



Research paper

Educational attainment and cognitive behavioral therapy treatment outcome in late-life depression: A secondary analysis of a randomized controlled trial

S.K. Gerhards^{a,*}, M. Lupp^a, A.E. Zülke^a, A. Pabst^a, M. Claus^{a,b}, B. Bewernick^c, M. Elsaesser^d, N. Zehender^d, M. Wagner^c, O. Peters^f, L. Frölich^e, E. Schramm^d, M. Hautzinger^g, F. Jessen^{h,i,j}, F.S. Dafsari^h, S.G. Riedel-Heller^a

^a Institute of Social Medicine, Occupational Health and Public Health (ISAP), Medical Faculty, University of Leipzig, Leipzig, Germany

^b Institute for Health and Nursing Science, Medical Faculty, Martin-Luther-University Halle-Wittenberg, Halle, Germany

^c Department of Old Age Psychiatry and Cognitive Disorders, University of Bonn, Bonn, Germany

^d Department of Psychiatry and Psychotherapy, Medical Center, University of Freiburg, Faculty of Medicine, Freiburg, Germany

^e Department of Geriatric Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany

^f Department of Psychiatry and Psychotherapy, Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

^g Department of Clinical Psychology and Psychotherapy, Eberhard Karls University, Tuebingen, Germany

^h Department of Psychiatry and Psychotherapy, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

ⁱ German Center for Neurodegenerative Disease (DZNE), Bonn, Germany

^j Cellular Stress Response in Aging-Associated Diseases (CECAD) Cluster of Excellence, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

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ABSTRACT

Aim: The aim of this study is to investigate the association of different levels of educational attainment with the impact of Cognitive Behavioral Therapy for Late-Life Depression (LLD-CBT) compared to a supportive unspecific intervention (SUI).

Methods: A secondary analysis of the multicenter, randomized controlled trial “CBTlate” was conducted with $n = 229$ participants aged 60 years and older with moderate to severe depression who received either LLD-CBT ($n = 115$) or SUI ($n = 114$). Depressive symptoms as outcome were assessed with the 30-item Geriatric Depression Scale (GDS). Educational attainment was categorized according to the school and vocational education based system (CASMIN). Intention-to-treat analysis was performed using multilevel mixed effects linear models.

Results: While the model showed no significant overall effect of education on treatment outcome, analysis revealed a significant treatment effect for the low educational attainment group (group*time interaction, $\chi^2(2) = 6.45$, $p = .040$) with LLD-CBT being superior to SUI in the reduction of depressive symptoms from baseline to the end of treatment (Estimated Marginal Mean Difference (EMMD) = -5.30 , 95 %-CI = -8.93 to -2.12) and to follow-up (EMMD = -7.34 , 95 %-CI = -11.24 to -3.43). There was no corresponding significant effect for the medium and high educational group. In the low remission and response rates were significantly higher in the LLD-CBT compared to the SUI group at follow-up.

Conclusion: Participants may have responded differently to LLD-CBT and SUI depending on their previous school and vocational education. This may be taken into account for future research and potentially when treating patients with LLD and individualizing interventions for this patient group.

1. Introduction

Late-Life Depression (LLD) is among the most frequently reported

mental health disorders at higher age (Volkert et al., 2013). Meta-analyses reveal a pooled prevalence of 17 % for late-life depressive disorders (Zenebe and Akele, 2021; Lupp et al., 2012). Facing an

* Corresponding author at: Institute of Social Medicine, Occupational Health and Public Health (ISAP), Medical Faculty, University of Leipzig, Philipp-Rosenthal-Straße 55, 04103 Leipzig, Germany.

E-mail address: sina.gerhards@medizin.uni-leipzig.de (S.K. Gerhards).

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increasing proportion of people of higher age in the world's population due to the demographic change, LLD is a major and growing public mental health concern.

Cognitive behavioral therapy (CBT) is an established form of psychotherapy for reducing depressive symptoms (Serfaty et al., 2009; Cuijpers et al., 2013; Gühne et al., 2014; Cuijpers et al., 2021). However, the efficacy of an LLD-specific CBT and the associated predictors of treatment outcome are insufficiently studied. A previous publication has shown that both cognitive behavioral therapy tailored for late-life depression (LLD-CBT) and a non-specific supportive intervention (SUI) were effective in reducing depressive symptoms in LLD (Dafsari et al., 2023). Yet, it is crucial to gain a deeper understanding of the predictors of treatment outcome in LLD in order to provide tailored, individualized treatment options for this patient group.

Educational attainment may play a role in the response to CBT and SUI in LLD. In epidemiological and public health research, education is often used as an indicator of socioeconomic status (SES) as the years of early educational attainment are closely related to future employment and income (Galobardes et al., 2006). Lower SES and lower education are associated with a higher risk of depression and higher levels of depressive symptoms (Freeman et al., 2016; Chlapecka et al., 2020). At the same time, studies show that individuals with lower SES and lower education have less access to mental healthcare services (Lorant et al., 2003). Additionally, in studies investigating the association of SES or educational attainment and psychotherapy treatment outcomes, participants with low SES or low educational attainment are often underrepresented.

Empirical results on the association of educational attainment and CBT treatment outcome for depressive disorders are inconclusive. A more recent systematic review and meta-analysis by Finegan et al. (Finegan et al., 2018) pointed out that three studies addressing education and psychological treatment response for depression showed no significant association between education and CBT treatment outcome (Button et al., 2012; Falconnier, 2009; Fournier et al., 2009). However, one of the three studies investigated internet-based therapy in 18 to 75 year-old adults and two studies did not include patients of higher age with depression at all. Studies investigating the association of educational attainment and CBT efficacy in the patients at higher age are scarce. In a single arm, non-controlled exploratory study, Marquett et al. (Marquett et al., 2013) reported that LLD patients with lower education showed less improvement when receiving CBT compared to participants with higher educational level. In a systematic review and meta-analysis by Tunvirachaisakul et al. (Tunvirachaisakul et al., 2018) addressing predictors of treatment outcome in LLD, education was not a predictor of treatment outcome in LLD. Bao et al. (Bao et al., 2011) reported a greater reduction of depressive symptoms in the less-educated patient group with depression compared to the college-educated patient group. In contrast, a study by Gilman et al. (Gilman et al., 2013) showed that higher education was associated with a better treatment outcome in terms of less depressive symptoms. However, these studies did not assess treatment outcome of CBT, but of treatment programs with interpersonal psychotherapy approaches.

