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Effect modification of an effective transdiagnostic cognitive behavioral psychotherapy in youths with common mental health problems: Secondary analyses of the randomized mind-my-mind trial

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Abstract
Mind My Mind (MMM) cognitive behavioral therapy (CBT) manualized treatment is effective in the management of common emotional and behavioral mental health problems in youth, yet not all individuals respond satisfactorily to treatment. This study explored potential effect modifiers, i.e., baseline factors associated with a differential treatment effect. We conducted secondary effect modifier analyses with MMM trial data, which involved randomization of 396 youths aged 6–16 years to either MMM CBT treatment (9–13 sessions) or management as usual in local community settings. We examined sociodemographic- (sex, age, family composition, ethnicity, parental education, and income) and clinical variables (mental disorders and duration of mental health problems) as potential effect modifiers of the a) change in parent-rated impact of mental health problems measured by the Strengths and Difficulties Questionnaire (SDQ) or b) response (reduction of ≥1 on SDQ-impact). In intention-to-treat analyses, superior treatment (net) benefits from the MMM intervention were found among youths who met criteria for any mental disorder at baseline (-1.25 [95%CI: -1.67;-0.82]) compared to youths that did not meet diagnostic criteria (-0.22 [95%CI:-1.09;0.65]). Comorbidity vs no comorbidity (-1.84 [95%CI:-2.58;-1.10] vs -0.72 [95%CI:-1.15;-0.29]) and longer duration of untreated mental health problems, i.e., more vs less than 6 months (-1.16 [95%CI:-1.55;-0.78] vs 0.43 [95%CI:-1.01;1.86]) were also associated with superior treatment benefits. The sociodemographic factors were not associated with differential treatment effects in the intention-to-treat analyses. These findings suggest that community-based programs like the MMM are well-suited for youths with substantial mental health problems. Clinical Trials Identifier: NCT03535805
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1. Introduction

Cognitive behavioral therapy (CBT) is the first-line treatment for common mental health problems of mild to moderate severity in youths, including anxiety, depression, and behavioral disorders (National Institute for Health and Clinical Excellence, 2013, 2019; Walter et al., 2020). CBT results in small- to- moderate effect sizes (Weisz et al., 2017), with CBT for anxiety showing moderate to large effect sizes (Weisz et al., 2017), followed by parent training for behavioral disorders (Furlong et al., 2013), and lastly interventions for depression showing smaller effect sizes (Eckshtain et al., 2020). However, not all youths can be expected to benefit equally from CBT. Although CBT aimed at common mental health problems is efficacious on a group level (Hetrick et al., 2016; James et al., 2020; Wuthrich et al., 2023), it is relevant to examine factors associated with differential outcomes across subgroups of patients receiving CBT - i.e., effect modifiers that might be associated with either increased or decreased effectiveness of the intervention. Despite decades of research on psychotherapy for youths, the beneficial effects of these

Glossary

CBT	cognitive behavioral therapy
DAWBA	Development and Well-Being Assessment
MAU	management as usual
MD	mean difference
MMM	Mind My Mind
RD	risk difference
SDQ	Strengths and Difficulties Questionnaire

interventions appear to not have developed to produce increased efficacy over time (Weisz et al., 2019). Hence, furthering our knowledge on effect modiefiers in CBT for youth is important to optimally target and personalize treatment efforts.

Numerous studies have attempted to identify potential effect modifiers related to sociodemographic (e.g., sex, age, ethnicity) and clinical (e.g., severity of psychopathology, comorbidity) factors, yet without consistent findings pointing at clinically meaningful effect modification rendered by specific factors in heterogeneous studies (Dedousis-Wallace et al., 2021; Norris and Kendall, 2021; Ollendick et al., 2008; Walczak et al., 2018).

The current study investigated potential sociodemographic and clinical effect modifiers of a transdiagnostic CBT intervention in a school-based non-university, non-hospital setting, using data from the Mind My Mind (MMM) randomized trial (Jeppesen et al., 2021). The MMM CBT intervention took place in a community and school-based setting and was directed at intervening early in emotional and behavioral problems in youth to reduce the impact of problems in the daily life and to prevent the problems to develop beyond the threshold of requiring specialist child and adolescent mental health services. The MMM trial included youths aged 6–16 years, who were self-/family-referred, assessed and randomized to the MMM transdiagnostic modular CBT for anxiety, depressive symptoms, or behavioral problems (MMM) versus enhanced management as usual (MAU). The main findings from the original effectiveness trial showed that transdiagnostic modular CBT at the municipal level was effective in reducing parent-reported impact of psychopathology compared to the MAU that varied depending on the local resources to meet the needs identified at the initial assessment (Jeppesen et al., 2021).

