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# Matching adolescents with a cannabis use disorder to multidimensional family therapy or cognitive behavioral therapy: Treatment effect moderators in a randomized controlled trial

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### ABSTRACT

**Background:** In a recent randomized controlled trial (Hendriks et al., 2011), multidimensional family therapy (MDFT) and cognitive behavioral therapy (CBT) were equally effective in reducing cannabis use in adolescents (13–18 years old) with a cannabis use disorder ( $n = 109$ ). In a secondary analysis of the trial data, we investigated which pretreatment patient characteristics differentially predicted treatment effect in MDFT and CBT, in order to generate hypotheses for future patient-treatment matching.

**Methods:** The predictive value of twenty patient characteristics, in the area of demographic background, substance use, substance-related problems, delinquency, treatment history, psychopathology, family functioning and school or work related problems, was investigated in bivariate and subsequent multivariate linear regression analyses, with baseline to month 12 reductions in cannabis use days and smoked joints as dependent variables.

**Results:** Older adolescents (17–18 years old) benefited considerably more from CBT, and younger adolescents considerably more from MDFT ( $p < 0.01$ ). Similarly, adolescents with a past year conduct or oppositional defiant disorder, and those with internalizing problems achieved considerably better results in MDFT, while those without these coexisting psychiatric problems benefited much more from CBT ( $p < 0.01$ , and  $p = 0.02$ , respectively).

**Conclusions:** The current study strongly suggests that age, disruptive behavior disorders and internalizing problems are important treatment effect moderators of MDFT and CBT in adolescents with a cannabis use disorder. If replicated, this finding suggests directions for future patient-treatment matching in adolescent substance abuse treatment.

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## 1. Introduction

Although the field of adolescent substance abuse treatment research is still relatively young, the number of well-designed, controlled studies in this area is rapidly growing. Overall, these studies have provided consistent empirical support for the efficacy of both family-based approaches and cognitive behavioral therapy, when compared to a minimal treatment control condition, but no clear evidence for the superiority of one of these treatment models over the other (Dennis et al., 2004; Liddle, 2001; Liddle et al., 2004, 2008; Kaminer et al., 2002; Thush et al., 2007; Waldron et al., 2001, 2005; Waldron and Turner, 2008). Recently, Stanger et al. (2009) investigated the efficacy of contingency management (CM) as an add-on

to motivational enhancement and cognitive behavioral therapy (MET/CBT), compared to MET/CBT without CM in adolescents with problematic marijuana use, and found superior outcomes associated with CM during treatment, but not during the post-treatment follow-up period.

In a recent randomized controlled study, we compared the effectiveness of outpatient multidimensional family therapy (MDFT) and individual cognitive behavioral therapy (CBT) in adolescents with a cannabis use disorder and found, in line with the conclusions above, significant pre- to post-treatment reductions in cannabis use and self-reported delinquency associated with both treatments but no differential treatment effect (Hendriks et al., 2011). Notably, in terms of 'treatment dose' (hours spent in therapy), adolescents and/or their system members in the MDFT-condition of this study had received three to four times as much therapy as those in the CBT-condition. Hence, we compared two treatments that differed considerably both in underlying treatment model and in intensity and duration, and nevertheless found no difference in results.

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This overall finding of lack of differential effect in randomized comparisons of active, well-established adolescent substance abuse treatments, often based on strongly diverging underlying models, points to an important, and increasingly acknowledged limitation of randomized controlled trials: they are, in a sense, based on a one-size-fits-all approach (Waldron and Turner, 2008). Within treatment groups, there is generally much heterogeneity in adolescent characteristics (e.g., age, ethnicity, substance use pattern, delinquency, psychiatric comorbidity) and adolescent subgroups in terms of these characteristics within each treatment condition may differ considerably in treatment outcome (Chan et al., 2008; Daudin et al., 2010).

