



Full length article

Cost-effectiveness of multidimensional family therapy compared to cognitive behavioral therapy for adolescents with a cannabis use disorder: Data from a randomized controlled trial

M. Goorden^{a,*}, E. van der Schee^b, V.M. Hendriks^{b,c}, L. Hakkaart-van Roijen^a

^a Institute for Medical Technology Assessment & Institute of Health Policy & Management, P.O. Box 1738, 3000 DR, Erasmus University Rotterdam, The Netherlands

^b Parnassia Addiction Research Centre (PARC), Brijder Addiction Treatment, Parnassia Group, P.O. Box 53002, 2505 AA The Hague, The Netherlands

^c Curium, Leiden University Medical Center, Department of Child and Adolescent Psychiatry, Leiden University, P.O. Box 37, 2300 AA Leiden, The Netherlands

ARTICLE INFO

Article history:

Received 2 September 2015

Received in revised form 1 March 2016

Accepted 3 March 2016

Available online 10 March 2016

Keywords:

Cost-effectiveness

MDFT

CBT

Cannabis use disorder

Adolescents

Delinquency

ISRCTN00179361

ABSTRACT

Objective: To evaluate the cost-effectiveness of Multidimensional Family Therapy (MDFT) for adolescents with a cannabis use disorder, compared to Cognitive Behavioural Therapy (CBT).

Methods: A parallel-group randomized controlled trial was performed. 109 adolescents with a DSM-IV cannabis use disorder (CBT n = 54; MDFT n = 55) were included. Assessments were conducted at baseline, and 3, 6, 9 and 12 months post-baseline, and included measures on cannabis and other substance use, delinquency, health care utilization, and general health related quality of life.

Results: Excluding those with missing cost-data, 96 participants (MDFT n = 49; CBT n = 47) were included. From a health care perspective, the average annual direct medical costs in the CBT group were €2015 (95% C.I. 1397–2714), compared to €5446 (95% C.I. 4159–7092) in the MDFT group. The average quality-adjusted life years (QALY's) gained were 0.06 QALY higher for the MDFT group, which led to an incremental cost-effectiveness ratio (ICER) of 54,308 Euro/QALY or €43,405 per recovered patient. Taking the costs of delinquency into account, the costs increased to €21,330 (95% C.I. 12,389–32,894) for the CBT group and to €21,915 (95% C.I. 16,273–28,181) for the MDFT group, which lead to an ICER of 9266 Euro/QALY or a cost per recovered patient of €7491.

Conclusions: This is the first comprehensive CEA of MDFT compared to CBT and it demonstrated that when costs of delinquency were included, the ICERS were modest. The results underline the importance of adopting a broader perspective regarding cost effectiveness analyses in mental health care.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

In the Netherlands, individual Cognitive Behavioral Therapy (CBT) is the first choice psychosocial treatment for substance abusing adolescents. However, environmental factors, like substance abusing peers and parent-child relationship, also influence substance abusing adolescents (Broman et al., 2006; Choquet et al., 2008; Kristjansson et al., 2013) and need to be addressed in therapy. Multidimensional Family Therapy (MDFT) is a promising treatment, as it not only targets the individual but also the systems surrounding the individual.

In a meta-analysis that evaluated the effectiveness of outpatient substance abuse treatments for adolescents, family therapy was the

most convincing and consistent effective treatment for substance abuse, and although CBT was more effective than any other non-family treatment, family therapy was superior (Tanner-Smith et al., 2013). Based on these findings, family therapy is the treatment with the strongest evidence of comparative effectiveness, although most types of treatment appear to be beneficial in helping adolescents reduce their substance use.

A randomized controlled study in the Netherlands showed that MDFT and CBT were equally effective in reducing cannabis use and delinquent behavior in adolescents with a cannabis use disorder (Hendriks et al., 2011). Regarding cost-effectiveness, only a limited number of studies assessed family interventions in adolescents. To date, there is one randomized trial that showed that MDFT was more costly and was equal in clinical effectiveness compared to CBT (Dennis et al., 2004). This study was limited to the monetary benefits compared on two clinical outcomes: days of abstinence after 12 months and 'being in recovery' at the end of the study

* Corresponding author at: Drs Maartje Goorden, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

E-mail address: Goorden@bmg.eur.nl (M. Goorden).

(defined by the authors as being abstinent and living in the community). In addition, as the study was conducted in the United States, the study findings cannot be generalized to the Dutch healthcare system without any consideration. Although studies evaluating the cost-effectiveness for MDFT are limited, the interest in cost-effectiveness analyses for relative expensive but commonly applied family treatments is strongly increasing as they compete with other (medical) treatments for health care budgets.

Next to difference in health care costs, cost savings may result from a decrease of adolescent criminal behavior. Cannabis and other substance use disorders in adolescents often coincide with delinquent behavior (Copeland and Swift, 2009). This relationship may reflect a common predisposition to addiction and delinquency, related to certain personality characteristics (e.g., impulsivity) and associated genetic factors (Sharma et al., 2014), decreased inhibitory control as a result of the acute effects of psychoactive substances or of chronic substance use (Volkow et al., 2003), an increased probability to commit crimes, to obtain money for buying drugs (Goldstein, 1985), as well as the influence of deviant peer affiliations on crime and substance use in adolescents (Fergusson et al., 2002). In any case, costs related to criminal involvement are important to include in a cost-effectiveness study of substance abuse treatment in adolescents.

The aim of the present study was to evaluate the cost-effectiveness of MDFT versus CBT in adolescents with a cannabis use disorder from a health care perspective. Additionally, the cost-effectiveness was assessed by including the costs of delinquency. We performed a cost-utility analysis, which has the advantage over a more general cost-effectiveness study in that the intervention is also comparable to interventions outside the mental health care system by using a generic outcome measure (quality of life). In addition, when treatments are equal in clinical effectiveness a cost utility study may add extra information on decisions for policy makers. Additionally we performed a cost-effectiveness analysis using a clinical outcome measure.

