Acceptance of two variants of medical cannabis by psychotic patients: a randomised cross-over study (N=12).

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The proposed experimental pilot study focuses on harm reduction in a specific subpopulation, i.e. in patients with schizophrenia (long-term psychotic disorder) with a suboptimal response to the currently available interventions, smoking a lot of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON44002

Source
ToetsingOnline

Brief title
Acceptance of medical cannabis

Condition

- Schizophrenia and other psychotic disorders

Synonym
hallucinations, schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: GGD Utrecht

Intervention

Keyword: Cannabis, Psychosis, Schizophrenia, Side effects

Outcome measures

Primary outcome

The primary question is whether the participant cannabis version with 8% CBD (Bediol) from the drop wants to smoke rather than by himself so far purchased cannabis variety.

Question 1. Would you take this cannabis in the sequel as a preferred alternative?

Question 2. If yes. Is this because of fewer side effects when smoking this variant or other reasons?

Secondary outcome

1. Experience with the cannabis just smoked (enough *high*, taste)? Different or similar to the kind you smoke normally?

2. Experiences during/after smoking the joints (less anxiety, panic, calm, drowsiness, excited, pleasant, stoned, dizziness, restlessness, lethargic, depressed or lethargic feeling, craving, sweating, nausea, dizziness, tremors, palpitations (Questionnaires see F9 + F10).

Study description

Background summary

Problem statement
Cannabis provokes psychotic symptoms, but is also used by psychotic patients to

dampen symptoms of the disease and side effects of the treatment. The ratio of THC:CBD in the cannabis smoked may be decisive for either induction or inhibition of psychotic symptoms. Cannabis varieties used in the Netherlands are often characterized by a high THC:CBD ratio and this may increase the probability of a psychotic relapse in patients with schizophrenia

Cannabis as causal agent in schizophrenia

Substantial epidemiological evidence shows that cannabis dose-dependently increases the risk of and provokes psychosis (Zammit et al., 2002; Fergusson et al., 2005; Henquet et al., 2005). The occurrence of schizophrenia in people smoking cannabis is increased (Moore et al., 2007) and chronic cannabis smokers show cognitive deficits similar to those seen in schizophrenic patients (Solowij and Michie, 2007). Moreover, cannabis use is associated with early onset of schizophrenia; young people with genetic vulnerability to schizophrenia are particularly sensitive to the physical and mental effects of cannabis (Degenhardt and Hall, 2006; Hollis et al., 2008). Nevertheless, the associations found in longitudinal cohort studies are difficult to interpret because of methodological problems, in particular the reliability of self-reported data and the possible role of (not measured) confounders. Finally, it seems the strong increase in the use of cannabis is not accompanied to have gone with a higher incidence of schizophrenia (Anonymous, 2011; van Amsterdam et al., 2004).

Cannabis as self-medication in schizophrenia

A substantial number of schizophrenic patients seem to use cannabis to self-medicate negative symptoms and anxiety. Therefore, a higher prevalence of cannabis use and cannabis dependence is seen in these patients as compared to the healthy population.

Studies, using self-report questionnaires to investigate motives of cannabis use among psychotic patients, indicate that the principal motives for use in this group are enhancement of positive affect, social acceptance and coping with negative affect (Spencer et al., 2002). Additional evidence that patients may use cannabis to self-medicate distress was reported in a population-based study where vulnerability for psychosis predicted future cannabis use in those who had never used cannabis before the onset of psychotic symptoms (Ferdinand et al., 2005).

Daily cannabis use predicted increases in positive affect in patients and controls, but decreases in negative affect and increases in hallucinatory experiences in patients only. Mood-enhancing properties of cannabis were acute, whereas psychosis-inducing effects were sub-acute. There was no direct evidence for self-medication effects in daily life. (Henquet et al., 2010).

