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Review

Depression and pain dynamics in lumbar degenerative disk disease: A systematic review and meta-analysis

Indira Karibayeva[1], Yerzhan Kuanyshbekov[2], Malika Idayat[3], Botagoz Turdaliyeva[4], Shayakhmet Makhanbetkhan[5]

[1]Department of Health Policy and Community Health, Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, GA, USA; [2]Department of Spinal Neurosurgery and Peripheral Nervous System Pathology, National center for Neurosurgery, Astana, Kazakhstan; [3]Department of Medicine and Healthcare, Al-Farabi Kazakh National University, Almaty, Kazakhstan; [4]Kazakh Scientific Center of Dermatology and Infectious Diseases of the Ministry of Health of the Republic of Kazakhstan, Almaty, Kazakhstan; [5]Central City Hospital, Almaty, Kazakhstan.

Abstract. *Background and aim:* This study systematically reviews the literature on changes in depression and pain scores in patients with lumbar degenerative disc disease (LDDD) after treatment initiation. *Methods:* A comprehensive review of PubMed, Web of Science, Science Direct, Academic Search Complete, and Google Scholar was performed. Pooled prevalence estimates, subgroup analysis, sensitivity analysis, and publication bias assessments were performed. *Results:* We identified eight eligible studies with 634 LDDD patients. Our meta-analysis indicated a slight reduction in the mean Beck Depression Inventory scores from baseline (11.51) to three months post-treatment (9.18). Conversely, there was a significant decrease in the mean Visual Analogue Scale back pain scores from baseline (6.72) to three months post-treatment (2.62). This suggests that treatment for LDDD may reduce pain levels in the short term; however, its effect on depression is limited. Additionally, patients in the conservative treatment group exhibited higher rates of depression both at baseline (12.32) and at the 3-month follow-up (9.45) than those in the operative treatment group (11.23 at baseline and 8.57 at the 3-month follow-up). In terms of pain, patients in the conservative treatment group reported lower pain scores at baseline (6.14) but higher scores at the 3-month follow-up (3.53) than those in the operative treatment group (7.68 at baseline and 1.45 at the 3-month follow-up). *Conclusions*: Our findings underscore the need for integrated treatment approaches that address both depression and pain to improve the outcomes of patients with LDDD. Although pain reduction is achievable, the management of depression remains a challenge. (www.actabiomedica.it)

Key words: lumbar degenerative disk disease, depression, pain, prevalence, systematic review, meta-analysis

Introduction

Degenerative spinal diseases, often driven by prolonged static and excessive dynamic loads, physical inactivity, and unique anatomical features like spine-pelvic imbalance, present considerable challenges to individuals' overall well-being (1). Lumbar degenerative disc disease (LDDD) is a common musculoskeletal disorder characterized by structural changes in lumbar intervertebral discs (2). These changes, including disc degeneration, herniation, and narrowing of the spinal canal are the most common causes of acute and chronic back pain, restricted mobility, and a decline in quality of life, especially in individuals over 40 (2). The prevalence of lumbar degenerative disc disease (LDDD) is shaped by several factors, including the patient's location, ethnicity, age, gender, and genetic background (3). LDDD ranked among the

top causes of disability, morbidity, and years lived with disability (4). Consequently, LDDD represents a major health concern, with a substantial socioeconomic burden (5, 6). Treatment for LDDD includes a variety of strategies, ranging from non-invasive treatments to more advanced surgical options (7). Some studies also suggest that modifiable factors, such as reducing elevated body mass index (BMI), controlling hypertension, managing dyslipidemia and diabetes mellitus, as well as quitting smoking, can decrease the risk of intervertebral disc degeneration and herniation (3). Despite these approaches, some individuals opt to forego treatment, highlighting the complex nature of this condition and the multitude of factors influencing treatment decisions and outcomes in those patients (8, 9). Notably, depression is a prevalent comorbidity in individuals with LDDD, surpassing the prevalence rates observed in the general population. Ajiboye and colleagues report that the prevalence of depression among symptomatic LDDD patients is 32% (10). This comorbidity significantly heightens pain perception and functional impairment, ultimately compromising treatment outcomes and leading to increased healthcare utilization (11).

Pain, both physical and psychological, constitutes a defining feature of LDDD (12). Chronic low back pain, radicular pain, and neuropathic pain contribute significantly to morbidity, diminishing the overall quality of life of affected individuals (12). Recent studies highlight the important role of the neuroimmune interface, particularly the neuroimmune communication between the peripheral and central nervous systems, in the development of chronic pain. Evidence suggests neuroimmune activation within the central nervous system in LDDD patients, even in the absence of systemic inflammation (13). Several cytokines are elevated in both cerebrospinal fluid and blood serum, with their levels correlating to back pain severity. The connection between depression and pain in LDDD is also deeply intertwined. Chronic pain can lead to or worsen depression, while depression can intensify pain perception by affecting central sensitization and disrupting neuroendocrine regulation (14). Understanding the dynamics of depression and pain in LDDD is crucial for tailoring effective patient care and treatment strategies. No meta-analysis has been conducted to investigate changes in depression and pain scores after treatment initiation in LDDD patients. Therefore, this study aimed to perform a systematic review and meta-analysis to explore the changes in depression and pain scores three months after treatment initiation, based on the Beck Depression Inventory (BDI) and Visual Analog Scale (VAS) back pain scores. We sought to shed light on the interplay between depression and pain in LDDD, providing valuable insights for clinical practice and enhancing patient outcomes (15, 16).