2. Material and methods

2.1. General study design

The cost-effectiveness analysis was conducted on data pertaining to the parallel-group randomized controlled study of Hendriks et al. (2011). This study was approved by the medical-ethical committee for research in mental health care settings of The Netherlands (METiGG; registration nr. 5238). This study was performed from March 2006 until October 2010 and evaluated the effectiveness of MDFT versus CBT. Eligible patients were randomly allocated (ratio 1:1) by the research group by using a computer-generated randomization list. Sample size calculation was based on Monte Carlo simulation techniques and resulted in a minimum of 100 and a maximum of 120 participants. 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. ≥ 75 days in the previous 90 days), using blocks of two patients.

2.2. Participants

Adolescents (13–18 years old) with a cannabis use disorder who applied for treatment at two treatment sites in The Hague were screened. The following inclusion criteria were used: using cannabis for at least 26 days in the 90 days before baseline, meeting the DSM-IV diagnostic criteria for past year cannabis abuse or dependence, and written informed consent. In this trial, 109 participants were included (CBT n = 54; MDFT n = 55). The detailed study

protocol and results of this trial have been described elsewhere (Hendriks et al., 2011, 2012).

2.3. Treatments

2.3.1. MDFT. The intervention involved individual outpatient therapy and sessions with the parents and/or family, twice a week, 1 h each, for 5–6 months. MDFT is not only aimed at the individual but also at the relationship with parents, family members or other extra-familial relevant contacts so extra-familial sessions involving school, work, drug using peers, the court and the juvenile justice system were arranged if necessary. Therapists were trained by the developers of MDFT in the United States and the original manual of MDFT was used during therapy (Liddle, 2002). In addition, trainers were contacted monthly, to receive feedback and consultation.

2.3.2. CBT (care as usual). CBT consisted of individual outpatient sessions, once a week, 1 h each, for 5–6 months. A non-system-oriented session to provide parents with information and support was held once a month. The first four sessions focussed on enhancing treatment motivation, building rapport, determining treatment goals and conducting an initial functional analysis. Until the 12th session, the main goal of treatment was to develop skills and achieve and maintain abstinence from cannabis. After this, treatment focussed on topics indirectly related to maintaining abstinence. The duration of treatment was also 5–6 months, to synchronize with MDFT. Therapists were trained and used a manual based on the Cannabis Youth Treatment (CYT) study (Webb et al. 2016; Sampl and Kadden, 2001; Dennis et al., 2004).

2.4. Outcome measure and assessments

The total duration of the study was 1 year (5–6 months treatment and 6–7 months of follow up). Data were collected by independent research assistants. Cost-effectiveness was determined by evaluating the quality of life and whether a person was in 'recovery', and by calculating the direct medical costs and costs related to delinquency. Data on quality of life was collected at baseline, 6, 9 and 12 months, data on the health care costs at 6 and 12 months and costs related to delinquency were collected at baseline, 3, 6, 9 and 12 months. The primary outcome measure was costs per quality-adjusted life year (QALY). Recovery was a secondary outcome measure and was based on the definition as used in the original trial of Hendriks et al. (2011).

2.4.1. Quality of life and recovery. Quality of life was assessed with the Euroqol 5 Dimensions (EQ-5D; Cheung et al., 2009). The EQ-5D is a standardized, validated instrument and encompasses five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is rated by the patient on three levels (no problems, some problems, and extreme problems). Thus, 243 distinct health states are defined, each with a unique utility score, ranging from 1 (perfect health) to 0 ('death'). Adolescents were considered to be 'in recovery' if they lived in the community and were abstinent from cannabis, heavy alcohol use (≥ 5 glasses a day) and any other substance use in the 30 days preceding the month 12 assessment.

2.4.2. Direct medical costs. Direct medical costs were measured with the Treatment Inventory of Costs in Psychiatric Patients (TiC-P), a validated instrument (Bouwman et al., 2013) that records self-reported number of contacts with health care providers during the previous three months. Unit costs were valued according to prices reported in the Dutch manual for cost research (Hakkaart-van Roijen et al., 2010), so the costs can be obtained by multiplying the unit prices with the volume. The costs of the MDFT and CBT

therapists were based on the gross wages per year, working hours, session length of 1 h, preparation and writing of reports, overhead and bonus, and education costs for both therapies. All unit costs were corrected for inflation.

2.4.3. Costs related to delinquency. To include costs related to delinquency, the Self Reported Delinquency (SRD) questionnaire was administered (Elliott et al., 1985; Wetenschappelijk Onderzoek en Documentatie Centrum, 1991). This questionnaire consists of questions aimed at mapping delinquent behavior in adolescents. Questions are categorized into: Internet offenses, drug offenses, discrimination, destruction/public order offenses, property offenses, traffic offenses and aggression, violent offenses and sex offenses. In each item of the questionnaire, the adolescent is asked at what age he or she first engaged in the specified delinquent behavior and the number of times this behavior was performed in the last 90 days. This number is translated into costs by specifying unit prices, which subsequently can be multiplied by the volumes to obtain costs. Unit prices are not yet available, so we estimated these costs based on two different sources (BIVV, 2011; Centraal, 2012). The Research and Documentation Centre (WODC) of The Netherlands provided an overview for expenses made for prevention, tracing, prosecution, going on trial, execution of verdict, support of suspects and perpetrators, support of victims, consulting of legal experts and other activities in The Netherlands. We matched the expense categories used by the WODC with the categories used in the SRD. As the expenses on support for suspects were already included in our health care costs, these were subtracted from the total costs. The WODC (2012) also provided the number of registered crimes, the number of suspects for certain crimes and the percentage of crimes that is registered (based on victim reports), so registered criminality could be corrected for multiple suspects and probability of not being detected. As percentage of crimes that are registered for traffic offenses were not included in the figures of the WODC, instead, the subjective chance of getting caught was used which was obtained from a different source (BIVV, Observatorium voor verkeersveiligheid 2011). These were added for different categories of criminal behavior according to the SRD. Additionally they provided the number of registered crimes that were subsequently adjusted for probability of registration of the crime and multiple suspects. For acquiring the unit costs, the total costs were divided by the total (adjusted) number of crimes and were subsequently indexed.

