of the quality of the studies
 - It is not a systematic review but a “selective literature review”. We have no idea of the studies that were excluded, and or why. They ignore 2 Cochrane Reviews on this topic (e.g. on AIDS wasting syndrome (Lutge et al., 2013) & MS (Mills et al., 2007))
- **Emerging evidence that cannabinoids may have anti-cancer effects, particularly anti-tumour effects [*therapeutic, rather than palliative care*]**
 - Mainly pre-clinical studies
 - Few human clinical trials have been published in this area
 - More trials are required to achieve certainty that cannabis or cannabinoids can be used as anticancer agents
(Machado Rocha et al., 2008)

2. Safety of medical cannabis (1)

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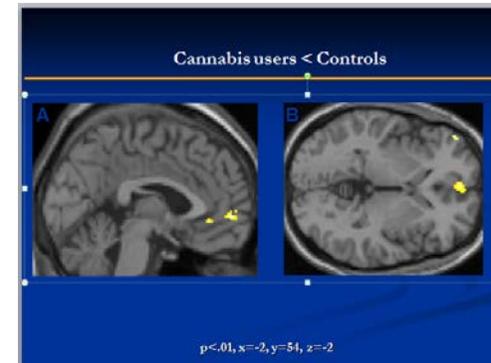


- **SAMRC Research**

- shown associations between cannabis use & road traffic injuries & other forms of trauma, crime (esp. property crime, murder), & sexual HIV risk behaviours
- but causal mechanisms were not clearly elucidated



- Unpublished research conducted at **SAMRC** Stress & Anxiety Unit, Stellenbosch U (Carey et al.) using fMRI showed cognitive deficits associated with cannabis use, even after participants had stopped using cannabis for several weeks



Safety of medical cannabis (2)

Building a healthy nation through science



Review

- Recent systematic review (Hall & Degenhardt, 2009) identified several adverse effects associated with cannabis use:
 - dependence syndrome; increased risk of motor vehicle crashes, impaired respiratory function & cardiovascular disease; adverse effects of regular use on adolescent psychosocial development and mental health
 - However, these harms should not be overstated, as they do not affect all users
- At community level the harms are less than those associated with alcohol & tobacco use (Nutt, 2011, 2014 – *Lancet*)

Adverse health effects of non-medical cannabis use

Weyre Hat, Luxembourg

For over two decades, cannabis, commonly known as marijuana, has been the most widely used illicit drug by young people in high-income countries, and has recently become popular on a global scale. Epidemiological research during the past 10 years suggests that regular use of cannabis during adolescence and into adulthood can have adverse effects. Epidemiological, clinical, and laboratory studies have established an association between cannabis use and adverse outcomes. We focus on adverse health effects of greatest potential public health interest— that is, those that are most likely to occur and to affect a large number of cannabis users. The most probable adverse effects include a dependence syndrome, increased risk of motor vehicle crashes, impaired respiratory function, cardiovascular disease, and adverse effects of regular use on adolescent psychosocial development and mental health.

Introduction

Psychoactive preparations of Cannabis sativa have been used for over 4000 years for medical and religious purposes. Over the past 50 years they have been increasingly adopted by adolescents and young adults for recreational use—in social settings to increase sociability and produce euphoric and intoxicating effects. Since cannabis use was first reported over 40 years ago by US college students, its recreational or non-medical use has spread globally, first to high-income countries, and recently to low-income and middle-income countries¹ (figures 1 and 2).

Uncertainties exist about the number of people who use cannabis because of lack of timely, good-quality data in most countries. The UN Office on Drugs and Crime has estimated that in 2006 cannabis was used by 166 million adults (1–9% of the global population aged 15–64 years)². Use was the highest in the USA, Australia, and New Zealand, followed by Europe. These countries reported higher rates of cannabis use than did the Middle East and Asia.³ Some African countries are also thought to have high rates of cannabis use.⁴ Because of these large populations, 11%, 20%, and 20% of the world's cannabis users are estimated to be from Asia, Africa, and the Americas, respectively, compared with 16% in Europe and 2% in Oceania² (figure 1).

