## **Gary Christian**

From: Sent: To: Subject: Gary Christian Friday, 27 March 2015 1:01 PM 'Brian Watters' INCB on Cannabis Legalisation

Brian

Here is the press release from the INCB re medical marijuana governed by States rather than Feds.

## PRESS RELEASES

UNIS/NAR/1023

8 February 2008

## Marijuana Vending Machines in Los Angeles are Contrary to International Drug Control Treaties, says INCB

VIENNA, 8 February (UN Information Service) -- "The International Narcotics Control Board (INCB) is deeply concerned about reports that computerized vending machines to dispense cannabis (marijuana) have been put into operation in Los Angeles," said Dr. Philip O. Emafo, President of the Board. The Board concludes its 91st session today in Vienna. "We know that the use of cannabis is illegal under federal law of the United States and we trust the authorities will stop such activities, which contravene the international drug control treaties," he added.

California is one of 11 states of the United States of America which allows medical use of cannabis, though such use continues to be illegal under federal law. In June 2005, the US Supreme Court confirmed the right of the Government to enforce the prohibition on the use of cannabis in a state that removed state-level criminal penalties on the use, possession and cultivation of cannabis for medical purposes.

Cannabis is included in Schedules I and IV of the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol (1961 Convention). Substances in Schedule IV are those considered particularly liable to abuse.

For some years there have been various claims about the therapeutic usefulness of cannabis or cannabis extracts. Scientific research concerning this question is in progress in several countries. So far, the results of research regarding the potential therapeutic usefulness have been limited.

INCB has confirmed in its annual reports that it welcomes sound scientific research on the therapeutic usefulness of cannabis. The Board requested governments concerned to share the results of such research, when available, with the Board, the World Health Organization (WHO) and the international community.

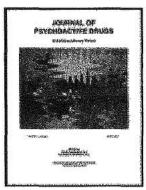
The Board has repeatedly expressed its concern that, without having reported conclusive research results to WHO, the Governments of Canada and the Netherlands authorized the use of cannabis for medical purposes. The Board is also concerned that cannabis is used for medical purposes in some jurisdictions of the United States without having definitive proof of its efficacy.

The control measures applied in California for the cultivation, production and use of cannabis do not meet the control standards set in the 1961 Convention to prevent diversion of narcotic drugs for illicit use. Such standards require, inter alia, the control of cultivation and production of cannabis by a national cannabis agency, and detailed record keeping and reporting on the activities with cannabis, including reporting to INCB.

The International Narcotics Control Board (INCB) is an independent control organ, established by the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol, for monitoring the implementation of the international drug control treaties by Governments and for providing assistance to Governments in this regard.

### Regards

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## Who Are Medical Marijuana Patients? Population Characteristics from Nine California Assessment Clinics

Craig Reinarman Rh.D.<sup>a</sup>, Helen Nunberg M.D.M.P.H.<sup>a</sup>, Fran Lanthier M.A.<sup>a</sup> & Tom Heddleston M.A.<sup>a</sup>

<sup>a</sup> Department of Sociology, University of California, Santa Cruz, CA, USA

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increased sharply. Recent estimates from the National Survey on Drug Use and Health show that 102,404,000 Americans have used this drug, 41% of the population aged 12 and over, or about half the adult population (SAMHSA 2010). This widespread use led to a gradual rediscovery of the therapeutic uses of cannabis, albeit largely without physician involvement.

Alongside the spread of nonmedical use, in 1964 scientists determined the precise chemical structure of delta-9 tetrahydrocannabinol (THC), thought to be the most significant psychoactive ingredient in cannabis (Gaoni & Mechoulam 1964). This stimulated research in the clinical pharmacology of cannabinoids. Many physicians in clinical practice also recognized the therapeutic potential of cannabis (Irvine 2006; Charuvastra, Freidmann & Stein 2005), specifically, for example, for pain (Woolridge et al. 2005), as an antiemetic for chemotherapy patients (Doblin & Kleiman 1991), or for symptoms of AIDS (Abrams et al. 2003). More recently a broader medical literature documenting the therapeutic properties of endogenous cannabinoids has developed (e.g., Nicoll & Alger 2004; Lehmann et al. 2002; Hall, Degenhart & Currow 2001). Numerous case reports in the medical literature also have suggested that cannabis has therapeutic potential for a variety of conditions. But rigorous experimental research that might determine more precisely the therapeutic efficacy of cannabis for specific conditions has been blocked by the Drug Enforcement Administration (see Zeese 1999; Alliance for Cannabis Therapeutics v. Drug Enforcement Administration 1994).

This combination of increasing therapeutic use and federal government opposition ultimately led to passage of new state laws providing for the medical use of cannabis upon physician recommendation. Since 1996, 15 U.S. states and the District of Columbia have passed such laws: California, Alaska, Oregon, Washington, Nevada, Colorado, Maine, Montana, Michigan, and Washington, DC by ballot initiative; Rhode Island, New Mexico, Vermont, Hawaii, and New Jersey by state legislation.

The first of these laws was California's Proposition 215, the Compassionate Use Act, passed in 1996 (San Francisco Chronicle 1996). This act made it legal under state law for patients to possess and use cannabis if recommended by their physicians. Numerous medical and scientific associations endorsed medical use of cannabis and/or supported further research into its therapeutic potential. These included the American College of Physicians (2008), the American Public Health Association (1995), the British Medical Association (1997), the Canadian Medical Association (2005), and the Institute of Medicine of the National Academy of Sciences (1999).

Such elections and endorsements notwithstanding, the Bush Administration's Office of National Drug Control Policy threatened to revoke the licenses of physicians who recommended cannabis to patients. One physician challenged this policy and the U.S. Court of Appeals ruled (in *Conant v. Walters*) in 2002 that it unconstitutionally infringed physicians' First Amendment rights to freedom of speech with their patients (McCarthy 2004). Subsequent legislation and case law have left medical marijuana (MM) patients and their physicians in legal limbo:

- In 2003, the California legislature passed SB 420 to provide specific implementation guidelines for Proposition 215, including how counties should handle MM patient ID cards.
- Most drug law enforcement is done by local police who enforce state, not federal, drug laws. In 2005, The California Attorney General ruled that Proposition 215 is the legitimate will of the voters and is therefore valid under the California Constitution for purposes of *state* law enforcement. He advised the Highway Patrol and other state law enforcement agencies that under California law MM patients were legally entitled to possess and use cannabis for therapeutic purposes (Hoge 2005).
- In 2006, Bush administration Attorney General Gonzales sought to invalidate state MM laws, and the U.S. Supreme Court ruled (*Gonzales v. Raich* 2006) that the Compassionate Use Act—its legitimate electoral provenance notwithstanding—neither supersedes nor invalidates federal laws that prohibit marijuana use (see Mikos 2009 for a legal analysis of the states' neglected power to legalize behavior that is criminalized under federal law).
- In 2008 the Supreme Court denied without comment an appeal by two California counties that had refused to implement Proposition 215 (*County of San Diego* v. San Diego NORML 2008), thereby letting stand a lower court ruling that upheld SB 420's provisions regarding counties issuing MM identification cards.
- In 2009, Attorney General Eric Holder issued a policy stating that federal drug control agencies would no longer raid MM dispensaries if they operated within state and local laws (Moore 2009).
- That policy notwithstanding, the DEA has continued to raid MM dispensaries in California into 2011 (e.g., Blankstein 2009).