2.5. Data analysis

Ninety-six adolescents (MDFT: 49; CBT: 47) were included in the study. As described in the paper of Hendriks et al. (2011), at month 9, the missing completely at random assumption (MCAR) was violated, and these data were subsequently excluded from the analyses. Patients were removed from analysis when there was insufficient information available regarding costs and effects, 1 measurement moment. As a result, a total of 13 adolescents were excluded from the analyses.

The health descriptions from the EQ-5D used to measure health-related quality of life were linked to empirical valuations of the Dutch general public, allowing utilities to be computed. Utilities are index based values that reflect the preference of one state to another. To obtain one utility score per patient, the area-under-the-curve method (AUC) was applied (Matthews et al., 1990). To obtain one utility per patient, the area under the curve of the utilities over the different points in time was determined using the Riemann sum. To calculate the incremental utilities; the utilities of the treatment groups (MDFT and CBT) were subtracted.

The numbers of missing values of the utilities at baseline and at the end of treatment were both low (0% and 7%, respectively). As

there were more missing values in between (51% after 6 months), the missing utility values at 6 and 12 months were estimated by interpolation. Interpolation is a method used to construct new data points within the range of a set of known data points using a (in this case) linear function.

Health care costs and costs related to delinquency were determined by multiplying the number of treatment contacts/number of crimes (over 3 months) by the reference unit prices of these services or crimes. For adolescents, health care use in general is low as they are, inherent to their age, generally healthier than adults. Based on this characteristic and the data distribution (frequency of zero's ranged from 65 to 100%), missing values at 6 months (36.5%) and 12 months (3.1%) were imputed with a zero value, meaning no costs. We did not perform a sensitivity analysis on the effect of the zero "imputations" as our dataset would become very small and we believe this would not add to a more accurate analysis."

A model predicting missing values more precisely cannot be generated as the discrete number of values is low because the data contained a lot of patients with zero costs (point mass is zero). To obtain health care costs for half a year, costs acquired by the TIC-P, covering 3 months, were doubled. The SRD did not provide a distinction between offenses that were committed by car or offenses committed by bike (although the difference in costs between these type of offenses is high). Therefore, information from the remarks of the SRD, was assessed to distinguish between these types of offenses. However, these remarks did not always contain this information. In addition, there was uncertainty about the probability of getting caught in traffic offenses and subsequently uncertainty in the unit costs. Therefore, there was much uncertainty around the costs of traffic offenses and a sensitivity analysis was performed, omitting these costs.

The uncertainty in the analysis was assessed using nonparametric bootstrapping (5000 times). This was expressed in a cost-effectiveness acceptability curve. The acceptability curve illustrates the probability that the cost-effectiveness ratio will be accepted for different cost limits (using the bootstrapped values) given a societal willingness to pay threshold. Including the costs of delinquency, the procedure was repeated.

An incremental cost-effectiveness ratio (ICER) was calculated to obtain the costs per quality Adjusted Life Year (QALY). The ICER was calculated by dividing the incremental costs by the incremental effects and represents the cost to achieve a unit of improved outcome in the intervention relatively to its comparator. The incremental costs per recovered patient were also calculated by dividing the incremental costs by the incremental number of recovered patients. Analyses were conducted using the Statistical Package for the Social Sciences 19.0 (SPSS 19.0) and Excel (2010).

3. Results

3.1. Demographics

The (consort) flow diagram in the Supplementary Material[i]describes the participant flow. The trial was ended within the planned 22 weeks treatment period and 1 year total study period. Table 1 summarizes the baseline demographic and clinical patient characteristics for the MDFT group and CBT group. At baseline, there were no significant differences between both groups.

3.2. Quality of life/recovery

Quality of life at baseline was 0.89 (0.13) for the CBT group and 0.88 (0.15) for the MDFT group.

The improvement in quality of life (EQ-5D) over time (effect, calculated with the AUC method) was -0.02 for the CBT group

Table 1
Sample characteristics at baseline.

	MDFT* (N=49)	CBT* (N=47)
	Mean (SD)/Percentage (%)	Mean (SD)/Percentage (%)
Age	16.7 (1.32)	17.0 (1.19)
Gender male (%)	77.6	76.6
Ethnicity (Dutch) (%)	72.3	72.7
Age of onset cannabis use	14.27 (1.50)	14.38 (1.34)
EQ-5D adolescents	0.88 (0.15)	0.89 (0.13)
Cannabis use past 90 days (#days)	61.7 (23.0)	62.5 (23.8)
Cannabis use past 90 days (#joints)	157.0 (119.5)	159.9 (133.4)
Cannabis dependence (%)	81.6	78.7
Ever convicted by court (%)	51.0	51.1
Parents living together (%)	38.8	40.4
Ever been in substance abuse treatment (%)	10.2	10.9
Ever been in psychiatric treatment (%)	34.8	37.0
Destruction and/public offenses past 90 days(#times)	32.5 (51.2)	19.9 (33.3)
Traffic offenses past 90 days (#times)	22.2 (36.1)	24.6 (36.7)
Aggression and violent offenses past 90 days (#times)	14.6 (30.1)	12.1 (26.4)

*MDFT = Multidimensional Family Therapy; CBT = Cognitive Behavioral Therapy; SD = Standard Deviation.

