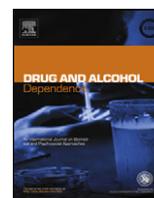




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# Treatment of adolescents with a cannabis use disorder: Main findings of a randomized controlled trial comparing multidimensional family therapy and cognitive behavioral therapy in The Netherlands

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### ABSTRACT

**Background:** To meet the treatment needs of the growing number of adolescents who seek help for cannabis use problems, new or supplementary types of treatment are needed. We investigated whether multidimensional family therapy (MDFT) was more effective than cognitive behavioral therapy (CBT) in treatment-seeking adolescents with a DSM-IV cannabis use disorder in The Netherlands.

**Methods:** One hundred and nine adolescents participated in a randomized controlled trial, with study assessments at baseline and at 3, 6, 9 and 12 months following baseline. They were randomly assigned to receive either outpatient MDFT or CBT, both with a planned treatment duration of 5–6 months. Main outcome measures were cannabis use, delinquent behavior, treatment response and recovery at one-year follow-up, and treatment intensity and retention.

**Results:** MDFT was not found to be superior to CBT on any of the outcome measures. Adolescents in both treatments did show significant and clinically meaningful reductions in cannabis use and delinquency from baseline to one-year follow-up, with treatment effects in the moderate range. A substantial percentage of adolescents in both groups met the criteria for treatment response at month 12. Treatment intensity and retention was significantly higher in MDFT than in CBT. Post hoc subgroup analyses suggested that high problem severity subgroups at baseline may benefit more from MDFT than from CBT.

**Conclusions:** The current study indicates that MDFT and CBT are equally effective in reducing cannabis use and delinquent behavior in adolescents with a cannabis use disorder in The Netherlands.

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## 1. Introduction

Although there are no recent data on the prevalence of cannabis use disorders among Dutch adolescents, the European School survey Project on Alcohol and other Drugs (ESPAD; Hibell et al., 2009) classified one out of ten Dutch past year adolescent cannabis users as having a high risk of developing cannabis-related problems. Of the adolescents who developed problematic cannabis use, an increasing number sought professional addiction care. From 2004 to 2008, the annual treatment demand of adolescents ( $\leq 18$  years old) and young adults (19–24 years old) for primary cannabis use problems in The Netherlands increased from 2161 to 3060, with the largest increase occurring in the subgroup of adolescents. In addition, of all adolescents seeking help for substance-related problems

in 2008, the majority (64%) sought help for primary cannabis use problems (Landelijk Alcohol en Drugs Informatie Systeem, 2010).

Various types of treatment are offered to individuals with a cannabis use disorder in The Netherlands, and these treatments – which include counselling, cognitive approaches, relapse prevention, and residential treatment – nearly all incorporate important elements of motivational enhancement therapy and cognitive behavioral therapy (CBT). Based on its effectiveness in adults with addictive behaviors (e.g., Miller and Wilbourne, 2002), outpatient CBT is considered the standard, first-choice treatment for adult patients, but empirical support for its effectiveness in adolescent cannabis abusers is still limited (e.g., Dennis et al., 2004a; Kaminer and Bursleson, 1999; Kaminer et al., 2002; Waldron et al., 2001; Waldron and Turner, 2008). Hence, to meet the treatment needs of the rapidly growing number of adolescents who seek help for cannabis use problems, new or supplementary types of treatment are needed. In the United States, several controlled studies in young cannabis abusers have shown promising results of a new family-based intervention named multidimensional family therapy (MDFT). In these studies, MDFT showed clinically relevant and significant benefits in terms of reduced cannabis and other substance

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use and less psycho-social and behavioral problems, compared to family education and adolescent group therapy (Liddle, 2001) and peer group treatment (Liddle et al., 2004, 2009). However, MDFT's effectiveness was similar to that of combined motivational enhancement/CBT and the adolescent community reinforcement approach in the cannabis youth treatment (CYT) study (Dennis et al., 2004a), while in another controlled comparison, MDFT was superior to CBT on some variables (e.g., psychological involvement with substances) but not on others (i.e., frequency of cannabis use) (Liddle, 2002; Liddle et al., 2008a). Given that almost all these results were obtained by one research group, independent replication studies are needed. In addition, it is unclear whether the positive outcomes of MDFT observed in the United States can be generalized to The Netherlands. Notably, the Dutch socio-cultural viewpoint on cannabis use differs from that in the United States, The Netherlands showing a more permissive attitude towards the use of soft drugs, which is expressed by, for instance, the possibility for adults to purchase cannabis in so-called 'coffee shops'.

The aim of the present study was to evaluate and compare the effectiveness of MDFT and CBT in The Netherlands in adolescents with a cannabis use disorder, in terms of cannabis use and use of other substances, delinquency, and treatment retention. The study is both a 'stand-alone' study in The Netherlands – the results of which are presented here – and part of a larger European research project in which MDFT's effectiveness is compared with that of treatment as usual in Belgium, France, Germany, Switzerland and The Netherlands (Rigter et al., 2010).