Within this grey area between conflicting state and federal laws, the number of patients who have received recommendations for medical marijuana from physicians has continued to grow, albeit by how much remains unknown. Over 1,000 MM dispensaries, delivery services, and cooperatives are said to be operating in California to meet the demand (NORML 2007). A rough estimate of the number of MM patients in California can be extrapolated from Oregon figures. Unlike California's Compassionate Use Act, Oregon's MM law set up an Oregon Medical Marijuana Program that requires centralized record keeping. As of July, 2009, some 2,983 Oregon-licensed physicians had approved 20,307 applications for MM (Oregon

# Who Are Medical Marijuana Patients? Population Characteristics from Nine California Assessment Clinics<sup>†</sup>

Craig Reinarman, Ph.D.\*; Helen Nunberg, M.D., M.P.H.\*\*; Fran Lanthier, M.A.\*\*\* & Tom Heddleston, M.A.\*\*\*

Abstract — Marijuana is a currently illegal psychoactive drug that many physicians believe has substantial therapeutic uses. The medical literature contains a growing number of studies on cannabinoids as well as case studies and anecdotal reports suggesting therapeutic potential. Fifteen states have passed medical marijuana laws, but little is known about the growing population of patients who use marijuana medicinally. This article reports on a sample of 1,746 patients from a network of nine medical marijuana evaluation clinics in California. Patients completed a standardized medical history form; evaluating physicians completed standardized evaluation forms. From this data we describe patient characteristics, self-reported presenting symptoms, physician evaluations, other treatments tried, other drug use, and medical marijuana use practices. Pain, insomnia, and anxiety were the most common conditions for which evaluating physicians recommended medical marijuana. Shifts in the medical marijuana patient population over time, the need for further research, and the issue of diversion are discussed.

Keywords --- anxiety, cannabis therapeutics, insomnia, medical marijuana, pain

Medicinal preparations containing marijuana (cannabis) were widely used in many societies for centuries. Dr. William O'Shaughnessy introduced it as a modern medicine in Europe in 1839. Marijuana was

\*\*Private practice, Santa Cruz, CA.

prescribed for therapeutic use in American medical practice for a variety of conditions from the mid-nineteenth century into the twentieth. Marijuana was admitted to the United States Pharmacopoeia in 1850 and listed in the National Formulary and the US Dispensatory. Major pharmaceutical companies including Lilly, Burroughs-Wellcome, and Parke-Davis produced cannabis-based therapeutic agents (Brecher et al. 1972).

In 1936, the Federal Bureau of Narcotics advocated a law prohibiting its use, which Congress passed in 1937, against the advice of the American Medical Association (Grinspoon & Bakalar 1993:9–11). This law, along with increased prescribing of aspirin and barbiturates, pushed cannabis out of the *United States Pharmacopoeia* and common medical practice by 1942.

After nonmedical cannabis use spread in the 1960s, the number of Americans reporting lifetime prevalence

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<sup>\*</sup>Professor and Chair, Department of Sociology, University of California, Santa Cruz.

<sup>\*\*\*</sup>Instructors and PhD candidates, Department of Sociology, University of California, Santa Cruz.

Please address correspondence and reprint requests to Craig Reinarman, Sociology Department, University of California, Santa Cruz, CA 95064; phone: (831) 459-2617, fax: (831) 459-3518, email: craigr@ ucsc.edu

	TABLE 1
D	emographic Characteristics of California Medical
	Marijuana Patients Compared to California
	Census 2000, Age 18 and Over {n = 1746}

	MM	U.S. Census
	Patients	2000 – California
Female	27.1%	50.7%
Male	72.9%	49.3%
White	61.5%	59.5%
Latino	14.4%	32.4%
African American	11.8%	6.7%
Native American	4.5%	1.0%
Asian/Pacific Islander	4.2%	11.2%
Other	4.3%	•
18-24 Years Old	17.9%	~17.1%
25-34 **	27.5%	15.4%
35-44 "	21.3%	16.2%
4554 "	20.4%	12.8%
55> "	12,6%	18.4%
<high school<="" td=""><td>8.8%</td><td>*</td></high>	8.8%	*
High School Graduate	42.2%	*
Some College	27.1%	*
College Graduate>	23.8%	*
Employed	64.8%	57.5%
Health Insurance	73.4%	+

African-Americans, conversely, are over-represented in this sample. This does not appear to stem from their prevalence of marijuana use, for representative national surveys show that Blacks generally do not have significantly higher prevalence of marijuana use than Whites (SAMHSA 2005). African-Americans may be more likely to seek MM for any of several reasons: because they are disproportionately poor, more often lack health insurance, are significantly less likely to be prescribed other medication for pain (Pletcher et al. 2008) or to receive treatment for cancer (Gross et al. 2008), and because African-Americans are a growing proportion of HIV/AIDS cases. Some of these same reasons may help to explain why Native Americans are also overrepresented, although their proportion of both this sample and the general population is too small to judge representativeness accurately.

In their medical history questionnaires, patients were asked "Which of the following best describe the therapeutic benefit you receive from medicinal cannabis? (Check the most important)." Patients typically reported more than one therapeutic benefit (mean = 3). Early studies showed most patients used MM to relieve symptoms of HIV/AIDS (Woolridge et al. 2005) or cancer, and it is likely that the majority of patients in our sample who reported "nausea" were cancer patients receiving chemotherapy. However, Table 2 suggests that cancer and AIDS patients are now a

#### TABLE 2 Patient Self-Reports of Therapeutic Benefits from Medicinal Marijuana\* Percent To Relieve: 82 6 Pain Muscle Spasms 41.1 Headaches 40.7 Anxiety 37.8 Nausea/Vomiting 27.7 Depression 26.1 19.0 Cramps Panic Attacks 16.9 Diarrhea 5.0 Itching 2.8 To Improve: 70.7 Sleep Relaxation 55.1 Appetite 37.7 Concentration/Focus 22.9 Energy 15.9 To Prevent: **Medication Side Effects** 22.5 Anger 22.4 6.2 Involuntary Movements Seizures 3.2 As Substitute for: Prescription Medication 50.9 Alcohol 13.0 \*N = 1,745; patients could report more than one benefit in more than one category.

significantly smaller proportion of the total (e.g., "to relieve nausea/vomiting" 27.7%, "to improve appetite" 37.7%) and that the MM patient population has become more diverse since the Compassionate Use Act was passed in 1996 (cf. Ware, Adams & Guy 2005, on MM use in the UK, and Grotenherman 2002 on MM use in Germany).

Instead, relief of pain, muscle spasms, headache, and anxiety, as well as to improve sleep and relaxation were the most common reasons patients cited for using MM. Chronic pain also topped the list of maladies for which MM was used in another California clinical sample (Reiman 2007b).

Table 3 shows the ICD-9 diagnostic codes most frequently recorded by evaluating physicians. Pain from back and neck injuries was the most frequently coded. This appears consistent with a nationally representative Medical Expenditure Panel Survey, which found a 19.3% increase in the prevalence of spine problems between 1997 and 2005 (Martin et al. 2008). Back and neck pain was followed in frequency by sleep disorders (also increasing), anxiety/depression, muscle spasms, and arthritis. Fully half of this sample reported using MM as a substitute Department of Human Services 2008). The population of California is 9.7 times that of Oregon (U.S. Census 2007), which yields a crude estimate of 196,978 MM patients in California. This is likely an underestimate because the California statute affords greater latitude to physicians regarding the conditions for which they can recommend MM ("... any other illness for which marijuana provides relief"). Americans for Safe Access (2008), a MM patient advocacy group, has estimated that there are well over 200,000 physician-sanctioned MM patients in California.