Materials and Methods

The study protocol was registered with the PROSPERO International Prospective Register of Systematic Reviews (ID: CRD42024561303).

The PROSPERO database was searched to identify similar studies, and no similar studies were found. We conducted a subsequent search of five major electronic literature databases: PubMed, Web of Science, ScienceDirect, Academic Search Complete, and Google Scholar. The literature search for the specified sources was initiated on January 1, 2024, and completed on June 1, 2024. The search strategy included the following keywords: "depression" and "degenerative disk disease"; "depressive disorder" and "degenerative disk disease"; "depression" and "degenerative disk" in all fields. The full search strategy is shown in Supplementary Table 1 (Table S1).

Methodologically, literature screening and synthesis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The inclusion criteria:

1. Cohort and cross-sectional studies, and database analyses.
2. Studies that included patients with LDDD.
3. Studies reporting specific outcomes, including mean scores on the Visual Analog Scale (VAS) for back pain and Beck Depression Inventory (BDI) scores at baseline and three months post-treatment.

Table 1. Summary of Included Articles Sorted by the Year of Publication.

Author, year	Country	Study design	Mean age of study group ± SD or age groups	Patient number	Outcome measures	Procedure type	Follow-up	Risk of bias
Falavigna, 2011 (19)	Brazil	prospective cohort	61.54 ± 9.78	52	VAS, BDI	Operative treatment	22 months	9,5
Misterska, 2013 (20)	Poland	prospectivestudy	43.47	90	BDI	Operative treatment	No	9
Engel-Yeger, 2016 (21)	Israel	a cross-sectional	46.96 ± 14.36	51	VAS, BDI	Conservative treatment	No	9,5
Jablonska, 2017 (22)	Poland	prospective cohort	42.7±10.99	188	VAS, BDI	Operative treatment	6 months	9,5
Comella, 2017 (23)	USA	open label study	51.5	15	VAS, BDI	Conservative treatment	12 months	10
Celenlıoglu, 2018 (15)	Turkey	prospective cohort	44,8	100	VAS, BDI	Conservative treatment	3 months	9,5
Sacaklidir, 2021 (24)	Turkey	prospective, observational	42.0 ± 9.5	58	VAS, BDI	Conservative treatment	3 months	9,5
Wu, 2021 (11)	China	retrospective trial	59.5 +-9.76	80	VAS, BDI	Operative treatment	24 months	9

Abbreviations: BDI – Beck Depression Inventory; SD – standard deviation; VAS – Visual Analogue Scale.

4. Studies published in English between January 2010 and March 2024.
5. Articles focusing on surgical interventions and conservative treatments.

The exclusion criteria:

1. Publications lacking essential information.
2. Studies duplicating previously reported findings.
3. Review articles or case reports involving fewer than ten patients.

In accordance with the PRISMA guidelines, two of the authors independently extracted the following information from the identified full-text articles using a standard data extraction form: (1) the first author's name, (2) publication year, (3) country, (4) study design, (5) sample size, (6) lesion location, (7) mean age, (8) mean ± SD BDI score pretreatment, (9) mean ± SD VAS back pain score pretreatment, (10) mean ± SD BDI score at 3-month follow-up, and (11) mean ± SD VAS back pain score at the 3-month follow-up. Any disagreements or conflicts were resolved by discussion and consensus.

Risk of bias

The Critical Appraisal Skills Programme (CASP) qualitative research checklist was employed to evaluate the methodological quality of the included studies (17). This checklist comprised ten questions covering various aspects, such as the study's objectives, methodology, research design, recruitment approach, data collection methods, researcher-participant relationships, ethical considerations, data analysis, research findings, and overall value. Each criterion was assessed with a rating of 'yes' when adequately described (scored as 1), 'no' when absent (scored as 0), and ' cannot tell' when unclear or incomplete (scored as 0.5). The total scores ranged from 0 to 10, with a score of at least 7 considered indicative of a satisfactory quality.

Statistical analysis

RStudio was used to calculate the pooled mean with 95% confidence intervals. We used a random effects model for the meta-analysis. We examined the following outcomes: BDI at baseline and 3 months and VAS Back

Pain at baseline and 3 months. Forest plots were used to display pooled estimates using the "RevMan5" layout function. Heterogeneity across studies was assessed using subgroup analysis for treatment type and meta-regression analysis for year of publication. Influence diagnostics analysis was performed by identifying an outlier study whose confidence interval did not overlap with the confidence interval of the pooled effect. Publication bias was evaluated through visual inspection of a funnel plot and statistical analysis using Egger's test to examine potential asymmetry in the distribution of the study results.