The transdiagnostic approach to CBT has the potential to help a large and heterogenous group of youths with complex and comorbid problems by adapting the treatment to their current individual needs (Dalgleish et al., 2020). Hence, such personalized treatment should ideally produce similar benefits across different classes of mental health problems and disorders. This study aimed to contribute to the emerging evidence base on the effect and potential modifiers of effects of transdiagnostic CBT in youths.

The specific objectives of the current study was to examine relevant sociodemographic factors (sex, age, family composition, parental mental health problems, ethnicity, parental education, and income) based on the rationale that social adversities are associated with a higher risk of developing mental health problems with a more detrimental course (Kessler et al., 2010; World Health Organization, 2014), and given that age and sex might influence the effects of the specific intervention. We also investigated clinical factors including duration of untreated mental health problems as well as diagnosable mental disorders as potential effect modifiers becausethese factors reflect high levels of persistence and impairment, which are usually regarded as poor prognostic factors (Kisely et al., 2006; Rubio and Correll, 2017).

2. Experimental procedures

2.1. Study design and interventions

Detailed information about the MMM trial, including study design, randomization procedures, the intervention and main findings have been published previously (Jeppesen et al., 2021). In short, the MMM modular CBT intervention consisted of a transdiagnostic manual, in which the youths and their parents/families, together with their therapist, identified a "top problem" within the domains of anxiety, depression, or conduct problems in order to target the problems most important to the families. The therapists could flexibly adapt the sessions using generic or problem-specific modules from the different domains. The MMM study was a pragmatic, open-label, analyst-masked, parallel, 2-arm, randomized superiority trial of MMM vs MAU for help-seeking children and adolescents (Clinical Trials identifier NCT03535805). In the MMM group, transdiagnostic modular CBT psychotherapy comprised 9–13 sessions delivered weekly by psychologists based in educational-psychological services in the local municipalities, followed by a booster-session within 4 weeks. In the MAU group, two additional care visits were organized to strengthen the coordination of usual community-based treatment in the local municipalities. The MMM intervention significantly reduced the child's parent-reported distress and impairment related to mental health problems according to the impact scale of the Strengths and Difficulties Questionnaire, SDQ (Goodman, 1999), in the intention-to-treat population after 18 weeks of treatment, compared to MAU. MMM further showed superior effectiveness for secondary outcomes, including the severity of mental health problems (anxiety, conduct, and depressive symptoms), school attendance, and daily and social functioning, including the six dimensions of the Weiss Functional Impairment Rating Scale - Parent Report of functioning: Family and home life, School and learning, Life skills, Self-Concept, Social activities, and Risk behaviors. The intervention was well-accepted, and 175 (88.8%) of the youths who were allocated to MMM completed the full intervention (i.e., completed 9–13 CBT sessions), whereas the youths in MAU received a mean of 1.6 (SD=0.6) coordinating visits.

2.2. Study population

The potential participants underwent a stage-based step-care recruitment procedure described in detail elsewhere (Wolf et al., 2021). Briefly, 573 parents completed the Strengths and Difficulties Questionnaire (SDQ) prior to randomization, and 75 (13%) rated their child below the SDQ cutoff (range 0–10, cutoff $\geq$1) for inclusion. Among the remaining 498 families, 4 dropped (1%) out, 52 (10%) youths were excluded due to having severe mental illness (prompting a referral to child and adolescent mental health services), and 43 (9%) were excluded due to other a priori criteria (Jeppesen et al., 2021). Additionally 3 individuals dropped out, and thus, 396 youths aged 6–16 years were randomized to either the MMM (n = 197) or MAU in the municipalities (n = 199), see online appendix 1.

2.3. Potential effect modifiers

All the variables listed below are further described in table-form in the prespecified Statistical Analysis Plan (online appendix 2, table A). Below, the different potential effect modifiers are listed and divided into sociodemographic- and clinical factors.

2.4. Sociodemographic factors

Basic dichotomous demographic variables were considered as potential effect modifiers: Sex, age group (6–10 years or 11–16 years), and Danish region of residence. Furthermore, several family factors were considered: parental immigrant status (one or both parents vs. none), number of children in the household (3≥ children vs. <3), level of education (one or both parents vs. neither parent with a bachelor's degree or higher), parents living together vs. apart, and self-reported parental mental health problems vs. no mental health problems.

2.5. Clinical factors

All youths included in the MMM trial were diagnostically assessed solely for research purposes using the Development and Well-Being Assessment (DAWBA) prior to initiating treatment (Goodman et al., 2000). The DAWBA is a comprehensive diagnostic assessment consisting of highly structured questionnaires within all major diagnostic constructs complemented by open-end questions that were completed online by parents. All available information was reviewed and integrated by an expert group of seven senior consultant child and adolescent psychiatrists working in pairs to determine whether the youth fulfilled the criteria for one or more mental disorders according to the Diagnostic and Statistical Manual of Mental Disorder IV/5 (DSM-IV/−5). For the current study, the following diagnostic (non-exclusive) groupings were considered: anxiety disorders, major depressive disorder, behavioral disorders, neurodevelopmental disorders (autism-spectrum disorders and attention-deficit/hyperactivity disorder, any disorder (i.e. any of the above), and comorbidity (fulfilling criteria for ≥2 disorders vs. ≤1 disorder). The following specific disorders within the above broader categories were also considered individually: attention deficit hyperactivity disorder, social anxiety disorder, and disruptive mood dysregulation disorder as defined in DSM-5.