Despite their growing numbers, however, the ambiguous legal status of MM patients renders them a half-hidden population whose characteristics are not well documented, with the partial exception of the San Francisco Bay Area (O'Connell & Bou-Matar 2007; Reiman 2007a). Medical marijuana will likely continue to be a contentious issue, but across fifteen states and the District of Columbia several hundred thousand people are using marijuana as a medicine recommended by physicians, and yet little is known about them as a patient population.

We intend this study as a modest contribution toward filling this gap. It presents data on the demographic characteristics, presenting symptoms, physician evaluations, conventional treatments tried, and MM use practices of patients from a network of MM assessment clinics in California.

#### METHODS

These data were drawn from 1,746 consecutive admissions to nine MM assessment clinics operating in California in July, August, and September 2006. These assessment clinics are not dispensaries and are not connected to dispensaries. They were located throughout the state-in the north and south, coast and central valley, and large and small cities: Modesto, Oakland, Sacramento, Hollywood, San Diego, Santa Cruz, Ukiah, San Francisco, and Santa Rosa. They charged \$100 to \$125 for an assessment. At the time our sample was drawn, these assessment clinics had evaluated over 54,000 MM patients. Without a comprehensive patient database or representative household surveys, there is no way to determine precisely how representative this sample is of the overall population of MM patients. Moreover, there is a large albeit unknown number of people who use marijuana medicinally but who have not sought physician recommendations or official patient ID cards, perhaps because of the expense of the assessment.1

Evaluating physicians interviewed potential patients and evaluated their patient medical histories for purposes of recommending MM and issuing patient identification cards under the Compassionate Use Act and SB 420. The evaluation instruments were (1) a basic patient-administered medical history questionnaire covering demographics, presenting symptoms or conditions, brief medical history, conventional and alternative medical treatments tried, drug use history, and MM use practices; and (2) a physician evaluation form using International Classification of Diseases codes (ICD-9). Each patient received and signed an extensive informed consent form noting confidentiality, which was approved by the clinics' IRB.

Most prior studies of MM patients are based on small, symptom-specific samples. Initially, the population of MM patients in the San Francisco Bay Area were people with HIV/AIDS and cancer (e.g., Harris, Mendelson & Jones 1998). Later, physicians began to recommend cannabis to patients with chronic pain, mood disorders and other psychiatric conditions (Gieringer 2002). The data reported here describe what is among the largest and most symptomatically and demographically diverse samples of medical cannabis patients to date (cf., O'Connell & Bou-Matar 2007).

#### RESULTS

As Table 1 indicates, the MM patients are three-fourths male and three-fifths White. Compared to the US Census of California, the patients in this sample are on average somewhat younger, report slightly more years of formal education, and are more often employed. The comparison also indicates that women, Latinos, and Asian Americans are underrepresented. Given the limitations of our data, we can offer only informed speculation as to why.

The underrepresentation of women may be in part an epidemiological artifact of the gender distribution of certain kinds of injuries (e.g., workplace, sports, and motorcycle accidents). It may also have to do with the double stigma women face in seeking MM—for using an illicit drug and for violating gender-specific norms against illegal behavior in general. Moreover, as with alcohol use, pregnant women and women considering pregnancy are likely to have health concerns and many may fear that MM could put them in jeopardy if discovered by child protection agencies.

Given the high poverty rate among Latinos and their concentration in the manual labor end of the occupational structure, Latinos are exposed to equal or greater risks of work-related injuries and to no less epidemiologic risk of other conditions for which MM is sometimes used. It seems likely that their under-representation has to do with the undocumented status of many Latinos in California. The undocumented often avoid contact with government agencies for fear of apprehension by law enforcement, for beyond arrest and incarceration this carries the risk of deportation. Such fears reduce the likelihood of Latinos accessing health care in general and MM in particular. Asian Americans are also underrepresented, but this may be because they have lower prevalence of marijuana use than other racial/ethnic groups and/or because they have their own venerable traditions of herbal medicine.

	TABLE	6		
Medical	Marijuana	Use	Practices	

Frequency of Medical Marijuana	Use (N == 1583)*
Daily	67.0% (1065)
<once a="" td="" week<=""><td>26.0% (409)</td></once>	26.0% (409)
<once a="" month<="" td=""><td>7.0% (109)</td></once>	7.0% (109)
On Days Used, Frequency per Day	(N = 1574)
1 To 2 Times Per Day	52.9% (833)
2 To 3 Times Per Day	29.0% (457)
>3 Times Per Day	10.0% (284)
Time Of Day Typically Used (N =	1745)
Prior To Sleep	56.1% (979)
Evenings	52.3% (913)
Depends on Symptoms	42.3% (739)
Mornings	25.7% (448)
Afternoons	20.1% (350)
After Work	12.4% (217)
Middle of the Night	6.5% (114)
All Day	5.3% (93)
Mode of Ingestion (N = 1745)	
Smoke	86.1% (1503)
Oral Ingestion	24.4% (426)
Vapor	21.8% (380)
Topical	2.8% (49)
Amount Used per Week (N = 143)	1)
0-3 Grams	40.1% (574)
4-7 Grams	36.5% (523)
>7 Grams	23.3% (334)

\*Total n = 1745, but N's vary across questions because patients could choose more than one response and because not all responded to each question.

#### DISCUSSION

## Rediscovery of Medicinal Utility and Diversifying Patient Population

Compared to earlier studies of MM patients, these data suggest that the patient population has evolved from mostly HIV/AIDS and cancer patients to a significantly more diverse array. The diffusion of marijuana as a medicine may have been slower than that of other medicines in conventional clinical practice because the flow of information from physician to patient is impeded by MM's ambiguous legal status. Thus, information about the potential therapeutic utility of cannabis is spread mostly via word of mouth and other informal means. This suggests that the patient population is likely to continue evolving as new patients and physicians discover the therapeutic uses of cannabis. Ironically, this trend toward increasing therapeutic uses is bringing marijuana back to the position it held in the U.S. Pharmacopeia prior to its prohibition in 1937.

### **Further Research**

Like other medicines, marijuana's therapeutic efficacy varies across conditions and patient groups. This variation seems more likely when supplies remain illicit because standardized dosages or other quality controls are more difficult to achieve. To gain maximum therapeutic potential across the growing range of conditions for which MM is being recommended, more systematic research is needed. Longitudinal, case control, and double-blind studies are required to rigorously assess marijuana's therapeutic efficacy for specific patient groups, conditions, and diseases. With regard to shifts in the patient population, it also would be very useful to have follow-up studies of patients accessing the assessment clinics in our sample and others drawn from similar assessment clinics.

### Diversion

Critics have argued that some MM patients are "gaming the system" to get marijuana for nonmedical use. Neither our data nor any other data we are aware of allow any clear-cut, empirical estimate of the scale of such diversion. Given the widespread nonmedical use marijuana in the general population (102,404,000 Americans report lifetime prevalence; see SAMHSA 2010) and the risk of arrest (847,864 Americans were arrested for marijuana offenses in 2008, 754,224 or 88.96% of them for possession alone; FBI 2009), it seems likely that at least some MM patients use MM dispensaries as sources of supply for nonmedical use.

