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A meta-analysis of the effectiveness of individually oriented Cognitive Behavioral Treatment (CBT) for severe aggressive behavior in adolescents

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This meta-analysis, including six studies (13 effect sizes) and 164 adolescents, examined the effectiveness of individually oriented treatment (which means that the intervention contained at least an individual component, possibly in combination with group and/or family therapy) with CBT-elements for adolescents with severe aggression problems. A large and homogeneous overall effect size was found ($d = 1.139$) indicating consistency across studies. The included studies examined the effect of three interventions, namely, mode deactivation therapy (MDT; four studies), stress-inoculation therapy (1), and the cell-phone program (1). This multilevel analysis demonstrated that only few individually oriented interventions have been developed and evaluated, while four of the included studies used a weak research design. Effective individually tailored interventions for youths with severe aggression problems (who are unsuitable for group treatment) are scant. There may be added value if group interventions are supplemented with more individually tailored evidence-based interventions.

Keywords: anger-management treatment; adolescents; cognitive-behavioral therapy; individual treatment; meta-analysis; RNR-principles

Introduction

Aggression is one of the most frequently occurring behavioral problems in adolescents (Blake & Hamrin, 2007). Aggression is associated with violence, extreme negativism, and oppositional and antisocial behavior. Severe aggressive behaviors can include various behaviors, such as starting rumors and excluding others. Notably, severe aggressive behaviors do not always involve

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physical contact with another person. Verbal aggression, such as bullying, threatening, striking back in anger, and using of strong-arm tactics, can be part of violent antisocial behavior. Youths with severe aggression problems often have other behavioral problems and/or have been arrested or convicted. In these youths, aggression problems are frequently related to various criminogenic factors (Andrews & Bonta, 2010), which are sometimes combined with psychiatric problems (Vreugdenhil, Doreleijers, Vermeiren, Wouters, & Van den Brink, 2004). Adolescents who commit violent crimes have a greater risk of displaying persistent criminal behavior throughout the rest of their lives (Garrido & Morales, 2007), and violent behavior is associated with high societal costs (Cohen & Piquero, 2009).

It is important to introduce effective interventions for youths with severe aggression problems (including violence) in order to reduce the negative impact of aggressive behavior (Loeber, Slot, Van der Laan, & Hoeve, 2008). Group treatment remains one of the most prominent modalities in both residential and outpatient (forensic) treatment of adolescents with severe aggression problems and violent behavior (Garrido & Morales, 2007; Hoogsteder, 2014). Group intervention programs can be effective and are efficient in both time and cost. Although group therapy has several advantages, it may not be effective in every situation. A more individual setting can be more appropriate for adolescents suffering from severe psychiatric disorders, because these adolescents may not be able to handle a group setting. Individual therapy should also be considered if group learning is too threatening for the adolescent and/or aggressive behavior can increase due to deviancy training (Dodge, Dishion, & Lansford, 2006; McGloin, Sullivan, Piquero, & Bacon, 2008; Souverein, Van der Helm, & Stams, 2013). Therefore, there is a need for additional individually oriented interventions for youths with severe aggression problems.

It is recommended that treatment for adolescents with severe aggression problems consists of cognitive behavioral therapeutic (CBT) elements. In fact, a large number of studies examining treatment of (severe) aggression problems has shown that applying CBT elements is effective (e.g. Foolen, Ince, & de Baat, 2012; Garrido & Morales, 2007; Lipsey, 2009; Litschge, Vaughn, & McCrea, 2010; Özabaci, 2011; Rotter & Carr, 2011). Cognitive behavioral therapy is based on the cognitive model: the way we perceive situations influences how we feel. CBT utilizes various techniques to change the clients' cognitive processes and behavior (Beck, 2011). CBT uses psycho-education (e.g. insight-offering questions), imitation learning (demonstrating examples of expected behavior), techniques developed in rational emotive therapy (recognizing cognitive distortions and criminogenic cognitive biases in combination with learning adequate cognitions, see Landenberger & Lipsey, 2005), and problem-solving skills training, for instance by means of role playing (e.g. Blake & Hamrin, 2007; Landenberger & Lipsey, 2005; Lipsey, 2009; Sukholdosky, Kassino, & Gorman, 2004). This article describes a meta-analysis to determine whether

individually oriented cognitive-behavioral interventions for adolescents with severe aggression problems are effective.