These findings corroborated well with a meta-analysis, which looked at the results of nine studies in which psychotic patients (N = 725) with and without a comorbid substance use disorder (SUD) were compared for the presence of each other positive and negative symptoms (Talamo et al., 2006). Psychotic patients with SUD had more positive symptoms, but less negative symptoms on the Positive and Negative Syndrome Scale (PANSS). Although tobacco and alcohol were

primarily used for social reasons, cannabis was 64 psychotic patients, mainly used because of the pleasure-enhancing effects
In psychotic patients with co-morbid substance use disorders (SUD), Talamo et al. showed that in 9 studies (N=725 subjects), SUD+ patients abused alcohol > cannabis > cocaine. Considering the PANSS score (Positive and Negative Syndrome Scale Scores), SUD+ patients had significantly higher PANSS-positive, and lower PANSS-negative scores. A study in 64 psychotic patients confirmed the pleasure enhancing effects of cannabis. Although tobacco was primarily used by them for coping motives and alcohol for social motives, cannabis was mainly taken for pleasure enhancement motives (Thornton et al., 2012).
Patients with psychosis are therefore more sensitive to both the psychosis-inducing and mood-enhancing effects of cannabis. The temporal dissociation between acute rewarding effects and sub-acute toxic influences may be instrumental in explaining the vicious circle of deleterious use in these patients (Henquet et al., 2010). Henquet et al. further showed that cannabis improved mood, particularly in psychotic patients. The combination of differential sensitivity in patients to the acute rewarding effects and the sub-acute negative influences of cannabis on psychotic symptoms (despite the fact that the majority of patients were using antipsychotic medication) may be helpful in explaining the model of cannabis use in patients with psychosis, as proposed by Spencer et al. (Spencer et al., 2002) According to this model, use of cannabis is driven by expectations that individuals may have about the (acute) effects of cannabis. The sub-acute negative psychotic effects may then be experienced as evidence that more use is necessary to bring about the anticipated rewarding effects. Hallucinatory experiences are strongly associated with negative affect (Delespaul et al., 2002), fuelling further use in order to experience acute improvement in mood. Other epidemiological work, however, has suggested that cannabis may reduce negative and affective symptoms in patients with schizophrenia (Compton et al., 2004). The reason for these differences in results is not clear.
Reports in the literature are, however, not conclusive about the effects of cannabis use by psychotic patients, because both positive (less negative and positive episodes) and negative (e.g. increases number of psychotic episodes) clinical outcomes have been reported (see below).

Cannabis use in high risk subjects and patients with schizophrenia
Negative outcome
The use of cannabis can trigger psychotic episodes in schizophrenic patients, which has been ascribed to THC. When given in very high dose (intravenously) to healthy humans, THC produces psychotic-like and anxiogenic effects (D'Souza et al., 2004; D'Souza et al., 2008). Indeed, most data demonstrate an unfavourable outcome in patients with schizophrenia and cannabis abuse, as indicated by more severe and refractory symptoms, poorer treatment-response, higher relapse rates and an overall worse prognosis (Linszen et al., 2004; Compton et al., 2004), including more hospitalisations (van Dijk et al., 2012).
In 1982, it was found that schizophrenic patients in South Africa experienced an increased frequency of acute psychotic episodes i.e. more hypomania and

agitation after the use of a variety of cannabis sativa virtually devoid of CBD (Rottanburg et al., 1982). Several studies confirmed that cannabis use is associated with a worsening of symptoms in subjects with psychotic disorder and have a negative impact on the course of the disease (Degenhardt et al., 2007; D'Souza et al., 2009).