Defining and measuring such diversion, however, is complicated at best. Given the high prevalence of nonmedical use, it is not surprising that most MM patients in our sample reported having used it recreationally before using it therapeutically. But as noted above, two-fifths had *not* been using marijuana recreationally prior to trying it for medicinal purposes. Their self-reported rates of other illicit drug use are slightly lower than those found among the general population, and their levels of educational attainment and rate of employment are comparable to the California population. Our data have clear limitations, but they contain no obvious signs that MM patients differ from the general population.

Nor is drug diversion unique to medical marijuana. A significant albeit unknown proportion of other patients obtain prescriptions for numerous drugs through legal medical channels that they then use for nonmedical purposes, for example, Valium and other benzodiazepines (Haafkens 1997), Ritalin and other stimulants prescribed for ADHD, and Oxycontin and other opiates prescribed for pain.

The diversion issue will likely become more important as the line between medical and nonmedical drug use is increasingly blurred (Murray, Gaylin & Macklin 1984). Beyond the spread of MM, Prozac and other SSRItype antidepressants, for example, are often prescribed

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### TABLE 3 Conditions Most Frequently Recorded by Physicians As Reasons for Approving Medical Marijuana Patient Identification Cards\*

	Percent	ICD-9 Codes
Back/Spine/Neck Pain	30.6%	[722.1-724.2]
Sleep Disorders	15.7%	[307.42, 327.0]
Anxiety/Depression	13.0%	[300.0, 311.0]
Muscle Spasms	9.5%	[728.85]
Arthritis	8.5%	[715.0, 721.2, 721.2]
Injuries (Knee, Ankle, Foot)	4.5%	[959.7]
Joint Disease/Disorders	4.4%	[716.1-719.49]
Narcolepsy	3.7%	[347.0]
Nausea	3.4%	[787.02]
Inflammation (Spine, Nerve)	2.9%	[724.4]
Headaches/Migraines	2.7%	[784.0, 346.0, 346.2]
Eating Disorders	1.1%	[783.0]

### TABLE 4 Other Treatment Modalities Tried for the Medical Condition(s) for Which Patients Seek Medical Marijuana\*

	%	N
Prescription Medication	79.3%	1383
Physical Therapy	48.7	850
Chiropractic	36.3	633
Surgery	22.3	389
Counseling	21.0	366
Acupuncture	19.4	338
Therapeutic Injection	15.4	269
Homeopathy	12.0	209
Other Types of Treatment	11.9	208

for prescription drugs, consistent with other studies (e.g., Reiman 2007a).

Table 4 indicates that the MM patients in the sample had tried a variety of other treatments, conventional and alternative, for the conditions for which they were seeking a MM identification card. Four in five (79.3%) reported having tried other medications prescribed by their physicians (almost half were opiates); about half (48.7%) had tried physical therapy; over a third (36.3%) had tried chiropractic; nearly one-fourth (22.3%) reported having had surgery for their condition.

Table 5 compares patient responses to the drug use questions to those in the 2006 National Survey on Drug Use and Health (SAMHSA 2007). Prevalence of tobacco

TABLE 5
Medical Marijuana Patients' Self-Reported
Current Nonmedical Drug Use, Compared to 2006
National Survey on Drug Use And Health
(SAMHSA 2007)

	<b>MM</b> Patients	NSDUH*
Tobacco	29.4%	25.0%
Alcohol	47.5	61.9
Cocaine	0.3	1.9
Methamphetamine	0.4	0.5
Heroin	0.1	0.3
Other Opiates	1.2	**
are percent responding " than one drug. Of smoker drinkers, 58.7% used =</th <td>ist month" prevalence use</td> <td>ould report more igarettes/day; of</td>	ist month" prevalence use	ould report more igarettes/day; of

use was somewhat higher than in the general population, but prevalence of alcohol use was significantly lower. Many patients reported that they valued MM because it allowed them to reduce their alcohol use. It is possible that self-reports on a self-administered instrument will underestimate illicit drug use, particularly if patients felt that admitting illicit drug use could reduce their chances of obtaining a MM identification card. Rigorous assessments of the reliability of such data must await further research, but limitations aside, these data suggest low prevalence of other illicit drug use among MM patients. While it is true that the great majority of our respondents had used marijuana recreationally, in response to a separate question over two-fifths (41.2%) reported that they had *not* been using it recreationally prior to trying it for medicinal purposes.

Table 6 presents data on patients' medical marijuana use practices. Amounts used per week varied from three grams or less (40.1%) to seven or more grams (23.3%). Two-thirds (67%) reported using MM daily while onefourth (26%) reported using less than once a week. Half (52.9%) reported using one or two times per day while one in ten (10%) reported using three or more times per day. Patients consumed MM primarily in the evenings (52.3%) or prior to sleep (56.1%). More than two in five (42.3%) reported that when they used depended on their medical symptoms. Patients ingested MM predominantly by smoking (86.1%), although one-fourth (24.4%) reported ingesting orally and nearly a fourth (21.8%) reported using a vaporizer. These latter figures suggest that at least some of the time, many MM patients are choosing modes of ingestion that reduce the perceived risk of harms from smoking (Tan et al. 2009; Hashibe et al. 2006).

#### Reinarman et al.

inhibits transient lower esophageal sphincter relaxations and reflux in dogs. *Gastraenterology* 123 (6): 1129–34.

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for patients who do not meet DSM criteria for clinical depression but who simply feel better when taking it. Such "cosmetic psychopharmacology" (Kramer 1993) is likely to grow as new psychiatric medications come to market. The line between medical and nonmedical drug use has also been blurred by performance enhancing drugs such as steroids, so-called "smart drugs" that combine vitamins with psychoactive ingredients, and herbal remedies like *ma huang* (ephedra) available in health food stores (Burros & Jay 1996).

These examples suggest that despite the best intentions of physicians and law makers, much drug use does not fit into two neat boxes, medical and nonmedical, but rather exists on a continuum where one shades into the other as patients' purposes shift to suit situational exigencies in their health and their daily lives. It is not clear where a border line between medical and nonmedical marijuana or other drug use might be drawn nor how it might be effectively policed (see Reinarman & Levine 1997: 334-44).

#### NOTE

1. We are grateful to one anonymous reviewer for pointing out that the cost of these assessments may well have prevented some potential MM patients—including many impoverished HIV/AIDS patients—from obtaining ID cards, which may have affected the demographics of this sample.

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## Articles

## Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study

Marta Di Forti, Arianna Marconi, Elena Carra, Sara Fraietta, Antonella Trotta, Matteo Bonomo, Francesca Bianconi, Poonam Gardner-Sood, Jennifer O'Connor, Manuela Russo, Simona A Stilo, Tiago Reis Marques, Valeria Mondelli, Paola Dazzan, Carmine Pariante, Anthony S David, Fiona Gaughran, Zerrin Atakan, Conrad Iyeqbe, John Powell, Craig Morgan, Michael Lynskey, Robin M Murray

#### Summary

Background The risk of individuals having adverse effects from drug use (eg, alcohol) generally depends on the frequency of use and potency of the drug used. We aimed to investigate how frequent use of skunk-like (high-potency) cannabis in south London affected the association between cannabis and psychotic disorders.