## 2. Methods

### 2.1. Design

One hundred and nine patients between 13 and 18 years old with a cannabis use disorder participated in a parallel-group randomized controlled trial (registration ISRCTN00179361) at two study sites. Following initial screening and baseline assessment, eligible patients were randomly allocated (ratio 1:1) by our research group to outpatient CBT (control group;  $n = 54$ ) or MDFT (experimental group;  $n = 55$ ) by using a computer-generated randomization list. Randomization was concealed and was conducted separately for the two study sites, and prestratified for age (13–14 vs. 15–18 years old), gender, ethnicity (Dutch/western vs. other) and frequency of cannabis use (<75 days vs.  $\geq 75$  days in the previous 90 days), using blocks of two patients. Both treatments had a planned duration of 5–6 months, and were followed by a naturalistic follow-up phase of 6–7 months. The primary endpoint of the study was 12 months after baseline.

### 2.2. Study sites and participants

Participants were recruited between March 2006 and July 2009 from the usual inflow of patients at Brijder Mistral Addiction Treatment, a substance abuse treatment facility for adolescents, and at De Jutters Palmhuis, a forensic treatment program for adolescents with mental health and behavioral problems, both situated in The Hague.

Eligible patients were 13–18 years old, had a history of cannabis abuse or dependence in the previous year according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994), recently used cannabis on a regular basis ( $\geq 26$  days in the 90 days preceding baseline), were willing to participate in the study and study treatments (written informed consent), and had at least one (step) parent or legal guardian who agreed to participate in the treatment and study assessments. Patients were barred from the study if they were currently psychotic (DSM-IV), suicidal or mentally retarded (clinical judgment), needed inpatient or opioid substitution treatment (clinical judgment), lived outside the catchment area of the treatment center, or insufficiently understood Dutch language.

### 2.3. Treatments

Control treatment consisted of 5–6 months outpatient CBT, focused on enhancing patients' motivation to change their addictive behavior, and on subsequently changing their maladaptive behaviors and cognitions by means of self control training, social and coping skills training and relapse prevention, based on the methods and treatment protocols of Miller and Rollnick (1991), Kadden et al. (1992) and Monti et al., 1989. Treatment was delivered by trained therapists who used a CBT treatment manual (De Wildt, 2002), and who were supervised by a highly experienced cognitive behavioral therapist. Weekly treatment sessions of 1 h were held

with the individual adolescent, and a monthly treatment session was scheduled for the adolescents' parents, to provide psycho-education and support. Notably, these parental sessions were support-oriented, and not system-oriented.

Experimental treatment consisted of 5–6 months outpatient MDFT. MDFT is a family-based and developmentally oriented treatment for adolescent substance use disorders and related problems, targeted at the adolescent as an individual, and at the relationship to his parent(s), other family members, and extra-familial contexts of influence, such as school, work, drug using peers and the juvenile justice system. MDFT-therapists had twice-weekly sessions (2 h total per week) with the individual adolescent, parent(s) and/or family, in addition to sessions or contacts with school, courts, and other persons. MDFT was delivered by trained and supervised therapists, who used a treatment manual developed by the original authors (<http://kap.samhsa.gov/products/manuals/cyt>), and were trained by the developers of MDFT at the Center for Treatment Research on Adolescent Drug Abuse (CTRADA) (Liddle et al., 2002). In addition, MDFT supervisors contacted trainers from CTRADA monthly during the study to receive feedback and consultation. The procedures used to monitor and optimize MDFT's treatment integrity in the study are described in detail elsewhere (Rigter et al., 2010).

### 2.4. Assessments

Study assessments took place at baseline and at 3, 6, 9 and 12 months (endpoint) following baseline, and were conducted by trained research assistants who used standardized instruments to minimize information bias. At baseline, they used the Adolescent Diagnostic Interview (ADI-Light; Winters and Henly, 1993) to obtain a DSM-IV (American Psychiatric Association, 1994) past year diagnosis of cannabis use disorder and other substance use disorders, the National Institute of Mental Health Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV; Shaffer et al., 2000) to determine the presence of a DSM-IV past year conduct disorder and oppositional defiant disorder, the Dutch version of the Family Environment Scale subscales Conflict (range: 0–11) and Cohesion (range: 0–11) (FES; Grotevant and Carlson, 1989; Jansma and De Coole, 1995; Moos and Moos, 1986) to assess family functioning, and the Personal Experiences Inventory subscale Personal Involvement with Chemicals (range: 0–87) (PEI; Winters and Henly, 1989) to determine the adolescents' level of psychological involvement with substances. At baseline and all subsequent time points, they administered the Parent and Adolescent Interview (Center for Treatment Research on Adolescent Drug Abuse, 1998), supplemented with items pertaining to substance use from the Addiction Severity Index (ASI; Hendriks et al., 1989; McLellan et al., 1992) and the Self-Report Delinquency Scale (SRD; Elliott et al., 1985; Wetenschappelijk Onderzoek en Documentatie Centrum WODC, 1991) to obtain information on substance use, social functioning, mental health problems, delinquency and treatment and juvenile justice history. In addition, the Timeline Follow-Back (TLFB; Sobell and Sobell, 1992) calendar method was used to collect detailed information about the adolescent's cannabis and alcohol use during the 90 days preceding each assessment. Lastly, urine samples were collected at month 12 and analyzed for the presence of tetrahydrocannabinol (THC). Adolescents received a maximum remuneration of 70 € (approx. 100 USD) for participating in the study assessments.

