

OPINION

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

C D H Parry, B J Myers

Charles Parry is Acting Vice-President (Intramural Research) at the South African Medical Research Council (MRC), Director of the Alcohol, Tobacco and Other Drug Research Unit (ATODRU) at the MRC, and an Extraordinary Professor in the Department of Psychiatry at Stellenbosch University, Tygerberg, Cape Town, South Africa. His interests include substance abuse epidemiology, alcohol and drug policy, and the effect of substance abuse on HIV and AIDS. Bronwyn Myers is a Chief Specialist Scientist in the ATODRU and an Honorary Associate Professor in the Department of Psychiatry and Mental Health at the University of Cape Town, South Africa. Her interests include alcohol and drug intervention and services research, and drug policy.

Corresponding author: C Parry (cparry@mrc.ac.za)

Inkatha Freedom Party MP Mario Oriani-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 wasting syndrome and other negative sequelae of HIV and AIDS are especially needed.

S Afr Med J 2014;104(6):399-400. DOI:10.7196/SAMJ.8135



On 19 February 2014, Inkatha Freedom Party MP Mario Oriani-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.^[1] 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 nabilone (Cesamet) 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 relieves symptoms quickly. Cannabinoids can also be ingested orally, inhaled through vapourisers (Nabidiolex), and used transdermally and via suppositories. Synthetic cannabis is 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.^[2]

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 as 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.^[3] We also have no medications approved by the Medicines Control Council that contain THC, other cannabinoids or even synthetic cannabinoids.^[4] 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 compound, particularly when smoked; and (iii) the negative health effects sometimes associated with cannabis use, particularly when smoked.^[5] 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,^[6] crime, particularly property crime and murder,^[7] and sexual HIV risk behaviours,^[8] 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 (Carey P, *et al.* – 'Functional magnetic resonance imaging (f-MRI) of abstinent cannabis, cannabis/methaqualone users, and normal controls',

presented at the 6-monthly meeting of the South African Community Epidemiology Network on Drug Use, 16 November 2005). In addition, a recent systematic review identified several adverse effects associated with cannabis use, including a dependence syndrome, an increased risk of motor vehicle crashes, impaired respiratory function, cardiovascular disease, and adverse effects of regular use on adolescent psychosocial development and mental health.^[9] However, these harms should not be overstated, as they do not affect all people who use cannabis. Certainly, at a community level the harms are a lot fewer than those associated with alcohol and tobacco use.^[10,11]

Impact of medical cannabis use on non-medical use

On the second issue, very few studies have examined whether allowing medical use of cannabis impacts on its non-medical use. A large study investigating the relationship between state legalisation of medical cannabis and cannabis use, abuse and dependence in the USA found that states that legalised medical cannabis had higher rates of use, but the authors acknowledged that this association was not necessarily causal.^[12] National surveys in Canada have indicated substantial use of cannabis for therapeutic purposes outside of the Health Canada programme, with an order of magnitude of between 13 and 33 persons for every one person in the programme.^[13]

Quality of the evidence supporting medical use of cannabis

The third important issue when considering whether to legalise the medical use of cannabis is the quality of the evidence in support of its effects on medical conditions. In his speech in Parliament, Oriani-Ambrosini referred to studies from Harvard cited in a Cannabis Position Paper presented to the Central Drug Authority in November 2013.^[14] This paper highlights various studies, mainly preclinical but some involving human subjects, that showed positive effects on a variety of conditions including Alzheimer's disease, amyotrophic lateral sclerosis, chronic pain, multiple sclerosis, diabetes mellitus, dystonia, fibromyalgia, incontinence, gastrointestinal disorders and various cancers, including lung cancer, the condition affecting Oriani-Ambrosini. Other conditions that have reportedly been positively affected by cannabis use include atopic dermatitis, brain injuries, eating disorders, epilepsy, glaucoma, Huntington's disease, neuromuscular disorders, rheumatoid arthritis, sleep disorders and Tourette's syndrome, though in many cases the supportive evidence is equivocal.^[15]

Cannabinoids are used for symptom management in cancer, while there is emerging evidence that cannabinoids may have anticancer effects, particularly antitumour effects.^[16] However, few human clinical trials have been published in this area, and more trials are required to achieve certainty that cannabis or cannabinoids can be used as anticancer agents.^[16] With regard to 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 and cannabinoids outperformed placebo treatment. However, few studies have compared cannabis or cannabinoids with conventional medications used to manage pain in cancer.^[16]

The effects of cannabis or cannabis extracts on AIDS wasting syndrome or weight loss from AIDS have been studied, mainly because cannabis or cannabinoids reportedly stimulate the appetite. A Cochrane review found that the seven studies included in the review suffered from bias and small sample size and lacked longitudinal data, limiting the extent to which conclusions could be drawn.^[17] The evidence is stronger regarding the positive effect of cannabinoids in treating chemotherapy-induced nausea and vomiting in cancer patients.^[16,18] Human studies suggest efficacy of cannabinoids in

the management of chemically induced nausea and vomiting, but further research aimed at developing new endocannabinoid-based anti-nausea and antiemetic therapies is still warranted.^[18]

Conclusions

There appears to be a divide between the reported medical benefits of cannabis use and well-executed studies on the benefits and risks of such use.^[13] Although evidence from preclinical studies points to the potential for cannabinoids to contribute to symptom alleviation and possible effects on disease status for a number of medical conditions, there are significant gaps in our understanding of the potential benefits and risks associated with their use. Most notable is the lack of evidence from human trials. That said, and in line with part of the reasoning behind the proposed legislation,^[1] the SA government should make it easier for researchers to conduct studies on the medical use of cannabinoids (including synthetic cannabinoids), and funding should be made available to support this research, especially where it could lead to medical innovation. This research should include: (i) an investigation of factors that led to the policy shifts in countries that have legalised the medical use of cannabis, and what their experiences have been of this policy shift; (ii) maintaining a watching brief on the literature in this area, as advances in scientific knowledge are taking place rapidly; (iii) establishing surveillance systems to assess the possible influences of medical cannabis use on non-medical cannabis use; and (iv) conducting both preclinical and human studies to study the effects of cannabinoids on symptom alleviation and disease status. For the latter, longitudinal studies that investigate the effects of cannabinoid inhalation and ingestion on the quality of life of patients with HIV/AIDS, where SA should lead the way, are especially needed.