Methods We applied adjusted logistic regression models to data from patients aged 18–65 years presenting to South London and Maudsley NHS Foundation Trust with first-episode psychosis and population controls recruited from the same area of south London (UK) to estimate the effect of the frequency of use, and type of cannabis used on the risk of psychotic disorders. We then calculated the proportion of new cases of psychosis attributable to different types of cannabis use in south London.

Findings Between May 1, 2005, and May 31, 2011, we obtained data from 410 patients with first-episode psychosis and 370 population controls. The risk of individuals having a psychotic disorder showed a roughly three-times increase in users of skunk-like cannabis compared with those who never used cannabis (adjusted odds ratio [OR] 2.92, 95% CI 1.52-3.45, p=0.001). Use of skunk-like cannabis every day conferred the highest risk of psychotic disorders compared with no use of cannabis (adjusted OR 5.4, 95% CI 2.81-11.31, p=0.002). The population attributable fraction of first-episode psychosis for skunk use for our geographical area was 24% (95% CI 17-31), possibly because of the high prevalence of use of high-potency cannabis (218 [53%] of 410 patients) in our study.

Interpretation The ready availability of high potency cannabis in south London might have resulted in a greater proportion of first onset psychosis cases being attributed to cannabis use than in previous studies.

Funding UK National Institute of Health Research (NIHR) Specialist Biomedical Research Centre for Mental Health, SLaM and the Institute of Psychiatry at King's College London, Psychiatry Research Trust, Maudsley Charity Research Fund, and th European Community's Seventh Framework Program grant (agreement No. HEALTH-F2-2009-241909 [Project EU-GEI]).

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#### Introduction

Cannabis is the most popular illicit drug in the world. Uruguay was the first country to legalise its use and several US states have done so or are in the process of doing similar.<sup>1</sup> Therefore, any harm caused by cannabis use should be quantified. Prospective epidemiological studies have consistently reported that use of cannabis increases the risk of schizophrenia-like psychosis.<sup>23</sup> In the UK, the investigators of the 2012 Schizophrenia Commission<sup>4</sup> concluded that cannabis use is the most preventable risk factor for psychosis, and research that aims to improve estimation of the drug's contribution to illness development should be pursued.

The aspects of exposure to cannabis (eg, age at first use, frequency of use, duration of use) that confer the greatest effect on risk of psychosis are unclear. Such information would be valuable for public education and to estimate the proportion of psychosis cases that could be prevented if harmful patterns of cannabis use were removed from the population. The few studies<sup>5,6</sup> that have tried to estimate the effect of cannabis use on the number of new cases of psychosis in specific populations have been limited by the scarcity of accurate information on patterns of cannabis use.

The risk of adverse effects for mental health and cognition posed by cannabis use has been suggested to depend on the potency of the type of cannabis used.<sup>7</sup> For example, in a previous study<sup>8</sup> of part of the population reported here, we noted that skunk-like types of cannabis, which contain very high concentrations of  $\Delta$ -9-tetrahydrocannabinol (THC), seemed to have a greater psychotogenic effect than did hash (resin), which is known to contain much less THC.

We analysed detailed data for history of cannabis use, aiming to: compare the patterns and types of cannabis used between patients with first-episode psychosis and a



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Department of Psychosis Studies (M Di Forti MD. A Marconi MD, E Carra MD, S Fraietta MD, A Trotta MSc. M Bonomo MSc. F Bianconi MSc. P Gardner-Sood PhD. O'Connor PhD. T R Margues PhD, P Dazzan PhD, Prof A 5 David MD, F Gaughran MD, Z Atakan MD, C lyegbe PhD, Prof R M Murray FRS). **Department of Health Services** and Public Health (5 A Stilo MD, Prof C Morgan PhD), Department of Psychological Medicine (V Mondelli PhD, Prof C Pariante PhD), Department of Neuroscience (Prof | Powell DPhil); Department of Addiction (Prof M Lynskey PhD), Institute of Psychiatry, Kings College London, London, UK; and Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA (M Russo PhD)

Correspondence to: Dr Marta Di Forti, Department of Psychosis Studies, Institute of Psychiatry, King's College, London SES 8AF, UK marta.diforti@kcl.ac.uk population control sample; use the data for pattern of cannabis use to develop a cannabis exposure measure that accurately estimates the risk of psychotic disorders; and calculate the proportion of cases of psychosis in our study area attributable to use of cannabis, particularly high-potency cannabis, if we assumed causality.

#### Methods

#### Study design and participants

As part of the GAP study,8 we did a case-control study at the inpatient units of the South London and Maudsley (SLaM) NHS Foundation Trust. We approached all patients aged 18-65 years who presented with first-episode psychosis. We invited patients to participate if they met the International Classification of Diseases 10 criteria for a diagnosis of non-affective (F20-F29) or affective (F30-F33) psychosis, validated by administration of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN)." We excluded individuals who met the criteria for organic psychosis (F09). If patients were too unwell to cooperate, we re-contacted them after the start of treatment.

We recruited controls using internet and newspaper advertisements and by distributing leaflets at train stations, shops, and job centres. None of the advertising material mentioned cannabis or illicit drug use. Volunteers were administered the Psychosis Screening Questionnaire10 and were excluded if they met the criteria for a psychotic disorder or if they reported a previous diagnosis of psychotic illness. This study is part of the GAP study, which was granted ethical approval by SLaM and Institute of Psychiatry Local Research Ethics Committee. All case and control individuals included in the study gave written informed consent.

#### Procedures

We obtained sociodemographic data using the Medical Research Council Schedule.<sup>11</sup> From March, 2006, we took a more detailed history of cannabis use by adding the Cannabis Experience Questionnaire modified version (CEQ<sub>m</sub>) to the assessment.<sup>8,12</sup> From the CEQ<sub>m</sub>, we derived information on history of use of tobacco, alcohol, other recreational drugs, and detailed information on cannabis use (age at first use, duration of use, frequency of use, type used).

Measures of cannabis use relevant to the analysis were: lifetime history of cannabis use-ie, had the individual ever used cannabis at any point in their life (no scores 0, yes scores 1); lifetime frequency of cannabis use-ie, the frequency that characterised the individual's most consistent pattern of use (none scores 0, less than once per week every week scores 1, at weekends scores 2, every day scores 3); and type of cannabis used-ie, the type most used by the subject (none scores 0, low potency [hash-type] scores 1, high potency [skunk-type] scores 2). This variable was grouped in accordance with the characteristics of the cannabis samples seized by the Metropolitan Police in London, as reported by Potter and colleagues13 and the See Online for appendix Home Office study (appendix)." Finally, we used a

seven-item composite cannabis exposure measure derived from the lifetime frequency of use and the most used type (none scores 0, hash less than once per week every week scores 1, hash at weekends scores 2, hash every day scores 3, skunk less than once per week scores 4, skunk at weekends scores 5, skunk every day scores 6) to investigate which patterns of use conferred the greatest risk.

#### Statistical analysis

We analysed data using Stata 13. We used  $\chi^2$  tests and t tests (or Mann-Whitney U tests) to test for associations between potential confounding variables and between presence of psychotic disorder and exposure to cannabis use. We also used these tests to establish whether missing data for the cannabis use exposure were associated with case-control status and therefore likely to bias the results.

We used logistic regression to analyse whether individual indicators of cannabis use (lifetime use, age at first use, duration and frequency of use, and most used type of cannabis) improved estimation of the likelihood of psychotic disorders (ie, case status), in comparisons of cannabis users with non-users.