Given this patient heterogeneity and the wide range of available treatment options, considerable efforts have been made in the adult addictions field to investigate “which treatment works best for whom.” The largest study ever conducted in this area, Project MATCH, tested 10 a priori primary patient-treatment matching hypotheses, but failed to find any interaction effects that impacted drinking outcome (Project MATCH Research Group, 1998; 1999). Likewise, several other large-scale, well-designed studies provided little evidence that psychosocial substance abuse treatment effectiveness could be enhanced by matching patients to different types of treatments (Crits-Christoph et al., 1999; Ouimette et al., 1999; UKATT Research Team, 2008). In addition, although matching effects have been found in some studies (Rychtarik et al., 2000), replication of findings is lacking. Hence, despite considerable efforts, adult substance abuse studies to date have failed to find robust matching effects that could be used in allocation guidelines in clinical practice.

In contrast with the adult addictions literature, adolescent substance abuse treatment evaluations to date have paid little attention to the role of potential moderators of differential treatment effect. The few studies that did, found inconsistent results. In a randomized study in dually diagnosed adolescent substance abusers, Kaminer et al. (1998) hypothesized that patients with externalizing disorders would have better substance use outcomes in group CBT, whereas those with internalizing disorders without co-occurring externalizing disorders would benefit more from interactional group treatment. Contrary to their hypothesis, no significant matching effects were identified. In another randomized study in adolescents, Kaminer et al. (2002) compared outpatient group CBT with group psychoeducational treatment (PET), and found CBT to be superior to PET in terms of substance use outcomes, but only for male and older (16 years and older) adolescents, and only at short-term follow-up. No significant treatment group differences in substance use outcomes were found on any of the investigated psychopathology predictor variables (e.g. externalizing disorders, conduct disorder, internalizing disorders). In the context of a randomized controlled comparison of the effectiveness of MDFT and CBT in adolescent drug abusers, Rowe et al. (2004) differentiated between adolescents with, at baseline, only a substance use diagnosis, adolescents with a comorbid internalizing disorder, adolescents with a comorbid externalizing disorder, and those with both a comorbid internalizing and externalizing disorder. Although the shape of the substance use change trajectories from baseline to month 12 follow-up differed substantially between the comorbidity subgroups, these effects were not moderated by treatment condition, nor by age or gender. Recently, Henderson et al. (2010) re-analyzed data from a randomized trial comparing MDFT and CBT (Liddle et al., 2008), and found MDFT to be more effective than CBT in decreasing psychological involvement with substances (“substance use problem severity”) in adolescent subgroups with high baseline psychological involvement and psychiatric comorbidity, but not in those with lower levels of involvement and comorbidity. In this study, however, no distinction was made between specific psychiatric diagnoses, and when actual frequency of substance

use was used as outcome parameter, no significant differences in treatment effect of MDFT and CBT were found for either predictor variable (Henderson et al., 2010). Overall, the studies described vary considerably in types of interventions investigated, outcome measures used, and analytical approach, which may account for the inconsistencies found.

To summarize, although there is much agreement in the literature that psychiatric comorbidity is associated with poorer treatment outcomes in adolescent substance abusers (Grella et al., 2001; White et al., 2004), studies to date provide little evidence that certain types of treatment are more effective than others in adolescents with or without (different types of) comorbid psychiatric disorders. In addition, no robust predictors of differential treatment effect have been found in the area of demographic background or other domains of functioning (e.g., delinquency). Hence, further investigations are needed to identify which substance abusing adolescents benefit most from which type of treatment.

In the present study, we used the data of our randomized controlled trial comparing the effectiveness of MDFT and CBT in The Netherlands in adolescents with a cannabis use disorder (Hendriks et al., 2011) to investigate which baseline patient characteristics differentially predicted treatment effect – reduction of cannabis use from baseline to month 12 follow-up – in MDFT and CBT, in order to generate hypotheses for future patient-treatment matching.

## 2. Methods

### 2.1. Design

The randomized controlled trial (registration ISRCTN00179361) was both a ‘stand alone’ study in The Netherlands and part of a larger European project (Rigter et al., 2010). The trial was conducted from March 2006 to October 2010, and included 109 adolescents with a cannabis use disorder who applied for treatment at two treatment sites in The Hague. Following randomization, patients received a treatment offer of 5–6 months outpatient CBT (control group;  $n = 54$ ) or MDFT (experimental group;  $n = 55$ ), both followed by a naturalistic follow-up phase of 6–7 months. The primary time point at which treatment outcome was determined was 12 months after baseline. For an extensive description of the study procedures, the reader is referred to the original publication (Hendriks et al., 2011).