Results

Description of the included studies

The initial database search yielded a total of 940 results. After removing 471 duplicates and 191 ineligible studies, 278 titles were screened for eligibility. Eight articles were included in the meta-analysis, based on the inclusion and exclusion criteria, 8 articles were included in the meta-analysis. A flowchart of the study selection is presented in Figure 1 (18).

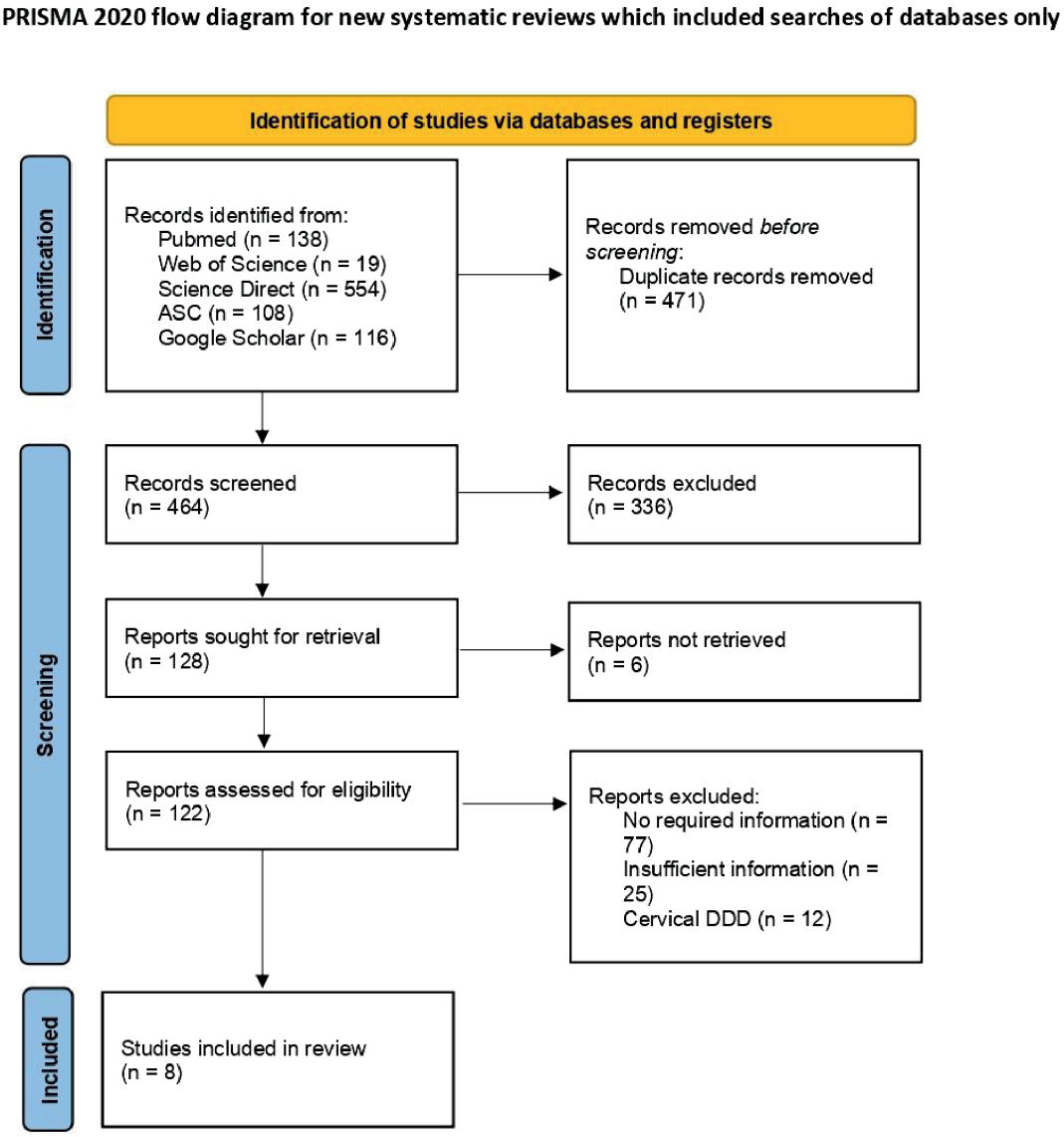

Figure 1. PRISMA flow chart of study selection (18).

Abbreviations: ACS: Academic Search Complete; DDD: Degenerative Disk Disease.

The study design and patient characteristics are presented in Table 1. All the included studies were published between 2011 and 2021. Geographically, the studies originated in diverse regions: three from South Asia, one from Latin America, two from Eastern Europe, one from North America, and one from East Asia. Among these studies, six were prospective, one was retrospective, and one was cross-sectional.