We used the punafcc command in Stata 13 to estimate the population attributable fraction (PAF), with confidence intervals, for each cannabis use variable. The PAF measures the population effect of an exposure by providing an estimate of the proportion of disorder that would be prevented if the exposure were removed. However, causality does not have to be proven before the PAF can be estimated, and this causation is not usually established when PAFs are estimated (indeed no single study could ever prove causation). Because the same proportion of disorder attributable to a specific risk factor can also be attributable to other factors with which the specific risk factor might interact, PAFs for multiple risk factors can add up to more than 100%. Furthermore, the PAF depends on both the prevalence of exposure (ie, measures of cannabis use) in cases and the odds ratio (OR) for the exposure, such that a risk factor with a modest OR can have a major population effect if the factor is common.

#### Role of the funding source

All funders contributed to data collection by providing the salaries of the research workers collecting the data. The funders of the study had no role in study design, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

#### Results

Between May 1, 2005, and May 31, 2011, we approached 606 patients with first-episode psychosis. Of these 606 patients, 145 (24%) refused to participate. Thus, we recruited 461 patients with first-episode psychosis. Patients who refused to participate were more likely to be men (p<0.004) and of Black Caribbean and Black African ethnic

an garana a sa an sa sa an garana sa sa sa sa Sa sa sa sa sa sa sa sa sa	First-episode psychosis group (n=410)	Control group (n=370)	p value
Age, years	27.1 (8.7)	30-0 (9-0)	0.0001
Gender	15229	с. М	0-004
Male	271 (66%)	209 (56%)	6468
Female	139 (34%)	161 (44%)	
Ethnicorigin	all. 1977		0.0001
White	132 (32%)	212 (57%)	1120
Black Caribbean	136 (33%)	73 (20%)	- 
Black African	98 (24%)	38 (10%)	1993 (N. 1993) 1993 (N. 1993)
Asian/other	44 (11%)	47 (13%)	14 I
Education	∴æ:	#	0.0003
No qualification	60 (15%)	8 (2%)	5.005
GCSEs	116 (28%)	31 (8%)	3 <b>5</b> 74
A levels or vocational training	153 (37%)	151 (41%)	
University	81 (20%)	180 (49%)	
Everemployed		4 4	0.001
Yes	361 (88%)	353 (95%)	
No	46 (11%)	15 (4%)	7.912 (99) - 1 1 <b>1 1</b> 1
No details	3 (1%)	2 (1%)	
Data are mean (SD) or n (%) unless :	stated otherwise.		

origin (p=0.001) than were those who consented. Therefore, in all the analyses, we tested for the potential confounding effects of ethnic origin and gender. During the same period and from the geographical area served by the clinical units, we recruited 389 control individuals, aged 18–65 years, who were similar to the local population in terms of ethnic origin, education, and employment status (table 1). The later addition of CEQ<sub>aw</sub> meant that there were data missing on detailed patterns of cannabis use for those participants recruited early in the project. The data we present here are therefore based on 410 (89%) of 461 patients with first-episode psychosis and 370 (95%) of 389 controls for whom we had data for cannabis use.

The patients with first-episode psychosis consisted of more men and were younger than the control group (table 1). As noted previously,<sup>15</sup> patients with first-episode psychosis were also more likely to be of Black ethnic origin (Caribbean or African) compared with controls, and less likely to have completed a high level of education than were controls (table 1).

A larger proportion of patients with first-episode psychosis (184 [45%] of 410 individuals) reported having smoked 100 tobacco cigarettes or more than did controls (60 [16%] of 370 individuals; p<0.0001), but the groups did not differ in lifetime history of other substance use (p=0.615), or alcohol units consumed per week (p=0.083). Patients with first-episode psychosis were no more likely than were controls to report a lifetime history of ever having used cannabis, but were more likely to use cannabis every day and to mostly use high-potency

	First-episode psychosis group (n=410)	Control group (n=370)	p value
Total population			
Lifetime history of cannabis use		1 a 1	0.277
Yes	275 (67%)	232 (63%)	34
No (never used)	135 (33%)	138 (37%)	
Frequency of use		20. AN	<0.0001
Less than once per week	68 (17%)	128 (35%)	3 <b>4</b>
At weekends	84 (20%)	63 (17%)	29
Every day	123 (30%)	41 (11%)	27
Most used type of cannabis	*		<0.0001
Neverused	135 (33%)	138 (37%)	34
Hash-like	57 (14%)	162 (44%)	200
Skunk-like	218 (53%)	70 (19%)	
Cannabis users			د وليو مسالية
Duration of use (years)	9.7 (7.4)	9-1 (7-8)	0.635
No details	3	1	
Age at first cannabis use (years)	16-1 (4-2)	16-6 (3-2)	0.146
No details	3	1	<u>.</u>
Age at first use <15 years			0.028
No	172 (63%)	178 (77%)	
Yes	100 (36%)	53 (23%)	••
No details	3	1	**
Data are n (%) or mean (SD) unless	stated otherwise.	1997 - 1997 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 -	

(skunk-like) cannabis (table 2). A small proportion of cannabis users (3 [0.6%] of 507 individuals) reported having used cannabis more than four days a week and they were included in the every day category.

Among cannabis users, the mean duration of use did not differ between patients with first-episode psychosis and controls (table 2). On average, both groups started using cannabis in their mid-teens, although distribution of the age at first cannabis use seemed to be skewed (mean 16·1 years, SD 4·2, median 16 years in the patients with first-episode psychosis *vs* mean 16·6 years, SD 3·2, median 17 years in the control group;  $Z=2\cdot88$ ;  $p=0\cdot146$ ). Patients with first-episode psychosis were more likely to start using cannabis at age 15 years or younger than were controls.

When we combined data on frequency of cannabis use and most used type into a single variable, the composite cannabis exposure measure, controls were more likely to be occasional users of low-potency cannabis (hash), and patients with first-episode psychosis were more likely to be daily users of high-potency cannabis (skunk; figure 1; p<0.0001).

A logistic regression, adjusted for age, gender, ethnic origin, number of cigarettes smoked, alcohol units and lifetime use of other illicit drugs, education, and employment history, showed that individuals who had ever used cannabis were not at increased risk of psychotic disorder compared with those who had never used For more on demographic composition of the local population see www.statistics. gov.uk/census

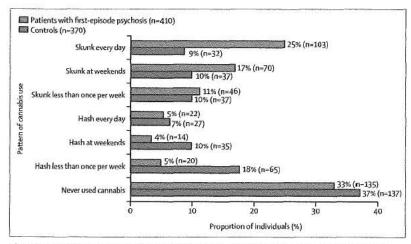


Figure 1: Patterns of cannabis use between patients with first-episode psychosis and population controls

	Odds ratio* (95% CI)	p value
Age at first use, years		
Never used	1	60
≥15 years	0.68 (0.34-1.37)	0.292
<15 years	1.55 (1.00-1.39)	0.048
Frequency of use		
Never used	1	11
ess than once per week	0.58 (0.25-1.32)	0.198
Weekends	1.04 (0.41-1.62)	0.929
Every day	3.04 (1.91-7.76)	0.020
Most used type		
Never used	1	55
Hash-like	0.83 (0.52-1.77)	0.903
škunk-like	2-91 (1-52-3-60)	0-001
Adjusted for age, gender, eth ther drugs used, education, a	nic origin, number of cigarettes nd employment status.	, alcohol unit

cannabis (n=775 [data for employment history was missing for five participants, OR 0.93, 95% CI 0.67–1.52, p=0.569). Individuals who started using cannabis at ages younger than 15 years had modestly, but significantly, increased risk of psychotic disorders compared with those who never used cannabis (table 3). People who used cannabis or skunk every day were both roughly three times more likely to have a diagnosis of a psychotic disorder than were those who never used cannabis (table 3).