The current study focuses on differences in treatment efficacy of LLD-CBT between different educational attainment groups. We aim to gain a deeper understanding of the association between educational attainment and CBT efficacy for LLD by exploring the following research questions.

- (1) Does the degree of educational attainment have an overall effect on the treatment efficacy of cognitive behavioral therapy tailored for late-life depression (LLD-CBT) compared to a supportive non-specific treatment (SUI) group in patients with LLD?
- (2) Are there differences in CBT vs. SUI treatment efficacy within three different educational attainment levels?

2. Methods

2.1. Study design and participants

This study is a secondary analysis of data from the multicentre, observer-blinded, randomized controlled trial Cognitive Behavioral Therapy for Late-Life Depression (CBTlate) (Dafsari et al., 2023; Dafsari et al., 2019). A more detailed account of the study design and methodology including a trial flowchart can be found in the study protocol (Dafsari et al., 2019) and the primary trial results (Dafsari et al., 2023). The study is registered at DRKS and [ClinicalTrials.gov](https://clinicaltrials.gov) with the registration numbers DRKS00013769 and NCT03735576, respectively. All participants provided written informed consent and the ethical committees of all study sites (Cologne, Bonn, Tuebingen, Berlin, Freiburg, Mannheim and Leipzig) approved the study.

Participants were recruited in collaboration with a network of psychiatrists and psychotherapists at seven trial sites in Germany (Cologne, Bonn, Tuebingen, Leipzig, Berlin, Freiburg, Mannheim). A trial flowchart of the inclusion process has been previously published in the main trial paper (Dafsari et al., 2023). Participants were at least 60 years old and met the diagnostic criteria of a moderate to severe depressive disorder as assessed with the Diagnostic and Statistical Manual of Mental Disorders (5th Edition, (Sheehan et al., 1998)). Furthermore, included participants had to score >10 on the 30-item Geriatric Depression Scale (GDS; (Yesavage et al., 1982)), >10 on the Quick Inventory of Depressive Symptomatology–Clinician Rating (Rush et al., 2003), and >25 on the Mini-Mental-Status-Test (Kessler et al., 1990). Criteria for exclusion were a diagnosis of bipolar depression, schizophrenia or other psychotic disorders, substance abuse or addiction, dementia, anxiety disorders or obsessive compulsive disorder. Further, individuals with a high likelihood of following regular use of benzodiazepines during the eight week treatment phase, planned psychotherapy apart from the study treatment or brain stimulation were excluded from study participation. Individuals with acute suicidality, severe or unstable medical conditions that impact depressive symptomatology or brain diseases with relevant functional impairment (e.g. Parkinson's Disease) were not included in the study. Participants who met the inclusion criteria were randomly assigned to either the LLD-CBT treatment group ($n = 126$) or the SUI active control group ($n = 125$) between October 1st 2018 and November 11th 2020. Of these, 22 participants dropped out before the end of treatment assessment due to severe health problems, newly emerging exclusion criteria, protocol violations, non-compliance or withdrawal of consent and were excluded from the analysis. This resulted in a sample of $n = 229$ participants with $n = 115$ in the LLD-CBT group and $n = 114$ in the SUI group for the intention-to-treat analysis.

2.2. Measures

Assessments were conducted at baseline, five weeks (intermediate), 10 weeks (end of treatment) and 6 months after the initial randomization (follow-up).

2.2.1. Depressive symptoms

Depressive symptoms were assessed with the Geriatric Depression Scale (GDS) consisting of 30 items that are rated “yes” (1) or “no” (0) and add up to a sum score ranging from 0 to 30, with higher scores indicating higher depressive symptoms. The GDS is used as the outcome variable in the analysis and an established self-report measure to assess depressive symptoms in older adults (Yesavage et al., 1982; Cuijpers et al., 2014).

2.2.2. Educational attainment

Educational attainment was assessed and categorized in line with the classification system Comparative Analysis of Social Mobility in Industrial Nations (CASMIN; 27, 28). The classification of education according to CASMIN is an internationally widely used and established certificate-oriented system that utilizes information on 1) general

education and 2) vocational education to categorize educational attainment levels into three categories: low, medium and high educational attainment. Qualifications classified as low educational attainment level are no formal education, vocational internship, lower secondary education with or without additional internship or vocational qualification such as technician training. Intermediate school certificates with or without additional vocational training or higher education certificates allowing for access to universities with or without additional vocational training classify as medium educational level, and higher vocational qualification from a university of applied science or engineering or any kind of academic university degree categorize as high educational level (Brauns and Steinmann, 1999).

2.2.3. Covariates

Sociodemographic data included age (in years) and sex (male/female). The number of therapy sessions attended by each participant was assessed by the therapists with a possible range from 0 to 15 sessions.

2.3. Interventions

The interventions included 15 manual-based sessions that were conducted twice a week for a duration of eight weeks for both LLD-CBT and SUI. The LLD-CBT intervention consisted of six cognitive behavioral therapy modules that were adapted to address age-specific topics and needs of patients with LLD, including the experiences of loss, physical impairment, life review, and reminiscence elements (Dafsari et al., 2023; Dafsari et al., 2019; Hautzinger, 2016). In contrast, the active control group SUI followed a therapeutic approach that focuses on basic therapeutic qualities such as congruence, empathy, and acceptance and primarily characterized by listening attentively. Consequently, it is a non-specific intervention with no given content or structure. More details on the interventions can be retrieved from the study protocol (Dafsari et al., 2023; Dafsari et al., 2019).

2.4. Statistical analysis

First, descriptive statistics are shown as mean and standard deviation or frequency with percentages as appropriate, stratified by educational attainment level and intervention group. Secondly, mean scores of GDS and respective standard deviations are reported for each time point for each treatment group (LLD-CBT and SUI) stratified by educational attainment group (low/medium/high). Additionally the mean change of GDS scores for the different time points in each treatment group stratified by educational attainment group are reported. T-tests are calculated in order to assess differences in the change of GDS score between the treatment groups (LLD-CBT and SUI) univariately without adjusting for potential confounders. Further, in an intention-to-treat analysis (at least one valid assessment after baseline), we performed multilevel mixed effects linear models to assess associations between the interventions (LLD-CBT or SUI) and the change in depressive symptoms over time as measured by the GDS and adjusted for covariates. The models comprised the baseline GDS score, age (in years), sex (female in reference to male) and the number of therapy sessions attended as covariates, as well as the intervention group, time, the group x time interaction term as fixed effects. Models included a participant ID as random intercept in order to adjust for within-subject correlations of observations over time. We stratified the analyses by educational attainment level according to the CASMIN-classification (low/medium/high) to identify potential differences in the effectiveness of the treatment groups across educational attainment groups. Corresponding marginal mean differences and contrast tests were calculated. To assess whether there is an overall effect of educational attainment level on the change in GDS scores over time in the treatment groups, we included and tested the three-way interaction term of treatment group x time x educational attainment level in an overall unstratified regression model with corresponding contrast tests. Standard errors were calculated using

the clustered sandwich estimator with study center as cluster variable.

