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Effective Components of Collaborative Care for Depression in Primary Care: An Individual Participant Data Meta-Analysis

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Key Points

Question What are the most effective components of collaborative care for adult patients with depressive symptoms in a primary care setting?

Findings This meta-analysis with individual participant data from 20,046 patients showed the biggest, significant effect size for the *therapeutic treatment strategy* component, with *manual-based psychotherapy* and *involvement of family* as key elements.

Meaning Collaborative care is effective for treating depression in primary care. Implementation should consider therapeutic treatment strategies, including manual-based psychotherapy and involvement of family and friends, as these elements can offer the greatest potential for improving depression and significantly impact the intervention's success.

Abstract

Importance: Collaborative Care is a multicomponent intervention for patients with chronic disease in primary care. Previous meta-analyses have proven the effectiveness of Collaborative Care for depression. However, individual participant data (IPD) is needed to identify which components of the intervention are the principal drivers of this effect.

Objective: To assess which components of collaborative care are the biggest drivers of its effectiveness in reducing symptoms of depression in primary care.

Data Sources: Data were obtained from Medline, Embase, Cochrane Library, PubMed, and PsycInfo, as well as references of relevant systematic reviews. We collected eligible data until March 14, 2024.

Study Selection: Two reviewer assessed for eligibility. We included randomized controlled trials comparing the effect of collaborative care and usual care among adult patients with depression in primary care.

Data Extraction and Synthesis: The study was conducted according to the PRISMA-IPD guidance. We collected IPD on demographics and depression outcomes measured at baseline and follow-ups from the authors of all eligible trials. Employing IPD, linear mixed models with random nested effects were calculated.

Main Outcomes and Measures: Continuous measure of depression severity assessed via validated self-report instruments at 4-6 months and standardized using the instrument's cut-off value for mild depression.

Results: We analyzed 35 datasets with 38 comparisons (N=20,046 participants [57% of all eligible, with minimal differences in baseline characteristics compared to non-retrieved data]).

A significant interaction effect with the biggest effect size was found between the depression outcome and the collaborative care component *Therapeutic Treatment Strategy* (-0.07, P≤.00), indicating that this was the most effective component of the intervention. For all other components we also saw significant interactions but with smaller effect sizes.

Conclusions and Relevance: We identified components of collaborative care most associated with improved effectiveness in reducing depressive symptoms. To optimize treatment effectiveness and resource allocation, a *Therapeutic Treatment Strategy* – such as manual-based psychotherapy or family integration may be prioritized when implementing a collaborative care intervention.

Introduction

Depression is one of the leading contributors to global health-related burdens, affecting individuals across all ages, sexes, and settings.[1,2] Primary care serves as the first contact point and key hub for outpatient depression treatment in many countries[3,4], including the US[5-7], Germany[3,8], and the UK, where up to 90% of mental health issues are managed.[9,10] However, patients often do not receive optimal care[11-13], highlighting the need for improvements in quality and patient-centered, proactive treatment.

A promising approach to achieve this is Collaborative Care[14], a multicomponent complex intervention typically implemented in primary care for depression. The concept involves a case manager who works with the primary care physician, acting as a link between patients and healthcare providers integrating relevant care services and disciplines.[15,16] Collaborative Care has been shown to be significantly more effective for depression than usual care[17] and it is part of several national guidelines[18-20] as well as recommendations by the World Psychiatric Association[21] and the World Health Organization[22]. However, its implementation remains rare, primarily due to limited resources and unclear understanding of its components.[23,24]

Robust insights are therefore needed to identify which components of collaborative care actually drive its effectiveness. While acknowledging that Collaborative Care must be tailored to its specific setting[24], identifying essential components and understanding their mechanisms of action remains critical to facilitate effective adoption in practice.

We used random effects models with individual participant data (IPD) for improved precision to investigate the components driving the effectiveness of Collaborative Care for depression in adult patients in primary care settings 4-6 months post randomization. Previous systematic reviews have assessed components of collaborative care[14,25-27], but they lacked a

comprehensive framework to assess the intervention systematically, are somewhat outdated, and did not integrate IPD, which we used to improve the precision of our estimations. [28]

Methods

The protocol of this IPD meta-analysis was registered in PROSPERO (CRD42024543787). However, the Principal Component Analysis and subsequent analyses represent a deviation from the protocol arising from exploratory analyses. The findings are reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses of Individual Participant Data (eSupplement eTable 1).[29] Secondary outcomes and subgroup analyses, requiring additional methodological considerations, will be addressed in future work.