SDQ measures (described in more detail as the outcome measure) of high vs. low impact score (3–10 vs. 0–2) and total score (14–40 vs 0–13) were also considered, along with SDQ-based measures of the duration of parent-reported problems (≥6 months vs. <6 months) and long-term duration of problems (≥12 months vs. <12 months). Finally, the co-defined top problems (anxiety, depression, or behavioral problems) were also individually considered as potential effect modifiers.

2.6. Outcomes - The Strengths and difficulties questionnaire (SDQ)

The outcomes in the current study were based on changes in parent/caregiver-reported impact of mental health problems from baseline to 18 weeks according to the SDQ (Goodman, 1999). The SDQ consists of 25 questions on strengths and difficulties pertaining to everyday life within five subscales: hyperactivity and inattention, conduct problems, emotional problems, peer problems, and prosocial behaviors. The total difficulties scale (range 0–40) sums up the difficulties across the four problem areas (not including pro-social behavior). The 25 questions are followed by an impact supplement enquiring about the distress and impairment of the reported difficulties across five different domains: home life, friendships, classroom learning, leisure activities, and child distress. An impact score ranging from 0 to 10 is then calculated by adding ratings of 'not at all' or 'a little' (score=0), 'a medium amount' (score=1), or 'a great deal' (score=2) of impact within each of the five domains. Thus, a 1-point reduction on the impact scale corresponds to a change from severe to moderate, or from moderate to little or no impact within one of five important aspects of a child's life. Two co-primary outcomes were utilized for the current study: 1) change in SDQ impact score on a continuous scale, and 2) SDQ-response defined as a clinically significant recovery of ≥1 on the SDQ impact scale, which was a priori set as the minimally clinical important difference when designing the MMM study (Jeppesen et al., 2021).

2.7. Ethical considerations

The trial was approved by the Danish Ethics Committee on June 20th, 2017 (Journal number: H-17,011,408). The European Union General Data Protection Regulation protocols were followed. Legal guardians provided written informed consent for all participants. We followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines (Jeppesen et al., 2021).

2.8. Statistical analyses

The statistical analyses (Christensen et al., 2021) and their rationale behind them were described in detail in a statistical analysis plan prior to analyses (online appendix 2). The main analyses were based on the intention-to-treat sample where missing data was handled with simple non-responder imputation (i.e., missing outcome data were conservatively replaced with the baseline score). For sensitivity, we also report findings on the 'as observed' population.

Differences between subgroup means net benefits for the continuous outcome (SDQ-impact change) were estimated from analysis of covariance (ANCOVA) models. We included the outcome value at baseline as a covariate, a main effect for allocated treatment group and the potential effect modifier, as well as the interaction term for the group and the potential effect modifier of interest. We calculated the contrast between subgroups together with the associated 95% confidence interval and the *P*-value, testing the null-hypotheses of no interaction between treatment group and the potential effect modifier (Christensen et al., 2021). For the dichotomous outcome (SDQ-response), a similar approach was used, based on the crude risk difference of the number of responders within the subgroups of participants (Christensen et al., 2021). All analyses were conducted in the statistical program R, version 4.1.2 (R-Core-Team, 2000).

3. Results

3.1. Baseline characteristics

As shown in Table 1, the baseline group characteristics were similar in the MMM and MAU groups. Mean age was 10.3 years (SD 2.37) and 190 (48%) were female. The majority (328; i.e., 82.2%) of the participants had a baseline duration of problems of more than one year according to parent reports. Also, a majority of the participants (317; i.e., 80.1%) fulfilled the criteria for a DAWBA-based diagnosis. Among youths with DAWBA-based mental disorders, 102 (32.2%) fulfilled criteria for two or more diagnoses within different domains.

Table 1 Baseline group characteristics for the Mind My Mind (MMM) and Management as Usual (MAU) groups. Abbreviations: DAWBA=Development and Well Being Assessment; SDQ=Strengths and Difficulties Questionnaire. Unless otherwise indicated, data are expressed as number (percentage) of patients. Percentages have been rounded and may not total 100.