### 2.2. Participants

Included patients were 13–18 years old, met diagnostic criteria for past year cannabis abuse or dependence disorder (DSM-IV; American Psychiatric Association, 1994), had used cannabis on at least 26 days in the 90 days preceding baseline, were willing to participate in the study (written informed consent), and had at least one (step) parent or legal guardian who agreed to participate in the study.

### 2.3. Treatments

CBT consisted of weekly outpatient treatment sessions of 1 h with the individual adolescent during 5–6 months. In addition, a monthly, non-system-oriented session was scheduled for the parents, to provide information and support. Treatment was delivered by trained therapists who used a manual based on the MET/CBT12 curriculum used in the Cannabis Youth Treatment (CYT) study (Dennis et al., 2004; Sampl and Kadden, 2001; Webb et al., 2002). To harmonize the planned treatment duration with that of MDFT (5–6 months) in our study, the number of CBT-sessions was extended to 20, with a similar sequence of session-topics as in the CYT-manuals, and the manual was modified for individual therapy. The

first four sessions consisted of MET, and focused on building rapport, enhancing treatment motivation, determining the treatment goal(s), and conducting an initial functional analysis. Sessions 5 through 12 consisted of CBT, targeted at developing skills directly related to achieving and maintaining abstinence from cannabis (e.g., cannabis use self-monitoring, refusal and craving coping skills, increasing social support and non-drug-related activities, problem solving training, coping with relapse). The remaining CBT sessions (13–20) were focused on topics and skills indirectly related to maintaining abstinence (e.g., anger/frustration and anxiety/depression management, delinquent behavior, impulse control, self-efficacy, effective communication).

MDFT consisted of twice-weekly outpatient treatment sessions of 1 h each during 5–6 months with the individual adolescent, parent(s) and/or family, supplemented with sessions or contacts with school, courts and other relevant extra-familial contexts. Treatment was provided by therapists who had been trained by the developers of MDFT in the United States (Liddle et al., 2002), and who used a treatment manual developed by the original authors (Liddle, 2002).

#### 2.4. Assessments

Study assessments were conducted by research assistants who were independent from the treatment staff, and took place at baseline, and after 3, 6, 9 and 12 months following baseline. For the purpose of the present paper, only the baseline and month 12 follow-up assessments are described here. At baseline, patient characteristics were assessed using the Adolescent Diagnostic Interview, substance use disorders section (ADI-Light; Winters and Henly, 1993), the substance use items of the Addiction Severity Index (Hendriks et al., 1989; McLellan et al., 1992), the Personal Involvement with Chemicals subscale (range: 0–87) of the Personal Experiences Inventory (PEI; Winters and Henly, 1989), the Environmental Factors (range: 0–4), Negative Moods (range: 0–4) and Positive Moods (range: 0–4) subscales of the Self-Efficacy List for Drug users (SELD; De Weert-Van Oene et al., 2000), the Diagnostic Interview Schedule for Children, conduct disorder and oppositional defiant disorder sections (DISC-IV; Shaffer et al., 2000), the Internalizing (range: 0–62) and Externalizing (range: 0–64) subscales of the Youth Self Report (YSR; Achenbach and Rescorla, 2001), the Conflict (range: 0–11) and Cohesion (range: 0–11) subscales of the Family Environment Scale (FES; Moos and Moos, 1986), and the Self-Report Delinquency Scale (SRD; Elliott et al., 1985). In addition, a set of questions from the Adolescent Interview (Center for Treatment Research on Adolescent Drug Abuse, 1998) was administered pertaining to the adolescents' functioning at school or work. Based on these questions, we determined whether the adolescent had been dismissed from school or work in the 90 days prior to baseline. With the exception of the SELD and the FES Cohesion subscale, higher scores on each scale reflect more problems.

Lastly, the Timeline Follow Back (TLFB; Sobell and Sobell, 1992) was administered at baseline and month 12 follow-up to assess cannabis use. The TLFB, currently a standard in addiction research, with high reliability and validity (Fals-Stewart et al., 2000; Donohue et al., 2007), provides detailed information about the adolescents' cannabis use during the 90 days preceding the assessments.