Data Sources

Searches were conducted in December 2023 in five databases (*MEDLINE, EMBASE, Cochrane Library, PubMed, and PsycINFO)* using the following concepts: *depression*, *collaborative care*, and *RCT* (eSupplement eTable 2). We also reviewed reference lists of related systematic reviews and contacted authors of eligible trials to identify additional studies (published or ongoing). The collection of eligible data was ongoing until May 2024.

Eligibility Criteria

Two reviewers assessed for study eligibility. We found studies to be eligible for inclusion if they fulfilled the following criteria:

1. Adult participants (≥ 18 years) with depression, mixed anxiety and mood disorder, or subthreshold symptoms thereof
2. (Co-) treated in a primary care setting
3. Receiving a collaborative care intervention (defined as multicomponent intervention, at minimum including a multiprofessional approach, and enhanced interprofessional communication)

4. Comparison treatment: (enhanced) usual care
5. Outcome: continuous depression score
6. Study design: (cluster) RCTs

Measuring of the Depression Outcome

All eligible studies assessed depressive symptoms with a validated score, namely the Patient Health Questionnaire-9[30], the Symptom Checklist[31], the Hamilton Depression Rating Scale[32], the Beck Depression Inventory-II[33], the Center for Epidemiologic Studies Depression Scale[34], the Clinical Interview Schedule-Revised[35], or the Patient-Reported Outcomes Measurement Information System – Depression[36]. We standardized the individual depression outcomes within each trial using the score-specific cut-off for mild depression and the pooled standard deviation of the study population at baseline. An overview table with all applied cut-offs, ranges, and references can be found in the supplement (eTable 3). Our outcome of interest was the assessment at 4 to 6 months of follow-up.

Systematic Assessment of the Collaborative Care Interventions' Components

For data extraction, we utilized a framework of collaborative care that assesses the interventions' components and their intensity. The framework is adapted from a widely accepted model of collaborative care[15] that consists of the following components:

- *Multiprofessional approach to patient care* (Involvement of a primary care physician and at least another health professional, e.g., a nurse, psychologist, psychiatrist, pharmacist)
- *Structured management plan* (Evidence-based guidelines and protocols, including pharmacological and non-pharmacological interventions)
- *Scheduled patient follow-ups* (Organized follow-up appointments for interventions, treatment adherence, and symptom monitoring)

- *Enhanced interprofessional communication* (Mechanisms for communication among professionals, e.g. team meetings, case-conferences, etc.)

We added the fifth component *increased patient and family activation* (strategies to empower patients and their families, including coping strategies, relapse prevention plans, involving family in care, and considering community or culture) to reflect recent developments in primary care trials and health policy that emphasize patient and carer involvement and empowerment[37-41]. We extracted all components as sum scores of dichotomous items, with all independent covariates treated as continuous variables. A detailed description of how the Collaborative Care Intensity Framework was applied, including the operationalization of each component, can be found in the appendices (eSupplement eTable 4, eTable 5).

Data Extraction and Preparation

We contacted the authors of all eligible trials via email and asked for the IPD of the following variables: treatment group, age, sex, and baseline and follow-up depression scores. Data were cleaned, converted to a uniform reporting format, and depression outcomes standardized. Before merging into a single dataset, we calculated initial separate analyses of the depression outcome to ensure consistency and completeness with reported original data. Missing data were retained as missing. We supplemented the IPD with information on the intervention's content derived from the full-texts using a standardized Excel sheet. The process of data extraction was piloted to ensure feasibility and afterwards conducted by two independent researchers. Initial interrater reliability was assessed by calculating Cohen's kappa for every intervention component item (average: 0.66). The respective contingency table can be found in the supplement (eTable 6). Afterwards, conflicts were noted, discussed, and resolved by a third reviewer if necessary. We compared data available to us with data unavailable on study population, outcome, intervention intensity, and common effect moderators to check for significant differences. Two independent reviewers checked the quality of the included trials

applying the Cochrane risk-of-bias 2 (RoB 2) tool (eSupplement eTable 7).[42] Further quality checks included depression severity baseline imbalance and missing data (eSupplement eFigure 1).