### 2.5. Outcome measures

The study's primary outcome measure was the frequency of cannabis use (i.e., days of cannabis use; number of joints smoked) in the 90 days preceding the month 12 assessment. Secondary outcome measures were (1) percentage of treatment responders, (2) percentage of recovered adolescents, (3) number of property and violent crimes committed in previous 90 days, and (4) treatment retention. Treatment responders were defined as participants who had at least 30% less cannabis using days in the 90 days preceding the month 12 assessment compared to baseline, provided that this reduction was not at the expense of a substantial increase (>6 days in the past month) in the use of other substances (i.e., alcohol ( $\geq 5$  glasses a day), cocaine, amphetamines, and ecstasy). Analogous to the definition used by Dennis et al. (2004a), adolescents were considered to be in recovery if they lived in the community (i.e., not incarcerated or in inpatient treatment) and were abstinent from cannabis, alcohol ( $\geq 5$  glasses a day) and any other substance use in the 90 days preceding the month 12 assessment. The outcome measures pertaining to cannabis use were based on the TLFB, which has shown excellent reliability and validity in adolescents (e.g., Dennis et al., 2004b; Levy et al., 2004). The criminality outcome measure was based on the SRD, which showed excellent internal consistency reliability in a study by Elliott et al. (1985), and generally high test–retest reliability (0.65–1.00) in a study by Huizinga and Elliott (1983).

Since the intensity of MDFT and CBT differed, various aspects of treatment retention were examined. First, treatment retention was defined as the number of weeks that a treatment session was attended by (1) the adolescent, and (2) the adolescent and/or others (i.e., parent(s), family, others). Second, we determined 'treatment dose', by calculating the total time of therapeutic contacts spent with (1) the adolescent, and (2) the adolescent and/or others. Adolescents were considered as treatment completers if they had attended a treatment session in at least 75% of the planned number of treatment weeks. Based on a planned treatment duration of at least 5 months (22 weeks), this amounted to a minimum of 17 treatment weeks. Lastly, the number of treatment weeks, treatment dose and percentage

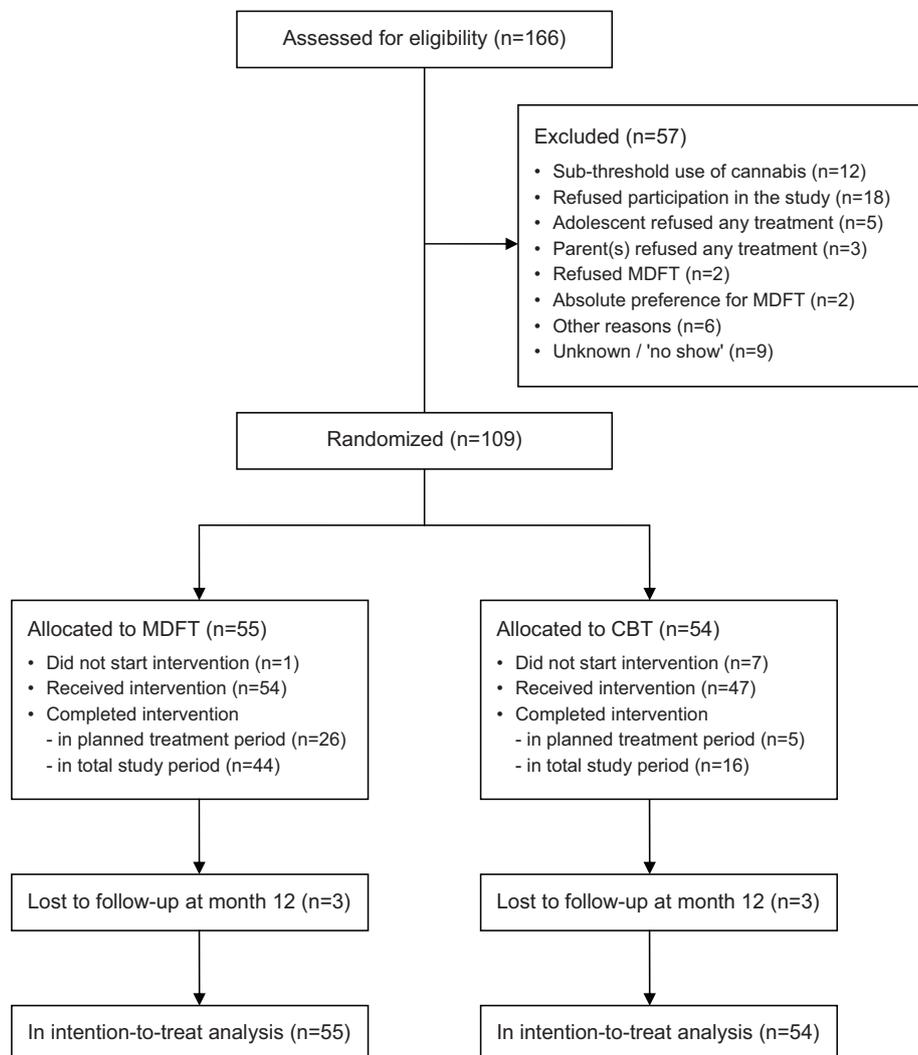


Fig. 1. Flow chart of the progress of participants in the trial.

treatment completers were determined separately for the planned treatment period of 22 weeks and the total study period of 12 months.