Empirical evidence shows that interventions that make use of the risk-need-responsivity-principles (RNR) have a positive impact on reducing severe aggressive behavior (Andrews & Bonta, 2010; Wong, Gordon, & Gu, 2007), especially in high-risk youth (Lipsey, 2009). Non-adherence to the RNR principles may even result in detrimental outcomes (Lowenkamp & Latessa, 2005). The risk principle informs therapists about the level of intensity. High-risk offenders should receive intensive treatment, whereas low-risk offenders should be given minimal or no care (Andrews & Bonta, 2010). The Need Principle refers to the importance of targeting dynamic criminogenic needs (Andrews & Bonta, 2010). The Responsivity Principle can be divided into general responsivity and specific responsivity. General responsivity represents the use of the most effective techniques to change the criminogenic needs (CBT). Specific responsivity means that the intervention should be tailored to the motivation, learning style, specific capabilities, and limitations of the delinquent, while there should be a match between the client and the therapist (Bonta & Andrews, 2007). It can be assumed that part of the target group will be more receptive (more responsive) to individually tailored interventions, because these interventions can more easily meet the specific responsivity principle (Bonta & Andrews, 2007). Meta-analyses of interventions targeting antisocial behavior or (mild) aggression of a broad population (e.g. students, nurses, school-age children, and adults) have shown that interventions with an individual treatment component are generally more effective than only group treatment (DiGiuseppe & Tafrate, 2003; Landenberger & Lipsey, 2005; Lipsey, Landenberger, & Wilson, 2007; McGuire, 2008). However, there is also research showing a positive effect of including group members in treatment, typically resulting in a reduction of aggressive behavior (Lee, Chmelka, & Thompson, 2010; Mager, Harris, & Howard, 2005).

Adding ‘relaxation’ and/or ‘mindfulness’ elements to CBT appears to further contribute positively to the effectiveness of interventions for aggression problems (Deffenbacher, 2011; Kelly, 2007; Novaco, 2001; Pellegrino, 2012; Singh et al., 2007). Relaxation refers to the reduction of stress symptoms through the application of stress management. Mindfulness exercises are also aimed at reducing stress, but are directed at ‘focusing attention’, as well as enhancing one’s consciousness of improving behavior. It has been shown that mindfulness exercises with aggressive youths lead to an improvement in self-regulation and reduction in stress (Himelstein, Hastings, Shapiro, & Heery, 2012).

Negative parent–child interactions increase the risk for developing and for the continuation of aggressive behavior (Compton, Snyder, Schrepferman, Bank, & Shortt, 2003; De Haan, Prinzie, & Deković, 2010; Eichelsheim, 2011; Kawabata, Alink, Tseng, Van IJzendoorn, & Crick, 2011). Interventions that (also) offer family treatment have been shown to be effective for the treatment

of (severe) aggression problems in adolescents (Foolen et al., 2012; Pellegrino, 2012; Weisz, Hawley, & Doss, 2004).

Finally, in determining the effectiveness of an intervention, it is relevant to assess the degree of program integrity, as the effect of an intervention can only be assessed if it is conducted as intended. Interventions that maintain a sufficient degree of program integrity appear to achieve better results (DiGiuseppe & Tafrate, 2003; Foolen et al., 2012). The quality of the study and the degree of independence of the researchers also seem to influence the outcome of research (Hoyle, Harris, & Judd, 2002). For instance, Petrosino and Soydan (2005) demonstrated that effect studies where researchers played a role in the development and/or implementation of the intervention showed substantially better results than those studies where this was not the case. These authors believe that this can be attributed to the fact that the implementation and program integrity are better maintained if researchers also play a role in the execution of the intervention. The present study is a meta-analysis examining whether interventions for adolescents with severe aggression problems are effective if they contain individual elements and apply CBT techniques. It is also examined whether the use of mindfulness, family intervention, and program-integrity influence the magnitude of the effect size. Furthermore, relevant background variables (such as age, gender, ethnic origin, and mental health condition), the quality of the study, and publication characteristics were examined to explore whether these moderators influence effectiveness. Three outcome measures were assessed, namely, externalizing behavior, physical aggression, and verbal aggression.