Characteristic	MMM ($n = 197$)	MAU ($n = 199$)	Total ($n = 396$)
Females	90 (45.7)	100 (50.3)	190 (48.0)
Immigration history of parents[†]:			
One or both	15 (7.6)	22 (11.1)	37 (9.4)
None	182 (92.4)	176 (88.9)	358 (90.6)
Age groups:			
11–16 years	88 (44.7)	94 (47.2)	182 (46.0)
6–10 years	109 (55.3)	105 (52.8)	214 (54.0)
Region:			
Vordingborg-Næstved	102 (51.8)	103 (51.8)	205 (51.8)
Holstebro-Helsingør	95 (48.2)	96 (48.2)	191 (48.2)
Top-problem (principal domain of problems):			
Anxiety	114 (57.9)	117 (58.8)	231 (58.3)
Depression	31 (15.7)	33 (16.6)	64 (16.2)
Behavioural dis.	52 (26.4)	49 (24.6)	101 (25.5)
Parents living together			
Yes	126 (64.0)	122 (61.3)	248 (62.6)
No[*]	71 (36.0)	77 (38.7)	148 (37.4)
Children in the household			
≥3 children	63 (32.0)	57 (28.6)	120 (30.3)
<3 children	134 (68.0)	142 (71.4)	276 (69.7)
Parents are academics			
One or both	148 (75.1)	130 (65.3)	278 (70.2)
None	49 (24.9)	69 (34.7)	118 (29.8)
Parental mental health prob.			
Yes	36 (18.3)	65 (32.7)	101 (25.5)
No	161 (81.7)	134 (67.3)	295 (74.5)
Child's DSM-IV/V mental disorders, based on DAWBA:			
Anxiety	102 (51.8)	118 (59.3)	220 (55.6)
Depression	25 (12.7)	33 (16.6)	58 (14.6)
Behavioural disorder	50 (25.4)	47 (23.6)	97 (24.5)
Autism/Attention Deficit Hyperactivity Disorder	25 (12.7)	32 (16.1)	57 (14.4)
Any mental disorder	153 (77.7)	164 (82.4)	317 (80.1)
Comorbidity, two or more	45 (22.8)	57 (28.6)	102 (25.8)
Duration of problems (SDQ, parent-reported):			
≥6 months	183 (92.9)	186 (93.5)	369 (93.2)
<6 months	14 (7.1)	13 (6.5)	27 (6.8)
Long-term duration of problems (SDQ, parent-reported):			
≥12 months	163 (82.7)	165 (82.9)	328 (82.8)
<12 months	34 (17.3)	34 (17.1)	68 (17.2)
The impact of problems in daily life (SDQ-impact, parent-reported)[†]:			
Impact score 3–10	144 (73.1)	151 (76.3)	295 (74.7)
Impact score 0–2	53 (26.9)	47 (23.7)	100 (25.3)
The emotional/behavioral problems (SDQ-total-difficulties, parent-reported)[†]:			
Total score 14–40	132 (67.0)	135 (68.2)	267 (67.6)
Total score 0–13	65 (33.0)	63 (31.8)	128 (32.4)
DSM-IV/−5 diagnosis of specific disorders, based on DAWBA:			
Social anxiety disorder	20 (10.2)	33 (16.6)	53 (13.4)
Disruptive Mood Dysregulation Disorder	12 (6.1)	14 (7.0)	26 (6.6)
Attention Deficit HyperActivity Disorder	18 (9.1)	28 (14.1)	46 (11.6)

[†] Missing data for one participant in the MAU group.
[*] Single parent/other/reconstituted family.

3.2. Potential effect modifiers

None of the sociodemographic variables of interest were statistically significantly associated with differential effects of the MMM treatment outcome in the intention-to-treat population. At a trend level, better treatment effects were found regarding change in SDQ-impact and SDQ-response for youths of parents without an academic educational background (Figs. 1& 2).

Several potential clinical effect modifiers were statistically significantly associated with a differential effect of MMM treatment when considering change in SDQ-impact (continuous outcome) for the intention-to-treat population (Fig. 1). Youths with problems of longer duration and who fulfilled the diagnostic criteria for mental disorders generally had a higher benefit from MMM treatment: Being diagnosed with any DAWBA mental disorder was associated with a more favorable response of MMM intervention versus MAU (difference in mean difference [MD] between subgroups −1.03 [95% CI −1.99 to −0.06]) as well as comorbidity, i.e. being diagnosed with two or more mental disorders vs. one or none (MD difference between subgroups −1.12 [95% CI −1.97 to −0.26]). Specifically, being diagnosed with anxiety disorder versus no anxiety disorder was associated with higher benefits of MMM, whereas this was not statistically significantly the case for depression and conduct disorders. Neurodevelopmental disorders (autism-spectrum disorder or attention deficit hyperactivity disorder combined) were also associated with a more favorable response to MMM intervention (MD difference between subgroups −1.13 [95% CI −2.21 to −0.05]). Higher baseline SDQ impact and SDQ total difficulties scores were not associated with differential outcome, nor did the top-problem defined by the therapists and families in cooperation.