(95% C.I., -0.05 to 0.02) and 0.04 for the MDFT group (95% C.I., 0.03–0.06), indicating that quality of life was not affected in CBT, but was improved in MDFT. The difference in improvement between both groups over time was 0.06 (95% C.I., 0.03–0.10). Over time the decrease in problems on the EQ-5D dimension pain/discomfort was higher (35% at baseline indicated no problems and 11% after 12 months) in the MDFT group than in the CBT group (23% at baseline indicated no problems and 16% after 12 months). Anxiety/depression also decreased more in the MDFT group (28% at baseline indicated no problems and 4% after 12 months) than in the CBT group (25% at baseline indicated no problems and 20% after 12 months). However, daily activities improved more in the CBT group (32% at baseline indicated no problems and 7% after 12 months) than in the MDFT group (20% at baseline indicated no problems and 13% after 12 months).

The percentage of recovered patients after 12 months was 6.4% for the CBT group and 14.3% for the MDFT group. The difference in effects was not significant, $\chi^2(1, N=96)=1.606, p=0.205$. The relative risk was 2.2, so the chance of recovery in the MDFT group was (although not significant) approximately twice as high as the chance of recovery in the CBT group.

Table 3
Mean annual cost per adolescent for both treatments based on unit prices of 2012.

	MDFT* (N=49)			CBT* (N=47)		
	Mean costs (€ _{SD})	Percentage of total costs (%)	Percentage of patients using the service (%)	Mean costs (€ _{SD})	Percentage of total costs (%)	Percentage of patients using the service (%)
MDFT therapy/CBT therapy**	3372 (1401)	62	98 ^a	896 (820)	44	89
(psychiatric) hospital days	1610(7327)	30	8	456(2181)	23	6
Social Worker	173(462)	3	33	112 (276)	6	23
General practitioner	46 (65)	1	49	41 (59)	2	40
Medication	28 (79)	1	31	13(43)	1	21
Medical Specialist	58 (121)	1	27	83 (194)	4	23
Paramedic care	49 (188)	1	10	7 (34)	0	4
Mental Health Care	80 (430)	1	4	317 (80)	16	13
psychologist/psychiatrist	20 (87)	0	4	12 (59)	1	4
Counselling centre for drugs alcohol	9 (66)	0	2	1 (8)	0	2
Occupational physician	1 (8)	0	2	1(8)	0	2
Alternative medicine	0(0)	0	0	28 (185)	1	2
Selfhelp group	0(0)	0	0	49 (334)	2	2
(parttime) day care	0(0)	0	0	0(0)	0	0
Total costs	€5446 (8032)			2015 (2807)		

*MDFT = Multidimensional Family Therapy; CBT = Cognitive Behavioral Therapy; SD = Standard Deviation.

^a There was 1 person who did not start treatment.

** $p < 0.01$.

Table 2

Unit costs-2009, sorted by height of costs, source (excluding therapists): Dutch manual for cost research (Hakkaart-van Roijen et al., 2010).

Category	Unit price (€)
(psychiatric) hospital day	232
Mental Health Care Institute contact	171
Medical Specialist contact	96.50
MDFT contact	67
CBT contact	66
Social Worker contact	65
Occupational physician contact	57
Alternative medicine contact	55
Paramedical contact	36
GP contact	28

3.3. Direct medical costs

The most relevant unit prices are summarized in Table 2. The costs of the MDFT and CBT therapists were based on the gross average wages per year (which were the same for both CBT and MDFT therapist) of €38,740, the working hours (1540), the session length of 1 h, the preparation and the writing of reports of both 20 min, overhead and bonus, and the education costs for both therapies.

Table 4
Delinquency unit costs in 2012.

Category	Unit price (€) ^a
Robbery and theft with violence	20,939
Simple and aggravated assault	4234
Simple theft/picket pocketing	1960
Destruction/vandalism of private/public property	1910
Threat	1819
Forced sexual contacts	1734
Receiving	1694
Arson	1449
Traffic offenses: Unauthorized driving	975
Traffic offenses: Driving under influence	213
Selling Harddrugs ^b	130
Discrimination	108
Nuisance	108
Selling softdrugs ²	41
General Traffic offenses	3

^a The unit costs contain costs of prevention, tracing, prosecution, going on trial, execution of verdict, support of suspects and perpetrators, support of victims, consulting legal experts and other activities.

^b In the Netherlands we make a distinction between soft drugs and hard drugs. Soft drugs are drugs that are less inhibiting and addicting than hard drugs, often being defined as causing psychological, but not physical addiction. Hard drugs are often defined as being both physically and psychologically addictive, while also posing serious risks to users.

Including all therapist-related costs, the cost of one MDFT session was estimated at €67 and the costs of one CBT session at €66.

The total average annual direct medical costs were €2015 (2807) for the CBT group. These costs were significantly higher for the MDFT group: €5446 (8032), mainly due to significantly higher treatment costs of MDFT treatment (see Table 3). Costs associated with (psychiatric) hospital admissions were higher in the MDFT group. However, costs associated with (additional) mental health care were higher in the CBT group.

3.4. Costs related to delinquency

An overview of the unit costs of delinquency is given in Table 4.

The mean number of self-reported illegal activities categorized by type of offense in the past 90 days and associated annual costs are presented in Table 5. The total annual costs were €16,469 (30,900) in the MDFT group and €19,314 (42,916) in the CBT group. Especially costs associated with traffic offenses (unauthorized driving, driving under influence and other traffic offenses) were higher in the CBT group.