Method

Selection of studies

Studies were included in the meta-analysis if they met the following criteria: (1) studies (1980 till 2011) had to address the effectiveness of treatments for adolescents with severe aggressive problems, often accompanied with conduct disorder (CD), (2) studies should have examined interventions that were individually oriented, which means that the intervention contained at least an individual component, possibly in combination with group and/or family therapy, (3) treatment had to include CBT-elements (an intervention was considered CBT if it involved anger-management training, skills training, and cognitive restructuring), (4) studies had to provide at least post-test scores and a control group (Treatment As Usual or regular care), (5) the control group should have received group therapy and/or individual treatment with no CBT-elements, (6) study samples had to include adolescents aged 12–18 years, and (7) studies should have provided the necessary data for the calculation of effect sizes. We excluded studies that specifically focused on prevention-based treatments for youth with conduct problems (e.g. Lochman, 1992).

Search strategy

First, we systematically searched the following electronic databases: psychINFO, MEDLINE, ERIC, Picarta, International Bibliography of Social Sciences, Adlib, Sciencedirect, Springerlink, Proquest Dissertation abstracts, and Google Scholar. We used the following keywords in various combinations: aggression treatment, anger-management training, chronic aggression, cognitive-behavior therapy, externalizing behavior in combination with the words adolescents, youth, juvenile, inpatient, incarcerated, and individual. We inspected all the references and citations of the articles we found in this first step. Second, we inspected the reference sections of relevant systematic reviews and meta-analyses in order to find more studies that had not been included yet. Third, we approached several researchers to obtain unpublished studies. The retrieved studies were examined to eliminate any potential duplicates or overlapping data. Potentially relevant meta-analyses were identified and screened for retrieval ($n = 24$; 1815 studies). We also identified 16 published and 15 unpublished studies (not included in any meta-analysis). We retrieved and reexamined the articles to determine their relevance for inclusion. Almost all studies were excluded (because of e.g. only group therapy, different target group, no CBT-elements, mentoring programs, family counseling, and only for children/adults). Ultimately, this search yielded six studies that met the inclusion criteria of our meta-analysis.

Coding the studies

Each study included in this meta-analysis was coded for intervention characteristics, publication characteristics, sample characteristics, the country where the study was conducted, study design characteristics, study quality, and type of setting. No studies could be coded for IQ and integrity-report, because of a lack of information. Each study consisted of a quasi-experimental design with a control group (a study was considered matched if the experimental and comparison group were comparable in at least gender, age, cultural background, and prevalence of conduct disorder). The control groups received (non-established) treatment as usual (i.e. standard care, psychotherapy, therapy with elements of cognitive behavior therapy, or dialectic behavior therapy). All included studies were conducted in the USA. None of the included studies reported that they were based on the principles of the RNR-model.

Categorical moderators were gender (male, female, and unknown), independence of authors (yes or no), published in peer reviewed journal (yes or no), study quality (weak, moderate, or strong; see next paragraph for more information), residential setting (yes or no), delinquent (yes or no), mental disorders (oppositional defiant disorder/ODD, CD or attention deficit hyperactivity disorder/ADHD, PTSS, and mix or none), and parallel treatment (yes or no). Continuous moderators were intervention characteristics: mindfulness

(yes or no), stress-management (yes or no), family intervention (yes or no), group component (yes or no) and average age, sample size, year of publication and impact factor, duration of treatment, proportion of ethnic minorities, proportion of treatment completers for both experimental and control group, and follow-up period.

The methodological quality of the studies was assessed using the Quality Assessment Tool for Quantitative Studies (Thomas, Ciliska, Dobbins, & Micucci, 2004), which classifies study design based on selection bias, study design, confounders, blinding, data collection method, and dropouts as weak, moderate, or strong.

Analysis

Cohen's d was calculated on the basis of mean scores and standard deviations or percentages to index differences between the experimental group and the control group. Cohens's d was adjusted for pre-test group differences in the outcome variables. Having calculated the effect sizes for each separate study on three outcomes (externalizing behavior, physical aggression, and verbal aggression), the overall combined effect size was calculated (Hox, 2002). Outlying effect sizes were identified on the basis of z values larger than 3.3 or smaller than -3.3 ($p < .005$; Tabachnick & Fidell, 2007). Outlying effect sizes were reduced to an effect size that was equal to the largest or smallest effect size within the normal range. An effect size of $d = .20$ was considered small, an effect size of $d = .50$ was considered medium, and an effect size of $.80$ was considered large (Cohen, 1988).