A longer duration of problems (≥6 months vs <6 months) according to the impact supplement of the SDQ was associated with a larger treatment benefit from MMM compared to MAU (MD difference between subgroups −1.59 [95% CI −3.08 to −0.10]). The findings also indicate that MMM and MAU were similarly efficacious in individuals with more recent emergence of problems, albeit with a large confidence interval (0.43 in favor of MAU [95% CI −1.01 to 1.86]).

The findings regarding the second primary outcome, the dichotomous SDQ-response (≥1-point reduction in SDQ-impact score), overall mirrored the directions of the above findings regarding the first, continuous, primary outcome. However, none of the statistically significant interactions described above for the continuous outcome SDQ-impact measure, were significant regarding the dichotomous SDQ-response (Fig. 2).

3.3. As observed population

Finally, to evaluate the robustness of the above-stated findings, we performed sensitivity analyses based on the 'as observed' sample data, i.e., without non-responder imputations, hence evaluating outcomes for 177 youths in the MMM and 166 in the MAU condition (response rates 89.8% and 83.4% respectively). The same overall patterns regarding directionality were found (online appendix 3 & 4), with some additional statistically significant findings: Regarding the social demographic variables, on the SDQ-response measure, children of immigrants (difference in RD between subgroups 0.33 [95% CI 0.08 to 0.58]) and children of parents with non-academic educational backgrounds (difference in RD between subgroups −0.26 [95% CI −0.45 to −0.06]) benefited significantly more from the MMM versus MAU intervention compared to those without these characteristics. Regarding the clinical variables, individuals who fulfilled criteria for attention deficit hyperactivity disorder had more beneficial effects regarding SDQ impact score change (MD difference between subgroups −1.41 [95% CI −2.68 to −0.14]), and behavioral disorders were associated with more beneficial effects regarding SDQ response (difference in risk difference [RD] between subgroups 0.24 [95% CI 0.03 to 0.45]). Furthermore, a substantial differential dropout was seen among youths with depression (9 in MAU vs 2 in MMM), and youths without depression benefitted more from the MMM regarding SDQ response compared to youths with depression (difference in RD between subgroups −0.31 [95% CI −0.58 to −0.04]). In sum the 'as-observed' findings are in line with the overall pattern of stronger beneficial effects for youths with more pronounced or persisting mental health problems. Furthermore, this pattern was robust across the continuous and dichotomous SDQ-impact measures in the 'as-observed' population.

4. Discussion

4.1. Main findings

The current study contributes by its examination of effect modifiers of a transdiagnostic CBT protocol for youth with mental health problems, delivered in a community setting. A majority of participants, consisting of 4 in 5 youths, fulfilled the criteria for DAWBA-based mental disorders, among which 1 in 3 had comorbidity across diagnostic groupings. At a group level, youths who had a longer duration of untreated mental health problems or fulfilled the criteria for one or more mental disorders benefitted more from MMM vs MAU than did youths who had a shorter duration of problems or youths who did not fulfill diagnostic criteria for mental disorders. We did not identify sociodemographic factors that modified the effects of the MMM treatment, except for findings in the sensitivity analyses based on 'as-observed' analyses that indicated superior benefits for children of parents with a history of immigration and of parents with non-academic educational backgrounds.

4.2. Methodological considerations

The identification of effect modifiers in psychotherapy trials faces an important challenge of lacking statistical power to identify interactions between a factor and the treatment. Although the MMM trial included a sizable, randomized population, statistical power was still limited, increasing the risk of type-2 errors. Hence, future meta-analytic approaches are warranted and needed (Christensen et al., 2021). However, such a meta-analytic approach might in turn be challenged by heterogeneity in both baseline and

