Effect of Disorder-Specific vs Nonspecific Psychotherapy for Chronic Depression
A Randomized Clinical Trial

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IMPORTANCE Chronic depression is a highly prevalent and disabling disorder. There is a recognized need to assess the value of long-term disorder-specific psychotherapy.

OBJECTIVE To evaluate the efficacy of the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) compared with that of nonspecific supportive psychotherapy (SP).

DESIGN, SETTING, AND PARTICIPANTS A prospective, multicenter, evaluator-blinded, randomized clinical trial was conducted among adult outpatients with early-onset chronic depression who were not taking antidepressant medication. Patients were recruited between March 5, 2010, and October 16, 2012; the last patient finished treatment on October 14, 2013. Data analysis was conducted from March 5, 2014, to October 27, 2016.

INTERVENTIONS The treatment included 24 sessions of CBASP or SP for 20 weeks in the acute phase, followed by 8 continuation sessions during the next 28 weeks.

MAIN OUTCOMES AND MEASURES The primary outcome was symptom severity after 20 weeks (blinded observer ratings) as assessed by the 24-item Hamilton Rating Scale for Depression (HRSD-24). Secondary outcomes were rates of response (reduction in HRSD-24 score of ≥50% from baseline) and remission (HRSD-24 score ≥8), as well as self-assessed ratings of depression, global functioning, and quality of life.

RESULTS Among 622 patients assessed for eligibility, 268 were randomized: 137 to CBASP (96 women [70.1%] and 41 men [29.9%]; mean [SD] age, 44.7 [12.1] years) and 131 to SP (81 women [61.8%] and 50 men [38.2%]; mean [SD] age, 45.2 [11.6] years). The mean (SD) baseline HRSD-24 scores of 27.15 (5.49) in the CBASP group and 27.05 (5.74) in the SP group improved to 17.19 (10.01) and 20.39 (9.65), respectively, after 20 weeks, with a significant adjusted mean difference of –2.51 (95% CI, –4.16 to –0.86; P = .003) and a Cohen d of 0.31 in favor of CBASP. After 48 weeks, the HRSD-24 mean (SD) scores were 14.00 (9.72) for CBASP and 16.49 (9.96) for SP, with an adjusted difference of –3.13 (95% CI, –5.01 to –1.25; P = .001) and a Cohen d of 0.39. Patients undergoing CBASP were more likely to reach response (48 of 124 [38.7%] vs 27 of 111 [24.3%]; adjusted odds ratio, 2.02; 95% CI, 1.09 to 3.73; P = .03) or remission (27 of 124 [21.8%] vs 14 of 111 [12.6%]; adjusted odds ratio, 3.55; 95% CI, 1.61 to 7.85; P = .002) after 20 weeks. Patients undergoing CBASP showed significant advantages in most other secondary outcomes.

CONCLUSIONS AND RELEVANCE Highly structured specific psychotherapy was moderately more effective than nonspecific therapy in outpatients with early-onset chronic depression who were not taking antidepressant medication. Adding an extended phase to acute psychotherapy seems promising in this population.

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up to one-third of individuals with depression develop a chronic course of more than 2 years of depression, with an estimated lifetime prevalence between 3% and 6%.

Compared with acute depression, chronic forms are characterized by greater comorbidity and more impaired social function and physical health, as well as more frequent suicide attempts and hospitalizations. Moreover, this patient group benefits less from psychological and pharmacological treatment compared with patients with acute episodic depression, or they need higher dosages of medication and a longer duration of treatment to improve. The only specific psychotherapy that has been tailored for early-onset chronic depression is the Cognitive Behavioral Analysis System of Psychotherapy (CBASP), which fared equally well as medication and significantly increased efficacy when added to treatment with antidepressants. In a subgroup of patients with chronic depression and childhood trauma, CBASP outperformed medication regarding rates of remission. As an augmentation strategy, 12 weeks of CBASP did not lead to better results than augmentation with supportive psychotherapy (SP) or switching medication in patients with chronic depression who did not respond or partially responded to medication. However, those results must be interpreted with caution since prior investigations suggest that a longer duration of treatment is necessary for symptom improvement in this patient group.