In conclusion, while in principle we are open to the idea of cannabis use for medical conditions, we need to strengthen the empirical evidence base in support of the benefits of such use, and find ways to minimise the risk of harms, before we can recommend legalising medical cannabis use in SA.

1. Oriani-Ambrosini MGR. Medical Innovation Bill: Publication and invitation for public comment (Notice 10 of 2014). Government Gazette No. 37349, 18 February 2014, Vol. 584.
2. Kellzy. Making cannabis oil in South Africa. <http://kitchencures.wordpress.com/2013/06/16/104/> (accessed 26 February 2014).
3. The Drugs and Drug Trafficking Act, 1992 (Act No. 140 of 1992).
4. Medicines and Related Substances Act, 1965 (Act No. 101 of 1965).
5. National Institute on Drug Abuse. DrugFacts: Is marijuana medicine? <http://www.drugabuse.gov/publications/drugfacts/marijuana-medicine> (accessed 25 February 2014).
6. Parry CDH, Phliddemann A, Donson H, Sukhai S, Marais S, Lombard C. Cannabis and other drug use among trauma patients in Cape Town, Port Elizabeth and Durban, South Africa, 1999-2001. *S Afr Med J* 2005;95(6):429-432.
7. Parry CDH, Phliddemann A, Louw A, Leggett T. The 3-Metros Study of Drugs and Crime in South Africa: Findings and policy implications. *Am J Drug Alcohol Abuse* 2004;30(1):167-185. [<http://dx.doi.org/10.1081/ADA-120029872>]
8. Parry CDH, Petersen P, Carney T, Dewing S, Needle R. Rapid assessment of drug use and sexual HIV risk patterns among vulnerable drug using populations in Cape Town, Durban and Pretoria, South Africa. *SAHARA-J: Journal of Social Aspects of HIV/AIDS* 2008;5(3):52-58. [<http://dx.doi.org/10.1080/17290376.2008.9724909>]
9. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet* 2009;374(9698):1383-1391. [[http://dx.doi.org/10.1016/S0140-6736\(09\)61037-0](http://dx.doi.org/10.1016/S0140-6736(09)61037-0)]
10. Lim SS, Vos T, Flaxman AD, et al. The burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions 1990-2010: A systematic analysis. *Lancet* 2012;380(9859):2224-2260. [[http://dx.doi.org/10.1016/S0140-6736\(12\)61766-8](http://dx.doi.org/10.1016/S0140-6736(12)61766-8)]
11. Nutt DJ, King LA, Phillips D. Drug harms in the UK: A multicriteria decision analysis. *Lancet* 2010;376(9752):1558-1565. [[http://dx.doi.org/10.1016/S0140-6736\(10\)61462-6](http://dx.doi.org/10.1016/S0140-6736(10)61462-6)]
12. Cerdá M, Wall M, Keyes KM, Galea S, Hasin D. Medical marijuana laws in 50 states: Investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug Alcohol Depend* 2012;120(1-3):22-27. [<http://dx.doi.org/10.1016/j.drugalcdep.2011.06.011>]
13. Walsh Z, Callaway R, Belle-Isle L, et al. Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use. *Int J Drug Policy* 2013;24(6):511-516. [<http://dx.doi.org/10.1016/j.drugpo.2013.08.010>]
14. Du Plessis A, Visser I, Smit A (on behalf of the South African Cannabis Working Group). Cannabis Position Paper 2013. <https://www.daggacouple.co.za/wp-content/uploads/2013/11/SANCWG-Cannabis-Position-Paper-of-2013.pdf> (accessed 25 February 2014).
15. Mayo Clinic. Drugs and supplements: Marijuana (*Cannabis sativa*). <http://www.mayoclinic.org/drugs-supplements/marijuana/evidence/hrb-20059701> (accessed 26 February 2014).
16. Machado Rocha FC, Stefano SC, De Cássia Haiek R, Rosa Oliveira LMQ, Da Silveira DX. Therapeutic use of *Cannabis sativa* on chemotherapy-induced nausea and vomiting among cancer patients: Systematic review and meta-analysis. *Eur J Cancer* 2008;17(5):431-443. [<http://dx.doi.org/10.1111/j.1365-2354.2008.00917.x>]
17. Lutge, EE, Gray A, Siegfried N. The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS. *Cochrane Database Syst Rev* 2013; Issue 4. Art. No.: CD005175. [<http://dx.doi.org/10.1002/14651858.CD005175.pub3>]
18. Sharkey KA, Darmani NA, Parker LA. Regulation of nausea and vomiting by cannabinoids and the endocannabinoid system. *Eur J Pharmacol* 2014;722:134-146. [<http://dx.doi.org/10.1016/j.ejphar.2013.09.068>]

Accepted 12 March 2014.