A total of 634 patients with LDDD were included in eight studies. The mean sample size was 79.25 patients, ranging from 15 to 188 patients per study. The mean age ranged from 42.0 to 59.5 years. The mean follow-up period ranged from 3 months to 2 years (Table 1).

Risk of bias (quality) assessment

All included studies had a CASP score of 9 or above, indicating high quality and a low risk of bias, as presented in Table 2.

Depression at baseline

Eight studies with ten groups presented the BDI scores at baseline. Based on the random-effects model, the pooled average mean of eight studies with ten groups on the BDI score at baseline in patients with LDDD was 11.51, 95% CI [9.31; 13.71], as presented in Figure 2. The test for heterogeneity suggested the presence of high heterogeneity: I^2=88%, Q (df = 9) = 72.40, p < 0.01.

Subgroup analysis based on the type of treatment was conducted to investigate the sources of heterogeneity among the studies. Using the random-effects model, the pooled average mean BDI score for the five groups in the conservative treatment subgroup indicated high heterogeneity, with a score of 12.32 (95% CI [6.93; 17.71]), I^2 = 93%, Q (df = 4) = 59.61, p < 0.01. In contrast, the operative treatment subgroup exhibited moderate heterogeneity with a pooled mean BDI score of 11.23 (95% CI [9.72; 12.75]), I^2 = 46%, Q (df = 4) = 7.43, p = 0.11, as shown in Figure 3.

Meta-regression analysis by year of publication revealed significant changes in the effect sizes over time (Figure S1). The analysis demonstrated that year of publication is a significant moderator, with newer studies showing higher effect sizes than older ones. The influence analysis assessed the robustness of the pooled estimates. The diagnostic evaluation of BDI scores at baseline did not reveal any influential studies (Figure S2). Upon visual inspection of the funnel plot, no asymmetry was evident (Figure S3), which was confirmed by non-significant Egger's test (p= 0.3767).

Table 2. The Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist.

Authors	Aim	Methodology	Design	Recruitment	Data collection	Relationship	Ethical	Data analysis	Finding	Values	Score
Celenlıoglu, 2018 (15)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	9,5
Engel-Yeger, 2016 (21)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	9,5
Falavigna, 2011 (19)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	9,5
Jablonska, 2017 (22)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	9,5
Comella, 2017 (23)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Misterska, 2013 (20)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	9
Sacaklidir, 2021 (24)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	9,5
Wu, 2021 (11)	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Yes	9

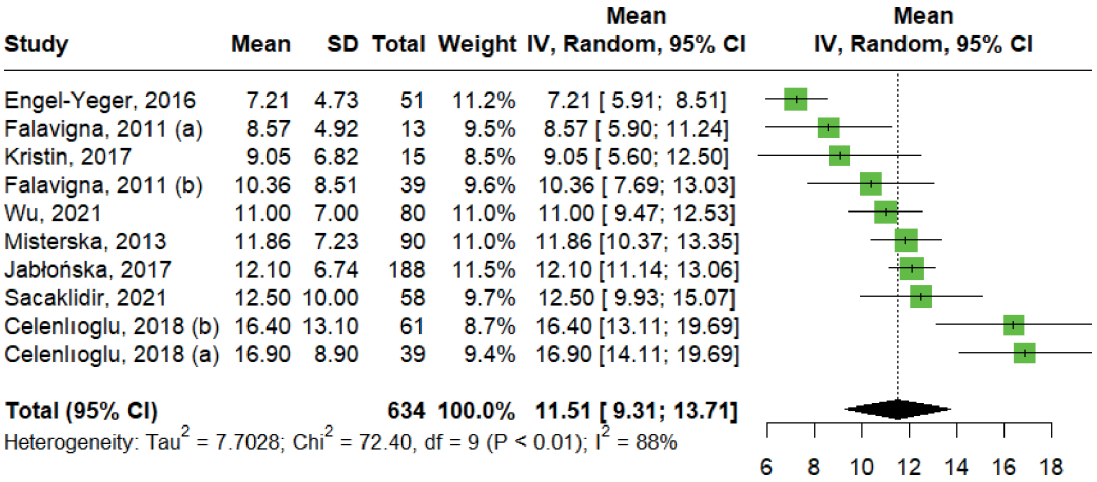

Figure 2. Pooled Baseline BDI Scores in Patients with LDDD.

Abbreviations: BDI: Beck Depression Inventory; C.I.: confidence interval; LDDD: lumbar Degenerative Disk Disease; SD: standard deviation.