Response (GDS score reduction from baseline to the time point of ≥ 50 %) and remission (GDS score ≤ 10) rates were calculated for the end of treatment and follow-up time point. Chi-squared tests were calculated to assess differences in response and remission rates between treatment groups (LLD-CBT vs. SUI) within the different educational attainment groups (low/medium/high). In order to assess whether a higher educational attainment level is associated with a higher likelihood to complete the LLD-CBT treatment (Jarrett et al., 2013), we conducted a non-completer analysis by conducting a binary logistic regression model and corresponding contrast tests at EOT and FU. In all analysis, p -values of < 0.05 are considered significant and all statistical analysis was performed using the Stata SE 16 software (Stata Statistical Software, 2019).

3. Results

3.1. Baseline characteristics

Relevant information on the baseline characteristics of the sample stratified by educational attainment and treatment groups can be found in Table 1. Across all educational attainment groups, there were more female participants compared to male participants with 34.1 % male and 65.94 % female individuals in the overall sample. 77.7 % of all participants were retired, and 22.3 % were employed of which 9.6 % worked fulltime, 7.0 % part-time and 5.7 % were in partial retirement, minor employment or working irregularly. In the low and medium educational attainment group, participants of the LLD-CBT group were slightly but not significantly younger compared to the SUI group. In the low educational attainment group, LLD-CBT participants were all retired compared to the SUI group where 75 % were retired ($\chi^2(1) = 4.80$, $p = .026$). Participants with high educational attainment level in the LLD-CBT group had slightly higher depressive symptoms on average compared to the SUI group ($t = -3.32$, $p = .001$).

3.2. Association of educational attainment groups and change in GDS scores in the treatment groups

Descriptive statistics of depressive symptom scores as measured with the GDS at different time points stratified by educational attainment group and treatment group as well as the mean change in GDS scores are shown in Table 2. Over the consecutive points of measurement from baseline to 6 months FU, descriptively there was an average mean decrease in GDS scores in all educational attainment groups and in both intervention conditions. In the low educational attainment group, there was a significant group difference between the mean change in GDS score in the LLD-CBT group and the SUI group, with participants in LLD-CBT showing a significantly higher mean reduction in the GDS score compared to the SUI group at the intermediate (INT), end of treatment (EOT) and 6 months FU time point (INT: $t = 2.20$, $p = .034$, EOT: $t = 2.62$, $p = .006$, FU: $t = 3.33$, $p = .001$). Effect sizes were large with Cohen's $d = -1.14$ (INT), Cohen's $d = -1.66$ (EOT) and Cohen's $d = -2.31$ (FU).

The unstratified multilevel mixed effects linear model showed that there was no overall modification of the treatment effect by educational attainment (intervention group x time x educational attainment: $\chi^2(4) = 6.26$, $p = .181$). The exploratory stratified multilevel mixed effects linear models showed significant marginal mean group differences in the GDS scores between the LLD-CBT and SUI group at all three time points (INT, EOT and FU) in the low educational attainment group (also see Fig. 1), but not in the medium and high educational attainment group (see Table 3). In the low educational attainment group, the analyses revealed a significantly greater reduction in the GDS score in LLD-CBT compared to the SUI group (group x time: $\chi^2(2) = 6.45$, $p = .040$). Estimated mean group differences at the time points intermediate, end of treatment and follow up were -3.62 (95 % CI: -5.37 ; -1.86), -5.30 (95 % CI: -8.39 ;

Table 1

Baseline Characteristics by educational attainment level and treatment group in the intention-to-treat sample (n=229).

	Educational attainment								
	Low (n = 41)			Medium (n = 114)			High (n = 74)		
	LLD-CBT (n = 17)	SUI (n = 24)	Group-difference	LLD-CBT (n = 58)	SUI (n = 56)	Group-difference	LLD-CBT (n = 40)	SUI (n = 34)	Group-difference
Sociodemographic characteristics									
Age; M (SD)	71.29 (7.44)	73.38 (7.41)	0.382	68.43 (7.44)	69.86 (7.06)	0.198	70.63 (6.89)	70.21 (5.94)	0.974
Sex; n (%)									
male	5 (29.41 %)	9 (37.50 %)	0.591	14 (24.14 %)	22 (39.29 %)	0.082	13 (32.50 %)	15 (44.12 %)	0.304
female	12 (70.59 %)	15 (62.50 %)		44 (75.86 %)	34 (60.71 %)		27 (67.50 %)	19 (55.88 %)	
Marital status; n (%)									
married/partner	7 (41.18 %)	10 (41.67 %)	0.710	32 (55.17)	30 (53.57)	0.711	22 (55.00 %)	19 (55.88 %)	0.274
single/separated/widowed	10 (58.82 %)	14 (58.33 %)		26 (44.83)	26 (46.43)		18 (45.00 %)	15 (44.12 %)	
Education in years; M (SD)	11.06 (1.69)	11.42 (2.30)	0.699	14.10 (1.90)	14.64 (3.66)	0.836	17.03 (1.86)	17.50 (2.08)	0.849
Retired (ref. employed); n (%)	17 (100 %)	18 (75.0 %)	0.026	44 (75.86 %)	46 (82.14 %)		29 (72.50 %)	24 (70.59 %)	0.856
Clinical characteristics									
Therapy sessions; M (SD)	12.24 (3.67)	13.38 (2.26)	0.301	13.43 (2.90)	13.59 (2.43)	0.411	13.70 (2.14)	13.68 (2.53)	0.451
Geriatric Depression Scale (GDS Score; M (SD))	20.53 (4.06)	19.88 (4.07)	0.307	20.78 (4.85)	21.79 (4.15)	0.883	21.60 (3.68)	18.71 (3.82)	0.001

Notes. LLD-CBT: Late-Life Depression specific Cognitive Behavioral Therapy, SUI: Supportive Unspecific Intervention; missing values: education n = 1 (0.44 %); group differences are calculated using *t*-tests, Wilcoxon rank-sum tests and chi square tests as appropriate, and *p*-value < .050 is considered significant.