Van der Meer et al. (van der Meer et al., 2012) recently conducted a systematic review of studies measuring the impact of cannabis use in a clinical high-risk (CHR) population on the transition to a first psychotic episode. Of 729 potentially relevant papers, 11 met inclusion criteria. The results of these studies were contradictory. In some studies, cannabis use was associated with more severe symptoms at baseline (the prodromal stage), increased pre-psychotic symptoms immediately after intoxication, and earlier onset of certain high-risk symptoms. In others, no significant association between cannabis use and baseline symptomatology was found. In one study, cannabis use was even significantly associated with a decrease in pre-psychotic negative symptoms, and with fewer symptoms of depression and anxiety. Four out of five studies reported no significant effect of cannabis use on transition to psychosis. It was concluded that cannabis use seems to provoke and enhance sub-clinical symptoms in CHR subjects. However, the results provide no consistent evidence for an association between cannabis use and transition to a first psychosis in CHR subjects (van der Meer et al., 2012). In a 4-year follow-up study of a small sample of 119 patients with recent onset of psychosis it was demonstrated that those patients who persisted in the use of cannabis had more positive (but not negative) symptoms and a more continuous illness at follow-up (Grech et al., 2005).

About the relationship between cannabis use and the development of psychotic disorder several studies have shown that co-morbid cannabis use disorder (CUD) affected the course of the disease in patients with schizophrenia negatively. Psychosocial functioning ("confusion" and "hostility") had deteriorated (Caspari, 1999), more severe psychotic symptoms occurred (Foti et al., 2010), more and earlier psychotic relapses were reported, more hospitalizations were noted (Caspari, 1999), and the patients showed less compliance (Linszen et al., 1994; Zammit et al., 2008). A retrospective study in schizophrenic patients (N=455) showed that those with a history of cannabis use disorder (CUD+; N=175) performed better on measures of processing speed, verbal fluency, verbal learning and memory than the CUD- group (N=280). The CUD+ group also scored better in Global Assessment of Functioning (GAF) scale than the CUD- group (DeRosse et al., 2010), suggesting that schizophrenic patients with co-morbid CUD may represent a higher functioning subgroup of schizophrenic patients (see also below).

Other studies on psychosocial functioning (eg in GAF scores) (Scheller-Gilkey et al., 2002; Dervaux et al., 2003; Machielsen et al., 2010) found no significant differences between patients with and without CUD. In patients with first-episode psychosis with CUD Compton et al. (Compton et al., 2004) found no difference in positive symptoms and general psychopathology, but they experienced less prominent negative symptoms than comparable patients without CUD.

Cannabis and alcohol use was associated with an increased risk of psychosis and delusions (Nunn et al., 2001). The results of a systematic review also suggested a link between cannabis use and psychosis, with the higher use associated with a higher risk (RR 2.09) (Moore et al., 2007). When administered in very high doses (intravenously) to healthy people THC induced psychosis-like and anxiogenic effects (D'Souza et al., 2004; D'Souza et al., 2008).

Conclusion

It seems that cannabis use in psychotic patients may lead to fewer negative symptoms and less anxiety, while there is a greater chance of positive symptoms (psychosis) and related admissions due to relapse. The positive relationship between cannabis use and psychosocial functioning that was sometimes found is probably a result of selection, where the better functioning patients are more able to obtain cannabis.