3.5. Cost-effectiveness analysis (CEA)

The average quality of life years (QALY's) gained was higher in the MDFT group. The direct medical costs in MDFT were also significantly higher compared to CBT, €3430 (95% C.I. 1962–5196), leading to an ICER of 54,308 Euro per QALY taking a health care perspective. The incremental costs per recovered patient were €43,405. An overview of the costs and effects are shown in Table 6. The incremental costs per extra recovered patient were €7491.

We first explored the incremental cost utility from a health care perspective. All of the ICERs (100%) fall in the northeast quadrant of the incremental cost-effectiveness plane, indicating that MDFT is more costly but also more effective than CBT, see Fig. 1.

When additional costs related to delinquency were included, total costs were not significantly higher in the MDFT group than in the CBT group, €585 (95% C.I. –12,271–11,426), and the ICER increased to 9266 Euro/QALY, see Table 7 (left).

Another way to present the uncertainty in the data is the acceptability curve in Fig. 2. This curve represents the probability that the ICER is acceptable at different (societal willingness to pay)

thresholds. For example, at a threshold of 100,000 Euro/QALY the probability that the ratio is acceptable is around 90%.

When including costs for delinquency, the probability that MDFT may be cost effective increases; 56% of the ratios fall into the northeast quadrant and 44% in the southeast quadrant, see Fig. 1 (right). When all ratios fall into the northeast quadrant of the cost-effectiveness plane, it means treatment is more costly and more effective. If all ratios fall into the south east quadrant, it means treatment is less costly and more effective.

Compared to the health care perspective, there is a higher probability that the ratio was acceptable up to a threshold of 65,000 Euro/QALY. However, taking a threshold higher than 65,000 Euro/QALY, the probability that the ICER becomes acceptable is slightly lower when costs for delinquency were included, see Fig. 2. This was due to higher uncertainty in the costs when costs related to delinquency were included. Overall, the probability that the ICER is acceptable is higher when costs of delinquency are included

3.6. Sensitivity analysis

A sensitivity analysis was conducted for the traffic offenses, as detailed information to estimate a weighted cost per offense was missing. The SRD did not provide a distinction between offenses that were committed by car or offenses committed by bike (although the difference in costs between these type of offenses is high). Therefore, information from the remarks of the SRD, was assessed to distinguish between these types of offenses. However, these remarks did not always contain this information. Therefore there was much uncertainty around the costs of traffic offenses and a sensitivity analysis was performed, omitting these costs. In addition, there was uncertainty about the probability of getting caught in traffic offenses and subsequently uncertainty in the unit costs. In our sensitivity analysis it was therefore assumed that these costs were zero. After the sensitivity analysis, the incremental costs increased to €4158 (95% C.I. –4664–12873), which lead to an (increased) ICER of 65,823 Euro/QALY. The cost-effectiveness plane and cost-effectiveness acceptability curve are included as Supplementary material.

4. Discussion

This study is the first cost-effectiveness analysis comparing MDFT to CBT in adolescents with a cannabis use disorder. The higher costs and larger effects in the MDFT group compared to the CBT group resulted in an ICER of 54,308 Euro/QALY and incremental costs per recovered patient of €43,405. This study is also the first to include relevant societal costs – related to delinquency – that go beyond the health care perspective. The results provide a first insight and indicate that inclusion of these costs, affect outcome: including costs related to delinquency resulted in an ICER of 9266 Euro/QALY and costs per recovered patient of €7491, as the difference of costs between both treatments decreased. As treatment of adolescents may have a preventive effect on future mental health problems and addiction (Liddle et al., 2004), the ICER may even improve in time. These results underline the importance of adopting a broader perspective regarding cost-effectiveness analysis in mental health care.

MDFT was more expensive which is consistent with MDFT being a more intensive treatment than CBT. Overall, health care costs were low in both groups, as adolescents do not have many physical health issues and subsequently do not often make use of health care providers. Only costs of (psychiatric) hospital admissions were high. Regarding the costs related to delinquency, costs of traffic offenses were much larger for MDFT compared to CBT. As there was much uncertainty around the costs for traffic offenses, we per-

Table 5

Mean number of times of engagement in illegal activity categorized by type of offense and associated costs for adolescents for both treatments in one year.