#### 2.5. Data analysis

As in the randomized controlled trial, the outcome measure of interest was change in cannabis use from baseline to month 12, in the 90 days prior to assessment. The month 12 follow-up, with a response rate of 94.5% in MDFT and 94.4% in CBT, was chosen as primary time point at which treatment outcome was determined, to allow for the examination of more durable, delayed or reduced effects of treatment. Two separate prediction analyses were

conducted, one with change in number of cannabis use days, and one with change in number of smoked joints as dependent variable. Study data were analyzed using an intention-to-treat approach, i.e., incorporating all patients that were notified about the result of randomization ( $n = 109$ ). Missing month 12 assessments pertaining to the primary outcome measure (TLFB cannabis use) were estimated by means of multiple imputation with five imputed datasets.

All baseline patient characteristics displayed in Table 1 were investigated in the prediction analysis, with the exception of history of earlier substance abuse treatment, given its low prevalence in the study sample. From these characteristics, all interval-level variables showed a non-linear relation with the outcome measure, and were dichotomized. For the Internalizing and Externalizing subscales of the YSR and the Conflict and Cohesion subscales of the FES, the dichotomy was based on normative scores (Achenbach et al., 2008; Jansma and De Coole, 1996). In addition, the two dichotomized subscales of the FES were combined into one variable: family (i.e., cohesion or conflict) problems. All remaining interval-level characteristics were dichotomized based on the observed median (Table 1).

To investigate which patient characteristics differentially predicted treatment outcome in MDFT and CBT, linear regression analyses were conducted, analogous to the two-step procedure suggested by Hosmer and Lemeshow (2000) for logistic models. First, bivariate linear regression analyses were performed for each patient characteristic separately, to determine which characteristics moderated the effect of treatment condition on change in cannabis use (i.e., number of days, number of joints) from baseline to month 12. Second, in order to identify a profile of adolescents more likely to benefit from MDFT than from CBT, and *vice versa*, all patient characteristics that interacted significantly with treatment condition in the bivariate analyses (using a lenient  $p$ -value of  $p < 0.25$ ; Hosmer and Lemeshow, 2000) were entered into a multivariate backward linear regression model. In addition, family functioning (combined Conflict and Cohesion subscales of the FES) was added to the model for reasons of clinical relevance, given MDFT's focus on the family system. All analyses were conducted with SPSS version 18.0.

### 3. Results

#### 3.1. Patient characteristics

Adolescents had a mean age of nearly seventeen years, were mostly male, and from a Dutch/western background (Table 1). They had used cannabis on nearly two-thirds of the 90 days preceding baseline, and their average use on a cannabis using day amounted to more than two and a half joints. All adolescents met DSM-IV criteria for past year cannabis use disorder (inclusion criterion), and more than three-fourths were cannabis dependent. Adolescents reported an average of more than six violent or property crimes during the 90 days prior to baseline, and nearly 40% had ever been detained. Thirty-eight percent of the adolescents was diagnosed with a past year DSM-IV conduct disorder or oppositional defiant disorder (CD/ODD).

#### 3.2. Overall between-groups effect

From baseline to month 12, cannabis use during the 90 days preceding the assessment decreased by an average of 20.1 days and 76.8 joints in MDFT and by 14.9 days and 59.1 joints in CBT. There was no differential effect over time between the treatment conditions on either outcome measure ( $2 \times 2$  repeated measures MANOVA: cannabis use days:  $F(1, 107) = 0.55$ ;  $p = 0.46$ ; Cohen's