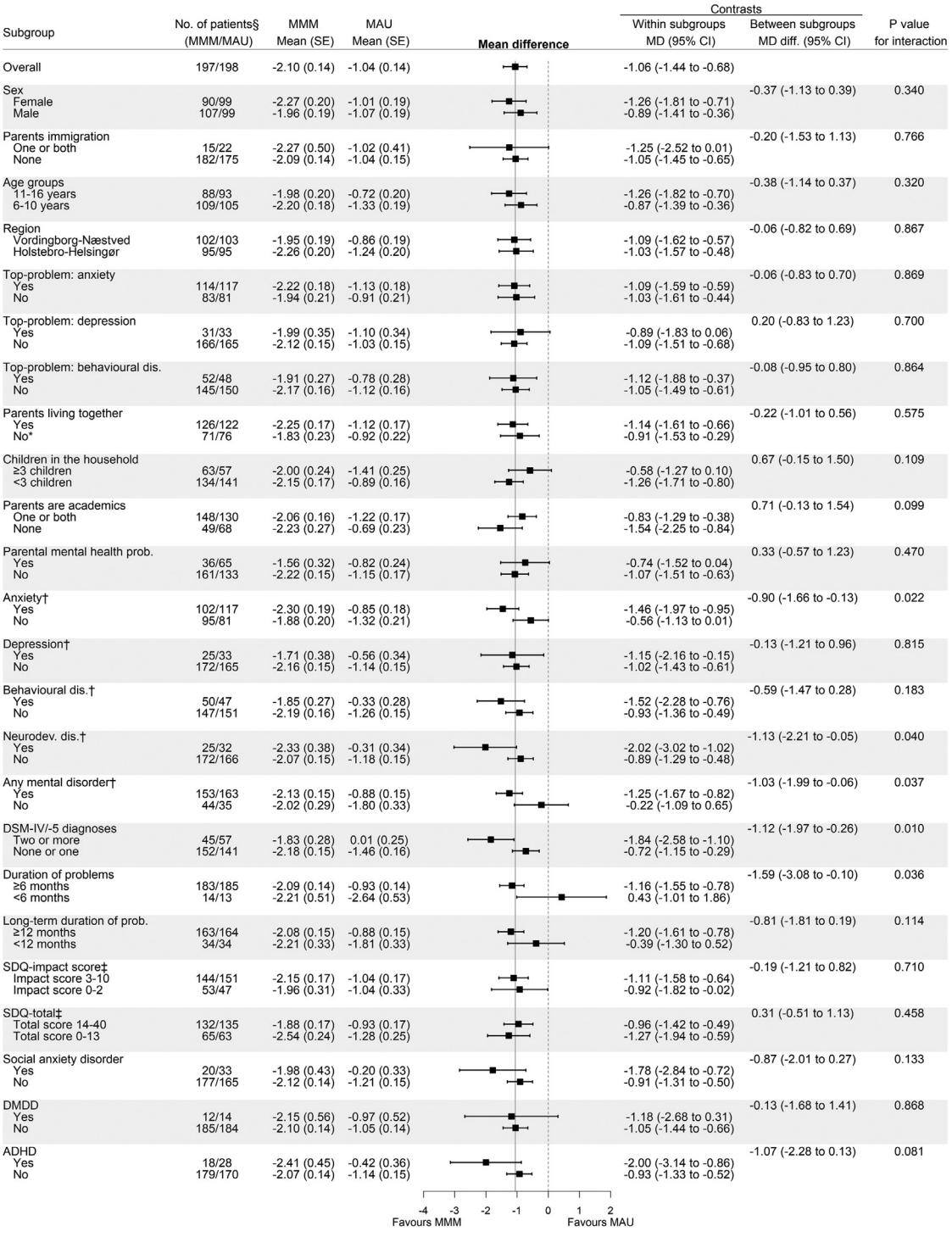

Fig. 1 Forest plot of the treatment effect (MMM vs MAU) across different potential effect modifiers regarding outcome of SDQ impact change. Abbreviations: ADHD=Attention Deficit Hyperactivity Disorder, DMDD=Disruptive Mood Dysregulation Disorder, MD=Mean Difference, MMM=Mind My Mind, MAU=Management as Usual, SDQ=Strengths and Difficulties Questionnaire. The ITT population includes only 198 from the MAU group, as one participant has missing data on SDQ change. *Single parent/other/reconstituted family. †DSM-diagnosis. ‡Parentreported. §Missing data for one participant in the MAU group for Parents immigration.