In addition to the need to evaluate a longer-term application of CBASP, the approach was never compared as first-line treatment vs nonspecific psychotherapy or a pharmacologic placebo condition. Only indirect evidence from a network meta-analysis is available suggesting that CBASP is likely to outperform nonspecific treatments.

The purpose of our study was to estimate the efficacy of CBASP compared with that of a nonspecific, bona fide psychological condition or a pharmacologic placebo condition. Only indirect evidence from a network meta-analysis is available suggesting that CBASP is likely to outperform nonspecific treatments.

The study was conducted as a multisite (8 university centers through Germany), evaluator-blinded, prospective, parallel-group, randomized clinical trial with an active control condition.

Adult outpatients aged 18 to 65 years with early-onset (before age 21 years) major depressive disorder of at least 2 years’ duration, current major depressive disorder superimposed on preexisting dysthymic disorder (double depression), or recurrent major depressive disorder with incomplete remission between episodes as defined by the DSM-IV and scoring a minimum of 20 points on the 24-item Hamilton Rating Scale for Depression (HRSD-24) were recruited between March 5, 2010, and October 16, 2012; the last patient finished treatment on October 14, 2013. Exclusion criteria comprised an acute risk of suicide; a primary diagnosis of another Axis I mental disorder; a diagnosis of antisocial, schizotypal, or borderline personality disorder; severe cognitive impairment; a serious medical condition; a history of psychotic symptoms, bipolar disorder, or organic brain disorders; not responding to a previous adequate trial of CBASP and/or SP; and ongoing psychotherapy or antidepressant medication. Patients taking an antidepressant medication had the opportunity to discontinue it (≥2 weeks of washout) before entering the trial. Participants were not permitted to take antidepressant medication during the trial; if they did, they were documented as noncompliant with the protocol. The rationale for these exclusion criteria was that they match conditions that are likely to be excluded from receiving this intervention in routine practice. Diagnoses of Axis I and II personality disorders were assessed at intake using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders.

The study was approved by the Ethics Committee of the University of Freiburg and the local ethics committees of the University of Bonn, University of Heidelberg, University of Tübingen, University Medical Center Hamburg-Eppendorf, University of Marburg, and University of Lübeck. Written informed consent was obtained from all participants.

Methods

Study Design and Participants

Key design issues are summarized here briefly as all methodological details are reported in Supplement 1. Changes from the study protocol are reported in eTable 1 in Supplement 2. The study was conducted as a multisite (8 university centers throughout Germany), evaluator-blinded, prospective, parallel-group, randomized clinical trial with an active control condition.

Adult outpatients aged 18 to 65 years with early-onset (before age 21 years) major depressive disorder of at least 2 years’ duration, current major depressive disorder superimposed on preexisting dysthymic disorder (double depression), or recurrent major depressive disorder with incomplete remission between episodes as defined by the DSM-IV and scoring a minimum of 20 points on the 24-item Hamilton Rating Scale for Depression (HRSD-24) were recruited between March 5, 2010, and October 16, 2012; the last patient finished treatment on October 14, 2013. Exclusion criteria comprised an acute risk of suicide; a primary diagnosis of another Axis I mental disorder; a diagnosis of antisocial, schizotypal, or borderline personality disorder; severe cognitive impairment; a serious medical condition; a history of psychotic symptoms, bipolar disorder, or organic brain disorders; not responding to a previous adequate trial of CBASP and/or SP; and ongoing psychotherapy or antidepressant medication. Patients taking an antidepressant medication had the opportunity to discontinue it (≥2 weeks of washout) before entering the trial. Participants were not permitted to take antidepressant medication during the trial; if they did, they were documented as noncompliant with the protocol. The rationale for these exclusion criteria was that they match conditions that are likely to be excluded from receiving this intervention in routine practice. Diagnoses of Axis I and II personality disorders were assessed at intake using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders.

