

The prevalence and incidence of medicinal cannabis on prescription in The Netherlands

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Abstract

Background A growing number of countries are providing pharmaceutical grade cannabis to chronically ill patients. However, little published data is known about the extent of medicinal cannabis use and the characteristics of patients using cannabis on doctor's prescription. This study describes a retrospective database study of The Netherlands.

WHAT THIS PAPER ADDS

What is already known on this subject

- As clinical support for the therapeutic use of cannabis or its isolated components such as THC is mounting, several countries are now providing herbal cannabis of pharmaceutical grade to chronically ill patients.
- Many other patients obtain cannabis from illicit sources and experiment with self-medication, without the supervision of a medical professional.
- Other than surveys based on self-selected participation, not much is known about characteristics or preferences of medicinal cannabis users.

What this study adds

- This study is the first one using objective data to study national medicinal cannabis consumption patterns, providing accurate data on the incidence, prevalence and characteristics of users of prescribed medicinal cannabis in The Netherlands.
- Understanding the background and preferences of cannabis patients may help medical professionals to decide about the role of medicinal cannabis in their own practice.

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Methods Complete dispensing histories were obtained of all patients with at least one medicinal cannabis prescription gathered at pharmacies in The Netherlands in the period 2003–2010. Data revealed prevalence and incidence of use of prescription cannabis as well as characteristics of patients using different cannabis varieties.

Results Five thousand five hundred forty patients were identified. After an initial incidence of about 6/100,000 inhabitants/year in 2003 and 2004, the incidence remained stable at 3/100,000/year in 2005–2010. The prevalence rate ranged from 5 to 8 per 100,000 inhabitants. Virtually all patients used some form of prescription medication in the 6 months preceding start of cannabis use, most particularly psycholeptics (45.5 %), analgesics (44.3 %), anti-ulcer agents (35.9 %) and NSAIDs (30.7 %). We found no significant association between use of medication of common indications for cannabis (pain, HIV/AIDS, cancer, nausea, glaucoma) and variety of cannabis used.

Conclusions This is the first nationwide study into the extent of prescription of medicinal cannabis. Although the cannabis varieties studied are believed to possess different therapeutic effects based on their different content of tetrahydrocannabinol (THC) and cannabidiol (CBD), no differences in choice of variety was found associated with indication.

Keywords Cannabis · Therapeutic use · Prevalence · Incidence · The Netherlands

Introduction

As the medicinal properties of the cannabis plant are increasingly being unraveled, the number of countries that provide an official source of cannabis to chronically ill patients is growing. Canada (since 2001) and The Netherlands (since 2003) have had a government-run program for the last decade, supplying quality-controlled herbal cannabis grown by specialized companies [1, 2]. Several countries are now following this

example, either by setting up their own program (Israel, Czech Republic) or by importing products from The Netherlands (Italy, Finland, Germany). In the United States, the number of states that have introduced laws to permit the medical use of marijuana has now grown to 17 plus the District of Columbia (DC), even though this development is not endorsed by the US federal government [3]. In contrast to these developments, little published data is known about the extent of medicinal cannabis use and the characteristics of patients using cannabis on doctor's prescription, other than survey data relying on self-selected participation and self-reports [4–9].

The medicinal cannabis program of The Netherlands, supervised by the Office of Medicinal Cannabis (OMC) of the Dutch Health Department, provides an opportunity to study such questions. The program offers pharmaceutical grade cannabis on prescription to chronically ill patients suffering from multiple sclerosis, cancer, HIV/AIDS, chronic pain, therapy-resistant glaucoma, and Tourette's syndrome [1]. The product is cultivated by contracted company Bedrocan BV, and dispensed through pharmacies in the form of dried female flowers (Cannabis Flos) packaged in 5 g containers. Patients are advised to administer medicinal cannabis by using a cannabis vaporizer or by preparing it as a tea [10, 11]. In a growing number of cases, costs are reimbursed by health insurance companies [12].