Pharmacological profile of THC and CBD

The psychotic effect of cannabis is closely related to the THC:CBD ratio: a higher proportion of THC is linked to the psychosis-facilitating potential. THC, the principal psychoactive constituent of the Cannabis sativa plant, stimulates the central cannabinoid CB1 receptor thereby inducing the characteristic psychomotor effects, and provokes (already existing) psychosis. CBD, the second most abundant psychoactive constituent of Cannabis sativa, has weak partial antagonistic properties at the CB1 receptor. CBD inhibits the reuptake and hydrolysis of anandamide, the most important endogenous CB1 receptor agonist. As such, CBD (partly) reverses many of the physiological and behavioural effects of CB1 receptor agonists, like THC, and more importantly CBD lacks the unwanted psychotropic characteristics of THC (and commonly used cannabis). Like SR141716, a selective CB1 receptor antagonist, CBD even retains anti-psychotic properties (Zuardi et al., 2006; Schier et al., 2012) which resemble that of atypical anti-psychotic drugs (Roser et al., 2010). Due to its antipsychotic property (recently critically reviewed by Zuardi c.s. (Zuardi et al., 2012)), CBD may be a therapeutic option in psychosis in general and in schizophrenia in particular (Zuardi et al., 2012).
A double-blind study, conducted in eight healthy volunteers by Zuardi c.s. in 1982 (Zuardi et al., 1982), demonstrated interactions between THC and CBD, with CBD (1 mg/kg) suppressing THC-induced anxiety and subjective alterations, like alertness, and feelings of being incompetent, discontent, clear minded and clumsy. This observation was later confirmed by various studies (Zuardi et al., 2006; Fusar-Poli et al., 2010; Bhattacharyya et al., 2010), case reports and in a clinical trial of Leweke et al. (Leweke et al., 2007). In the latter trial in 42 patients with acute paranoid schizophrenia, 200 mg CBD given during 2-4 weeks induced a similar decrease of symptoms as treatment with the antipsychotic drug amisulpiride, but showed fewer side effects. Bhattacharyya c.s reported that pre-treatment of 15 healthy men with minimal earlier exposure to cannabis with CBD (10 mg p.o.) prevented the acute induction of psychotic symptoms by THC (Bhattacharyya et al., 2010). Some 20 clinical trials are registered in 2012 for the use of synthetic CBD for a variety of medical

conditions (finalised or on-going) (Clinical trials, 2012). Possibly, these results indicate that the CBD may suppress the negative effects of THC in patients with schizophrenia.
Finally, CBD seems to counteract some of the drug-seeking effects of THC in humans. This was shown in smokers of high CBD:THC cannabis strains who when intoxicated showed reduced attentional bias to drug and food stimuli compared with smokers of low CBD:THC. Note that those smoking higher CBD:THC strains also showed lower self-rated liking of cannabis stimuli on both test days (Morgan et al., 2010a). The low reinforcing potency of CBD was confirmed in rodent studies (Vann et al., 2008), where CBD reversed the conditioned place preference effect induced by THC in CBD:THC ratios of 1:1 and 1:10 (Vann et al., 2008).

THC:CBD ratio in cannabis strains
The geographic origin and growing conditions (temperature, inside, outside) can make considerable difference in terms of the THC content in cannabis. For example, cannabis produced in the Netherlands (Nederwiet) contains about 15-16% THC (imported cannabis 5.7%) and virtually no CBD (0.3%), whereas hash imported from Nepal, Afghanistan or Morocco contained a slightly higher proportion of THC (17%), but also contained up to 9% CBD (mean 6.9%) (Niesink and Rigter, 2012).
Despite the negative effects of cannabis in psychotic patients mentioned above, there are also indications that the composition of cannabis i.e. the THC:CBD ratio is decisive for the clinical outcome. Associations between the use of certain strains of cannabis and the occurrence of psychotic symptoms have been found in three 'naturalistic' studies in the United Kingdom and the Netherlands in 2010 and 2011 (Schubart et al., 2011; Morgan et al., 2010b; Morgan et al., 2011). These studies did, however, not clarify the effect of different strains of cannabis on psychotic symptoms in chronic psychotic patients.
High THC:CBD ratio*s have also been associated with a higher risk of a first psychotic episode (Di Forti et al., 2009), while cannabis with high CBD content was associated with fewer psychotic experiences (Schubart et al., 2011). Cognitive deficits emerged in individuals who smoked cannabis with a low-CBD content, whereas high-CBD cannabis smokers tested in memory tasks under acute intoxication performed similarly than when tested in a drug-free environment (Morgan et al., 2010b).
The impact of the ratio THC:CBD was nicely demonstrated by Morgan and Curran (Morgan and Curran, 2008) who analysed hair samples to examine levels of THC and CBD in 140 individuals. Three clear groups emerged: *THC only*, *THC+CBD* and those with no cannabinoid in hair. The THC only group showed higher levels of schizophrenia-like symptoms (anhedonia, hallucinations, and delusions) compared with the no cannabinoid and *THC+CBD* group. Except a lower score for anhedonia for 'THC + CBD' group compared with no cannabinoids, the two groups did not differ from each other.
Patients with schizophrenia frequently encounter difficulties initiating or maintaining sleep are encountered. Depending on the degree of psychotic symptomatology, disturbed sleep can be found in 30-80% of schizophrenic