Statistical Analysis

We conducted a one-stage meta-analysis using linear mixed models (LMMs) with one random intercept for study and an additional random effect for treatment nested within study. We chose this approach to account for between-study heterogeneity in treatment that was otherwise not captured by the fixed effects via a random slope.

Our approach is in line with recommendations by methodology literature.[43] The model we designed contains homoscedastic error variance between studies, as no indication for heteroscedasticity was found while checking graphically (eSupplement eFigure 2).

First, we ran an exploratory LMM with IPD outcome data to empirically test the previously described operationalization of the received collaborative care intensity used for data extraction. The dependent variable was the individual depression outcome after 4-6 months, while the independent variables were the five collaborative care components based on the received intervention according to the modified framework, controlled for the participants' age, sex, and depression severity at baseline. We thus ran a LMM, combining study-level and patient-level covariates. Details on this LMM analysis can be found in the appendices (eSupplement eTable 8, eTable 9).

This exploratory allocation led to suppression effects which we found to stem from pronounced collinearity particularly between two components (Pearson correlation Coef.: 0.61, eSupplement eTable 10), making interpretation difficult. We thus decided to conduct a principal component analysis (PCA) for dimensionality reduction.[44] PCA assigns items to components based on their empirical correlations, ensuring that highly correlated items are grouped together.[45]

We used Parallel Analysis to determine the number of components for PCA, resulting in four components. Details on the PCA and the Parallel Analysis are described in the appendices (eSupplement eTable 11). The resulting allocation of items was then applied to the LMM.

For analyses, we used R packages *psych*[46] and *ImerTest*[47] as well as Stata Version 17.0[48].

Before analysis, we descriptively assessed the course of depression, stratified by treatment group over time using all individual depression outcomes across all available assessment points ranging from month 1 to month 48 after randomization via the R package *ggplot2*[49].

Results

As shown in Figure 1, we found a total of 74 RCTs (35,395 participants) with 78 comparisons to be eligible for our IPD meta-analysis. Based on the recommended[50] funnel plot for these studies, we could not detect evidence for significant asymmetry (Egger's test [SE], −0.09 [0.08]; P =.27) (eSupplement eFigure 3). We collected data from 35 trials (20,273 participants [57.3% of total]) including 38 comparisons. A complete list of included studies can be found in the supplement (eTable 12). In total, 227 individuals (1.1%) were excluded from the analyses due to their age <18 years or because only the depression subgroup of the trial was eligible for our purpose, resulting in 20,046 unique cases.

Baseline characteristics and Comparison between Available and Unavailable Data

Eighteen studies stem from the US, 11 from Europe, 3 from India, 2 from Australia, and 1 from Canada. Most participants (13,709 [69.1%]) were female with a mean age of 50.8 years (SD 16.5; range: 18-95). We did not encounter any important issues related to data accuracy or completeness while checking the IPD. Details on the characteristics of all studies as well as their duration can be found in the supplement (eSupplement eTable 13, eTable 14). We compared available and unavailable studies based on population, design, intervention content, and outcomes, informed by previous reviews, which identified these factors as potential effect

modifiers in collaborative care.[14,27] As shown in Table 1, we did not find any significant differences except for the intervention content (represented as Collaborative Care Intensity Framework). A higher percentage of more intense trials provided IPD.

Course of depression over time

In our data, the treatment group receiving collaborative care showed reduced depression severity compared to the usual care group at each assessment time point persisting for the first 24 months (Figure 2). A corresponding forest plot for the overall effect of Collaborative Care at 4-6 months confirmed this pattern with Collaborative Care having a small significant effect over usual care (standardized mean difference -0.20 [95%CI, -0.26 to -0.15]; I^2= 58.4%) (eSupplement eFigure 4). Information on data availability at each assessment time point can be found in the supplement (eTable 15).