### 2.6. Data analysis

Study data were analyzed using an intent-to-treat approach, which included all patients that were notified about their randomized group allocation ( $n = 109$ ). Missing data at follow-up amounted to 46.8% (MDFT: 50.9%; CBT: 42.6%) at month 3, 50.5% (MDFT: 49.1%; CBT: 51.9%) at month 6, 50.5% (MDFT: 40.0%; CBT: 61.1%) at month 9, and 5.5% (MDFT: 5.5%; CBT: 5.6%) at month 12. Follow-up attendance at month 3, 6 and 12 was neither related to cannabis use at baseline or previous assessment, nor to treatment retention status or treatment group, but did differ significantly between the treatment groups at month 9, with a particularly low follow-up rate in CBT. Given this violation of the missing completely at random (MCAR) assumption, month 9 data were excluded from the analyses. Missing data at month 3, 6 and 12 were estimated by means of a multiple imputation procedure, using five imputed datasets (SPSS version 18.0; SPSS Inc., 2010).

Efficacy of MDFT vs. CBT in terms of the primary outcome measure was analyzed by means of a 2 (treatment: MDFT vs. CBT)  $\times$  2 (time: baseline vs. month 12) repeated measures MANOVA, using the baseline and imputed month 12 datasets. Difference in percentage treatment responders between the study groups at month 12 was analyzed in a logistic regression model, with treatment group as independent variable and treatment response (imputed dataset) as outcome variable. The same approach was used for analyzing the difference in percentage of recovered adolescents at month 12. Differences in delinquency (property and violent crimes) between the study groups at month 12 were tested using the same analytical approach as described for the primary outcome measure (i.e., repeated measures MANOVA). In a secondary analysis, Generalized Estimation Equation (GEE), based on an unstructured correlation matrix, was used to investigate whether the temporal course of cannabis use and delinquent behavior differed between MDFT and

CBT during the 12 months study period. In all MANOVA- and GEE-analyses, we tested whether treatment site (forensic vs. addiction treatment site) modified (a) the relation between treatment group and outcome, and (b) the time effect.

In American MDFT trials, effect-sizes of  $D = 0.6$ – $0.7$  were reported with regard to substance use (Liddle, 2009; Liddle et al., 2009). Given the socio-cultural differences between the US and The Netherlands with regard to cannabis use, and a possibly more problematic Dutch cannabis using population, a more conservative between groups effect-size of  $D = 0.5$  was anticipated in the current study. Based on this effect size (corresponding to a mean difference between the study groups in pre- to post-treatment change scores of 12–13 days, and a standard deviation of 25 days), a two-sided alpha of 0.05 and a  $(1 - \beta)$  power of 0.80, we estimated that 64 participants were needed in each study group (Cohen, 1988; Pocock, 1983). All statistical analyses were conducted with SPSS version 18.0 (SPSS Inc., 2010).

### 3. Results

One hundred and sixty six patients were assessed for eligibility and 57 patients were excluded prior to randomization (Fig. 1), mostly because either the adolescent, the parent(s) or both refused to participate in the study or study treatments ( $n = 28$ ). Of the 109 randomized patients in the intent-to-treat sample, one participant in MDFT and seven participants in CBT never started treatment, and many more patients completed treatment in MDFT than in CBT, both within the planned 22 weeks treatment period and 1 year total study period.

The baseline characteristics of the participants are summarized in Table 1. Adolescents were primarily male, Dutch/western, with a