**Table 1**  
Patient characteristics at baseline ( $n = 109$ ).<sup>a</sup>

	MDFT ( $n = 55$ ) %/mean (sd)	CBT ( $n = 54$ ) %/mean (sd)	Total sample ( $n = 109$ ) %/mean (median)
<b>Demographic background</b>			
Age (range 13–18 yrs) (yrs)	16.6 (1.3)	16.9 (1.2)	16.8 (16.8)
Gender male (%)	80.0%	79.6%	79.8%
Ethnicity Dutch/western (%)	72.7%	70.4%	71.6%
<b>Substance use</b>			
Age of onset regular cannabis use (yrs)	14.2 (1.6)	14.4 (1.3)	14.3 (14)
Cannabis use past 90 days (days)	63.1 (22.8)	62.3 (23.6)	62.7 (64)
Cannabis use past 90 days (# 'joints')	168.0 (129.6)	155.1 (128.7)	161.6 (122)
Cannabis dependence (%)	76.4%	77.8%	77.1%
Any other substance use past 30 days (%) <sup>b</sup>	51.9%	41.8%	46.8%
<b>Substance-related problems</b>			
Psychological involvement with chemicals (PEI; 0–87)	36.9 (18.2)	36.9 (17.2)	36.9 (37)
Self-efficacy: environmental factors (SELD; 0–4)	2.1 (1.1)	2.0 (1.0)	2.0 (2)
Self-efficacy: negative moods (SELD; 0–4)	2.1 (1.2)	2.0 (1.1)	2.1 (2)
Self-efficacy: positive moods (SELD; 0–4)	2.6 (1.1)	2.6 (1.0)	2.6 (2.5)
<b>Delinquency</b>			
Violent/property crimes past 90 days (# crimes)	6.3 (13.4)	6.6 (18.2)	6.4 (1)
Ever in prison (%)	42.6%	37.0%	39.8%
<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%
<b>Psychopathology</b>			
Internalizing symptoms (YSR; 0–62)	13.4 (9.4)	13.1 (8.5)	13.2 (11)
Externalizing symptoms (YSR; 0–64)	22.8 (10.0)	20.8 (8.4)	21.8 (21)
Conduct or oppositional defiant disorder (%)	43.5%	31.9%	37.6%
<b>Family functioning</b>			
Family cohesion (FES; 0–11)	6.9 (2.8)	6.9 (2.0)	6.9 (7.7)
Family conflict (FES; 0–11)	4.9 (2.7)	5.0 (2.4)	4.9 (5.0)
<b>School or work related problems (%)</b>			
	23.6%	31.5%	27.5%

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

<sup>b</sup> Any other substance use: cocaine, amphetamines, ecstasy, heroin, and alcohol ( $\geq 5$  g/day).

$D = 0.14$ ; smoked joints:  $F(1, 107) = 0.46$ ;  $p = 0.50$ ; Cohen's  $D = 0.13$ ; Hendriks et al., 2011).

### 3.3. Moderators of between-groups effect

Table 2 (upper part) shows the results of the bivariate regression analyses with number of cannabis use days as dependent variable. From the twenty baseline variables investigated, six variables met the criterion for entering the multivariate analysis ( $p < 0.25$ ), and four of these variables showed a significant ( $p < 0.05$ ) interaction effect with treatment condition on treatment outcome in the bivariate analyses. Older adolescents (17–18 years old) showed greater mean reductions in cannabis use days in CBT than in MDFT (–20.8 and –4.1 days, respectively), while younger adolescents (13–16 years old) showed greater reductions in MDFT than in CBT (–34.6 and –9.0 days, respectively;  $p = 0.002$ ). In addition, patients with above median scores on the PEI and those with externalizing problems on the YSR had greater reductions in cannabis use days in MDFT (–33.5 days and –22.8 days, respectively) than in CBT (–14.4 days and –2.7 days, respectively), whereas patients with below median PEI scores and those without externalizing problems showed greater PEI reductions in CBT (–18.6 and –31.2 days, respectively) than in MDFT (–7.00 and –17.4 days, respectively;  $p = 0.033$  and  $p = 0.021$ , respectively). Lastly, adolescents with CD/ODD showed a decrease in cannabis use days in MDFT (–34.4 days), and an increase in CBT (7.8 days), whereas those without CD/ODD showed a greater reduction in CBT (–23.2 days) than in MDFT (–7.5 days;  $p = 0.000$ ).