Patients in The Netherlands typically utilise only a single pharmacy for obtaining all their prescription medicine, making it possible to track patients over time and construct complete medication histories including both GP and specialist prescriptions [13]. Therefore, using the Dutch cannabis program as a well-documented source of data, this study aims to analyse the incidence and prevalence of prescription medicinal cannabis use, as well as the demographics and characteristics of patients using cannabis on prescription.

Methods

The data collection covered the period of September 2003 (when medicinal cannabis first became officially available on prescription in The Netherlands) to the end of December 2010. Data on dispensing was collected from two sources. The main source was the Dutch Foundation for Pharmaceutical Statistics (Stichting Farmaceutische Kengetallen; SFK); an independent organization collecting data from community pharmacies in The Netherlands for policy and research purposes. Medication dispensed through hospital pharmacies and nursing homes for in-house patients are not registered in the SFK database and are therefore not covered in our study. The second source of data was the only Dutch pharmacy specialized in dispensing of medicinal cannabis (Hanzeplein pharmacy, Groningen). Since 2007 this pharmacy has been active in dispensing the same medicinal

cannabis for a reduced price (as a result of cheaper packaging, distribution and labour cost) through mail-order to patients located all over The Netherlands.

Data collected from both sources included date of dispensing, variety and amount of medicinal cannabis dispensed, and patient characteristics (age, gender, and geographical location by zip code). Complete comedication dispensed through the pharmacy was collected for SFK data only from 6 months preceding the first medicinal cannabis dispensing until the end of medicinal cannabis use. Comedication was coded according to the WHO ATC/DDD methodology and grouped accordingly [14]. All data were anonymized and patients were not financially or otherwise compensated.

In the period covered by this study (2003–2010), four different varieties of cannabis were available to patients, each containing a standardized amount of the known active ingredients tetrahydrocannabinol (THC) or cannabidiol (CBD) [15]. These varieties were: *Bedrocan*[®] (ca. 19 % THC; introduced 2003); *Bedrobinol*[®] (ca. 12 % THC; introduced 2005); and *Bediol*[®] (ca. 6 % THC, 7.5 % CBD; introduced 2007). Variety *SIMM18* (ca. 11 % THC; introduced 2003) was only available until 2006, after which it was replaced by *Bedrobinol*[®].

Incident use of medicinal cannabis was defined as the first dispensing date available in the database. Since the database covers the complete period of availability of medicinal cannabis in The Netherlands, this refers to actual new users. Year-by-year prevalence was determined by counting the number of patients with at least one dispensing of a medicinal cannabis preparation in a calendar year. Total duration of cannabis use was defined as the time difference between the first and last dispensing of medicinal cannabis, supplemented with the number of days needed to consume the last dispensed amount (assuming an average daily use as shown in Table 1). Average dosage of cannabis per day per patient was calculated by dividing the total dispensed dose (in grams) of each individual, by the total duration of use (in days) calculated for that same individual.

Results

Demographics

Table 1 shows demographic data of the study population. Over the 2003–2010 study period, 5,540 individual patients were identified receiving a combined total of approximately 35,000 medicinal cannabis dispensations. The majority of patients (5,255; 94.9 %) received their product through regular community pharmacies, the remaining patients (285; 5.1 %) had their prescription filled in by the specialized cannabis pharmacy. More females (56.8 %) compared to males (42.7 %) used medicinal cannabis on prescription. The mean (median) age of the study population was 55.6 (55) years, with

Table 1 Demographics and medicinal cannabis use in the study population from 2003 to 2010

	N=(%)	Average duration of use (days)	Average number of dispensations	Average daily use (grams)
Study population	5,540 (100)	251	6.43	0.68
Sex				
Male	2,366 (42.7)	244	6.70	0.71
Female	3,149 (56.8)	258	6.26	0.65
Age				
≤ 20	93 (1.7)	181	5.57	0.82
21–40	846 (15.3)	316	8.73	0.72
41–60	2,551 (46.0)	304	7.44	0.66
61–80	1,722 (31.1)	174	4.51	0.67
>80	303 (5.5)	99	3.01	0.74

a range of 14 to 93 years. The zip code information available for each patient indicated that medicinal cannabis users were fairly equally distributed, without noticeable agglomeration in specific geographical locations (data not shown).