**Table 1**  
Baseline characteristics of study sample (n = 109).<sup>a</sup>

	MDFT (n = 55) Mean (sd)/%	CBT (n = 54) Mean (sd)/%	Total sample (n = 109) Mean (sd)/%
<b>Demographic background</b>			
Age (range 13–18 years) (years)	16.6 (1.3)	16.9 (1.2)	16.8 (1.3)
Aged 13–14 (%)	10.9%	9.3%	10.1%
Gender male (%)	80.0%	79.6%	79.8%
Ethnicity Dutch/western (%)	72.7%	70.4%	71.6%
Single parent family (%)	34.5%	46.3%	40.4%
Currently attending school (%)	74.5%	72.2%	73.4%
<b>Substance use</b>			
Age of onset regular cannabis use (years)	14.2 (1.6)	14.4 (1.3)	14.3 (1.4)
Lifetime duration regular cannabis use (months)	24.5 (15.7)	22.3 (16.6)	23.4 (16.1)
Cannabis use past 90 days (days)	63.1 (22.8)	62.3 (23.6)	62.7 (23.1)
Cannabis use past 90 days (# 'joints')	168.0 (129.6)	155.1 (128.7)	161.6 (128.7)
Any alcohol use past 90 days (days)	11.0 (15.5)	8.9 (10.4)	9.9 (13.2)
Any alcohol use past 90 days (glasses/units)	71.7 (115.5)	53.1 (98.3)	62.4 (107.1)
Alcohol use ( $\geq 5$ gl/day) past 30 days (days)	2.3 (3.8)	2.6 (5.3)	2.4 (4.6)
Other substance use past 30 days (%) <sup>b</sup>	10.9%	7.4%	9.2%
<b>Delinquency</b>			
Violent/property crimes past 90 days (#crimes)	6.3 (13.4)	6.6 (18.2)	6.4 (15.9)
Arrested for property crimes past 90 days (%)	10.9%	5.6%	8.3%
Arrested for violent crimes past 90 days (%)	13.0%	9.1%	11.0%
Ever in prison	42.6%	37.0%	39.8%
Referred to treatment by court (%)	12.7%	18.5%	15.6%
<b>Treatment history</b>			
Ever been in substance abuse treatment (%)	9.1%	9.4%	9.3%
Ever been in psychiatric treatment (%)	34.6%	34.0%	34.3%
Study treatment in addiction treatment site (%)	43.6%	46.3%	45.0%
Study treatment in forensic treatment site (%)	56.4%	53.7%	55.0%
<b>DSM-IV diagnosis (past year)</b>			
Cannabis abuse (%)	25.5%	22.2%	23.9%
Cannabis dependence (%)	74.5%	77.8%	76.1%
Severity cannabis use disorder (range 0–11) <sup>c</sup>	6.8 (2.5)	7.1 (2.1)	6.9 (2.3)
Alcohol abuse (%)	10.9%	3.7%	7.3%
Alcohol dependence (%)	5.5%	11.1%	8.3%
Other substance use disorder (%)	5.5%	1.9%	3.7%
Conduct disorder (CD) (%)	34.8%	22.9%	28.7%
Oppositional defiant disorder (ODD) (%)	19.6%	14.9%	17.2%
CD and/or ODD (%)	43.5%	31.9%	37.6%

<sup>a</sup> MDFT, multidimensional family therapy; CBT, cognitive behavioral therapy; SD, standard deviation.

<sup>b</sup> Other substance use: cocaine, amphetamines, ecstasy or heroin.

<sup>c</sup> Severity of cannabis use disorder was determined by adding up the number of DSM-IV criteria (seven dependence and four abuse criteria) endorsed by each participant.

high frequency of cannabis use, and relatively little other substance use. They reported an average of more than six violent or property crimes in the 3 months prior to baseline, and a substantial minority was diagnosed with a conduct disorder or oppositional defiant disorder.

### 3.1. Cannabis use

Table 2 shows the baseline to month 12 changes in cannabis use in the 90 days prior to each assessment. The number of cannabis using days in the 90 days prior to month 12, compared to baseline, decreased by 20.1 days in MDFT, and by 14.9 days in CBT. In the  $2 \times 2$  repeated measures MANOVA, there was a significant effect of time for both treatment conditions combined ( $F(1, 107) = 24.8$ ;  $p < 0.001$ ), but no differential effect over time between MDFT and CBT on number of cannabis using days at month 12 ( $F(1, 107) = 0.55$ ;  $p = 0.46$ ) (Cohen's  $D = 0.14$ ). Similarly, there was a significant decrease in number of joints smoked from baseline to month 12 across the two treatment conditions, but no significant interaction between treatment condition and time ( $F(1, 107) = 0.46$ ;  $p = 0.50$ ) (Cohen's  $D = 0.13$ ). In both analyses, treatment site (forensic vs. addiction treatment) did not modify the relation between treatment group and month 12 outcome, but site did interact significantly with time (cannabis using days:  $F(1, 107) = 8.5$ ;  $p < 0.01$ ; number of joints smoked:  $F(1, 107) = 14.8$ ;  $p < 0.001$ ), with larger reductions in cannabis use occurring in the addiction treatment site. Additional analyses (not in Table 2) indicated that 18.2% of

the adolescents in MDFT were abstinent from cannabis during the 90 days prior to month 12, compared to 14.8% of those in CBT ( $\chi^2 = 0.22$ ;  $p = 0.64$ ), and the results of urinalysis at month 12 were in line with these self-report findings: 25.6% cannabis-negative urines in MDFT and 25.7% negative urines in CBT.

A secondary analysis of number of cannabis using days at each assessment point (i.e., at baseline, month 3, 6 and 12) between and across the two treatment conditions, using GEE, similarly showed a significant decrease of cannabis use over time (Wald = 49.01;  $df = 4$ ;  $p < 0.001$ ) and no interaction between treatment and time on treatment outcome (Wald = 2.55;  $df = 4$ ;  $p = 0.64$ ), indicating that the overall shape of the changes over time was similar for both treatment conditions.