In the second step of the prediction analysis, all seven variables displayed in the upper part of Table 2 were entered into the multivariate backward regression model. The patient characteristic-by-treatment interactions that remained in the model were age ( $t = 2.32$ ;  $p = 0.02$ ; 13–16 years old: Cohen's

$D = 0.68$ , and 17–18 years old:  $D = 0.51$ ) and CD/ODD ( $t = -3.55$ ;  $p = 0.00$ ; CD/ODD present:  $D = 1.13$ , and CD/ODD absent:  $D = 0.48$ ); all other patient characteristic-by-treatment interactions were not significant at  $p < 0.05$  and, hence, removed from the model.

The same set of predictor variables and same analytical procedures were used in the second prediction analysis, with number of smoked joints as dependent variable. From the seven variables that met the criterion ( $p < 0.25$ ) for entering the multivariate regression model (Table 2, lower part), two patient characteristic-by-treatment interactions remained in the multivariate model: age ( $t = 3.09$ ;  $p = 0.002$ ; 13–16 years old: Cohen's  $D = 0.68$ , and 17–18 years old:  $D = 0.61$ ) and YSR internalizing problems ( $t = -2.82$ ;  $p = 0.005$ ; adolescents with internalizing problems: Cohen's  $D = 0.66$ , and adolescents without internalizing problems:  $D = 0.30$ ). Older adolescents and those without internalizing problems had greater mean reductions in number of smoked joints in CBT (–88.2 and –72.5 joints, respectively) than in MDFT (–19.9 and –36.6 joints, respectively), whereas younger adolescents and those with internalizing problems showed greater reductions in MDFT (–127.8 and –149.5 joints, respectively) than in CBT (–29.9 and –46.8 joints, respectively) (age:  $p = 0.001$ ; internalizing problems:  $p = 0.018$ ).

Cross-validation of the two multivariate models indicated that age and CD/ODD were also significant predictors when entered in a multivariate model with number of smoked joints as dependent variable ( $t = 2.18$ ;  $p = 0.03$ , and  $t = -2.55$ ;  $p = 0.01$ , respectively), and similarly, that age and YSR internalizing problems were significant predictors in the model with cannabis use days as dependent variable ( $t = 3.13$ ;  $p = 0.002$ , and  $t = -2.28$ ;  $p = 0.03$ , respectively).

To explore the practical implications of our findings for treatment allocation, we investigated baseline to month 12 changes in



paper, however, indicated that age, CD/ODD and internalizing problems differentially predicted baseline to month 12 changes in cannabis use associated with these treatments, with greater cannabis use reductions in younger adolescents (13–16 years old) and those with CD/ODD or internalizing problems in MDFT, and, conversely, greater cannabis use reductions in older adolescents (17–18 years old) and those without these coexisting psychiatric problems in CBT.

These results extend our findings of an exploratory analysis of the trial data, reported earlier (Hendriks et al., 2011), and suggest that age and coexisting psychiatric problems in the areas of disruptive behavior disorders and internalizing problems are important moderators of differential treatment outcome associated with a family-based intervention and cognitive behavioral therapy in adolescents with a substance use disorder. Our findings concerning age are in line with those reported in a randomized controlled study by Kaminer et al. (2002), who found lower relapse rates in older adolescents assigned to CBT than in those assigned to a psychoeducation intervention. According to Kaminer et al. (2002), older adolescents are likely to be in a more advanced stage of cognitive development, and may therefore be better able to grasp the cognitive component of the CBT curriculum than younger ones. Alternatively, older adolescents are clearly more likely to be in a transitional phase from living in a family context to living on their own, and may therefore benefit less from interventions with a strong focus on the family system, such as MDFT, than younger adolescents.

With regard to conduct and oppositional defiant disorder, the literature consistently shows that these disruptive behavior disorders, particularly if severe and with an early onset (American Academy of Child and Adolescent Psychiatry, 1997; Lahey et al., 1998), are difficult to treat (Burke et al., 2002), and are associated with a poor long-term prognosis (Myers et al., 1998; Satterfield et al., 2007). In addition, much of the literature converges on the notion that multicomponent or family-based interventions are currently probably the best available treatments for these behavior disorders (Eyberg et al., 2008; Henggeler and Sheidow, 2003; Pappadopulos et al., 2003; Rowe et al., 2004). However, little research exists about the role of co-occurring disruptive behavior disorders as potential effect moderator in adolescent substance abuse treatment, and studies investigating this role in direct comparisons between family-based interventions and CBT in this field are lacking.