The program MLwiN was used for conducting multilevel analysis, applying a multilevel random effects model for the calculation of combined effect sizes (Hox, 2002; Van den Noortgate & Onghena, 2003). The multilevel random effects model accounts for the hierarchical structure of the data, in which the effect sizes are nested within studies. We conducted a test for heterogeneity of effect sizes to detect variation in effect sizes across individual studies (Rosenthal, 1991). Studies were homogeneous when effect sizes were constant across the different studies. In case of heterogeneity, it is imperative to run a moderator-analysis to explain variances between studies.

Publication bias

It is commonly known that studies with no positive results are less likely to be published than studies with the more appealing significant effects. This type of bias has been designated as the file drawer problem (Rosenthal, 1995). Part of this problem was resolved by the inclusion of non-published studies in the current meta-analytic study. Additionally, we applied one of the conventional methods to examine the possibility of publication bias, the fail-safe number (Rothstein, 2008). The fail-safe number estimates the number of unpublished

studies, presumably reporting null results, needed to reverse the outcomes to non-significance (Lipsey & Wilson, 2001). There should be no file drawer bias if the fail-safe number is larger than $5*k + 10$.

Results

Information about the included studies

Systematic literature searches yielded six studies ($N = 164$) that met the inclusion criteria. The included studies examined the effect of three interventions, namely, mode deactivation therapy (MDT; 4 studies), stress-inoculation therapy (1 study), and the cell-phone program (1 study).

Mode Deactivation Therapy (MDT; Apsche & Ward Bailey, 2004) is designed to treat the complex interplay between trauma, personality factors, and a child's belief system that often leads to conduct problems, such as aggression. Apsche and Ward Bailey (2004) observed that the most aggressive youth are not responsive to the traditional procedures of cognitive restructuring, because of their defensive characteristics and complex problems. Moreover, Young, Klosko and Weishaar (2003) found that personality-disordered clients, especially borderline and narcissistic clients, continue to experience significant emotional distress following treatment. Therefore, a key component of MDT is the deactivation of negative cognitive/affective/motivation/behavioral responses aimed at reducing conduct disordered behaviors and emotional deregulation. MDT is a treatment that combines basic elements from Beck's 'theory of modes' (Beck & Clark, 1996); traditional Cognitive Behavioral Therapy and Schema Therapy (Alford & Beck, 1997); Dialectical Behavior Therapy (Linehan et al., 1999); and Functional Analytic Behavior Therapy (Nezu, Nezu, Friedman, & Haynes, 1997). MDT includes centering, imagery, and relaxation techniques (mindfulness) to facilitate cognition. This is followed by balance training, which teaches youngsters to balance their perception and interpretation of information. MDT focuses on individuals, but also offers an alternative form, namely family MDT. Family MDT uses the same model, with additional group components and meetings with the family.

Stress-inoculation therapy is an individual cognitive behavioral therapy to help adolescents control their stress and anger. In the first part of the treatment, the adolescents are educated about anger and aggression, the causes and consequences, and about alternative methods of control. In the second part adolescents learn a variety of coping skills that are useful in managing stress and aggressive behavior. The treatment helps the adolescent to tackle the anger and stress in an early stage. Finally, adolescents receive practice in applying these coping skills during *exposure* to simulated provocations (Schlichter & Horan, 1981).

The cell-phone program is a cognitive training supplemented with a cell-phone coach reducing recidivism of aggressive behavior. The cell-phone

program is an intervention centered on the idea that behavior drives beliefs. Phone calls are used to monitor behavior and to remind individuals of their goals during the six-week cognitive training. The phone calls also serve as aftercare (1 year) when the training has been completed. Most adolescents receive two phone calls per day; each call consists of three short questions. First, the phone coach asks if the adolescent has followed the goal since the last phone call. Second, the coach asks how much effort the adolescent has put forth to achieve the goal. Finally, the phone coach asks what results the efforts have produced. A prerecorded positive message is played if there has been progress; a prerecorded encouragement message is played if the adolescent needs encouragement. These messages can be recorded by friends and family, and can be regularly updated. Adolescents can always receive immediate face to face care from a professional therapist (Burraston, Cherrington, & Bahr, 2010).