–2.20) and – 7.34 (95 % CI: –11.24; –3.43), respectively.

In the treatment non-completer analysis by conduction of a binary logistic regression model and corresponding contrast tests at EOT and FU there was no significant difference between completers and non-completers in terms of educational level (EOT: $\chi^2(2) = 1.25$, $p = .536$; FU: $\chi^2(2) = 1.29$, $p = .525$).

3.3. Remission and response across educational attainment groups

Remission and response rates stratified by educational attainment group for end of treatment and FU are shown in Table 4. Remission and response rates in the low educational attainment group were higher in the LLD-CBT group compared to the SUI condition, both at the end of treatment (remission: 50.00 % vs. 30.43 %; response: 56.25 % vs. 26.09 %) and at FU (remission: 53.85 % vs. 17.39 %; response: 53.85 % vs. 8.07 %). However, only the remission and response rate differences between LLD-CBT and SUI at FU reached statistical significance (remission: $\chi^2(1) = 5.20$, $p = .023$; response: $\chi^2(1) = 9.03$, $p = .003$). There was no significant difference in response or remission between LLD-CBT and SUI in the medium or high educational attainment group.

4. Discussion

The aim of this secondary analysis of a multicenter, randomized, controlled trial was to investigate the effect of educational attainment on the efficacy of the different psychotherapeutic treatments LLD-CBT and SUI for late-life depression. While there was no overall effect of educational attainment group on treatment efficacy, we found evidence for the superiority of LLD-CBT compared to SUI in treating late-life depression patients with low educational attainment. In the medium and high educational attainment group, there was no significant difference in treatment efficacy between LLD-CBT and SUI.

Our results are in line with Bao and colleagues (Bao et al., 2011) who showed that lower educational level (no college education) showed better treatment outcomes in terms of lower depressive symptoms compared to higher education (college education) in individuals with

minor or major depression who were 60 years and older. In contrast to our findings, Gilman et al. (Gilman et al., 2013) reported that higher education was associated with better treatment outcome to a primary care based treatment program in patients of higher age with depressive symptoms. However, Bao et al. and Gilman et al. did not assess the effectiveness of cognitive behavioral therapy but a collaborative depression care management (DCM) program for clinically relevant depressive symptomatology, which is not equivalent to the comparison of LLD-CBT and SUI in our study. A recent study by Gellert et al. (Gellert et al., 2024) on psychotherapy effectiveness in community-dwelling older adults with depression reported no effect of education (operationalized with the ISCED in three categories: low, medium, high) on treatment outcome. To integrate these findings in our results, it is important to mention that testing possible associations of education and treatment effectiveness was not the focus of their investigation. Thus, they reported associations of education and depression within a mixed model with education as control variable, providing results for high education in reference to low/medium educational level and not testing with an overall Wald test. Moreover, only a low percentage of 8.0 % in the intervention and 13.8 % in the control group showed a low education level. This underrepresentation of people with a low educational level is a common phenomenon in psychotherapy research resulting in a limited generalizability for this educational group. Our present study advantageously included 14.8 % with low educational level in the intervention group and 21.1 % in the control group.

Our findings are highly relevant and may show the importance of reducing potential barriers for psychotherapy access for patients with low educational level. Contrary to the findings suggesting that lower education is associated with worse treatment outcomes (Marquett et al., 2013), LLD-CBT may indeed be effective in the low educational attainment group and even superior to SUI. While Marquett et al. (Marquett et al., 2013) investigated the treatment response in the same age group as our study, they did not have a control condition they tested against, and applied a less nuanced operationalization of education (“high school or less” and “some college or more”). It is unclear whether this group even included people with low educational attainment level.

Table 2
Change in the Geriatric Depression Scale (GDS) Score over time stratified by educational attainment and treatment group.

	Educational attainment					
	Low		Medium		High	
LLD-CBT	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Baseline	17	20.53 (4.06)	58	20.78 (4.85)	40	21.60 (3.68)
Intermediate	17	14.41 (7.25)	56	14.61 (6.43)	39	17.51 (6.21)
End of Treatment	16	11.31 (7.17)	54	12.41 (7.87)	39	15.85 (7.04)
Follow Up	13	10.38 (6.96)	52	14.33 (7.89)	36	14.81 (6.70)
SUI						
Baseline	24	19.88 (4.07)	56	21.79 (4.15)	34	18.71 (3.82)
Intermediate	23	17.61 (5.95)	56	16.95 (5.29)	34	16.50 (5.25)
End of Treatment	23	15.70 (7.25)	55	14.15 (6.72)	32	13.22 (6.94)
Follow Up	23	17.26 (7.01)	50	14.76 (6.72)	32	13.38 (5.66)
Change in GDS score from baseline to INT LLD-CBT	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
	17	-6.12 (6.18)	56	-5.96 (5.67)	39	-4.26 (5.66)
SUI	23	-2.43 (4.43)	56	-4.84 (5.36)	34	-2.21 (5.48)
Group difference		p = .034		p = .283		p = .122
Change in GDS score from baseline to EOT LLD-CBT		Mean (SD)		Mean (SD)		Mean (SD)
	16	-9.69 (7.10)	54	-8.39 (7.24)	39	-5.64 (6.74)
SUI	23	-4.35 (5.61)	55	-7.52 (7.59)	32	-5.47 (7.65)
Group difference		p = .006		p = .272		p = .460
Change in GDS score from baseline to FU LLD-CBT		Mean (SD)		Mean (SD)		Mean (SD)
	13	-10.54 (8.40)	52	-6.61 (7.87)	36	-6.36 (7.38)
SUI	23	-2.91 (5.376)	50	-6.66 (7.27)	32	-5.31 (6.58)
Group difference		p = .001		p = .512		p = .270

Notes. LLD-CBT: Late-Life Depression specific Cognitive Behavioral Therapy, SUI: Supportive Unspecific Intervention; Change in GDS score was calculated by subtracting the GDS Score at baseline from GDS Score at end of treatment and follow-up, respectively with those cases included that had valid values for both assessments; Group differences between LLD-CBT and SUI were assessed using t-tests. Abbreviations: GDS: Geriatric Depression Scale; INT: intermediate measurement point at week 5; EOT: End of treatment, FU: Follow up; SD: Standard Deviation.

Additionally, the vast majority of participants had a high educational level with 91 % being allocated to the category “some college or more”, complicating scientifically valid and reliable statements about the CBT treatment efficacy in the low educational attainment category.