Association between Depression Outcome and Intervention Components

To resolve collinearity observed with the intervention components, we rearranged their extracted items via PCA, which yielded the following four components, also described in more detail in Table 2 and the appendices (eSupplement eTable 16):

- *Patient-Centered Care* (Individualized care respecting patient preferences, needs, values),
- *Therapeutic Treatment Strategy* (Structured therapeutic approaches and support for effective depression management),
- *Measurement-based Care* (Systematic data-driven monitoring and treatment plan adjustments),
- *Integrated Mental Healthcare* (Comprehensive linkage for primary mental health care).

When applying the LMM with random nested effects, a statistically significant association was found between the *therapeutic treatment strategy* component and the standardized depression outcome (-0.07, p-value≤0.00) (Table 3) indicating that this component may be particularly effective in reducing depression severity. The primary items that loaded most heavily on this component were *manual-based psychotherapy*, and *involvement of family or friends* (eSupplement eTable 11). We also saw significant effects for the other components but with smaller effect sizes of -0.04 each, indicating a decrease in depression severity when the component is more intensively implemented.

Discussion

This IPD meta-analysis found that the derived collaborative care component labeled *therapeutic treatment strategy*, including its main items *manual-based psychotherapy* and *involvement of family or friends*, was most effective for reducing depression severity in primary care. While the reported individual effect of this key component may appear modest, it is straightforward to implement and has the potential to benefit a large number of patients in the primary care setting.

Furthermore, we found evidence that the other derived components contribute to the effectiveness of collaborative care to some degree as well, albeit with smaller effects on reducing depression severity. Considering these findings and potentially positive interactions between these components, we believe that all components should be implemented to some extent. However, our findings clearly indicate that the *therapeutic treatment strategy* warrants greater intensity and resource allocation to improve patient depression outcomes.

Comparison with Existing Systematic Reviews

The effectiveness of Collaborative Care for depression in primary care has been well-established in the literature.[17,25]

The question of the most effective components of collaborative care has been addressed already, however findings have so far remained inconclusive.[51,52] Previous studies have employed various methodological approaches, including descriptive or narrative syntheses of systematic reviews[53-56], observational studies[51,57,58], and meta-regressions with aggregated data[25-27,59]. These studies as well as similar studies on the Chronic Care Model[60] have provided valuable groundwork despite facing certain methodological challenges, such as limited causal inference[53] or reliance on pre-selected components[14,25-27]. Our study contributes to this ongoing effort by systematically assessing the components of collaborative care for depression and incorporating IPD for improved model estimations.

A primary finding of our analysis was that *Therapeutic Treatment Strategy* was the most effective component for reducing depression severity, particularly its main items *manual-based psychotherapy* and the *involvement of family and friends*. This aligns with a prior meta-analysis[27], which highlighted psychological interventions as the only significant predictor of improved depression outcomes in collaborative care among 10 pre-selected predictors. Similar findings are reported by a systematic review[55]. Our results support and extend these findings by also identifying the critical role of family and friend involvement - a previously understudied component in collaborative care.[61] This aspect, which may range from psychoeducation to active participation in patient care, has been shown to bring tangible clinical benefits to patients' mental health outcomes in the literature[62], and also appears to enhance the effectiveness of collaborative care interventions.

Implications for Clinicians, Policymakers, and Researchers

Considering that collaborative care components can be implemented with varying intensities, we provide valuable insights into where resources could be more intensively allocated to improve depression outcomes. The most influential component—therapeutic treatment

strategy, with its key items of manual-based psychotherapy and involvement of family or friends—should be prioritized for implementation.

While our findings do not suggest that other components are completely ineffective or should be disregarded, identifying the most influential components is crucial for improving complex interventions such as collaborative care. Practitioners and policymakers should ensure this key component is consistently included in future intervention designs to optimize effectiveness. Additionally, these findings offer an initial basis for engaging health insurers to evaluate coverage decisions. Funding critical components may enhance the impact of collaborative care on depression outcomes and support sustainable implementation in routine practice.

In terms of research implications, it may be helpful to further untangle collaborative care, separating active ingredients from delivery approaches to assess their relative importance. This may require experimental approaches that manipulate specific intervention components, such as factorial experiments (e.g., 2x2, 3x3) [63,64], allowing for testing of combinations and interactions of core components, or adaptive approaches, including Sequential Multiple Assignment Randomized Trials[65], and the Multiphase Optimization Strategy[66]. Coupled with data on real-world implementation[67], which has already been shown to be particularly important in the collaborative care field[68], such an approach may confirm our results and inform the development and broader adoption of structured depression care.