Pattern of cannabis use

In the USA, rates of cannabis use in young adults peaked in 1979, which was followed by a long decline until the early 1990s, when use increased again, before levelling off towards the end of the decade.⁵ A similar rise in its use in the early 1990s, followed by decline or stabilisation in recent years, has been reported in Australia and western Europe⁶. Research in the USA has indicated that about 10% of those who ever use cannabis become daily users, and 30% to 50% become weekly users.⁷ Cannabis use in the USA typically begins in the middle to late teenage years and peaks in the early and middle 20s. Use declines sharply after young people enter full-time employment, energy and have children.⁸

No reliable information exists about the concentration of Δ-9-tetrahydrocannabinol and other cannabinoids (eg, cannabidiol) in commonly used cannabis products.

Search strategy and selection criteria

We searched PubMed and Thompson Business Web of Science (current indexes) for articles published in the past 10 years on adverse health effects of cannabis, with the search terms: "cannabis", "marijuana abuse", "marijuana smoking", "psychoactive", "adverse effects", "substance-related disorder", "drug abuse", "respiratory disorder", "cardiovascular disease", "marijuana dependence", "marijuana addiction", "marijuana abuse", "marijuana dependence", and "marijuana". Most selected studies were published in English since 1997. Additional publications were identified from the references selected and from books, other works, and reports in the field.

www.thelancet.com Vol 374 October 12, 2009

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Safety of medical use of cannabis (3)

- **Have to look at studies of side effects of medical cannabis - not studies of side effects of recreational cannabis**
- **Reviews of medicinal cannabis used under essentially controlled conditions indicate that frequencies of both side effects & dependence are low**
- **Need to compare side effects of cannabis vs symptoms if no treatment vs side effects of conventional meds**
- **MDs & pharmacists will require further education about medical cannabis & how to instruct patients in its use. Criteria for patient selection will need development**



Safety of medical use of cannabis (4)

- As c/ opioid analgesics, risks of diversion of medicinal cannabis must be minimised. But is hard to envisage how significant diversion will be necessary when cannabis is very easy to obtain
- In US states that have passed medical cannabis laws, no increase was found in the prevalence of use overall or among adolescents (**Lynne-Landsman et al., 2013**)
- In general, medical cannabis policies reduce cannabis consumption, but states that allow dispensaries &/or allow home cultivation can completely offset positive effect on cannabis consumption (**Pacula et al., 2013**)
- In US states' legalization associated with an 8-11% drop in traffic fatalities (from alcohol) (**Anderson et al., 2012**)
- We need to separate out the health affects of synthetic cannabis vs cannabis; and smoked vs taken up in other ways

3. Cost

effectiveness of med cannabis

- No data on cost effectiveness yet
- But likely to be cost effective
 - vapourizers not cheap (Pens -- \$100+ for kit but save on cannabis)

4. Supply & regulation

- Need supply of consistent, high quality cannabis leaf
 - Import?
 - NDoH to produce?
 - License to SA companies to cultivate & produce in compliance with clear standards + be subject to strict quality control under NDoH control



5. *Route of administration*

- Smoking is not an accurate dosage method + is not acceptable to many patients, nor is it medically acceptable
- **Oral absorption poor, slow, unpredictable, less acceptable to patients**
- Vaporisation in an electrically heated vaporiser produces comparable results & is preferable



- 1. Commend** late MP for bringing attention to issue of medical cannabis, but we don't support Bill in its current form
- 2. Argue** that issue of medical cannabis should be separated from legalisation of cannabis or commercial cultivation
- 3. As a public health research organization we *do not support* smoking of cannabis for recreational purposes, just as we do not support tobacco smoking**



Conclusion (2)

Building a healthy nation through research



4. *Acknowledge* increasing evidence of value of medical cannabis (using extracts such as oils, tablets, patches or vapourizers) in providing palliative care for various conditions
4. *Recommend* a Cochrane Review be undertaken **by SAMRC** to evaluate quality/strength of evidence for use of cannabinoids/cannabis for both palliative care and therapeutic use
4. *Believe* that the Medicines Control Council (MCC) needs to consider the evidence (before registering cannabinoids/cannabis in South Africa)

7. **SAMRC** should take the leading role in coordinating further research and clinical trials on the use of medical cannabis
8. **SAMRC** should also monitor possible influences of medical cannabis use on non-medical use (especially among adolescents)