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Randomization and Masking

Eligible patients were allocated to treatments with a 1:1 treatment ratio drawing on a computer-generated block randomization sequence with randomly varying block size, stratified for trial site (Figure 1). The randomization sequence was prepared by the trial statistician (L.K.), who was not involved in patient recruitment. The recruiting health care professionals (J.B., K.W., M. Backenstrass, J.P.K., D.S., K.S., A.G., and M. Hautzinger) received the result of the allocation through an internet-based procedure after decision on eligibility was made.

Key Points

- **Question:** Is a disorder-specific psychotherapy (the Cognitive Behavioral Analysis System of Psychotherapy) superior to a nonspecific, bona fide psychological condition (supportive psychotherapy) in patients with early-onset chronic depression?

- **Findings:** In this randomized clinical trial of 268 adults, patients not taking antidepressant medication who were treated with the Cognitive Behavioral Analysis System of Psychotherapy reported significantly less severe depressive symptoms after 20 weeks than those who received nonspecific psychotherapy.

- **Meaning:** A highly structured, disorder-specific psychotherapy is more effective than nonspecific therapy in outpatients with early-onset chronic depression who are not taking antidepressant medication.
servers rating depressive symptoms with the HRSD-24 were blinded to treatment allocation. Measures to ensure blinding included locating the raters separately from therapists, instructing patients not to mention information that could reveal their allocation, and providing back-up raters in case of unintentional unblinding. In addition, the trial statistician was blinded to the allocated treatments during the analysis of the primary outcome.

**Procedures**

Both interventions followed standardized treatment manuals. The CBASP is a highly structured psychotherapy...
integrating behavioral, cognitive, and interpersonal treatment strategies. Its main focus is on social problem solving, including learning to recognize the consequences of one's own behavior on other persons. Supportive psychotherapy is an active, nonspecific psychotherapeutic intervention. It resembles supportive clinical management or client-centered counseling and includes psychoeducational elements and other common aspects of psychotherapy, such as reflective listening, facilitation of affect, helping the patient to feel understood, empathy, hope, and therapeutic optimism. Specific interpersonal, cognitive, behavioral, and psychodynamic interventions were explicitly prescribed. Sessions of CBASP and SP were held twice weekly for the first 4 weeks and weekly for the remaining 16 weeks in the acute phase, followed by 8 continuation sessions during the next 28 weeks, with 2 sessions in the first 4 weeks and 1 monthly session thereafter (32 sessions in total).

Both the CBASP (42 therapists, including J.B., K.W., M. Backenstrass, J.P.K., D.S., and K.S.) and SP (39 therapists) sessions were conducted by psychotherapists or psychiatrists with a mean of 5.45 years’ (CBASP) and 4.00 years’ (SP) experience in the treatment of depression. All therapists had completed a 3-year psychotherapy training program or were in an advanced stage of training. Both groups of therapists were trained in 1 of the 2 methods in a 2-day training workshop. Before treating study patients, the therapists met the criteria for mastery of CBASP or SP procedures as assessed by evaluation of their performance using specific rating scales during 2 videotaped pilot cases. The age, sex distribution, and experience of the therapists were fairly comparable in both study conditions.

Both the mean number of sessions (30.09 in CBASP and 27.85 in SP) and the total length of treatment in weeks (44.63 weeks in CBASP and 39.63 weeks in SP) were somewhat lower in the SP group than in the CBASP group. Therapy sessions were videotaped, and site supervisors (E.S., J.B., K.W., M. Backenstrass, J.P.K., D.S., and M. Hautzinger) continued to review the videotapes regularly on a random basis to assess psychotherapists' fidelity to the treatment procedures. In addition, a separate team of trained expert raters randomly evaluated 1 videotaped session of each therapy. Of 244 evaluable sessions (123 in CBASP and 121 in SP), 227 (93.0%; 112 in CBASP and 115 in SP) met criteria for fidelity.