Sample

The sample of the included studies consisted of males (62.5%; rest is not reported) adolescents, between 12 and 18 years of age, who received treatment (in- or out-patient). The average age was 15.8 years, 41% was of African-American origin, 24% American, and 5% Latino (in 30% of the studies no information on the cultural background was provided). Mental disorder was reported by 74.2% ($n = 153$) of the sample; 64% was diagnosed with conduct disorder (CD), 26% with oppositional defiant disorder (ODD), 47% with a post-traumatic stress disorder (PTSD), and in 30% of the cases comorbid diagnoses were assessed. The control groups received treatment as usual, which consisted of individual therapy (no CBT-elements; 2×) or grouptherapy with elements of cognitive-behavioral therapy (4×).

Table 1. Effect sizes of the included studies.

Study ^a	Outcome	<i>N</i>	ES
1	Externalizing	20	1.51
2	Externalizing	39	1.63
4	Externalizing	59	1.18
6	Externalizing	13	2.70
1	Fysical aggression	20	.66
2	Fysical aggression	39	.30
3	Fysical Aggression	18	.13
3	Fysical aggression	18	.53
4	Fysical aggression	59	1.18
5	Fysical aggression	15	3.13
3	Verbal aggression	18	-.06
3	Verbal aggression	18	1.00
5	Verbal aggression	15	1.46

^aSee Table 2 for information of the study number.

Table 1 shows an overview of the relevant study characteristics of the included 6 studies ($N = 164$). The overall effect size for the effectiveness of individual interventions for adolescents with several aggressive problems was $d = 1.139$, $z = 4.538$, $p < .01$, which is a large effect (Cohen, 1988). The individual study effect sizes ranged from $d = -.06$ to $d = 3.13$; (see Table 2). The test for heterogeneity of effect sizes to detect variation in effect sizes across individual studies showed that the effect size was homogeneous ($z = 1.135$, $p > .05$), indicating that the effect sizes were constant across the different studies. Therefore, we did not conduct moderator analyses. The *fail-safe* number of the overall effect size ($k = 13$) was 140, which is larger than 75 ($5 * k + 10$) and indicates that publication bias is unlikely.

Discussion

A multilevel meta-analysis was conducted to examine the effectiveness of individual cognitive behavioral interventions for adolescents with severe aggression problems. A large and homogeneous overall effect size was found, supporting the hypothesis that adolescents with severe aggression problems benefit from an intervention with CBT elements and an individual component (Landenberger & Lipsey, 2005; Sukhodolsky, Kassinove, & Gorman, 2004). Homogeneity indicated that effect sizes were consistent across different studies; (Family) MDT, the cell-phone program, and stress inoculation were equally effective. However, some results of Stress inoculation were less convincing; the intervention reduced verbal and physical aggression on three self-report scales, but there were no effects on the behavior ratings by staff.

The current study demonstrated that no individually tailored behavioral interventions for adolescents describe the extent to which they have incorporated the RNR-principles of effective judicial interventions. Most studies examining the effectiveness of judicial interventions in adolescents are primarily focused on group-based interventions (Garrido & Morales 2007; McGuire, 2008; Sukhodolsky et al., 2004). It also became apparent that few individually tailored interventions have been developed (particularly none that are explicitly based on the RNR model). These findings lead to the question whether the current intervention programs sufficiently serve youths with severe aggression problems. After all, group therapy does not seem appropriate in every situation. A more individually orientated treatment should be considered if adolescents cannot handle treatment in a group or are negatively affected by a deviant peer group (Dishion, McCord, & Poulin, 1999).

This multilevel meta-analysis revealed that little is known about the effectiveness of individually tailored interventions with CBT elements for adolescents with a severe aggression problem. More studies involving individual interventions were found, but these interventions were aimed at other target groups (mild aggression problems, children or adults) or did not comprise CBT elements (e.g. psychotherapy without CBT or mentoring).

Table 2. Overview of the included studies.