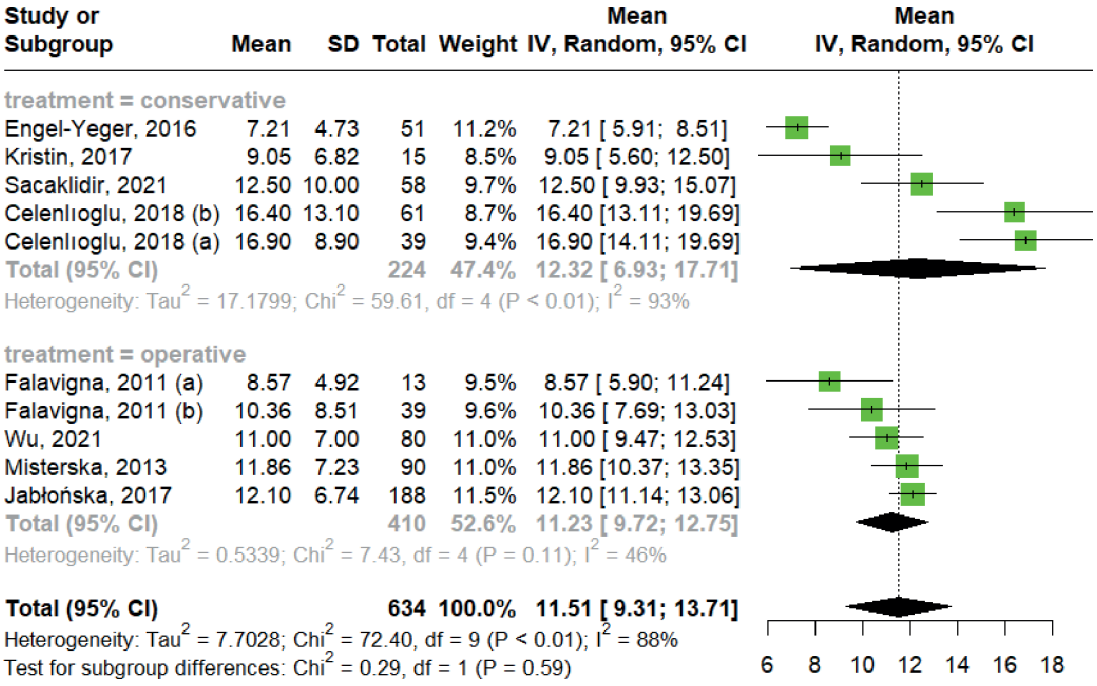

Figure 3. Subgroup Analysis of the BDI Score at Baseline in Patients with LDDD by Treatment Type.

Abbreviations: BDI: Beck Depression Inventory; C.I.: confidence interval; LDDD: lumbar Degenerative Disk Disease; SD: standard deviation.

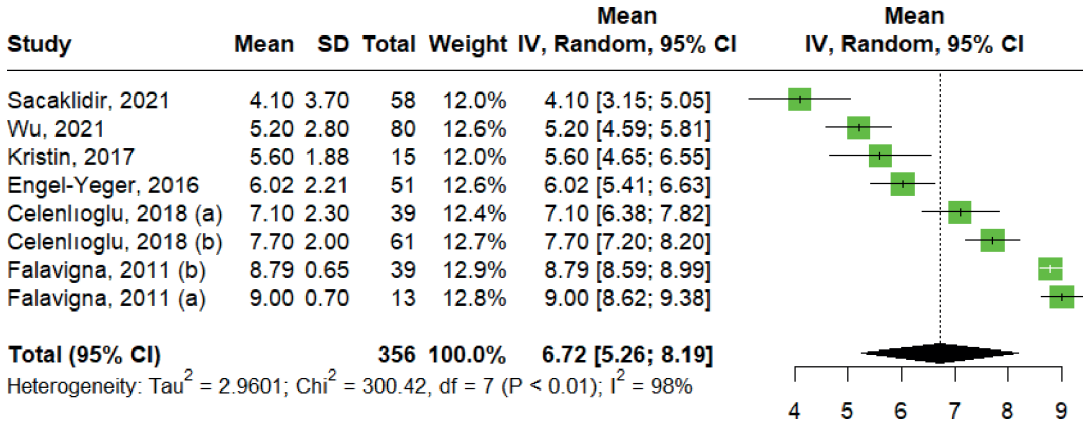

Figure 4. Pooled Baseline VAS Back Pain Scores in Patients with LDDD.

Abbreviations: C.I.: confidence interval; LDDD: Lumbar Degenerative Disk Disease; SD: standard deviation; VAS: Visual Analogue Scale.

Pain at baseline

Six studies with eight groups presented the VAS back pain scores at baseline. Using the random-effects model, the pooled mean VAS back pain score at baseline for patients with LDDD was 6.72 (95% CI [5.26, 8.19]) (Figure 4). The test for heterogeneity indicated a high level of heterogeneity, I^2 = 98%, Q (df = 7) = 300.42, p < 0.01.