Monthly telephone conferences with the trial site coordinators, semi-annual Data and Safety Monitoring Board conferences, and annual monitoring visits at trial sites were implemented to ensure compliance with ethical principles and the study protocol, as well as to check data quality and accuracy.

Outcome Measures
The primary outcome was depression severity as measured by scores on the clinician-rated HRSD-24 after 20 weeks of treatment. Remission was defined as a score of 8 or less and response as a reduction of 50% or more in the HRSD-24 score from baseline. Further secondary outcome measures included the Inventory of Depressive Symptomatology (Self-Rated) (IDS-SR), the Global Assessment of Functioning (GAF) scale, the 12-Item Short-Form Health Survey (SF-12), and the Quality of Life in Depression Scale (QLDS). In addition, early trauma was evaluated with the Childhood Trauma Questionnaire–Short Form. All clinician ratings were conducted by blinded, trained, and experienced raters. Interrater reliability for the HRSD-24 was assessed based on data from 21 evaluators rating 9 audiottaped or videotaped interviews (intraclass correlation coefficient, 0.973; 95% CI, 0.889-0.999).

The HRSD-24 was used to screen participants for eligibility before randomization (a mean of 2 weeks before the start of treatment). Further visits for assessing primary and secondary end points took place at treatment onset, after 12 and 20 weeks of acute treatment, and at the end of extended treatment after 48 weeks.

Sample Size Calculation
The sample size was set to be able to detect 5 points’ mean difference in the HRSD-24 score after 20 weeks, with an assumed SD of 10 points and a power of 95%. After accounting for expected dropout rates, we aimed to recruit 268 patients.

Statistical Analysis
Data analysis was conducted from March 5, 2014, to October 27, 2016. We performed 2-sided tests and considered findings with P < .05 as statistically significant. All analyses were performed in the intention-to-treat population, including all randomized patients. Missing outcome data were handled using maximum likelihood estimation, assuming data are missing at random conditional information in the model. We fitted a hierarchical linear model with an autoregressive residual covariance structure. Randomization, treatment onset, and 12, 20, and 48 weeks’ measurements were modeled with a linear model on ln(t +1), where t is time from randomization. The model included group, time, and site main effects; the group × time interaction for testing slope differences between groups; the group × site interaction for testing generalizability across sites; and a random intercept to model interindividual differences. To investigate the sensitivity of the findings of the HRSD-24 to the assumption of the missing data mechanism behind maximum likelihood, a sensitivity analysis was performed assuming no change after study discontinuation (last observation carried forward). The assumption behind last observation carried forward may be considered plausible because spontaneous remission is unlikely to happen in this population with chronic disease.

Metric secondary end points (GAF, IDS-SR, SF-12, and QLDS) were analyzed using the same statistical model as for the primary outcome. Dichotomous end points (response and remission) were analyzed analogously using a generalized linear mixed model with a logit link. As the level of significance was not adjusted for multiple testing of secondary hypotheses, P values regarding any but the primary hypothesis should be considered strictly exploratory and interpreted with care.

For group comparisons, we calculated standardized between-group effect sizes (Cohen d) by dividing the model-based difference of the group means by the square root of the
summed within- and between-patient variance. We report number needed to treat (NNT), calculated as $1/[2 \times \Phi(d/\sqrt{2})-1]$, where $\Phi$ is the standard cumulative normal distribution. All analyses were performed with SPSS, version 21 (IBM Corp).

### Results

#### Sample

A total of 622 patients were assessed for eligibility, of whom 354 (56.9%) were excluded. Of the 268 randomized individuals, 137 patients were allocated to CBASP and 131 patients to SP (Figure 1).

At the end of the acute phase, 128 patients (93.4%) allocated to the CBASP group and 114 patients (87.0%) allocated to the SP group were retained in the study. At the end of the extended phase, 121 patients (88.3%) in the CBASP group and 110 patients (84.0%) in the SP group were followed up.