Strengths and Limitations

We believe this study is the most rigorous methodological examination of the most effective collaborative care components to date and the first attempt to synthesize these data also incorporating IPD.[27] We exploratorily employed an a priori, conceptually developed model of

collaborative care, which we then contrasted with an empirically driven, data-derived model offering a complementary perspective.

Our sole focus on primary care adds a new, clear perspective. To address potential biases, we tested for funnel plot asymmetry, finding no significant publication bias, and employed comprehensive literature searches (i.e., major databases, snowballing, author requests) with strict, piloted inclusion criteria to mitigate study selection bias. Using LMMs incorporating random nested effects, alongside controlling for key covariates using IPD, we were able to improve our model precision.[28] Although robust, our findings should be interpreted cautiously, as complete elimination of all biases could not be assured, with mainly four notable limitations remaining.

First, we accessed 57% of IPD across requested RCTs, which is below the recommended recruitment target (i.e. 80% of published data)[50] but comparable to similar meta-analyses[69,70]. While baseline characteristics showed minimal differences between studies with and without IPD, unmeasured factors may still affect our findings, highlighting the need for improved data sharing. Second, while we assessed the interventions systematically, the complexity and inconsistent reporting of collaborative care[17,71,72] posed some challenges in recording details uniformly. Integrating IPD with study-level data was essential for our research, though it reduced variance and impacted statistical power. Thirdly, while our framework captured key components of collaborative care, it did not account for variables such as the physician-patient relationship[73] or the trustworthiness between collaborative care stakeholders[74-76]. These factors, shaped by trust, familiarity, and clear role definitions, may significantly influence intervention outcomes and merit further exploration. Additionally, while we included age, gender, and baseline depression severity as covariates in our analyses, other potentially important factors, such as employment status[77], were not consistently available across studies. Future research with more consistent data availability could provide a more

comprehensive understanding of the factors influencing the effectiveness of collaborative care interventions. Finally, our data did not allow us to fully disentangle the cluster components combining specific intervention content with intensity. Despite this limitation, our analysis provides critical insights into the active ingredients of collaborative care, which have remained unclear until now.[17,59]

Conclusion

To the best of our knowledge, this IPD meta-analysis provides the most rigorous and conclusive insights into the most effective components of collaborative care for depression in primary care that should be considered by implementers of this complex intervention. A strong focus should thus lie on the derived component labeled therapeutic treatment strategy including patient and family involvement (e.g., in the form of psychotherapy, psychological short interventions, involvement of family members, and coping skills training).

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Author Contributions

Ms Schillok had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of Interest Disclosures

The authors declare that they have no competing interests.

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Disclaimers

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Figure Legends

Figure 1. Flowchart

Figure 2. Depression Course over time shown with IPD.

Red line representing Control Group (Usual Care), blue line representing Intervention Group (Collaborative Care). Depression score is standardized with y-axis indicating the number of standard deviations the score is above the cut-off for light depression. X-axis represents months after baseline.