### 3.2. Delinquent behavior

Baseline to month 12 changes in number of property and violent crimes were also analyzed in a  $2 \times 2$  repeated measures MANOVA (Table 2). Again, time was significant across both treatment conditions ( $F(1, 107) = 8.4$ ;  $p < 0.01$ ), and the interaction between treatment and time on the number of property/violent crimes at month 12 was not significant ( $F(1, 107) = 0.00$ ;  $p = 1.00$ ) (Cohen's  $D = 0.00$ ). Treatment site did not modify the relation between treatment condition and month 12 outcome, nor the time effect. As with cannabis use, additional analyses using GEE showed a significant decrease of delinquent behavior over time (Wald = 12.95;  $df = 4$ ;

**Table 2**  
Main outcome measures in adolescents according to treatment condition ( $n = 109$ ).<sup>a</sup>

	MDFT Mean (sd)	CBT Mean (sd)	Time Baseline vs. month 12	Treatment × time Baseline vs. month 12
<b>Cannabis use past 90 days (days)</b>				
Baseline	63.1 (22.8)	62.3 (23.6)		
Month 3	42.0 (23.7)	45.4 (23.0)		
Month 6	40.6 (21.8)	42.9 (20.6)		
Month 12	43.0 (33.3)	47.4 (33.3)	$F = 24.8; p = 0.00 (D = 0.61)$	$F = 0.55; p = 0.46 (D = 0.14)$
<b>Cannabis use past 90 days ('joints')</b>				
Baseline	168.0 (129.6)	155.1 (128.7)		
Month 3	108.2 (89.0)	106.8 (82.3)		
Month 6	108.8 (134.5)	92.9 (64.6)		
Month 12	91.2 (94.2)	96.0 (100.8)	$F = 27.1; p = 0.00 (D = 0.60)$	$F = 0.46; p = 0.50 (D = 0.13)$
<b>Property/violent crimes past 90 days</b>				
Baseline	6.3 (13.4)	6.6 (18.2)		
Month 3	4.2 (3.8)	4.9 (7.6)		
Month 6	3.9 (3.8)	3.4 (3.4)		
Month 12	1.7 (3.1)	2.1 (4.2)	$F = 8.4; p < 0.01 (D = 0.39)$	$F = 0.00; p = 1.00 (D = 0.00)$
	MDFT (%)	CBT (%)		Treatment <sup>b</sup> Month 12
<b>Treatment response</b>				
Month 3	51.6%	43.6%		
Month 6	58.9%	54.8%		
Month 12	41.8%	44.4%		$\beta = -0.11; p = 0.78$
<b>Treatment recovery</b>				
Month 3	9.1%	7.4%		
Month 6	5.5%	3.7%		
Month 12	14.5%	5.6%		$\beta = 1.06; p = 0.13$

<sup>a</sup> MDFT, multidimensional family therapy; CBT, cognitive behavioral therapy.

<sup>b</sup> Reference category: CBT.

$p = 0.01$ ), but no difference in overall shape of the changes between the two treatment conditions (Wald = 6.45;  $df = 4$ ;  $p = 0.17$ ).

### 3.3. Treatment response and treatment recovery

Table 2 shows the percentage of adolescents who met the criteria for response and recovery at each follow-up. Logistic regression analysis of response and recovery at month 12 showed no significant differences between MDFT and CBT for either measure (response:  $\beta = -0.11$ ;  $p = 0.78$ ; recovery:  $\beta = 1.06$ ;  $p = 0.13$ ), and no significant interaction between treatment condition and treatment site. In addition, there were no significant differences between the treatment conditions in response and recovery at month 3 and 6 (not shown in Table 2).

### 3.4. Treatment retention and treatment dose

There were highly significant differences between MDFT and CBT on all investigated indicators of treatment retention and received 'treatment dose' (Table 3). Adolescents in MDFT attended a treatment session in approximately twice as many weeks as those in CBT in both the planned treatment period (15.2 and 7.9 weeks, respectively;  $p < 0.001$ ) and the total study period (23.4 and 10.6 weeks, respectively;  $p < 0.001$ ), and this was also the case regarding attendance of the adolescents and/or their system members (parent(s), other family members, others). In terms of treatment dose - hours spent in therapy - adolescents and/or their system members in MDFT received three to four times as much therapy as those in CBT (Table 3). Similarly, the rate of treatment completers was approximately three to five times higher in MDFT than in CBT, depending on the period considered.

A linear regression analysis was conducted to determine whether number of cannabis using days prior to month 12 was related to treatment duration. Since treatment duration was substantially higher in MDFT than in CBT, treatment condition was added as covariate in the model. Results showed that treatment retention, when controlled for treatment condition, was not sig-

nificantly related to treatment outcome ( $\beta = -0.53$ ;  $p = 0.15$ ). In addition, pre- to post-treatment changes in cannabis using days among treatment completers did not differ between MDFT and CBT ( $F(1, 58) = 0.50$ ;  $p = 0.48$ ).