Subgroup analysis based on the type of treatment revealed significant heterogeneity among the studies. Using the random-effects model, the pooled mean VAS score for the four groups in the conservative treatment subgroup was lower than that in the operative subgroup. Both subgroups exhibited high heterogeneity, with scores of 6.14 (95% CI [4.41; 7.87]), I^2 = 98%, Q (df = 5) = 9.71, p < 0.01, and 7.68 (95% CI [2.39; 12.97]), I^2 = 98%, Q (df = 2) = 125.2, p < 0.01, respectively, as shown in Figure 5.

Meta-regression analysis by year of publication revealed significant changes in effect sizes over time, as depicted in Figure S4. Studies published in earlier years have reported larger effect sizes than those reported in more recent studies. Sensitivity analysis was used to assess the robustness of the pooled estimates. The influence diagnostics of the VAS Back Pain Score at baseline did not reveal any influential studies (Figure S5). Upon visual inspection of the baseline VAS back pain funnel plot, asymmetry was evident, suggesting a non-symmetric distribution of the study results around the estimated effect size (Figure S6), which was confirmed by a significant Egger's test (p=0.001).

Depression at a 3-month follow up

Six studies with eight groups presented the dynamics of BDI scores at the 3 month follow up. Utilizing the random-effects model, the pooled average mean of these six studies, comprising eight groups, revealed a BDI score of 9.18 (95% CI [7.73; 10.64]) among patients with LDDD (Figure 6). A test for heterogeneity indicated significant heterogeneity (I^2 = 54%, Q (df = 7) = 15.36, p = 0.03).

Subgroup analysis based on the type of treatment revealed significant variability among studies. Using the random-effects model, the pooled average mean BDI score for the four groups in the conservative treatment subgroup was higher than that in the operative subgroup, with scores of 9.45 (95% CI [5.94; 12.96]), I^2 = 69%, Q (df = 3) = 9.71, p = 0.02, and 8.57 (85% CI [7.31; 9.83]), I^2 = 18%, Q (df = 3) = 3.64, p = 0.02, respectively (Figure 7). Notably, heterogeneity within the operative treatment group was low.

Meta-regression analysis of the BDI score dynamics at 3 months by year of publication revealed significant changes in effect sizes over time, as depicted in Figure S7. Studies published in earlier years have reported larger effect sizes than those reported in more recent studies.

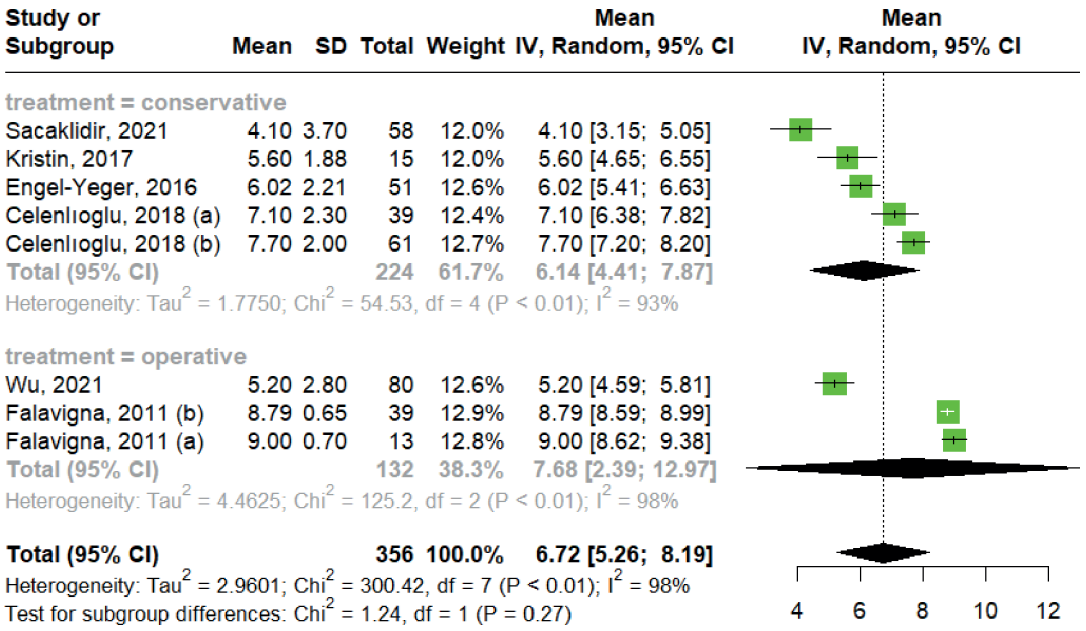

Figure 5. Subgroup Analysis of the VAS Back Pain Score at Baseline in Patients with LDDD by Treatment Type

Abbreviations: C.I.: confidence interval; LDDD: Lumbar Degenerative Disk Disease; SD: standard deviation; VAS: Visual Analogue Scale.