With respect to internalizing problems, Kaminer et al. (1992) reported poorer substance abuse treatment outcomes in dually diagnosed adolescents without depression or anxiety disorders, whereas Rowe et al. (2004) reported that, independent from treatment condition, adolescents with combined externalizing and internalizing disorders had the poorest outcomes. Hence, few studies investigated the role of internalizing problems as moderator of (differential) treatment outcome, and the ones that did, found inconsistent results.

If replicated in future studies, our findings may provide a basis for future patient-treatment matching, both to improve the effectiveness of the investigated interventions, to prevent unnecessary long or intense treatment, and to enhance their cost-effectiveness. Although at this stage still tentative, the most important clinical implication of our findings is that – based on standardized assessment at intake – young adolescents with a diagnosis of CD/ODD or with YSR internalizing scores in the clinical range (Achenbach et al., 2008) may probably best be referred to MDFT, and older adolescents without these coexisting psychiatric problems to CBT. In addition, given that MDFT is a more intensive treatment, but, compared to CBT, in our study did not result in greater reductions in cannabis use in younger adolescents without these coexisting psychiatric problems or older adolescents with these psychiatric

problems, CBT may be considered as preferred treatment option for these adolescent subgroups as well.

With respect to matching research in adolescent substance abuse treatment, much work is still needed. Researchers should make more use of the option to conduct secondary analyses of existing trial data, and investigate whether observed post hoc matching effects can be replicated in subsequent prospective studies. An advantage of the analytical approach followed in this paper is that dichotomization of interval-level predictor variables – where possible based on normative scores – allows a relatively easy translation of the findings into practical guidelines for treatment allocation. Based on previous matching attempts in the addiction field, important additional recommendations for future matching research include (a) to investigate interventions that are sufficiently distinct in terms of underlying treatment model or intensity, (b) to maximize patient heterogeneity, and, hence, external validity, by using lenient exclusion criteria, (c) to develop a priori matching hypotheses, which (d) if feasible given the larger sample size needed, should also address higher order interactions than the single patient characteristic-by-treatment interactions tested in most studies (Finney, 1999; Hall, 1999; Orford, 1999; Bühringer, 2006). Clearly, the search for targeted, more effective, treatments poses a considerable and exciting challenge to the adolescent substance abuse field.

#### 4.1. Limitations

The main limitations of the randomized controlled study (including: mostly self-reported outcome data; treatments of unequal intensity and duration; lack of a no-treatment control condition) have been discussed in our earlier paper (Hendriks et al., 2011). The trial was designed to study the main effects of MDFT versus CBT, and, consequently, statistical power to detect patient characteristics associated with differences in treatment outcome was limited. Power would have been enhanced if the pooled data of the international MDFT evaluation could have been used. However, control treatments differed substantially between the participating countries (The Netherlands, Belgium, France, Germany and Switzerland) in both theoretical orientation (e.g., a predominantly psychodynamic approach in France, integrative psychotherapy in Switzerland) and number of sessions provided, and, hence, the pooled data would not have allowed a comparison of MDFT with a well-described, manualized treatment as in our study. Notwithstanding the limited power in our study, however, we did find statistically significant differential treatment effects in subgroups of adolescents, and the observed moderate to large between-treatment effect sizes in these subgroups suggest clinical relevance.

#### 5. Conclusion

The current study, based on data from a randomized controlled trial in which MDFT and CBT were equally effective in reducing cannabis use, strongly suggests that age, disruptive behavior disorders and internalizing problems are important treatment effect moderators of MDFT and CBT in adolescents with a cannabis use disorder. If replicated, this finding suggests directions for future patient-treatment matching in adolescent substance abuse treatment.

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This study was commissioned and financed by the Netherlands Ministry of Health, Welfare and Sports. The Ministry had no further role in study design, nor in the collection, analysis and interpretation of the data or in the writing of the report.

## 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.

## 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.

## Conflict of interest

No conflict declared.

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