### 3.5. Post hoc analyses of subgroups and effect

Given the general lack of treatment effect observed between MDFT and CBT in this study, we conducted several exploratory analyses to investigate whether subgroups could be identified that differentially benefited from MDFT or CBT. For this purpose, we defined 'high' and 'low' severity problem subgroups in terms of baseline days of cannabis use (above or below the median of 64 days), substance use problem severity (PEI Personal Involvement with Chemicals subscale score above or below the median of 38), criminality (adolescents with or without self-reported violent or property crimes in the 90 days prior to baseline), psychiatric co-morbidity (adolescents with or without a conduct disorder (CD) and/or oppositional defiant disorder (ODD)), and family functioning (absence or presence of family dysfunctioning on the FES Conflict and/or Cohesion subscales, according to Dutch norm groups). In each of the baseline high severity subgroups, MDFT resulted in a greater reduction in the number of cannabis using days from baseline to month 12, compared to CBT, while this was not the case in any of the low severity subgroups. These greater reductions in MDFT than in CBT amounted to 9.8 days in the high severity cannabis use subgroup (Cohen's  $D = 0.28$ ), 19.1 days in the high PEI substance use problem severity subgroup ( $D = 0.53$ ), 7.3 days in the criminality subgroup ( $D = 0.18$ ), 42.2 days in the high severity psychopathology subgroup ( $D = 1.16$ ), and 16.1 days in the FES high severity family dysfunctioning subgroup ( $D = 0.44$ ). From the three variables with at least a moderate effect size in the high severity subgroup, i.e. PEI, CD/ODD and FES, the differential treatment effect of MDFT and CBT (high vs. low severity subgroup) was statistically significant for substance use problem severity on the PEI and psychiatric co-morbidity.

**Table 3**  
Participation in treatment ( $n = 109$ ).

	MDFT <sup>a</sup> ( $n = 55$ ) Mean (sd)/%	CBT <sup>a</sup> ( $n = 54$ ) Mean (sd)/%	$p$ -Value <sup>b</sup>
<i>Planned treatment period (5 months; 22 weeks)</i>			
<b>Adolescent</b>			
Treatment started (%)	98.2%	87.0%	.03
At least one treatment session attended (weeks)	15.2 (4.2)	7.9 (5.9)	<.001
Treatment dose (h)	24.1 (11.2)	7.7 (6.7)	<.001
Treatment completion (%) <sup>c</sup>	47.3%	9.3%	<.001
<b>Adolescent/parents/family/others</b>			
At least one treatment session attended (weeks)	16.7 (3.9)	8.5 (6.2)	<.001
Treatment dose (h)	33.7 (14.3)	9.0 (8.4)	<.001
<i>Total study period (12 months; 52 weeks)</i>			
<b>Adolescent</b>			
At least one treatment session attended (weeks)	23.4 (8.7)	10.6 (9.0)	<.001
Treatment dose (h)	35.1 (15.9)	10.4 (9.7)	<.001
Treatment completion (%) <sup>c</sup>	80.0%	29.6%	<.001
Treatment completion (%) <sup>d</sup>	90.9%	27.8%	<.001
<b>Adolescent/parents/family/others</b>			
At least one treatment session attended (weeks)	26.0 (8.8)	11.5 (9.5)	<.001
Treatment dose (h)	48.7 (20.2)	12.5 (12.0)	<.001

<sup>a</sup> MDFT, multidimensional family therapy; CBT, cognitive behavioral therapy; SD: standard deviation.

<sup>b</sup>  $p$ -Values are based on Fisher's Exact Test (dichotomous variables) and Mann–Whitney  $U$  test for (non-normal) interval variables.

<sup>c</sup> Treatment completion is defined as participation in at least one treatment session per week by the adolescent in at least 75% of the planned (22) treatment weeks; i.e., at least 17 treatment weeks.

<sup>d</sup> Treatment completion as defined by the therapist.

#### 4. Discussion

This study represents the first randomized controlled comparison between the efficacy of MDFT and that of CBT outside the United States. The study incorporated a range of features aimed at maximizing the validity of the findings, including the use of DSM diagnosis to define the target population, the use of manual-guided, supervised interventions, MDFT-training by the original developers of the intervention, the use of pre-specified outcome measures, derived from standardized and broadly accepted instruments that were administered by independent, trained research assistants, additional outcome assessment by means of urinalyses, and the application of an intent-to-treat data analysis approach.

In this study in adolescents with a cannabis use disorder, both MDFT and CBT showed significant and clinically relevant pre- to post-treatment effects, with moderate effect sizes (Cohen's  $D$  ranging from 0.39 to 0.61) in terms of reducing days and frequency of cannabis use, less delinquent behavior pertaining to property and violent crimes, and a substantial and clinically meaningful percentage of adolescents (43%) who met the criteria for treatment response (i.e., at least 30% less cannabis use and no considerable increase of other substance use, compared to baseline) at 1-year follow-up. In terms of complete recovery, i.e., total abstinence and living in the community, the results of both interventions were less favorable, with only 10% of the adolescents meeting these criteria at 1-year follow-up. This latter finding indicates that neither intervention was sufficient to fully interrupt the targeted problem behaviors in most participants, which, in turn, suggests that continued care and repeated interventions may be needed to establish a more comprehensive and long-lasting treatment effect (e.g., McLellan et al., 2000). Compared to earlier studies investigating CBT and/or MDFT in adolescents, the pre- to post-treatment effect sizes for cannabis use observed in our study are similar to those reported by Liddle et al. (2008a) and somewhat larger than those found by Dennis et al. (2004a) and by Waldron et al. (2001), although in the latter study, significant pre- to post-treatment changes in cannabis use were only found for functional family therapy (FFT), combined FFT and CBT, and group therapy,

but not for CBT-alone. Taken together, these results suggest that both MDFT and CBT can be effective in reducing cannabis use in adolescents.