patients (Cohrs, 2008). Cannabis is known to induce sleepiness, but only few data could be retrieved from literature. The hypnotic effects of THC were evaluated in the 1970s, and it was shown that THC increased Stage 3 sleep and reduced REM sleep (Feinberg et al., 1975). Smoked marijuana and oral Delta-9-tetrahydrocannabinol (THC) reduce REM sleep. Moreover, acute administration of cannabis appears to improve deep sleep (stage 3 and 4) (Schierenbeck et al., 2008).

Conclusion
The use of cannabis is detrimental for patients with chronic psychotic disorders, but the degree of damage is probably related to the ratio of THC and CBD in cannabis. To improve the treatment of these patients it is necessary to understand the effects of cannabis products with different THC: CBD ratio on well-being of these patients.

Problem analysis
In the Utrecht mental health institutions Altrecht and Victas there are reportedly some 80 patients with chronic psychotic disorder and severe cannabis dependence are treated who:
1. hardly respond to currently available interventions,
2. (almost) daily visit the coffee shops, and
3. use considerable quantities of cannabis, including cannabis with a composition which provokes rather than prevents psychotic episodes.

Various studies (Barnes et al., 2006; Mauri et al., 2006; Talamo et al., 2006; Wade et al., 2007) have shown that many patients with a psychotic disorder and substance use (these studies did not specifically examine cannabis but also to other psychotropic substances) are able to become abstinent which initiates better functioning. Especially patients with a first psychotic episode benefit from stopping substance use. Conversely, they may, for reasons of compliance and side effects of medications, also benefit from controlled use of cannabis with a high CBD content (see studies of Leweke). This raises the need for a clinical trial to investigate the therapeutic potency of CBD-enriched cannabis.
A meta-analysis of the available studies on substance use and psychotic disorders (Mullin et al., 2012), however, showed no significant reduction of symptoms in patients with a prolonged psychotic disorder who discontinued substance use. Although the authors also raised methodological arguments (too small number of enrolled longitudinal studies, limitations of cross-sectional studies and poor quality of many studies), it can not be excluded that quitting substance use is only effective when it occurs in the early phase of the disease. Those who use cannabis may, however, benefit from the prescription of cannabis with a different composition (i.e. a low THC:CBD ratio).

For literature references see Dutch section

Study objective

The proposed experimental pilot study focuses on harm reduction in a specific subpopulation, i.e. in patients with schizophrenia (long-term psychotic disorder) with a suboptimal response to the currently available interventions, smoking a lot of cannabis. Cannabis variants with lower THC / CBD ratios would be significantly better for these patients than the coffeeshop variant (with a high THC content and a relatively low CBD content) that is usually used by this group of patients. This relates to anxiety and panic effects and more psychotic symptoms. Before starting a RCT on the effects of replacement of cannabis with high THC / CBD ratio by cannabis with a low THC / CBD ratio it must first be examined whether the latter variant is accepted by these patients. In addition, with this pilot study a first impression about the possible differences in the (sub) acute effects of the two variants offered cannabis will be obtained.
The primary aim of this pilot study was therefore to determine the degree of acceptance of cannabis varieties with different THC / CBD ratios by patients with schizophrenia who (almost) daily use cannabis. Secondary readouts are self-reporting of (sub) acute onset of fear, anxiety, pleasure / enjoyment and psychotic symptoms. Under (sub) acute effects are thought to effects that occur after use within 2 hours, with probably the CBD antianxiety effects likely to occur (approximately 15 minutes) than the THC dissociative effects (60 minutes).