Average cannabis use and duration

Data on cannabis use are also shown in Table 1. Patients received on average 6.4 prescriptions of medicinal cannabis with a median of 10 g dispensed per prescription. Overall, medicinal cannabis was prescribed for an average duration of 251 days. Patients had an average daily dose of 0.68 g per day dispensed. Male patients (0.71 g) were found to consume slightly more medicinal cannabis daily than female patients (0.65 g). Despite the differences in composition of active ingredients, no clear differences in average daily dose were observed between the four cannabis varieties offered (data not shown).

Incidence and prevalence

After an initial incidence of about 1,000 new users per year at the start of the cannabis program in 2003 and 2004 (equalling 6 per 100,000 persons per year), the number of new users stabilized somewhat lower around 500 per year, (3 per 100,000 per year). The number of patients receiving at least one prescription of medicinal cannabis per year ranged from 800 to 1,300 per year, which translates into a yearly prevalence rate of 5–8 per 100,000 persons as shown in more detail in Fig. 1.

Comedication and correlation with cannabis varieties

Virtually all patients used at least some form of prescription medication, other than cannabis, in the 6 months preceding the first cannabis prescription. Comedication observed most

often were psycholeptics (ATC code N05; used by 45.5 % of study population), analgesics (N02; 44.3 %), anti-ulcer agents (A02B; 35.9 %) and NSAIDs (M01; 30.7 %).

Because the Dutch program provides multiple cannabis varieties, each with different content of THC and CBD, this may (tentatively) allow us to identify correlations between these pharmaceutically active components and particular symptoms under treatment, by studying the comedication used in the period before start of cannabis treatment. We therefore selected those indications that are specifically mentioned by the Office of Medicinal Cannabis, and that can be fairly unambiguously recognized by the (co)medication used. These included severe pain (as identified by use of opioid and non-opioid pain medication), cancer (oncolytics), HIV/AIDS (HIV-medication), nausea (anti-nausea medication) and glaucoma (eye drops). Other indications, such as MS or Tourette syndrome, were not investigated here because there is no specific comedication that unambiguously indicates these conditions.

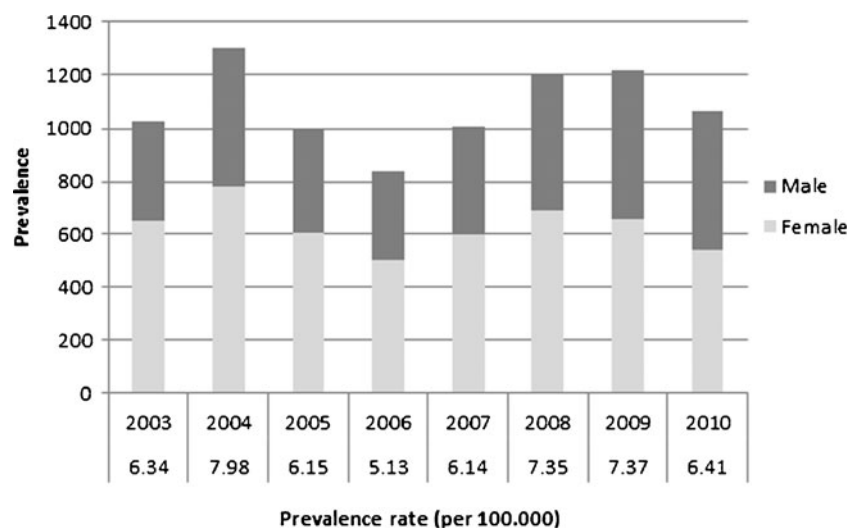
As shown in Table 2 (which includes the 5,250 patients from the SFK database only), pain medication was used by 53.6 % of all cannabis users, which was further broken down into non-opioids (40.5 % of cannabis users), and weak (21.8 %) or strong opioids (21.2 %). Although cancer and HIV/AIDS are often mentioned in popular media in relation to medicinal cannabis use, oncolytics (2.7 %) and HIV medication (0.9 %) were only used by a small proportion of cannabis users. Glaucoma medication was seen in 2.2 % of users. In contrast, medication prescribed to treat nausea was used by 15.5 % of all cannabis users.