Tables

Table 1. Comparison of Studies providing IPD and those not providing IPD

Variable		Data Available (n = 35)	Data Unavailable (n = 39)	Statistical Test	P Value
Participants, No.		20,046	15,122		
Country: United States, No. (%)		18 (51.4%)	21 (55.3%)	$\chi^2_1 = 0.108$	0.74
Publication date, year					
	Mean (SD)	2010.7 (7.6)	2010.8 (7.9)	$t_{71} = -0.026$	0.98
	Median (range)	2012.0 (1995 - 2022)	2010.5 (1995 - 2022)		
Depression Instrument used					
	PHQ-9, No. (%)	15 (42.9%)	9 (23.7%)	$\chi^2_1 = 3.035$	0.08
Retention Rate, (%)					
	Mean (SD)	82.7 (11.3)	84.5 (8.8)	$t_{72} = -0.749$	0.46
	Median (range)	85.8 (40.8 – 96.3)	84.0 (61.1 – 98.9)		
Population Size					
	Mean (SD)	572.7 (604.8)	397.9 (368.4)	$t_{55.2711} = 1.476$	0.15
	Median (range)	329 (65 – 2486)	345 (74 – 2365)		
Percentage of Female Participants per trial (%)					
	Mean (SD)	69.1 (18.0)	70.0 (19.3)	$t_{71} = -1.021$	0.31
	Median (range)	72.1 (3.4 - 82.9)	71.6 (3.5 - 100)		
Mean Age of Participants, years					
	Mean (SD)	50.8 (16.49)	55.5 (12.11)	$t_{71} = -1.137$	0.26
	Median (range)	48.3 (35.6 - 77.9)	55.3 (37.4 - 77.3)		
Physical Condition Present, No. (%)		11 (31.4%)	8 (21.1%)	$\chi^2_1 = 1.019$	0.31
Intervention Duration					
	Mean (SD)	8.6 (4.4)	8.9 (6.6)	$t_{71} = -0.201$	0.84
	Median (range)	7 (3 - 24)	6 (2 - 36)		
Collaborative Care Intensity Framework Score					
	Mean (SD)	10.8 (2.4)	9 (2.5)	$t_{71} = 3.213$	0.002
	Median (range)	11 (5 - 16)	9 (2 - 14)		
Self-reported significant outcome, dichotomized, No. (%)		29 (82.9%)	29 (76.3%)	$\chi^2_1 = 0.478$	0.49

Abbreviations: No, Number; SD, Standard Deviation; Group comparisons were conducted using t-tests or chi²-tests, with prior variance homogeneity assessed via Levene's tests.

Table 2. Components of Collaborative Care after PCA

Components	Items	Dichotomized Outcome	
Patient-Centered Care	Consideration of Patient Preference	No	Yes
	Involvement of community or cultural background	No	Yes
	Goal setting	No	Yes
	Automatization process for Follow-Up	No	Yes
	Form of Monitoring	By phone	In person
	Supervising Mental Health Specialist	No	Yes
	Regularly scheduled Patient Reviews	No	Yes
	Written documentation / Team Meeting	No	Yes
Therapeutic Treatment Strategy	Manual-based Psychotherapy	No	Yes
	Involvement of Family / Friends	No	Yes
	Organization of treatment team	Centralized	Locally
	Counseling (≤ 8 sessions) [additional to potential medication therapy]	No	Yes
	Routine Follow-Up with Case Manager (every 2 to 4 weeks)	No	Yes
	Disease-related coping strategies	No	Yes
Measurement based Care	Intensive Follow-up with Case Manager (at least every 2 weeks)	No	Yes
	Ad hoc emergency communication	No	Yes
	Shared Medical Record	No	Yes
Integrated Mental Healthcare	Case Manager with Mental Health Background	No	Yes
	Co-Treatment by Mental Health Specialist	No	Yes
	Relapse Prevention Plan	No	Yes

Table 3.

Linear mixed model with nested random effects examining the effect of the four components of collaborative care according to the principal component analysis on depression outcome adjusted for patient-level age, gender, and baseline depression

	Estimate	Std. Error	Df	t value	Pr(>|t|)	
Intercept	-0.02	0.06	37.43	-0.32	0.75	
Patient-Centered Care	-0.04	0.02	18.88	-2.33	0.03	*
Therapeutic Treatment	-0.07	0.02	13.63	-4.08	0.00	***
Measurement based Care	-0.04	0.02	37.24	-2.45	0.02	*
Integrated Mental	-0.04	0.02	20.35	-2.85	0.01	*
Age	0.00	0.00	12908.93	Feb 52	0.01	
Female	0.01	0.02	13502.21	0.34	0.73	
Depression baseline score	0.47	0.01	13144.15	55.88	0.00	

Abbreviations: Std. Error, standard error; Df, Degrees of freedom; "*" indicates a p-value ≤ 0.05; "**" indicates a p-value ≤ 0.01, "***" indicates a p-value ≤ 0.001, all indicating statistical significance; table indicates higher levels of depressive symptoms among females and with increasing age (years). With all other factors remaining constant, the estimated effect implies a decrease in depressive symptoms by 0.07 standard deviations when the therapeutic treatment component is increased by one standard deviation. Other estimates to be interpreted analogously.