Hypotheses
Patients with schizophrenia prefer smoking cannabis with relatively low THC / CBD ratio, because it has a favorable effect profile with less anxiety, panic and unrest and a beneficial effect on dissociative and prepsychotic symptoms. Therefore, it is expected that patients with schizophrenia are willing to replace the cannabis which they commonly use by variants with a lower THC / CBD ratio.

Study design

In a randomized and blinded design 12 male patients with schizophrenia (the participants) smoke two types of cannabis; of each kind two joints (total of four joints; 0.25 grams of cannabis per joint). The two use cannabis strains are:
A. Medicinal cannabis I: Bedrobinol (13.5% THC, CBD 0%). This species is very similar to the coffee shop cannabis and serves as a reference.
B. Medicinal cannabis II: Bediol (6.3% THC, 7.5% CBD)
Smoking takes place in hostels of the addiction institution Victas in Utrecht.
In addition, participants will be asked which cannabis he usually smokes. A sample of this cannabis will be purchased by the researcher at the coffee-shop to assay the content of THC and CBD in this cannabis.

Study Medication
The Slotervaart-pharmacy (head: Prof. JH Beijnen) buys the two medicinal cannabis varieties Bedrobinol® and Bediol® at the firm Fagron Pharmaceuticals, Nieuwerkerk aan de IJssel; the producer is Bedrocan). Bediol is sold in granular form (the dried flowers are ground into particles having a size of up

to 5 millimeters). The Bedrobinol is granulated in the pharmacy, so both types of cannabis look the same (for blinding). The Slotervaart pharmacy is responsible for drug accountability. Bedrobinol® and Bediol® are according to Dutch law registered as medicinal raw material. Both products are batch analysis certificates and (highly confidential) IMPD files available.
Bedrobinol and Bediol already off label prescribed several years by doctors prescription to patients for medical purposes, and is reimbursed by various health ensurance companies.
After approval by the METC in Leiden and Erasmus METC in the Netherlands earlier clinical trials conducted with the medicinal cannabis Bedrocan® variant, which has the same legal status as Bedrobinol®. Trial Registry number Bedrocan (Erasmus University) NTR783. Title Influence of Medicinal Cannabis (Bedrocan) on the pharmacokinetics of irinotecan and docetaxel in cancer patient's (METC 2003-171 Erasmus MC).
http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=bedrocan
METC Leiden protocol number P11.007 and P13.262.

Blinding, randomization and issuance
The study has a randomized design with a classic cross-over model (6 x AABB en 6x BBAA). After purchasing the two types of medicinal cannabis and granulating Bedrobinol by the Slotervaart pharmacy both cannabis strains are dispensed in portions of 0.25 grams in sealed jars (with open tear strip) and stickered.
This total of 12 x 2 x 2 = 48 pots are randomized and blinded investigator. The 48 jars are randomized and transferred in three rounds to the researcher, to each record on the transfer form. The latter has to do with the fact that the treatment institution may have no more than 5 grams of cannabis at stock.
On the examination day, the participant of the research employee receives a coded jar of cannabis. The participant rolls himself with his own tobacco, rolling papers and "turn technique" the joint and smokes in the hostel of the institution attended by the research assistant.

timeline

T1 T2 AB C. Analysis Description Reporting
I I I I I I I I I

T1
Pre-selection, recruitment and inclusion after informed consent.
Purchase of 0.5 gram of cannabis the coffee shop that is normally used by the participants for the determination of the content of THC and CBD. Up to this are 12 different weed samples.
Purchase of the two types of medicinal cannabis by Slotervaart pharmacy.

T2
Baseline assessment. Participants complete questionnaires on demographic, physical and psychological characteristics and medical treatment of psychosis (see Questionnaire F1-F8).