The results in Table 2 were further broken down for the different cannabis varieties available. Varieties *Bedrobinol* and *SIMM18* were combined because of their similar THC content. For ease of interpretation, only data of patients who had used one single cannabis variety is shown, which covered 4,507 (85.8 %) of all subjects. Of the remaining subjects, 682 (13.0 %) patients had used 2 different varieties, while 98 (1.9 %) had used 3 or 4 varieties. Although some minor differences between varieties are visible, there seemed to be no clear correlation between content of THC/CBD and any of the comedication we studied.

Discussion & conclusion

This first nationwide study into the extent of prescription of medicinal cannabis provides us with a characterization of patients using medicinal cannabis on prescription in The Netherlands, including demographics, average use and information on varieties and indications. A strength of this study is the virtual nationwide coverage of the data-collection, with the SFK data statistically covering about 85 % of the total Dutch population [Dutch Foundation for Pharmaceutical Statistics, personal communication]. Before conclusions may be drawn,

Fig. 1 Prevalence (vertical bars) and prevalence rate (secondary horizontal axis) of medicinal cannabis use in The Netherlands, 2003–2010



however, the potential limitations of the study must be clearly addressed. Our study was performed based on the assumption that Dutch patients receive all their medication from one pharmacy only. Although this is generally considered to be typical for the Dutch pharmacy system, we cannot exclude that at least a proportion of patients visited multiple pharmacies over the study period. When a patient visits a new pharmacy, the person is entered into the database under a new identifier, which in our study would have been interpreted as a new user. Also, it should be noted that obtaining cannabis from the Dutch outlets known as coffee shops remains a (pseudo-legal) option for patients [16]. A recent large-scale international survey among 953 patients performed by the International Association for Cannabinoid Medicines (IACM) indicated that the street market (including coffee shops), as well as growing your own cannabis, remain widely popular even among those patients who have access to cannabis on prescription [4].

Despite these limitations, we believe this was the first time objective data was used to study national medicinal cannabis consumption patterns, in contrast to surveys based

on self-selected participation. Indeed, the differences between these two approaches can be significant. For example, the average daily use determined in our study was 0.68 g. In contrast, the international IACM survey found an average daily use ranging from 2.4 to 3.8 g per day, depending on the administration form used [4]. Unfortunately, in our current study the administration form of the cannabis was not known; although patients are advised to inhale their cannabis by using a vaporizer or to prepare tea [1], we cannot be certain they follow these instructions. We also noticed a significant difference in age of subjects between the IACM survey (mean 40.7 years) and our own study (mean 55.6 years). Other surveys have found similar results for higher daily consumption [7, 17] or younger mean age, compared to the database approach described here [18–20]. Such differences may indicate that surveys based on self-selected medicinal cannabis users, at least to some extent, inadvertently attract younger patients who have an above-average interest in herbal cannabis, and use more liberal amounts of cannabis on a daily base.