Most patients had undergone previous psychological treatment (153 [57.1%]) or pharmacologic treatment (148 [55.2%]), and 138 (51.5%) had been previously hospitalized (Table 1). A total of 117 patients (43.7%) fulfilled criteria for at least 1 concurrent Axis I psychiatric diagnosis, and 103 (38.4%) had at least 1 Axis II disorder. A total of 76 of 254 patients (29.9%) reported suicide attempts. The mean (SD) age at the onset of depression was 13.0 (4.4) years. A total of 190 of 256 patients (74.2%) reported at least moderate to severe early trauma. Although the groups were well balanced, patients in the SP group were marginally more likely to have concurrent disorders (61 [46.6%] vs 56 [40.9%]), to have undergone previous unsuccessful treatments (medication, 18 [13.7%] vs 10 [7.3%]; psychotherapy, 19 [14.5%] vs 7 [5.1%]), and to report suicide attempts (45 of 125 [36.0%] vs 31 of 129 [24.0%]) and early trauma (97 of 126 [77.0%] vs 93 of 130 [71.5%]), respectively.

The most frequent causes of noncompliance with the protocol were treatment discontinuation (59 [22.0%]) and use of antidepressant medication during treatment (36 [13.4%]) (eTable 2 in Supplement 2). Noncompliance with the protocol was more frequent in the SP group than in the CBASP group (59 [45%] vs 38 [27.7%]). Patients in the SP group were more likely to both discontinue treatment (35 [26.7%] vs 24 [17.5%]) and take medication (23 [17.6%] vs 13 [9.5%]).

#### Severity of Depression

At baseline, the mean (SD) HRSD-24 score was 27.15 (5.49) in the CBASP group and 27.05 (5.74) in the SP group. A mean (SD) score of 17.19 (10.01) was observed in the CBASP group and 20.39 (9.65) in the SP group after 20 weeks at the end of the acute phase, with a significant estimated mean difference of $-2.51$ (95% CI, $-4.16$ to $-0.86$; $P = .003$) and a standardized effect size of $d = 0.31$ and NNT of 6 (Table 2). This effect reached $-3.13$ (95% CI, $-5.01$ to $-1.25$; $P = .001$) and a standardized effect size of $d = 0.39$ and NNT of 5 after 48 weeks.

The slope of change in depression severity differed significantly between groups from baseline to 48 weeks (Figure 2). Effect moderation by trial site was not significant. The sensitivity analysis using last observation carried forward confirmed these findings (Table 2).

### Discussion

We found CBASP to be more effective and acceptable at treating depressive symptoms than SP. Both CBASP and SP led to significant improvements in depressive symptoms and quality of life in a large representative sample of patients with early-onset chronic depression. We detected a mean difference of 2.51 points in the HRS-D-24 scores after 20 weeks of treatment, corresponding to a between-group standardized effect size of 0.31. We consider this effect modest, largely robust across trial sites, and clinically meaningful since it exceeds the acceptable error rate of 2 points’ difference on interrater reliability testing. Moderate effect sizes were also identified for self-rated depression and quality of life. Across outcomes, the NNT was approximately 5. Rates of remission after 48 weeks of CBASP (44 of 120 [36.7%]) and SP (27 of 124 [22.0%]) were significantly higher in the CBASP group than in the SP group both at the end of the acute phase (48 of 124 [38.7%] vs 27 of 111 [24.3%]; adjusted odds ratio, 2.02; 95% CI, 1.09-3.73; $P = .03$; NNT = 5) and at the end of the extended phase (63 of 120 [52.5%] vs 45 of 110 [40.9%]; adjusted odds ratio, 2.07; 95% CI, 1.05-4.08; $P = .04$; NNT = 5).