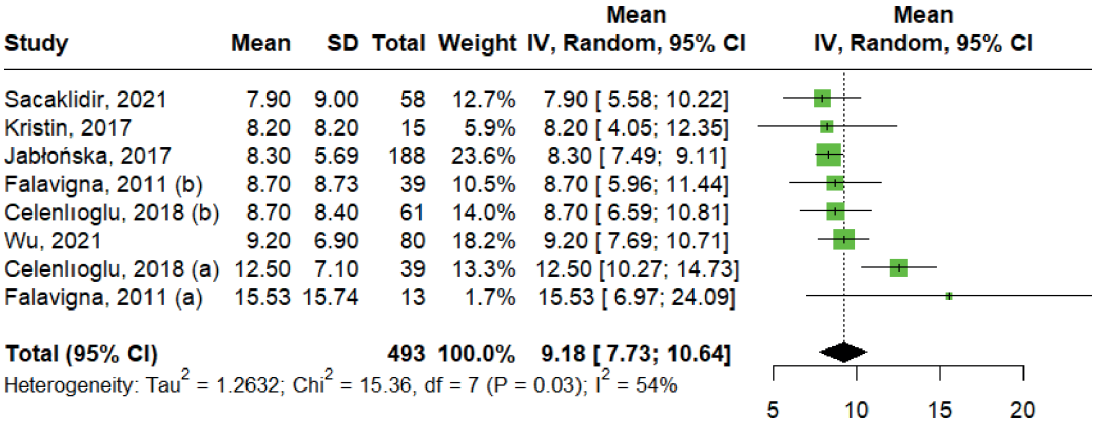

Figure 6. Pooled BDI Scores in Patients with LDDD at a 3-month Follow-up.

Abbreviations: BDI: Beck Depression Inventory; C.I.: confidence interval; LDDD: lumbar Degenerative Disk Disease; SD: standard deviation.

Sensitivity analysis was used to assess the robustness of the pooled estimates. The influence diagnostics of the BDI score dynamics at three 3-months revealed that Celenlioglu, 2018 (15) (study #7) was an outlier (pooled average mean BDI score = 12.50, 95% CI [10.27; 14.73]), as shown in Figure S8. A visual inspection of the funnel plot for BDI score dynamics at 3 months suggested a symmetric distribution of study results around the estimated effect size, which was confirmed by non-significant Egger's test p = 0.2397 (Figure S9).

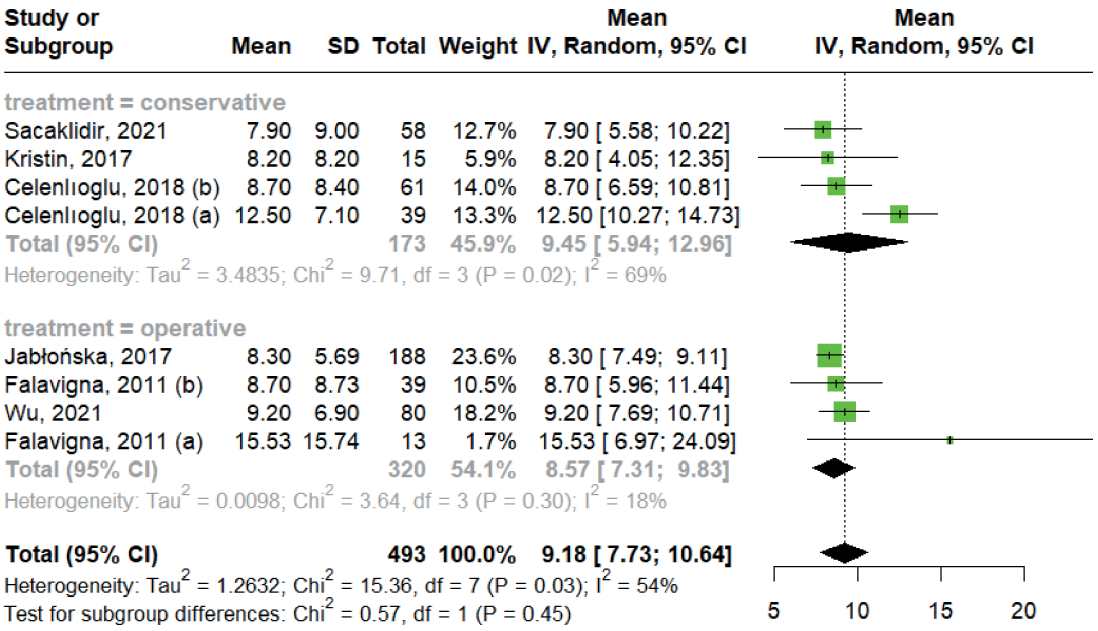

Figure 7. Subgroup Analysis of BDI Score Dynamics at a 3-Month Follow-Up in Patients with LDDD by Treatment Type.

Abbreviations: BDI: Beck Depression Inventory; C.I.: confidence interval; LDDD: lumbar Degenerative Disk Disease; SD: standard deviation.