However, contrary to our expectations based on MDFT's more intense and comprehensive treatment offer, MDFT was not found to be superior to CBT on any of the outcome measures (i.e., cannabis use, delinquent behavior, treatment response, treatment recovery) and on any of the time points (i.e., after 3, 6 and 12 months). Additional analyses, in which we investigated the percentage of adolescents who were completely abstinent from cannabis, alcohol ( $\geq 5$  g/l/day) and/or other substances at follow-up did not reveal any significant outcome differences between the treatment groups either, both based on self-report and – for cannabis – on the results of urinalyses.

Our findings are in line with the results of the CYT study (Dennis et al., 2004a), in which the efficacy of MDFT was equivalent to that of CBT on all investigated outcome variables, but are in contrast with those reported by Liddle (2002) and Liddle et al. (2008a). In the latter trial, MDFT and CBT did not differ in reducing frequency of cannabis use either, but the authors did observe a differential treatment effect favoring MDFT in terms of less psychological involvement with alcohol and drugs. This effect continued for 12 months following treatment termination, suggesting that adolescents who received MDFT retained their treatment benefits in this sense more effectively than those who received CBT. Post hoc analyses using GEE in our study sample suggested no post-discharge effect of treatment group on frequency of cannabis use or delinquent behavior after the month 6 follow-up.

Our findings are particularly relevant given the observed considerably longer treatment retention and higher treatment dose – and consequently, higher treatment costs involved (e.g., French et al., 2002) – of the participants in MDFT than those in CBT, the former having received 3–4 times as much therapy. Hence, we compared more intense, longer lasting MDFT with less intense, shorter lasting CBT and found no difference in treatment outcome.

In a secondary analysis of two earlier trials (Liddle et al., 2008a,b), Henderson et al. (2010) found MDFT to be more effective than the comparison treatments in adolescents with high baseline substance use and psychiatric comorbidity, but not in those

with lower levels of substance use and comorbidity, suggesting that MDFT may be most beneficial for more severely problematic adolescents (Henderson et al., 2010). Compared to almost all American MDFT trials (Dennis et al., 2004a; Liddle, 2002; Liddle et al., 2004, 2008a, 2009), our sample consisted of more severe cannabis users – with cannabis consumption on an average of 63 days in the 90 days prior to intake, compared to for example 38 out of 90 days in the CYT-study (Dennis et al., 2004a), and to 11 out of 30 days in Liddle et al. (2008a). Nevertheless, in post hoc analyses of our study sample, patients with high baseline substance use problem severity and high psychiatric severity, and patients from a highly dysfunctional family background showed greater reductions of cannabis use in MDFT than in CBT (Cohen' *D* of 0.53, 1.16 and 0.44, respectively). These greater reductions are probably clinically relevant, although due to a lack of power they were only significant for the substance use problem severity and psychiatric severity subgroups.

#### 4.1. Limitations

Several limitations of the study should be considered. First, most of our data were obtained by means of self-report. However, we did analyze month 12 urine samples for presence of cannabis metabolites and found results consistent with those from self-report. Second, relatively low follow-up rates were obtained at the month 3 and 6 assessments. Nevertheless, similarly low follow-up rates were obtained by Liddle et al. (2008a), and while the missed intermediate assessments may have caused some bias in the shape of the change trajectories, we did succeed in reaching nearly all adolescents (94.5%) at our primary endpoint, after 12 months. Third, we did not investigate treatments of equal intensity, but, instead, a more intense and longer lasting treatment – MDFT – with a less intense and shorter lasting treatment – CBT, and our study findings should be interpreted within this context. Fourth, we managed to recruit 109 from the 128 adolescents needed according to our power calculation, hence, our study was somewhat underpowered (observed power 0.73). On the other hand, the between treatments effects observed in this study were sufficiently small that even a substantially larger sample would not have resulted in statistically significant effects. Fifth, in a strict sense, we are uncertain whether the observed reductions in cannabis use and delinquency could have been achieved as well without treatment, since we did not include a no-treatment control condition in our study. Sixth, the generalizability of our findings may be limited to the particular sample of adolescents in our study: youngsters with (a) a high frequency of cannabis use but relatively little concurrent substance use, (b) often a history of delinquent behavior, (c) predominantly a Dutch/western background, and (d) a sizeable minority having a history of earlier psychiatric treatment(s). In addition, it is important to note that the findings were obtained in a country with a relative permissive socio-cultural attitude towards cannabis use ('soft drug'; Dutch 'coffee shops').

#### 5. Conclusion

The current study indicates that MDFT and CBT are equally effective in reducing cannabis use and delinquent behavior in adolescents with a cannabis use disorder in The Netherlands. Despite some limitations, we are confident that the results are robust and valid for the majority of treatment-seeking adolescents with problematic cannabis use in The Netherlands. Given that this study also found indications of a differential treatment effect in high problem severity subgroups, further research should focus on the effectiveness and cost effectiveness of MDFT in more problematic adolescents and families.

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#### Contributors

All authors were responsible for analysis and interpretation of the data, and contributed to and approved the final manuscript. Vincent Hendriks and Peter Blanken were also responsible for concept and design of this study.

#### Conflict of interest

No conflict declared.

#### Ethical approval

The study was approved by the medical-ethical committee for research in mental health care settings of The Netherlands (METiGG; registration nr. 5238). All participants provided written informed consent.

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