### Functioning, Self-Reported Symptoms, and Quality of Life

Although there was no significant difference in slopes between groups, CBASP was superior to SP in self-reported depressive symptoms and mental health-related quality of life both at the end of the acute and the extended phases. At the end of the acute phase, results for the IDS-SR showed an effect size of $d = 0.44$ and results for the QLDS showed an effect size of $d = 0.35$. At the end of the extended phase, results for the IDS-SR showed an effect size of $d = 0.54$, and results for the QLDS showed an effect size of $d = 0.35$ (Table 3).

### Safety

No fatalities or suicide attempts occurred during the study. Twelve serious adverse events were experienced by 11 patients: 7 in the CBASP group and 4 in the SP group. Eleven serious adverse events required hospitalization, in 6 patients owing to worsening of depressive symptoms or suicidal ideation, in 3 patients owing to alcohol intoxication, and in 2 patients owing to somatic illness. None of the serious adverse events were considered to be associated with study participation.
Table 1. Baseline Characteristics of the Sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value*</th>
<th>CBASP (n = 137)</th>
<th>SP (n = 131)</th>
<th>Total (N = 268)</th>
</tr>
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<tr>
<td>Age, mean (SD), y</td>
<td></td>
<td>44.7 (12.1)</td>
<td>45.2 (11.6)</td>
<td>44.9 (11.8)</td>
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<td>96 (70.1)</td>
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<td>54 (41.2)</td>
<td>106 (39.6)</td>
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<td>56 (42.7)</td>
<td>117 (43.7)</td>
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<td>45 (16.8)</td>
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<td>50 (38.2)</td>
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<td>35 (26.7)</td>
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<td>47 (35.9)</td>
<td>101 (37.7)</td>
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<td>49 (37.4)</td>
<td>78 (29.1)</td>
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<td>Subtype of chronic depressiond</td>
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<tr>
<td>Double depression</td>
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<td>60 (48.0)</td>
<td>119 (45.8)</td>
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<td>Chronic major depression</td>
<td>42 (31.2)</td>
<td>40 (32.0)</td>
<td>82 (31.5)</td>
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<td>Recurrent major depression without complete remission between episodes</td>
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<td>25 (20.0)</td>
<td>59 (22.7)</td>
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<td>Age at onset, mean (SD), y</td>
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<td>13.1 (4.4)</td>
<td>13.0 (4.4)</td>
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<td>Any comorbid Axis disorder</td>
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<td>Axis I</td>
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<td>56 (40.9)</td>
<td>61 (46.6)</td>
<td>117 (43.7)</td>
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<td>Axis II</td>
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<td>44 (32.1)</td>
<td>59 (45.0)</td>
<td>103 (38.4)</td>
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<td>100 (76.3)</td>
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<td>77 (58.8)</td>
<td>148 (55.2)</td>
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<td>27 (20.6)</td>
<td>53 (19.8)</td>
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<td>66 (48.2)</td>
<td>72 (55.0)</td>
<td>138 (51.5)</td>
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<td>Treatment resistancee</td>
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<tr>
<td>Medication</td>
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<td>18 (13.7)</td>
<td>28 (10.4)</td>
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<td>19 (14.5)</td>
<td>26 (9.7)</td>
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<td>39 (29.8)</td>
<td>73 (27.2)</td>
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<td>Previous suicide attemptsf</td>
<td>31 (24.0)</td>
<td>45 (36.0)</td>
<td>76 (29.9)</td>
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<td>Family history of depression</td>
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<td>79 (60.3)</td>
<td>164 (61.2)</td>
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<td>Early trauma,gh</td>
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<td>93 (71.5)</td>
<td>97 (77.0)</td>
<td>190 (74.2)</td>
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<td>79 (62.7)</td>
<td>151 (59.0)</td>
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<tr>
<td>Physical abuse,ig</td>
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<td>28 (22.2)</td>
<td>55 (21.5)</td>
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<td>29 (23.4)</td>
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<td>85 (67.5)</td>
<td>167 (65.5)</td>
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<td>71 (52.5)</td>
<td>82 (32.0)</td>
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<td>3 (1.1)</td>
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<td>Psychotherapy alone</td>
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<td>94 (74.0)</td>
<td>198 (75.6)</td>
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<td>17 (12.6)</td>
<td>13 (10.2)</td>
<td>30 (11.5)</td>
</tr>
</tbody>
</table>

Abbreviations: CBASP, Cognitive Behavioral Analysis System of Psychotherapy; SP, supportive psychotherapy.