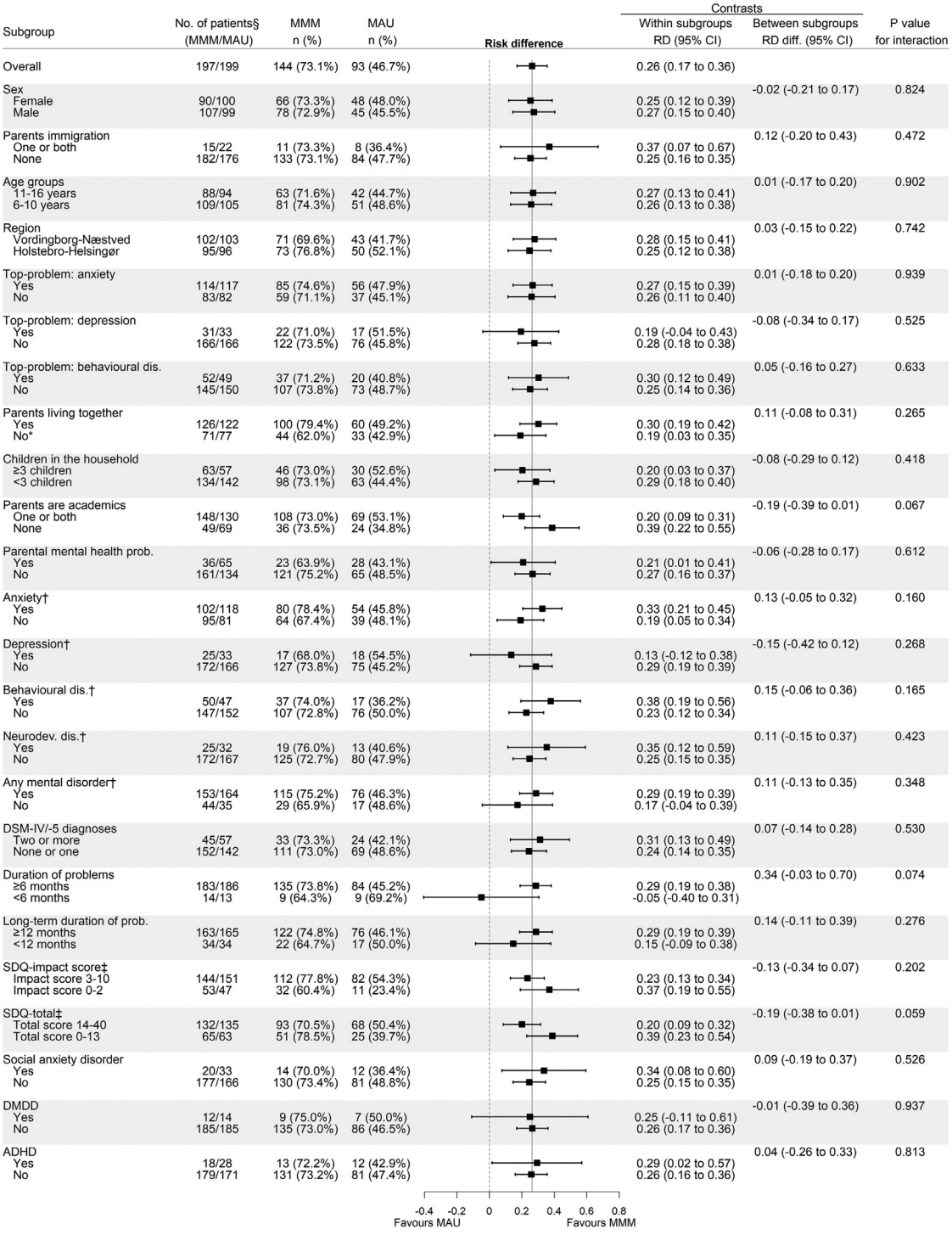

Fig. 2 Forest plot of the treatment effect (MMM vs MAU) across different potential effect modifiers regarding outcome of SDQ impact response. Abbreviations: ADHD=Attention Deficit Hyperactivity Disorder, DMDD=Disruptive Mood Dysregulation Disorder, RD=Risk Difference, MMM=Mind My Mind, MAU=Management as Usual, SDQ=Strengths and Difficulties Questionnaire. *Single parent/other/reconstituted family. †DSM-diagnosis. ‡Parent-reported. §Missing data for one participant in the MAU group for Parents immigration, SDQ-impact score, and SDQtotal.

outcome measures as well as diverse target groups. Conversely, there is also a risk of type-1 errors given that we analyzed numerous (predetermined) potential effect modifiers, increasing the risk of chance findings. Acknowledging the difficult balance between the risk of type-1 and type-2 errors described above, we chose not to adjust for multiple testing, given the inevitably limited statistical power. Altogether, this fact calls for cautious considerations when

discussing the implications of the current work, and we encourage readers to consider our findings as part of a larger evidence-base that is being built about effect modifiers for transdiagnostic CBT in community-based settings for youths. Nonetheless, confidence in our main findings is strengthened by the data indicating that more severe (diagnosable) problems at baseline with a longer duration were associated with a more sizable response to treatment were consistent across several of the clinically relevant baseline variables.

It cannot be ruled out that the finding that treatment effects were greater for youths with more severe psychopathology/comorbidity and longer duration of symptoms might partly be explained by the natural tendency of higher levels of problems to approach a lower level over time, i.e. regression towards the mean (Barnett et al., 2005). However, we statistically adjusted for baseline values of the outcome variables, and higher baseline SDQ-impact and SDQ-total difficulties scores per se were not associated with differential treatment response, suggesting that our findings are not likely to reflect regression to the mean to a strong degree.

Finally, we included potential adverse upbringing conditions, such as parental mental health problems and family upheaval, as potential effect modifiers and found no differential treatment effects for these groups. It would have been valuable to include information on childhood trauma, e.g., abuse, neglect, or domestic violence. However, these data were not available in the current sample. Childhood trauma constitutes an important avenue for future research, given the likely substantial causal role of childhood adversities in the development of substantial mental health problems (Dragioti et al., 2022).