LLD-CBT and SUI both reduced depressive symptoms over the course of treatment and at follow-up in all educational groups. In the low educational group however, LLD-CBT seems to provide a benefit that goes beyond common factors of psychotherapy as used in SUI. LLD-CBT is a highly structured treatment including psychoeducational elements, behavioral activation, structuring everyday life and problem solving (Dafsari et al., 2023; Hautzinger, 2016). A factor that may explain the additional benefit of LLD-CBT in the low educational attainment group may be the degree of structure provided by the LLD-CBT intervention. Written material used in LLD-CBT may have contributed to LLD-CBT being easier to follow compared to the less structured SUI, which is not supplemented by written material. The self-structuring ability is an ability that generally may be strengthened with prolonged school carrier path and longer duration of being exposed to the school system, making

it necessary to use learning, self-structuring and planning strategies. Evidence suggests that a longer duration of education is for example accompanied by higher self-structuring ability and improved goal setting ability (Lourenço and Paiva, 2024; García-Pérez et al., 2021). The highly structured and exercise-based LLD-CBT treatment that uses psychoeducational elements and trains the ability to self-regulate cognitively and emotionally might be the reason for the superiority of LLD-CBT in the low educational attainment group with less duration in the school system. The low educational attainment group might be able to improve their cognitive and emotional self-management skills to self-structure in the LLD-CBT treatment. They might be more open to a more externally determined, less self-determined approach like LLD-CBT. SUI requires more activity and initiative by the patients with respect to the content and procedure of the sessions (e.g. bringing in topics to work on, setting goals, etc.) which may overwhelm older patients with low educational background.

There is evidence that mental health stigma is more prevalent in groups with lower educational and vocational attainment, which not only leads to reduced psychotherapy utilization (Jagdeo et al., 2009; Leppänen et al., 2022) but is also associated with greater suffering and suicidal ideation (Oexle et al., 2017). Studies show that CBT-based interventions can be particularly effective in reducing self-stigma, especially in depression (Mills et al., 2020). One possible explanation is that self-stigma was higher in the low educational and vocational attainment group compared to the medium and high groups, and CBT may have been successful in reducing self-stigma, thereby alleviating suffering. Larger confirmatory studies are needed for clarification.

Another explanatory approach may be that patients with higher educational level may already have acquired knowledge about strategies to reduce depressive symptoms, tried to use a variety of them and this may have been followed by resignation if those strategies were unsuccessful. This resignation hypothesis would be in line with Marquett et al. (Marquett et al., 2013), who reported that active coping is associated with worse treatment outcome and suggested that this is due to the mentioned resignation and insufficient flexibility to try other strategy options.

Finally, evidence suggests that a higher education level is associated with a higher level of autonomy since students are gradually more responsible for their learning achievements (Fujii, 2024). This may result in a higher need for autonomy in adult life including the professional activities they pursue. Thus, LLD patients with higher educational level might be used to a higher level of autonomy in their previous work life. It might be possible that they are not as open to the highly structured and action-oriented approach that LLD-CBT offers.

4.1. Strengths and limitations

A particular strength of the study is the longitudinal design of a multicenter randomized controlled trial with rater-blinding, monitoring of manual-adherence and a follow up assessment. Our study also included a large number of patients suffering from moderate to severe depression, strengthening the scientific value of our findings. Importantly, to the best of our knowledge, this analysis is the first that specifically focuses on the influence of educational attainment levels on the treatment efficacy of LLD-CBT or SUI for LLD. We assessed the educational and vocational level with the widely known and used classification system CASMIN (Brauns and Steinmann, 1999; Brauns et al., 2003) that goes beyond the surface-level measure of education duration and taps into the quality, type, and content of education that can influence how individuals process information and engage in therapeutic interventions. Furthermore, we included a relatively high percentage of people with low educational level compared to previous studies.

The current findings should be considered in the context of several limitations. First, we did not include a waitlist condition or a less intense control group, which does not allow us to compare the effects with the natural course of depressive disorders in later life. Second, we cannot