	MDFT ^a (N = 49)		CBT ^a (N = 47)	
	Number of times engaged 1 year (SD)	Average costs (€, SD) per adolescent	Number of times engaged 1 year (SD) ^a	Average costs (€,SD) per adolescent
Drug offenses	15.4 (38.0)	852 (2305)	4.9 (15.6)	556 (2008)
Selling softdrugs ^b	12.9 (35.7)	529 (1462)	0.9 (3.0)	38 (123)
Selling harddrugs ^b	2.5 (14.0)	324 (1818)	4.0 (15.5)	518 (2009)
Discrimination	0.3 (0.8)	26 (84)	0.1 (0.3)	7 (27)
Calling names	0.3 (0.8)	26 (84)	0.1 (0.3)	7 (27)
Fighting	0 (0)	0 (0)	0(0)	0 (0)
Destruction/public order offenses	45.6 (65.8)		35.2 (60.6)	
Nuisance	9.2 (30.1)	923 (3007)	2.6 (3.5)	260 (350)
Destruction private property	0.0 (0.2)		0.1 (0.3)	
Destruction public objects	0.1 (0.4)		0.1 (0.3)	
Vandalism public or private objects	1.3 (4.4)	2846 (9209)	0.7 (3.8)	1666 (7542)
Fare dodging	33.9 (55.6)		30.8 (56.2)	
Fire work offense	0.8 (2.7)		0.9 (3.0)	
Arson	0.2 (0.8)	296(1145)	0.1 (0.4)	154(543)
Property offenses	3.1 (5.4)	5849(10,272)	3.5 (8.9)	6665 (17,119)
Simple theft	2.0 (3.9)	3920 (7706)	2.8 (7.7)	5470 (15,036)
Shop	0.9 (2.6)	1840 (5192)	0.8 (2.6)	1585 (5164)
School/work	0.3 (1.0)	640(2016)	1.8 (7.0)	3593 (13,629)
Without break-in private objects	0.7 (2.1)	1440 (4192)	0.2 (0.5)	292 (999)
Theft with or without break-in with or without theft	0.1 (0.4)	200 (721)	0.0 (0.2)	42 (286)
Receiving	1.0 (2.9)	1729 (4872)	0.7 (2.2)	1153 (3656)
Traffic offenses	39.4 (67.0)	410 (870)	27.5 (59.3)	3975 (23,426)
Unauthorized driving	0.3 (0.8)	268.6 (802.7)	3.3 (19.7)	3,225.8 (19,230.4)
Driving under influence	0.1 (0.3)	23.9 (73.0)	3.2 (19.7)	686.6 (4202.8)
General	39.0 (66.9)	117.1 (200.6)	20.9 (45.1)	62.7 (135.5)
Aggression and violent offenses	14.4 (39.8)		13.5 (36.3)	
Threat	0.4 (1.1)	742 (1962)	0.3 (0.7)	581 (1320)
Pocket-picking	0.1 (0.2)	120 (475)	0.0 (0.2)	42 (286)
Robbery/theft with violence	0.0 (0.1)	427 (2991)	0 (0)	0(0)
Weapon possession	13.0 (39.6)			
Simple or aggravated assault	0.9 (2.7)	3975 (11,544)	1.3 (4.3)	5405 (18,386)
Injury with weapon	0 (0)			
Sex offenses, forcible	0 (0)	0 (0)	0 (0)	0(0)
Total costs ^c	16,469 (30,900)		€19,314 (42,916)	

^aMDFT=Multidimensional Family Therapy; CBT=Cognitive Behavioral Therapy; SD=Standard Deviation.^b In the Netherlands we make a distinction between soft drugs and hard drugs. Soft drugs are drugs that are less inhibiting and addicting than hard drugs, often being defined as causing psychological, but not physical addiction. Hard drugs are often defined as being both physically and psychologically addictive, while also posing serious risks to users.^c The sum of the costs do not exactly equal the total costs because of rounding.**Table 6**

Overview costs and incremental effects of adolescents for both groups from a health care perspective.

	MDFT [*]	CBT [*]
Costs	€5446 (95% C.I. 4159 to 7092)	€2015 (95% C.I. 1397 to 2714)
Incremental effect	0.06 (95% C.I. 0.03–0.10)	
ICER	54,308 Euro/QALY	
Incremental costs per recovered patient	€43,405	

^{*}MDFT = Multidimensional Family Therapy; CBT=Cognitive Behavioral Therapy.**Table 7**

Overview costs and incremental effects of adolescents for both groups by including costs of delinquency.

	MDFT [*]	CBT [*]
Costs	€21,915 (95% C.I. 16,273 to 28,181)	€21,330 (95% C.I. 12,389 to 32,894)
Incremental effect	0.06 (95% C.I. 0.03–0.10)	
ICER	9266 Euro/QALY	
Incremental costs per recovered patient	€7491	

^{*}MDFT = Multidimensional Family Therapy; CBT=Cognitive Behavioral Therapy.

formed a sensitivity analysis. As the difference in costs increase, the ICER also increased to 65,823 Euro/QALY. These costs per QALY were still within the range of 80,000, the commonly applied threshold of the Council for Public and Health Care (RVZ). Based on the sources used for estimating the costs related to delinquency, it was not possible to estimate the costs of internet offenses, so we did not

include these costs in our analyses. Probably, this does not have a large effect on the results, given that the probability of getting caught for internet offenses is small. Productivity costs were not included in the study because these costs were expected to be negligible as most adolescents (14–19) do not have a day to day job. Although the costs related to delinquency were lower in the MDFT

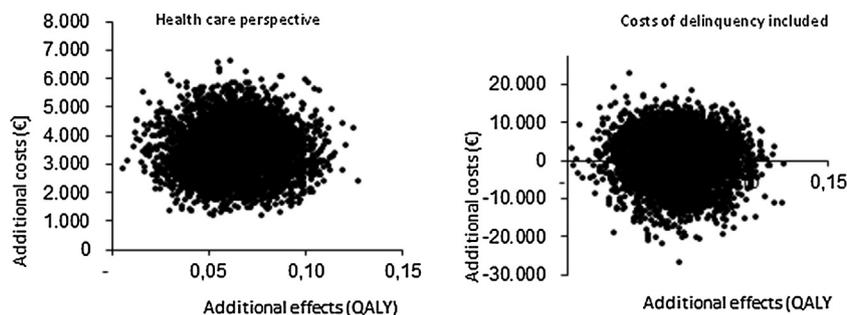


Fig. 1. Cost-acceptability planes (left: health care perspective, right: costs of delinquency included).