4.3. Implications

While keeping the above limitations in mind, potential lessons of clinical value can be deducted from these secondary analyses of the MMM study. Given that youths with the most severe mental health problems were excluded prior to randomization and referred to child and adolescent mental health services, it may seem counterintuitive that four in five in the randomized population fulfilled DAWBA-based diagnoses. It is worth considering though that anxiety disorders and other emotional disorders as well as behavioural disorders should be addressed in the primary and educational sectors before they can be referred to the child and adolescent mental health services in the Danish system. Further, when considering the exclusion criteria, the individuals with neurodevelopmental disorders who participated in the RCT likely had problems at the less severe end of the spectrum. Importantly, we identified a consistent and robust pattern of superior benefits of MMM compared to MAU for the subgroups of youths with more unfavorable clinical characteristics, perhaps indicating a poorer prognosis prior to the initiation of treatment. However, the minority groups of youths with mental health problems that had more recently emerged according to parent reports (i.e., within the last 6 months) or did not fulfill the criteria for any mental disorder, had no beneficial effects of MMM over MAU. Given that the MMM intervention is relatively high-intensity and costly (Wolf et al., 2022) this implies that an intervention such as the MMM is suitable for youths with long lasting problems or problems that are associated with distress and impact on the everyday life of the child. These findings are in line with prior evidence regarding youths who received community-based mental health services suggesting that high-intensity interventions, characterized by more contact with mental health professionals, are beneficial for a group of high-risk youths with more severe mental health problems, but not for youths with less severe problems (Bonadio and Tompsett, 2018).

The findings from the current study, should also be considered in the context of the development of the intervention and the training of the psychologists who performed the treatment. Although the treatment was carried out in local municipalities by community-based psychologists, the MMM intervention manual, and the training of the local psychologists were developed by specialists with extensive experience from clinical psychology, and the ongoing supervision was provided by psychologists from child and adolescent mental health services. This can certainly be considered a strength of the MMM study in terms of internal and external validity of the findings concerning the implementation of quality CBT for an impaired population of help-seeking youths, yet one should also consider that such relatively high level training is not always readily available.

Most research on effect modifiers of CBT treatments aimed at youths were conducted in trials targeting specific symptom/diagnostic constructs. Meta-analytic findings on parent training programs for children with behavioral disorders suggested that treatment effects regarding the outcome of conduct problems were not hampered by comorbidity (Leijten et al., 2020). Similarly, the overall results of systematic reviews of the effects of CBT for anxiety disorders in youths did not find that comorbidity reduced treatment effects regarding anxiety symptoms (Ollendick et al., 2008; Walczak et al., 2018). It is reassuring that the current study examining a transdiagnostic manual in a school- and community-based context was able to produce benefits for youths with substantial comorbidity and persistence of problems.

Whereas fulfilling diagnostic criteria of emotional, behavioral, and neurodevelopmental disorders were identified as effect modifiers in the current study, this was not the case for the small group of youths with depressive symptoms. These findings coincide well with the meta-analytic evidence finding the highest effect sizes for anxiety disorders, and the lowest effect sizes for depression (Weisz et al., 2017). However, the type of top-problem as defined by the families in cooperation with their therapist (anxiety, behavioral problems, or depressive symptoms) showed no indication of differential outcome, suggesting that the transdiagnostic nature of the modularized CBT intervention in MMM was equally well adapted to the individual needs of the child in all three domains of problems. The therapist and the families had no knowledge of the DAWBA-based diagnoses during the course of treatment. Hence, in sum, the findings support that the transdiagnostic CBT intervention was well-suited for improving the overall impact of mental health problems when the therapy targeted the individual top-problem.

Finally, the studied sociodemographic factors were not associated with differential response to MMM in the main analyses. Hence, similar benefits of the MMM were found

for boys and girls, and the treatment had similar effects for children and adolescents, adding to the notion of MMM as a broadly efficacious, and hence scalable, intervention for school-aged youths. Further, the negative findings regarding some potential adversities (parents not living together or parent reports of own mental health problems) suggest that youths who might more often experience less support in, e.g., completing homework in psychotherapy, did not benefit less from treatment in this study. On the contrary, in the sensitivity analyses of the 'as observed' population there was some indication that youths from potentially vulnerable families (immigrant families and families with lower levels of education) benefitted more from MMM. A prior study of the participants in the MMM study, found that families with these exact characteristics were underrepresented compared to a matched background population (Wolf et al., 2021). Hence these findings underline the importance of increasing efforts to actively recruit and enroll more diverse youths and families including from potentially disadvantaged groups to participate in research in general and in interventions such as MMM and to further study their role as potential treatment effect modifiers (Patriarca et al., 2022).

5. Conclusions and future directions

Future studies examining potential effect modifiers of CBT interventions, might benefit from considering several effect modifiers simultaneously, rather than simply considering potential effect modifiers individually (Mullarkey and Schleider, 2021). Nonetheless, our findings provide the important information that mental health professionals should not be deterred from offering manualized CBT when encountering youths who present with persistent and substantial problems in a community setting - quite to the contrary. Furthermore, the null findings regarding lack of effect modification via sociodemographic characteristics, such as socioeconomic status, indicate that treatment should likely be offered irrespectively of these factors.

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Supplementary materials

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