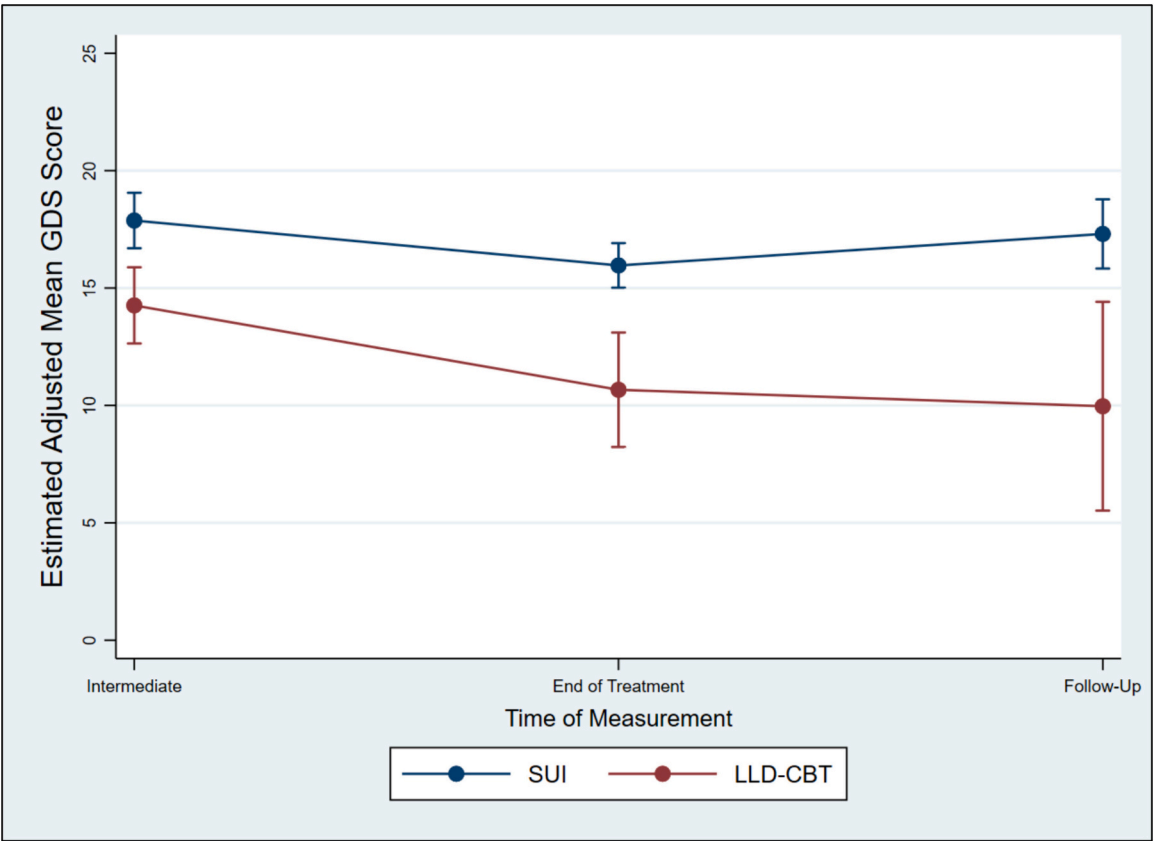


Fig. 1. Estimated adjusted mean scores of GDS with 95% Confidence Intervals adjusted for baseline GDS score, age, gender and sessions attended over three consecutive time points in the low educational attainment group.
Note. The x-axis starts at 'Intermediate' because the model was adjusted for GDS baseline scores and is therefore not included in the estimation or the corresponding figure.

Table 3
Estimated adjusted mean group differences in Geriatric Depression Scale score stratified by educational attainment level.

	Educational attainment								
	Low			Medium			High		
	Diff	CI	<i>p</i>	Diff	CI	<i>p</i>	Diff	CI	<i>p</i>
GDS									
Intermediate	−3.616	−5.369; −1.862	<0.001	−1.223	−2.779; 0.332	0.123	0.214	−0.773; 1.200	0.671
End of Treatment	−5.296	−8.393; −2.199	0.001	−0.800	−3.031; 1.431	0.482	1.955	−1.070; 4.980	0.205
Follow Up	−7.338	−11.244; −3.432	<0.001	0.266	−4.370; 4.902	0.910	1.336	−0.419; 3.091	0.136
Interaction group x time	$\chi^2(2) = 6.45, p = .040$			$\chi^2(2) = 0.50, p = .778$			$\chi^2(2) = 2.39, p = .303$		
Interaction group x time x education ^c	$\chi^2(4) = 6.26, p = .181$ ($\chi^2(2) = 3.80, p = .150$)								

Notes. Diff = adjusted mean difference in GDS Score (LLD-CBT vs. SUI); CI = 95 % Confidence Interval; ^aassessed with multilevel mixed-effects linear regression models adjusted for baseline GDS score, age, gender and number of received therapy sessions; ^bas assessed with the Geriatric Depression Scale (GDS), ^cEducational Attainment level as categorized according to the Comparative Analysis of Social Mobility in Industrial Nations (CASMIN), group-by-time-by-education interaction was tested with Wald tests with categorical CASMIN group (and continuous education in years) in the overall model.

completely rule out the influence of potential confounding factors. However, we conducted additional further analyses on the effect of baseline cognition, income, comorbidities and marital status, which did not significantly change results. Third, this is a post hoc analysis of the CBTlate trial and the results from these secondary analyses are exploratory. As such, they are hypothesis-generating, but not confirmatory. Moreover, it needs to be considered that the Geriatric Depression Scale is a self-administered tool and as such assesses the subjective perception of depressive symptoms. We would argue that this is the most relevant factor from a clinicians point of view since CBT should aim at reducing the subjective level of suffering. The absence of alpha error correction for multiple testing allows for explorative analysis but needs to be taken into account when interpreting the results. We thus point out the need

for further RCT's to confirm or challenge the results and evaluate the association between educational attainment level and treatment outcome, response and remission in different psychotherapies for LLD.

5. Conclusion

To the best of our knowledge, this is the first study to demonstrate differential treatment effects of LLD-CBT and SUI in LLD as a function of the educational attainment level before treatment. Our results show, that response to psychotherapy in LLD is heterogeneous and patients with different educational levels may respond differently to psychotherapeutic interventions. Our results should be taken into account when treating patients with LLD and individualizing interventions for

Table 4

Remission and Response rates by educational attainment level at the end of treatment and at follow up.

	Educational attainment					
	low		medium		high	
	n	%	n	%	n	%
End of Treatment						
Remission						
LLD-CBT	8/16	50.00	24/54	44.44	7/39	17.95
SUI	7/23	30.43	16/55	29.09	12/32	37.50
Group difference	$\chi^2(1) = 1.526, p = .217$		$\chi^2(1) = 2.765, p = .096$		$\chi^2(1) = 3.428, p = .064$	
Response						
LLD-CBT	9/16	56.25	22/54	40.74	8/39	20.51
SUI	6/23	26.09	17/55	30.91	9/32	28.13
Group difference	$\chi^2(1) = 3.627, p = .057$		$\chi^2(1) = 1.146, p = .284$		$\chi^2(1) = 0.559, p = .455$	
Follow Up						
Remission						
LLD-CBT	7/13	53.85	18/52	34.62	10/36	27.78
SUI	4/23	17.39	14/50	28.00	8/32	25.00
Group difference	$\chi^2(1) = 5.202, p = .023$		$\chi^2(1) = 0.518, p = .472$		$\chi^2(1) = 0.067, p = .796$	
Response						
LLD-CBT	7/13	53.85	16/52	30.77	10/36	27.78
SUI	2/23	8.07	16/50	32.00	8/32	25.00
Group difference	$\chi^2(1) = 9.030, p = .003$		$\chi^2(1) = 0.018, p = .893$		$\chi^2(1) = 0.067, p = .796$	

Notes. LLD-CBT: Late-Life Depression specific Cognitive Behavioral Therapy, SUI: Supportive Unspecific Intervention; remission indicates a GDS Score ≤ 10 at EOT or FU, respectively; response indicates a GDS Score reduction of $\geq 50\%$ from baseline to EOT or FU respectively; group differences were calculated using chi-squared tests.

this patient group. While patients with low educational level seem to have benefited significantly more from LLD-CBT compared to SUI, there was no significant difference in treatment outcome in LLD-CBT and SUI in patients with medium and high educational levels. Therapists should consider the potential influence of education attainment levels when treating patients with LLD. Considering individual differences in educational attainment before treatment as one factor might significantly improve treatment efficacy for this patient group when selecting a therapeutic modality for LLD patients.

Since LLD-CBT seems to be significantly more effective in the low educational attainment group, it may be important to reduce barriers for utilizing mental health care services particularly for LLD patients with low educational attainment in order to have access to a CBT treatment. Evidence suggests that mental health related stigma and associated attitudinal reasons might contribute to a lower access to psychotherapy and higher barriers for people with low socioeconomic status and/or low educational and vocational attainment (Jagdeo et al., 2009; Leppänen et al., 2022). Therefore, it seems particularly relevant to enable this group of LLD patients with low educational attainment to access CBT psychotherapy in particular. Further research is needed to better understand the barriers to accessing psychotherapy in the older population with a depressive disorder, so that more patients can benefit from psychotherapy and to reduce mental health burden in later life.