Because the SFK database did not cover the entire Dutch general population (totaling 16.6 million inhabitants in 2010),

Table 2 Use of comedication categorized per cannabis variety. Results are expressed as percentage of total users in each category

	All users ^a	Users of high THC: ^b <i>Bedrocan</i>	Users of low THC: ^b <i>Bedrobinol/SIMM</i>	Users of THC+CBD ^b <i>Bediol</i>
Total (N=)	5,250	2,136	1,933	438
Associated comedication (%)				
Pain medication	2,801 (53.4)	1,119 (52.4)	1,072 (55.5)	220 (50.2)
-Non-opioid	2,125 (40.5)	814 (38.1)	841 (43.5)	168 (38.4)
-Weak opioid	1,147 (21.8)	470 (22.0)	423 (21.9)	99 (22.6)
-Strong opioid	1,114 (21.2)	476 (22.3)	430 (22.2)	95 (21.7)
HIV medication	48 (0.9)	24 (1.1)	9 (0.5)	4 (0.9)
Oncolytics	139 (2.6)	66 (3.1)	50 (2.6)	9 (2.1)
Nausea medication	806 (15.4)	337 (15.8)	335 (17.3)	68 (15.5)
Glaucoma medication	116 (2.2)	49 (2.3)	40 (2.1)	10 (2.3)

^aAll users for which comedication information was available (SFK database patients only)

^bFor exact THC and CBD content, see [Methods](#)

and at least a proportion of patients is believed to consume cannabis obtained from non-official sources, our calculated prevalence rate of 5–8 per 100,000 should be considered a very conservative estimate. By comparison, prevalence rates (unofficially) reported in some other countries where medicinal cannabis use is registered by national authorities are 35 (per 100,000) for Canada and 80 for Israel, while in some US states prevalence rates of over 100 are claimed [21]. However, these numbers likely include significant numbers of pseudo-patients who, other than Dutch consumers, do not have the opportunity to obtain cannabis from legal street sources like the Dutch coffee shops. Importantly, the low average daily dose (0.68 g) found in our study points to a low potential of misuse, and a seeming absence of widespread development of tolerance. By comparison, an average Dutch cannabis cigarette used for recreational purposes contains about 0.26 g of cannabis mixed with tobacco [22]. The slightly higher daily consumption by male patients compared to females may be explained by differences in average body weight between both sexes.

By studying the comedication prescribed in the period right before first onset of cannabis use, we identified pain and nausea as common medical indications correlated with cannabis use. This may not be surprising given the fact that nausea (together with vomiting and lack of appetite) is a clinically proven indication for THC, e.g. in the form of Marinol[®], while preparations containing THC and/or CBD were shown to be clinically effective for several pain indications, including severe chronic noncancer pain [23], various neuropathic pains [24], postoperative pain [25] and MS [26]. Surprisingly, the differences between varieties, in terms of average daily consumption or associated comedication, were found to be minimal. Although the cannabis varieties are believed to possess different therapeutic effects based on their different content of THC and CBD, only a minority of patients (14.9 %) had tried more than one single variety. It is unknown whether this means that the first choice of variety was already sufficiently effective in most patients, or that patients were generally not interested in trying another variety of cannabis in case the first variety failed to provide proper relief. Alternatively, doctors may have lacked sufficient information to make an informed decision, or may have refused to write another prescription after the first variety was found to be ineffective.

The Dutch program is currently unique in the world for providing a choice of standardized and quality controlled cannabis varieties to patients. Nevertheless, based on our study it should be concluded that the differences between these varieties are still insufficiently recognized. In contrast, it is important to realize that although our data accurately show *what* (how much, how often, what variety) doctors have prescribed, it cannot reveal whether the prescribed products were actually effective or not in treating the intended

symptoms. Large population-based surveys, preferably among the same well-documented Dutch patient population, are needed to further describe the intentions and experiences of medicinal cannabis patients. Eventually, properly designed clinical trials are needed to provide a better understanding of the link between specific combinations of cannabinoids and medical indications. In the meantime, an increased effort to educate medical users as well as prescribers about the medicinal use of cannabis may further strengthen the Dutch model of providing pharmaceutical-grade cannabis to chronically ill patients.

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