We used logistic regression (n=775) to test whether the composite cannabis exposure measure predicted risk of psychotic disorder more accurately than the individual markers, frequency of cannabis use and most used type of cannabis, alone. Individuals who mostly used low-potency (hash-like) cannabis occasionally (p=0.493), at weekends (p=0.102), or daily (p=0.626) had no increased likelihood of psychotic disorders compared with those who never used cannabis (figure 2).

Compared with those who never used cannabis, individuals who mostly used skunk-like cannabis were nearly twice as likely to be diagnosed with a psychotic disorder if they used it less than once per week (p=0.020), almost three times as likely if they used it at weekends (p=0.008), and more than five times as likely if they were daily users (p=0.001; figure 2).

Based on the estimated adjusted OR for daily cannabis use (3.04, 95% CI 1.91-7.76), we calculated that, if we assumed causality, 19.3% (13.1-27.0) of psychotic disorders in the study population were attributable to exposure to daily cannabis use. The PAF of psychotic disorders in the study population that were attributable to high potency cannabis use was 24.0% (17.4-30.6) and the PAF for the two exposures combined, skunk use every day, was 16.0% (14.0-20.3; table 4). If causality is assumed, this finding suggests that skunk alone was responsible for the largest proportion of new cases (24%) of psychotic disorder in the study population, an effect driven by its high prevalence among patients with first-episode psychosis who used cannabis (218 [53%] of 410 patients).

#### Discussion

The results of our study support our previous conclusions from analysis of part of the sample;<sup>8</sup> use of high-potency cannabis (skunk) confers an increased risk of psychosis compared with traditional low-potency cannabis (hash). Additionally, because of the increased sample size in the present study, we were able to combine information on frequency of use and type of cannabis used into a single measure. This combined measure suggested that the strongest predictor of case-control status (ie, predictor of whether a random individual would be case or control) was daily-skunk use. Figure 2, which shows the adjusted ORs for psychotic disorders for each of the composite cannabis exposure measure groups, shows how the ORs for skunk users increase with the frequency of use.

Samples of skunk seized in the London area in 2005,13 2008,14 and more recently, as reported by Freeman and colleagues,16 contained more THC than did samples of hash, and virtually no cannabidiol. Use of cannabis with a high concentration of THC might have a more detrimental effect on mental health than use of a weaker form. Indeed, in line with epidemiological evidence,23 the results of experimental studies<sup>17,18</sup> that investigated the acute effects of intravenous administration of THC in non-psychotic volunteers showed that the resulting psychotic symptoms were dependent on the dose. Furthermore, the scarcity of cannabidiol in skunk-like cannabis might also be relevant because evidence suggests that cannabidiol ameliorates the psychotogenic effect of THC and might even have antipsychotic properties.19,20 The presence of cannabidiol might explain our results, which showed that hash users do not have any increase in risk of psychotic disorders compared with non-users, irrespective of their frequency of use. Morgan and colleagues21 previously reported that, in healthy volunteers who smoked cannabis, individuals with

hair traces of THC and cannabidiol had fewer schizophrenialike symptoms than those with hair traces of THC only.

In our results, a combined measure of exposure to cannabis, daily use of high-potency cannabis, predicted a greater risk of psychotic disorders than did the single measures of either frequency or potency. However, a simple yes-or-no question of whether people use skunk might be more useful to identify those at increased risk to develop psychosis because of their cannabis use. In view of the high prevalence of skunk use in our study population, if a causal role for cannabis is assumed, skunk use alone was responsible for 24% of those adults presenting with first-episode psychosis to the psychiatric services in south London.

South London has one of the highest recorded incidence rates of psychosis in the UK.<sup>22</sup> Boydell and colleagues<sup>23</sup> showed that the incidence of schizophrenia had doubled since 1965,<sup>24</sup> and that one possible contribution to this was the increase in cannabis use among individuals who developed schizophrenia. In the present study, we identified an increased estimate for the PAF accounted for by cannabis (24%) compared with previous studies, which reported PAFs of 6 · 2% in Germany.<sup>25</sup> 8% in New Zealand,<sup>26</sup> and 13 · 3% in Holland.<sup>5</sup> This finding could be caused by, not only the greater use of cannabis, but also the greater use of high-potency (skunk-like) cannabis in south London than in these other countries in earlier periods.<sup>77</sup>

Hickman and colleagues<sup>6</sup> suggested that the number of people who need to be treated to stop their cannabis use to prevent one case of schizophrenia is large, but would become substantially lower if more was understood about which individuals are at greatest risk because of their pattern of use or their susceptibility to psychosis.<sup>6</sup> In relation to susceptibility to schizophrenia, Henquet and colleagues<sup>25</sup> calculated that the PAF for individuals in the general population with a predisposition for psychosis at baseline was more than double (14·2%) that of the total population (6·2%). Our data suggest that the potency of the cannabis used also needs to be taken into account in calculations of the PAF.

The strategy we used for control recruitment, based on a variety of advertising strategies rather than on random selection, might have biased the findings. However, the final sample of controls was similar, according to the last UK census data, to the population from which the cases were drawn. Moreover, rather than this approach undersampling individuals who used cannabis, the proportion of controls with a history of cannabis use (63%) was more than the national average (40%) for similar age groups,<sup>28</sup> showing the high prevalence of cannabis use in south London. Furthermore, if we had oversampled individuals who used cannabis, this oversampling would have caused underestimation of the effects of cannabis use on risk of psychotic disorders.

A theoretical explanation of why skunk might have been preferred by patients with first-episode psychosis is that, when they began to experience their illness prodrome, these

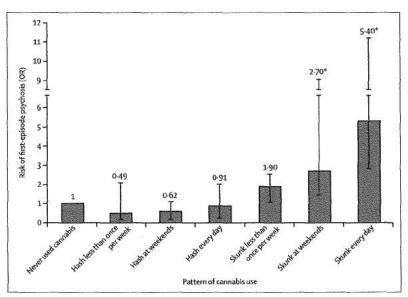


Figure 2: Probability of individuals having a psychotic disorder by pattern of cannabis use OR adjusted for age, gender, ethnic origin, education, employment status, and tobacco use. OR=odds ratio. \*p<0.05.

an a	Odds ratio* (95% Cl)	Prevalence of exposure in patients with first- episode psychosis	Population attributable fraction (95% CI)
Daily cannabis use	3.04 (1.91-7.76)	123/410 (30%)	19.3% (13.1-27.0)
Skunk use	2.91 (1.52-3.60)	218/410 (53%)	24.0% (17.4-30.6)
Skunk use every day	5.40 (2.80-11.30)	103/410 (25%)	16-0% (14-0-20-3)

Table 4: Population attributable fraction for daily use of cannabis, skunk use, and skunk use every day

individuals might have sought increased concentrations of THC to self-medicate. However, experimental studies show that THC induces psychotic symptoms, while cannabidiol ameliorates them and reduces anxiety.<sup>36-39</sup> That people who already have prodromal symptoms would choose a type of cannabis that is high in THC and has little cannabidiol (such as skunk), which might exacerbate their symptoms, rather than a cannabidiol-containing type (such as hash), would seem counterintuitive.