CRediT authorship contribution statement

S.K. Gerhards: Writing – review & editing, Writing – original draft, Visualization, Formal analysis. **M. Lupp:** Writing – review & editing, Supervision. **A.E. Zülke:** Writing – review & editing, Conceptualization. **A. Pabst:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **M. Claus:** Writing – review & editing. **B. Bewernick:** Writing – review & editing, Supervision, Conceptualization. **M. Elsaesser:** Writing – review & editing, Investigation. **N. Zehender:**

Writing – review & editing, Investigation. **M. Wagner:** Writing – review & editing, Supervision, Conceptualization. **O. Peters:** Writing – review & editing, Supervision. **L. Frölich:** Writing – review & editing, Supervision. **E. Schramm:** Writing – review & editing, Supervision. **M. Hautzinger:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **F. Jessen:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **F.S. Dafsari:** Writing – review & editing, Supervision, Conceptualization. **S.G. Riedel-Heller:** Writing – review & editing, Supervision, Conceptualization.

Statement of ethics

The study protocol was reviewed and approved by the Institutional Review Board/Institutional Ethical Committee (IRB/IEC) of the University of Cologne (Project No. 18-129) and by all other local IRB/IEC at the participating sites prior to initiation of the trial. All participants provided written informed consent.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Data availability

Due to ethical restrictions, data is not publicly available but can be inquired from the author upon reasonable request with the need to fill out an individual permission form from the study sites ethical boards.

References

Bao, Y., Alexopoulos, G.S., Casalino, L.P., et al., 2011. Collaborative depression care management and disparities in depression treatment and outcomes. *Arch. Gen. Psychiatry* 68 (6), 627–636. <https://doi.org/10.1001/archgenpsychiatry.2011.55>.
Brauns, H., Scherer, S., Steinmann, S., 2003. The CASMIN educational classification in international comparative research. In: Hoffmeyer-Zlotnik, J.H.P., Wolf, C. (Eds.), *Advances in Cross-National Comparison: A European Working Book for Demographic and Socio-Economic Variables*. Springer US, Boston, MA, pp. 221–244.
Brauns, H., Steinmann, S., 1999. Educational reform in France, West-Germany and the United Kingdom: updating the CASMIN educational classification. *ZUMA Nachrichten* 23, 7–44.
Button, K.S., Wiles, N.J., Lewis, G., Peters, T.J., Kessler, D., 2012. Factors associated with differential response to online cognitive behavioural therapy. *Soc. Psychiatry Psychiatr. Epidemiol.* 47 (5), 827–833. <https://doi.org/10.1007/s00127-011-0389-1> (PMID: 21541696).
Chlapeccka, A., Kagstrom, A., Cermakova, P., 2020. Educational attainment inequalities in depressive symptoms in more than 100,000 individuals in Europe. *Eur. Psychiatry* 63 (1), e97. <https://doi.org/10.1192/j.eurpsy.2020.100>.
Cuijpers, P., Berking, M., Andersson, G., Quigley, L., Kleiboer, A., Dobson, K.S., 2013. A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *Can. J. Psychiatr.* 58 (7), 376–385. <https://doi.org/10.1177/070674371305800702> (PMID: 23870719).
Cuijpers, P., Karyotaki, E., Weitz, E., Andersson, G., Hollon, S.D., van Straten, A., 2014. The effects of psychotherapies for major depression in adults on remission, recovery and improvement: a meta-analysis. *J. Affect. Disord.* 159, 118–126. <https://doi.org/10.1016/j.jad.2014.02.026> (PMID: 24679399).