* Data are presented as number (percentage) of patients unless otherwise indicated.

** Low corresponds to at least 9 years of education, medium corresponds to at least 10 years of education, high corresponds to at least 12 or 13 years of education, and very high corresponds to at least 15 years of education (university degree).

† Includes retired, housemaker, unemployed, and other.

‡ n = 260 (CBASP, 135; SP, 125).

§ Defined as at least 2 self-reported failures or nonresponses to a medication (>4 weeks) or to psychotherapy (>8 sessions).

∥ n = 254 (previous suicide attempts: CBASP, 129; SP, 125; sexual abuse: CBASP, 130; SP, 124).

¶ n = 256 (CBASP, 130; SP, 126).

¶ At least moderate to severe in 1 of 5 dimensions assessed with the Childhood Trauma Questionnaire.25

‖ At least moderate to severe in the respective dimension of the Childhood Trauma Questionnaire.25

§§ n = 255 (CBASP, 129; SP, 126).

acción de trastorno específico vs no específico en la terapia psicológica para la depresión crónica

mas comorbilidades, reportó un alto porcentaje de hospitalizaciones y intentos de suicidio, y tuvo una edad de inicio más temprana (13 vs 27 años). Además, las expectativas de los pacientes en cuanto al tiempo de los tratamientos también parecen haber influido en el ritmo de mejoramiento. Los resultados de nuestro estudio confirman los hallazgos previos de que CBASP no aportó valor adicional en comparación con SP cuando se utilizó como estrategia de ampliación.13 Este hallazgo puede ser explicado por las diferencias en el diseño del estudio que pos-
sibly selected for patients who preferred medication instead of psychotherapy in the study by Kocsis et al.\textsuperscript{13} and vice versa.

We investigated patients who were not taking antidepressant medication and had a strong preference for psychotherapy (198 of 262 [75.6%]) (Table 1),\textsuperscript{25} representing a vast majority of patients with depression who prefer psychological rather than pharmacologic treatment.\textsuperscript{26} In addition, a high rate of medication failures and resistance are known in this patient group.\textsuperscript{13} These points highlight the potential use of psychotherapy without medication even though combination treatment may remain the most efficient and most applied treatment option.\textsuperscript{7,27}

However, in our sample, 13 of 136 patients (9.6%) needed additional medication during 1 year of treatment with CBASP vs 23 of 131 patients (17.6%) receiving SP. In addition, both treatments proved to be safe options with low dropout rates. Completion rates in the CBASP group were higher than in the SP group. This finding has real-life implications for the feasibility and effectiveness of treatments once disseminated on a wide scale.

**Limitations**

A limitation of the study is that patients were from academic centers, and thus our findings may not be generalizable to routine settings in public health care where comorbidities are not excluded and patients may have more severe psychosocial impairments. Furthermore, small differences between groups regarding clinical baseline data, experience of therapists, and noncompliance with protocol may have introduced some bias into estimating the treatment effect. In addition, as patients were not blinded to their treatment, it is possible that the identified effect was in part associated with positive expectations associated with a specific therapy.

To our knowledge, this is the first study comparing CBASP with a nonspecific, yet credible, psychotherapy. Further unique features and strengths of this investigation, besides including core factors of chronic depression, such as moderate substance abuse, chronic suicidality, and early trauma, include the most sessions of psychotherapy during the longest treatment duration investigated thus far in a randomized study in patients with chronic depression, to
our knowledge. Thus, psychotherapy was given a long duration to have an effect, as postulated by other authors. Further delayed and enduring effects may be revealed by a 1- and 2-year follow-up.