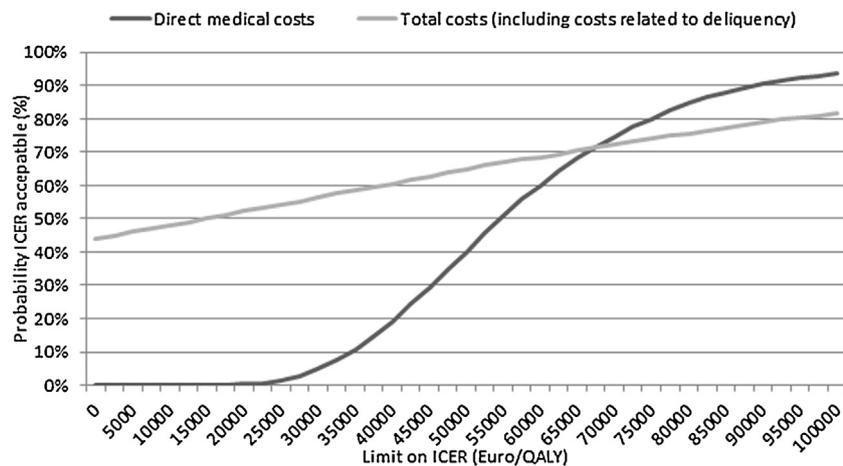


Fig. 2. Cost-acceptability curves.

group, the total number of offenses in nearly every category was larger in the MDFT group, compared to the CBT group (i.e., drug offenses, discrimination, destruction, traffic offense, aggression). However, the subcategories show that the CBT group is engaged in more severe and subsequently costly offenses.

It is also interesting to note that although the percentage of recovered patients did not significantly differ between the two treatment groups, we did find a (just) significant effect on quality of life in the MDFT group, compared to the CBT group. Although various clinical outcomes found in the study of Hendriks et al. (2011) were in favour of MDFT, there were no significant effects. Instruments like the Youth Self report (YSR; Achenbach and Rescorla, 2001) are validated and widely used instruments for substance abuse treatment. Although according to the user guide of the EQ-5D (Van Reenen et al., 2014), this instrument can be used for adolescents, the EQ-5D is not specifically validated for substance abuse treatment yet, and a recent study suggests a small to moderate significant association between clinical effect measures and quality of life for adolescents with persistent major depression, replications are necessary (Byford, 2013). In this study, quality of life decreased more due to a decrease in pain/discomfort and anxiety/depression. More research is needed to replicate these findings and in general on the usefulness of the EQ-5D in adolescents.

Limitations of the randomized controlled trial are extensively discussed in the paper of Hendriks et al. (2011). A first limitation of the present cost-effectiveness study is the relatively short time-frame of 1 year. As substance abuse treatment may prevent future service use and delinquency, it would be interesting to assess future costs and effects. Secondly, outcomes were mostly self-reported. However, we have no reason to expect a bias as this method was used in both treatment groups. Additionally, it was not possible to include subgroup analyses in our study because of a combina-

tion of small sample size and skewness. As the study of Hendriks et al. (2012) indicated that matching these subgroups to MDFT or CBT may lead to better results (less cannabis use), future cost-effectiveness studies based on these post-hoc analysis should also assess its impact. Thirdly, we only obtained health care costs over three months at 6 and 12 months. These costs were linearly interpolated. However, as the duration of both treatments was 5–6 months, the situation in which the patients were in treatment or not in treatment, was the same during the period of interpolation it seems reasonable to assume that interpolation may not have a significant effect on the results. Fourthly, we interpolated our missing utilities. In most cases a sensitivity analysis is needed to determine the impact of these missing values. However, in this case a complete case analysis would have resulted in almost no power in the analysis. Generally, in most studies, the number of missing values increase in time. However, in the present study the amount of missing values at both baseline and at the end of the study were both low, subsequently adding information in our analysis about the value of the missing values in between. The values in between were therefore estimated by using interpolation. As information on baseline and at the end of the study period was used to estimate these values (in this case utilities), it is believed that the impact of these missing values is low. Fifthly, treatment intensity was not equal between both treatments, as MDFT was much more intensive which may have contributed to the superior effect (quality of life) of MDFT. Finally, although the results suggest that MDFT is more cost-effective than CBT in the Dutch healthcare context where CBT is the standard model of care it may be premature to conclude that these results can be generalized to other settings and contexts.

This is a first comprehensive CEA of MDFT compared to CBT and it demonstrated that by including the costs of delinquency the ICERS were modest. The study provides a first insight into the

impact of including costs beyond the health care perspective and the importance of adopting a more broad perspective. Future studies should adopt a longer time frame, include costs for delinquency and should also be aimed at subgroups to acquire a more detailed picture of the cost-effectiveness of MDFT versus CBT.

Role of funding source

The study was funded by The Netherlands Organization for Health Research and Development (ZONMW).

Contributors

All authors contributed to and approved the final manuscript. VH was also responsible for concept and design of this study.

Conflict of interest

None.

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.

Acknowledgements

We thank Sylvia Cool of the stichting jeugdinterventies in assisting us with the collection of information to determine the unit costs of both treatments.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugalcdep.2016.03.004>.