- Cuijpers, P., Quero, S., Noma, H., et al., 2021. Psychotherapies for depression: a network meta-analysis covering efficacy, acceptability and long-term outcomes of all main treatment types. *World Psychiatry* 20 (2), 283–293. <https://doi.org/10.1002/wps.20860>.
- Dafarsi, F.S., Bewernick, B., Biewer, M., et al., 2019. Cognitive behavioural therapy for the treatment of late life depression: study protocol of a multicentre, randomized, observer-blinded, controlled trial (CBTlate). *BMC Psychiatry* 19 (1), 423. <https://doi.org/10.1186/s12888-019-2412-0> (PMID: 31881995).
- Dafarsi, F.S., Bewernick, B., Böhlinger, S., et al., 2023. Cognitive behavioral therapy for late-life depression (CBTlate): results of a multicenter, randomized, observer-blinded, controlled trial. *Psychother. Psychosom.* 1–13. <https://doi.org/10.1159/000529445> (PMID: 37004508).
- Falconier, L., 2009. Socioeconomic status in the treatment of depression. *Am. J. Orthop.* 79 (2), 148–158. <https://doi.org/10.1037/a0015469> (PMID: 19485632).
- Finegan, M., Firth, N., Wojnarowski, C., Delgado, J., 2018. Associations between socioeconomic status and psychological therapy outcomes: a systematic review and meta-analysis. *Depress. Anxiety* 35 (6), 560–573. <https://doi.org/10.1002/da.22765> (PMID: 29697880).
- Fournier, J.C., DeRubeis, R.J., Shelton, R.C., Hollon, S.D., Amsterdam, J.D., Gallop, R., 2009. Prediction of response to medication and cognitive therapy in the treatment of moderate to severe depression. *J. Consult. Clin. Psychol.* 77 (4), 775–787. <https://doi.org/10.1037/a0015401> (PMID: 19634969).
- Freeman, A., Tyrovolas, S., Koyanagi, A., et al., 2016. The role of socio-economic status in depression: results from the COURAGE (aging survey in Europe). *BMC Public Health* 16 (1), 1098. <https://doi.org/10.1186/s12889-016-3638-0>.
- Fujii, A., 2024. Exploring autonomy support and learning preference in higher education: introducing a flexible and personalized learning environment with technology. *Discov. Educ.* 3 (1), 26. <https://doi.org/10.1007/s44217-024-00111-z>.
- Galobardes, B., Shaw, M., Lawlor, D.A., Lynch, J.W., Davey, Smith G., 2006. Indicators of socioeconomic position (part 1). *J. Epidemiol. Community Health* 60 (1), 7–12. <https://doi.org/10.1136/jech.2004.023531> (PMID: 16361448).
- García-Pérez, D., Fraile, J., Panadero, E., 2021. Learning strategies and self-regulation in context: how higher education students approach different courses, assessments, and challenges. *Eur. J. Psychol. Educ.* 36 (2), 533–550. <https://doi.org/10.1007/s10212-020-00488-z>.
- Gellert, P., Lech, S., Hoppmann, F., O'Sullivan, J.L., Kessler, E.-M., 2024. Effectiveness of psychotherapy for community-dwelling vulnerable older adults with depression and care needs: findings from the PSY-CARE trial. *Clin. Gerontol.* 1–15. <https://doi.org/10.1080/07317115.2024.2353702>.
- Gilman SE, Bruce ML, Have T ten, et al. Social inequalities in depression and suicidal ideation among older primary care patients. *Soc. Psychiatry Psychiatr. Epidemiol.* 2013; 48(1): 59–69 [doi:<https://doi.org/10.1007/s00127-012-0575-9>] (PMID: 22948560).
- Gühne, U., Lupp, M., König, H.-H., Hautzinger, M., Riedel-Heller, S., 2014. Ist Psychotherapie bei depressiven Erkrankungen im Alter wirksam? *Psychiatr. Prax.* 41 (08), 415–423. <https://doi.org/10.1055/s-0034-1370113>.
- Hautzinger, M., 2016. *Depression im Alter: Psychotherapeutische Behandlung für das Einzel- und Gruppensetting*, 2nd edition. Beltz, Weinheim.
- Jagdeo, A., Cox, B.J., Stein, M.B., Sareen, J., 2009. Negative attitudes toward help seeking for mental illness in 2 population-based surveys from the United States and Canada. *Can. J. Psychiatr.* 54 (11), 757–766. <https://doi.org/10.1177/070674370905401106> (PMID: 19961664).
- Jarrett, R.B., Minhajuddin, A., Kangas, J.L., Friedman, E.S., Callan, J.A., Thase, M.E., 2013. Acute phase cognitive therapy for recurrent major depressive disorder: who drops out and how much do patient skills influence response? *Behav. Res. Ther.* 51 (4), 221–230. <https://doi.org/10.1016/j.brat.2013.01.006>.
- Kessler, J., Folstein, S.E., Denzler, P., 1990. MMST. Mini-Mental-Status-Test, Deutschsprachige Fassung.
- Leppänen, H., Kampman, O., Autio, R., et al., 2022. Socioeconomic factors and use of psychotherapy in common mental disorders predisposing to disability pension. *BMC Health Serv. Res.* 22 (1), 983. <https://doi.org/10.1186/s12913-022-08389-1>.
- Lorant, V., Deliege, D., Eaton, W., Robert, A., Philippot, P., Anseau, M., 2003. Socioeconomic inequalities in depression: a Meta-analysis. *Am. J. Epidemiol.* 157, 98–112. <https://doi.org/10.1093/aje/kwf182>.
- Loureço, A.A., Paiva, M.O., 2024. Academic performance of excellence: the impact of self-regulated learning and academic time management planning. *Knowledge* 4 (2), 289–301. <https://doi.org/10.3390/knowledge4020016>.
- Lupp, M., Sikorski, C., Luck, T., et al., 2012. Age- and gender-specific prevalence of depression in latest-life – systematic review and meta-analysis. *J. Affect. Disord.* 136 (3), 212–221. <https://doi.org/10.1016/j.jad.2010.11.033>.
- Marquett, R.M., Thompson, L.W., Reiser, R.P., et al., 2013. Psychosocial predictors of treatment response to cognitive-behavior therapy for late-life depression: an exploratory study. *Aging Ment. Health* 17 (7), 830–838. <https://doi.org/10.1080/13607863.2013.791661>.
- Mills, H., Mulfinger, N., Raeder, S., Rüsch, N., Clements, H., Scior, K., 2020. Self-help interventions to reduce self-stigma in people with mental health problems: a systematic literature review. *Psychiatry Res.* 284, 112702. <https://doi.org/10.1016/j.psychres.2019.112702>.
- Oexle, N., Rüsch, N., Vierung, S., et al., 2017. Self-stigma and suicidality: a longitudinal study. *Eur. Arch. Psychiatry Clin. Neurosci.* 267 (4), 359–361. <https://doi.org/10.1007/s00406-016-0698-1>.
- Rush, A.J., Trivedi, M.H., Ibrahim, H.M., et al., 2003. The 16-item quick inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. *Biol. Psychiatry* 54 (5), 573–583. [https://doi.org/10.1016/S0006-3223\(02\)01866-8](https://doi.org/10.1016/S0006-3223(02)01866-8).
- Serfaty, M.A., Haworth, D., Blanchard, M., Buszewicz, M., Murad, S., King, M., 2009. Clinical effectiveness of individual cognitive behavioral therapy for depressed older people in primary care: a randomized controlled trial. *Arch. Gen. Psychiatry* 66 (12), 1332–1340. <https://doi.org/10.1001/archgenpsychiatry.2009.165> (PMID: 19996038).
- Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatry* 1998; 59 Suppl 20: 22–33; quiz 34–57 (PMID: 9881538).
- Stata Statistical Software, 2019. Release 16. StataCorp LLC, College Station, TX.
- Tunvirachaisakul, C., Gould, R.L., Coulson, M.C., et al., 2018. Predictors of treatment outcome in depression in later life: a systematic review and meta-analysis. *J. Affect. Disord.* 227, 164–182. <https://doi.org/10.1016/j.jad.2017.10.008> (PMID: 29100149).
- Volkert, J., Schulz, H., Härter, M., Włodarczyk, O., Andreas, S., 2013. The prevalence of mental disorders in older people in Western countries - a meta-analysis. *Ageing Res. Rev.* 12 (1), 339–353. <https://doi.org/10.1016/j.arr.2012.09.004> (PMID: 23000171).
- Yesavage, J.A., Brink, T.L., Rose, T.L., et al., 1982. Development and validation of a geriatric depression screening scale: a preliminary report. *J. Psychiatr. Res.* 17 (1), 37–49. [https://doi.org/10.1016/0022-3956\(82\)90033-4](https://doi.org/10.1016/0022-3956(82)90033-4).
- Zenebe Y, Akele B, W/Selassie M, Necho M. Prevalence and determinants of depression among old age: a systematic review and meta-analysis. *Ann. General Psychiatry* 2021; 20(1): 55 [doi:<https://doi.org/10.1186/s12991-021-00375-x>].