A
Processing of medicinal cannabis by the Slotervaart pharmacy (grinding, weighing, distribute evenly, blinding, randomization, labeling). Transfer of 12 x 2 x 2 = 48 servings medical cannabis from 0.25 grams to the researcher (a total of 12 grams of cannabis) on three different days, to capture transfer forms.

Week B and C
In these two weeks are smoked in total four joints (two joints per week, each on one morning). The research assistant and the participant are unaware (blind) of the contents of the joint.

The participant smokes his joint in the room (hostel of the institution) and just before (t = -5 min) and three times after smoking (t = 15, 60 and 120 minutes after smoking) questioned by the research assistant on the feelings and experiences of smoke (see Questionnaires F9 and F10). The participant will also be asked to write down how he feels a day later (questionnaire F9).

Sizes (baseline)
Self-report at the start of the study (baseline assessment) on the basis of the following set of questionnaires (F1 - F8; fall time: 45-60 minutes):
F1. Demographic, physical and psychological characteristics and medical treatment, incl. Drug use
F2. Smoking cannabis in the last month and last week (number of joints smoked, cannabis type, price per gram of cannabis, spent amount) and use of other resources.
F3. Motivation cannabis use and the relationship between cannabis smoking and eliciting positive and negative symptoms.
F4. Questionnaire to smoke (QSU)
F5. Questions List psychotic symptoms (CAPE)
F6. Questionnaire measured anxiety and depression (HADS)
F7. sleep disturbance; shortened questionnaire
F8. Quality of Life (QOL)

Just before each smoking session.
F9. Did you use drugs in the last 24 hrs. If yes, how much?

Decrease 5 min before and 4 x after smoking
F10 Sense and drug effect, incl. Liking, high, stoned, relaxation, anxiety (VAS). The participant will also be asked to write down a day later how he feels.

At 2 hours after smoking
F11 rating and acceptance of this joint. Four short questions.

Intervention

12 patients receive frpm the investigator in total 4 joints (two with Bediol and two with Bedrobinol) that they smoke in the presence of the researcher on four different days.

Study burden and risks

No risk and no special burden.
Participants complete questionnaires and smoking a joint on four different days (a total of four joints). The joints consist of two different types of medicinal cannabis.
Except for some nausea or dizziness - no problems or side effects are anticipated. All participating patients are experienced cannabis users with a (very) high THC and low CBD (particularly "Dutch weed" with an average content of 15% THC). The two medical cannabis variants (Bedrobinol® and Bediol®) have a similar or lower THC content of 13.5% and 6.3% respectively. Therefore, there are no specific risks to be expected with the use of these variants. All participants smoke the cannabis under the supervision of the researcher in the treatment center, where medical staff can help quickly if (unexpected) that would have serious side effects. If the result of the study is positive, it is possible to launch a follow-up study into the potential clinical benefit of high CBD / low THC cannabis for this group to determine patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. males aged 18 to 65
2. At present (almost) daily (at least 4-5 times a week) use of Dutch weed (cannabis containing THC virtually only)
3. Chronic psychotic disorder and is currently in a treatment / care program
4. According to the practitioner a suboptimal response to currently available interventions, eg, persistent psychotic symptoms, psychotic decompensations frequent and / or severe impairment in social functioning
5. Willing to smoke two medicinal cannabis variants that differ in THC / CBD ratio. On four different days one joint is smoked (two joints a variant, a total of 4 joints).

Exclusion criteria

1. suffering from a serious neurological or medical illness (other than schizophrenia)
2. heavy use of alcohol (> 60 gram per day) or regular use (> 2x per week) of amphetamine, cocaine or opiates

Study design

Design

Study type: Interventional

Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2016

Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bedrobinol® and Bediol® (cannabis sativa)
Generic name:	THC and CBD

Ethics review

Approved WMO Date:	19-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-005540-17-NL
CCMO	NL51295.018.15