	EG+	CG+	N	N	CG	Age	Gender		Migrants	CD	Duration	Follow-up	Residential	Family	Group	Mindfulness	Stress management	Study quality	Independent research
							Male	(%)											
1. Murphy and Siv (2007)	MDT	PT	10	10	10	15.3	100	65%	80%	52	Yes	Yes	Yes	No	No	Yes	No	Weak	Yes
2. Apsche and Bass (2006)	MDT	TAU	19	20	20	16.3	100	80%	917%	48	No	No	Yes	No	No	Yes	No	Moderate	No
3. Schlichter and Horan (1981)	Stress inoculation	TAU	10	8	8	15.5	100	U++	U	10	No	No	Yes	No	No	No	Yes	Weak	Yes
4. Burraston et al. (2010)	Cell-phone	TAU	28	31	31	15.7	11.8	U	U	52	Yes	Yes	Yes	No	Yes	No	No	Moderate	No
5. Apsche, Bass, and Houston (2007)	MDT	TAU	8	7	7	U	100	U	U	20	No	No	No	Yes	Yes	Yes	No	Weak	No
6. Apsche, Bass, and Siv (2006)	MDT	TAU	7	6	6	16.3	100	23%	77%	26	No	No	No	Yes	Yes	Yes	No	Weak	No

+EG = Experimental Group, CG = control group, ++ = Unknown.

Researchers who have conducted meta-analyses on the effect of interventions for children and adolescents (or adolescents and adults) and discussed the effect of an individual component primarily based their conclusions for a large extent on studies conducted with children (e.g. Beck & Fernandez, 1998; Lipman et al., 2006) or adults (e.g. Deffenbacher, Oetting, & DiGiuseppe, 2002; DiGiuseppe & Tafrate, 2003).

The overall effect size was homogeneous; it was therefore not necessary to test whether particular moderators had an influence on the effectiveness of the intervention. The homogeneity may be explained by the fact that only three (partly similar) interventions and a limited number of studies with a small sample size were included, resulting in both lack of variance and lack of statistical power. Therefore, these results do not mean that – on the basis of this meta-analysis – adding a family component (Eichelsheim, 2011; Kawabata et al., 2011) or applying mindfulness (Pellegrino, 2012) will not have a positive effect on individually tailored interventions for youths with severe aggression problems. This needs to be studied further in a study with more power.

Noteworthy is that none of the included studies reported on the level of program integrity. This means there was no clarity about the quality of the programs offered and to what extent relevant components of the interventions was provided.

Although the overall effect size established seemed promising for the specific target group, these findings should be interpreted with caution due to a number of limitations of this meta-analysis. First, it was impossible to test for publication bias in a robust way (by means of a funnel plot) due to a relatively low number of studies (Duval, & Tweedie, 2000a, 2000b; Moreno et al., 2009). Thus, the large overall mean effect size could be an overestimation of the actual effect size. Nevertheless, an attempt was made to include as many studies as possible by including both experimental and quasi-experimental studies, and both published and non-published studies to prevent a possible file-drawer bias. Notably, the fail-safe number of the overall effect size was not indicative of a file-drawer problem.

A second limitation of the current study was that this multilevel analysis was performed using a small sample of studies, including few subjects. Furthermore, four of the included studies used a weak research design according to the Quality Assessment Tool for Quantitative Studies (Thomas et al., 2004). These four studies gave no specific information about selection bias, possible confounders, and missing data. There was no blinding and no information about reliability and validity of the instruments that were used.

Thirdly, there was little diversity within the research group. Most of the studies evaluating effects of MDT aimed at a specific target group, that is, adolescents with severe aggression problems and, for a substantial part, PTSD. A final limitation was that four of the included studies were conducted by dependent researchers. Petrosino and Soydan (2005) demonstrated that dependent researchers report more positive results compared to independent researchers.

There are a number of explanations for this, such as differences in the quality of research (RCT, length of follow-up; Eisner, 2009), degree of program integrity, or methodological bias through conflicts of interest (Gorman & Conde, 2007).

The majority of the current evidence-based judicial intervention programs are group-based. However, this meta-analysis indicates that group interventions that are supplemented with a number of (elements of) individually tailored evidence-based interventions, which meet requirements of the RNR model, and make use of essential CBT elements are effective. Additions such as these may lead to more positive treatment outcomes for aggressive adolescents who do not benefit (enough) from group treatment. Individually tailored evidence-based interventions are more easily tailored to their risk of recidivism, the presence of criminogenic needs and psychiatric problems (trauma-related disorders), and responsivity. The results of this meta-analysis provide some support for the (continued) development of and research into the effectiveness of such individually tailored interventions.

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