A possible limitation of our study is the absence of data on number of joints or grams used per day. However, because we collected information about use over a period of years and not about present use, the reliability of such detailed information would probably have been confounded by recall bias to a greater extent than was the general description of pattern of use that we obtained. The fact that we were able to collect detailed information on other environmental factors and control for their potential confounding effects is a key strength of our study.

Our findings show the importance of raising public awareness of the risk associated with use of high-potency cannabis (panel), especially when such varieties of cannabis are becoming more available.<sup>29</sup> The worldwide Panel: Research in context

#### Systematic review

We searched PubMed for studies that estimated the effect of cannabis use on the number of new cases of psychosis arising in specific populations, using both the terms "population attributable fraction", and "number needed to treat". We also searched for studies that investigated the association between the "high potency and/or skunk" type of cannabis and psychosis. We included all studies available on PubMed until Sept 31, 2014. We identified three studies,<sup>28,15</sup> all of which met our inclusion criteria.

#### Interpretation

The association between cannabis use and increased risk of developing schizophrenia-like psychosis has been consistently reported by prospective epidemiological studies.<sup>23</sup> Our previous study was the first to show that use of high-potency (skunk-like) cannabis carries the highest risk for psychotic disorders.<sup>8</sup> In the present larger sample analysis, we replicated our previous report and showed that the highest probability to suffer a psychotic disorder is in those who are daily users of high potency cannabis. Indeed, skunk use appears to contribute to 24% of cases of first episode psychosis in south London. Our findings show the importance of raising awareness among young people of the risks associated with the use of high-potency cannabis. The need for such public education is emphasised by the worldwide trend of liberalisation of the legal constraints on cannabis and the fact that high potency varieties are becoming much more widely available. Finally, in both primary care and mental health services, a simple yes-or-no question of whether people use skunk might be more useful to identify those at increased risk to develop psychosis because of their cannabis use.

trend of liberalisation of the legal constraints on the use of cannabis further emphasises the urgent need to develop public education to inform young people about the risks of high-potency cannabis.

#### Contributors

In collaboration with the Genetics and Psychosis Study (VM, TRM, SAS, MR, AM, JO'C, CI, PD, CP) and the PUMP study (FG, ZA, PG-S) teams, MDF, AT, and SAS collected the data and MDF prepared the data for the analysis. MDF did the data analysis with CM. MB and FB contributed to the data entry. ML and RMM supervised MDF in the interpretation of the results. EC and SF contributed to the literature review and to the selection of the references. ASD and JP reviewed the manuscript and contributed to its final draft. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

#### **Declaration of interests**

RMM reports honoraria from Otsuka, Lundbeck, and Janssen, which he received for lecturing on the report of the Schizophrenia Commission. All other authors declare no competing interests.

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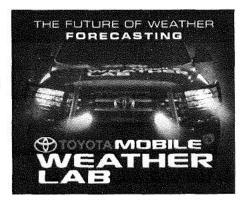
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LOS ANGELES (CBSLA.com) - In a CBS2 News exclusive, Investigative Reporter David Goldstein uncovers medical marijuana being sold to school-aged kids in broad daylight, within walking distance of local schools.

He reported the city was quick to act when he brought his disturbing findings to officials.

Goldstein recorded many instances of adults buying the marijuana and quickly turning around and reselling it to the underage kids.

The students were shown, many times, smoking the pot minutes after leaving their schools.

The student's faces were covered because most appeared to be under 18 - the legal age for receiving doctor's approval to buy medical marijuana without a parents' consent.

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Who's Hiring!

So exactly how did these kids get their hands on it?

Our hidden cameras caught the students paying someone else to get it for them --- like this one man who didn't want his face shown on TV.

On most afternoons, residents of the area say kids like these gather on Barton Avenue, near Western in Hollywood.

On a map, it's easy to see the area is walking distance to several schools.

With their sneakers, skateboards and backpacks, it looks like any afterschool meeting place. Until you see what's taking place on the corner -- Natural Remedies Caregivers, a marijuana dispensary.

Goldstein reports, "we saw plenty of activity."

In one instance, a group of young women is shown handing a man on a skateboard some money. He gets on the skateboard, then walks into the store. A few minutes later, he comes out carrying a white bag. He passes out what looks like pill jars to the girls on the street

The jars are similar to one Goldstein found in the bushes near the dispensary. They're used as containers for the pot.

It says right on the label, "Not for children - Keep out of reach."

But that didn't seem to stop the seller or the buyers.

The girls are shown opening up the jars and smelling their newly-purchased medical marijuana.

Goldstein and his producer also observed a customer leaving the dispensary two times in one afternoon to hand off the contents inside his white bags.

The man is shown delivering the jars to two kids on the street — then he just crumples up the bag and throws it over his head.

One teen is still holding his school notebook under his arm when he is shown tossing a jar to his friend who takes a whiff to check it out.

On another occasion, Goldstein saw two teens buying and selling what appears to be medical marijuana - exchanged openly in broad daylight.

On another day, our cameras caught a group of teens collect their money. Their connection comes up to grab it. He goes into the dispensary and comes out with the tell-tale white bag.

He distributes the contents to his teenaged customers.

Goldstein then confronts the man. "You just went into the dispensary and bought pot for these guys, didn't you?" he asks.

"I don't know what you're talking about," the man replies.

Goldstein tries again. "We just saw you go in there and you bought pot for these guys."

This time the man hit our camera and also made an obscene gesture.

The teens also had nothing to say.

"How old are you?" he asked several.

Goldstein then asked to speak to a manager at the dispensary.

He was told the manager "wasn't around" and that a security guard hired by the store to police the area said he didn't see anything going on.

"You are the security guard, you don't see these people coming in here and then selling to kids right around the corner?," Goldstein asks, "and you don't see anything, right?"

The guard closed the door.

Residents said they see it and complained to police and nothing was done.

"Well, it's very frustrating," said resident Dazzier Jimenez, "because you know, we have kids around the area, so they see that. It's a bad example for our youth."

Goldstein asked City Attorney Mike Feuer why this dispensary was allowed to remain open.

His office oversees LA's Prop D marijuana law. He said the dispensary complies with all the written requirements, as far as being a safe distance from schools and parks.

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After we told him what was going on, authorities acted.

"I can report that because you provided us with that location," Feuer said, "the police conducted an investigation at the site and last evening they arrested an individual, an adult for allegedly selling medical marijuana to a minor just outside the facility."

The manager of the dispensary also emailed Goldstein.

"We are doing everything in our power to stop the illegal patient solicitations outside of the building and to also stop second-hand transactions from happening," the manager wrote.

Residents wonder why it took so long.

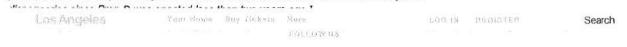
"Why are there now arrests when there haven't been any in the past?," said Jimenez.

"Quite frankly," says LAPD Commander Andrew Smith, "it was not a big problem location. It was not known to us as a problem location."

Police and prosecutors told Goldstein that after seeing CBS2's undercover video, they are now cracking down.

#### David Goldstein, CBS2 News

#### [Editor's note: The City Attorney's office has shut down more than 400 medical marijuana





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