References

- Achenbach, T.M., Rescorla, L.A., 2001. *Manual for the ASEBA School-age Forms and Profiles University of Vermont. Research Center for Children, Youth, and Families, Burlington, VT.*
- BIVV, Observatorium voor verkeersveiligheid, 2011. *Kerncijfers Verkeersveiligheid 2010, Brussel Vragenlijst Internationaal Onderzoek Selfreport Delictgedrag, [Questionnaire International Study Self-Report Delinquency] 1991, Wetenschappelijk Onderzoek en Documentatie Centrum (WODC), Den Hague.*
- Bouwman, C., de Jong, K., Timman, R., Vlasveld, M., van der Feltz-Cornelis, C.M., Tan, S.S., Hakkaart-van Roijen, L., 2013. *Feasibility, reliability and validity of a questionnaire on health care consumption and productivity loss in patients with a psychiatric disorder (TiC-P).* BMC Health Serv. Res. 13, 217.
- Broman, C.L., Reckase, M.D., Freedman-Doan, C.R., 2006. *The role of parenting in drug use among black, Latino and white adolescents.* J. Ethn. Subst. Abuse 5, 39–50.
- Byford, S., 2013. *The validity and responsiveness of the EQ-5D measure of health-related quality of life in an adolescent population with persistent major depression.* J. Ment. Health 22, 101–110.
- Centraal Bureau voor de Statistiek (CBS), en het Wetenschappelijk Onderzoek- en Documentatiecentrum van het Ministerie van Justitie (WODC), 2012. *Criminaliteit En Rechts-handhaving, Boorn uitgevers, Den Haag.*
- Cheung, K., Oemar, M., Oppe, M., Rabin, R., 2009. *Eq-5D User Guide Basic Information On How To Use EQ-5D.* EuroQol Group.
- Choquet, M., Hassler, C., Morin, D., Falissard, B., Chau, N., 2008. *Perceived parenting styles and tobacco: alcohol and cannabis use among French adolescents: gender and family structure differentials.* Alcohol Alcohol. 43, 73–80.
- Copeland, J., Swift, W., 2009. *Cannabis use disorder: epidemiology and management.* Int. Rev. Psychiatry 21, 96–103.
- Dennis, M., Godley, S.H., Diamond, G., Tims, F.M., Babor, T., Donaldson, J., Liddle, H., Titus, J.C., Kaminer, Y., Webb, C., Hamilton, N., Funk, R., 2004. *The cannabis youth treatment (CYT) study: main findings from two randomized trials.* J. Subst. Abuse Treat. 27, 197–213.
- Elliott, D.S., Huizinga, D., Ageton, S.S., 1985. *Explaining Delinquency and Drug Use* Sage. Publications Beverly Hills, CA.
- Fergusson, D.M., Swain-Campbell, N.R., Horwood, L.J., 2002. *Deviant peer affiliations, crime and substance use: a fixed effects regression analysis.* J. Abnorm. Child Psychol. 30, 419–430.
- Goldstein, P.J., 1985. *The drugs/violence nexus: a tripartite conceptual framework.* J. Drug Issues 39, 143–174.
- Hakkaart-van Roijen, L., Tan, S.S., Bouwmans, C.A.M., 2010. *Handleiding Voor Kostenonderzoek: Methoden En Standaard Kostprijzen Voor Economische Evaluaties in De Gezondheidszorg. College voor zorgverzekeringen, Diemen.*
- Hendriks, V., van der Schee, E., Blanken, P., 2011. *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.* Drug Alcohol Depend. 119, 64–71.
- Hendriks, V., van der Schee, E., Blanken, P., 2012. *Matching adolescents with a cannabis use disorder to multidimensional family therapy or cognitive behavioral therapy: treatment effect moderators in a randomized controlled trial.* Drug Alcohol Depend. 125, 119–126.
- Kristjansson, A.L., Sigfusdottir, I.D., Allegrante, J.P., 2013. *Adolescent substance use and peer use: a multilevel analysis of cross-sectional population data.* Subst. Abuse Treat. Prev. Policy 8, 8–27 (27–597X).
- Liddle, H.A., Rowe, C.L., Dakof, G.A., Ungaro, R.A., Henderson, C.E., 2004. *Early intervention for adolescent substance abuse: pretreatment to posttreatment outcomes of a randomized clinical trial comparing multidimensional family therapy and peer group treatment.* J. Psychoact. Drugs 36, 49–63.
- Liddle, H.A., 2002. *Multidimensional Family Therapy for Adolescent Cannabis Users. Cannabis Youth Treatment (CYT) Series Center for Substance Abuse Treatment Substance Abuse and Mental Health Services Administration, Rockville, MD.*
- Matthews, J.N.S., Altman, D.G., Campbell, M.J., Royston, P., 1990. *Analysis of serial measurements in medical research.* BMJ 300, 230–235.
- Sampl, S., Kadden, R., 2001. *Motivational enhancement therapy and cognitive behavioral therapy for adolescent cannabis users: 5 sessions.* In: Cannabis Youth Treatment (CYT) Series. Center for Substance Abuse Treatment Substance Abuse and Mental Health Services Administration, Rockville, MD.
- Sharma, L., Markon, K.E., Clark, L.E., 2014. *Toward a theory of distinct types of impulsive behaviors: a meta-analysis of self-report and behavioral measures.* Psychol. Bull. 140, 374–408.
- Tanner-Smith, E.E., Wilson, S.J., Lipsey, M.W., 2013. *The comparative effectiveness of outpatient treatment for adolescent substance abuse: a meta-analysis.* J. Subst. Abuse Treat. 44, 145–158.
- Van Reenen, M., Janssen, B., Oppe, M., Kreimeier, S., Greiner, W., 2014. *EQ-5D-Y User Guide: Basic Information On How To Use The EQ-5D-Y Instrument.* Springer, New York.
- Volkow, N.D., Fowler, J.S., Wang, G.J., 2003. *The addicted human brain: insights from imaging studies.* J. Clin. Invest. 111, 1444–1451.
- Webb, C., Scudder, M., Kaminer, Y., Kadden, R., 2016. *The Motivational Enhancement Therapy And Cognitive Behavioral Therapy Supplement: 7 Sessions Of Cognitive Behavioral Therapy For Adolescent Cannabis Users. Cannabis Youth Treatment (CYT) Series. Center for Substance Abuse Treatment Substance Abuse and Mental Health Services Administration, Rockville, MD.*
1991. *Wetenschappelijk Onderzoek En Documentatie Centrum, WODC), Vragenlijst Internationaal Onderzoek Selfreport Delictgedrag [Questionnaire International Study Self-Report Delinquency] WODC. Ministry of Justice, Den Hague.*