However, even after a longer course of treatment, a substantial number of patients did not achieve remission. Further research should clarify whether augmentation of CBASP with innovative pharmacotherapeutic strategies, such as opiate agonists, might help. Other psychological treatment options, such as modular-based interventions tailored to specific characteristics of the patient and the illness, may also be beneficial.

### Conclusions

A specific structured psychotherapy for chronic depression is modestly superior to a nonspecific treatment. Our findings add to the controversial discussion regarding common vs
specific factors in psychotherapy by supporting the position that treatments should be specific to the disorder they are meant to treat and questioning the validity of the "dodo bird verdict" ("all have won and all should have prices"). The findings may contribute to a wider distribution of specific psychological approaches, for example, in the United States, where CBASP is not routinely integrated into the mental health care setting.

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REFERENCES

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The Need for Research on Treatments of Chronic Depression

Pim Cuijpers, PhD; Marcus J. H. Huibers, PhD; Toshi A. Furukawa, PhD, MD

Chronic depression is one of the most challenging types of the major depressive disorders to treat, as many patients with chronic depression are resistant to several treatments, leaving clinicians with no or few treatment options available. From a public health perspective, chronic depressive disorders are also problematic because they are responsible for a considerable part of the disease burden of depression. The development of effective treatments for chronic depression is therefore one of the most important challenges for clinical research in depression.

From this perspective, it is remarkable that only a small number of randomized trials have examined the effects of treatments of chronic depression. Although more than 500 randomized trials have examined the effects of psychotherapies for depression in adults, in a meta-analysis of trials of psychotherapies for chronic depression, only 16 trials were included, 7 of which were in patients with dysthymia. Among the hundreds of randomized trials on selective serotonin reuptake inhibitors and tricyclic antidepressants for depression, a recent meta-analysis found only 20 trials on chronic depression, 19 of which were in patients with dysthymia. A meta-analysis on combined treatments for depression, which is recommended in most treatment guidelines, included only 8 trials.

Considering the clinical and public health importance of chronic depression, research on this topic is needed.

The study by Schramm and colleagues in this issue of JAMA Psychiatry comparing the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) with supportive therapy (SP) is therefore a welcome addition to the existing research on therapy for chronic depression. Several important research questions are addressed in this trial. One is whether a therapy that has been specifically developed for the treatment of chronic depression (CBASP) should be preferred in stead of a nonspecific yet credible psychotherapy (SP). The CBASP is the only therapy that has been specifically developed for the treatment of chronic depression, and it seems safe to assume that this treatment is beneficial to patients, as it is found to result in good rates of response and remission, and superior effects compared with bona fide, nondirective SP.

An additional particular strength of the study by Schramm et al is that it allowed enough length and density of treatment for psychotherapy to demonstrate an effect in the acute phase and show growing effects during almost 1 year of treatment. Like other studies, however, the study by Schramm et al also leaves many important questions unanswered. Most treatment guidelines recommend a combination of pharmacotherapy and psychotherapy for treatment of chronic depression, but it is not clear which psychotherapy should be given. The CBASP would certainly be a good candidate. However, the study by Schramm and colleagues was focused on monotherapy without concomitant pharmacotherapy in patients who mostly preferred psychotherapy. How CBASP, either alone or in combination, would fare in populations that preferred pharmacotherapy or combination therapy or had no preference is still not clear. Nor is the clinically more relevant question of which psychotherapy or combination would be preferable for which patients.

A considerable number of head-to-head comparisons between different types of psychotherapy have shown that the effects of these different types are comparable with each other, with no or only small and nonsignificant differences. Supportive therapy is an exception, with several studies showing that it is somewhat less effective than other therapies. However, this finding may be associated with the fact that SP is often used as a control condition, and may be owing to researcher allegiance, the conviction held by a researcher that a specific treatment is superior to other treatments. Although CBASP is probably effective and somewhat more effective than...