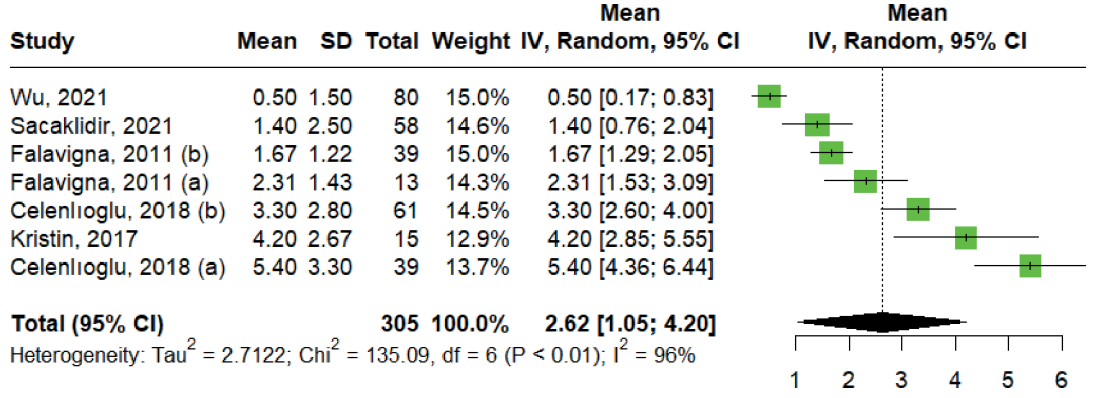

Figure 8. Pooled VAS Back Pain Scores in Patients with LDDD at a 3-month Follow-up.

Abbreviations: C.I.: confidence interval; LDDD: Lumbar Degenerative Disk Disease; VAS: Visual Analogue Scale

Pain at 3-month follow-up

Five studies with seven groups presented the VAS Back Pain score dynamics at the 3-month follow-up. Based on the random-effects model, the pooled average mean VAS back pain score at 3 months in patients with LDDD was 2.62 (95% CI [1.05; 4.20]). A test for heterogeneity indicated a high level of heterogeneity (I^2 = 96%, Q (df = 6) = 135.09, p < 0.01), as shown in Figure 8.

Subgroup analysis based on the type of treatment revealed significant heterogeneity among the studies. Utilizing the random-effects model, the pooled average VAS back pain score at the 3-month follow-up

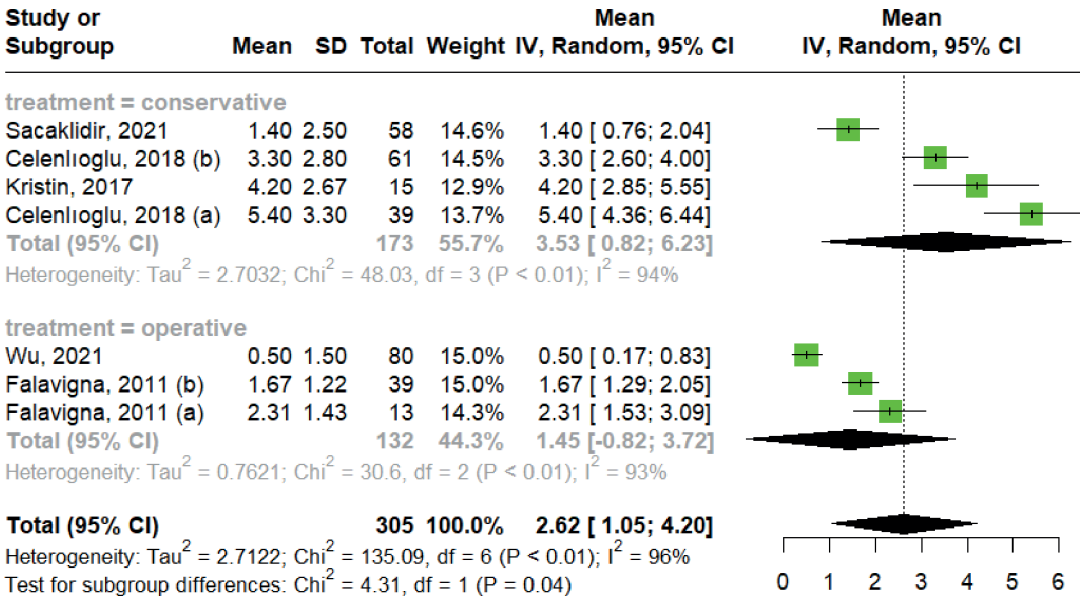

Figure 9. Subgroup Analysis of VAS Back Pain Score Dynamics at a 3-Month Follow-Up in Patients with LDDD by Treatment Type.

Abbreviations: C.I.: confidence interval; LDDD: Lumbar Degenerative Disk Disease; SD: standard deviation; VAS: Visual Analogue Scale.

for the four groups in the conservative treatment subgroup was higher than that in the operative subgroup. The scores were 3.53 (95% CI [0.82; 6.23]), I^2 = 94%, Q(df=3)=48.03,p<0.01,and1.45(95%CI[-0.82;3.72]), I^2 = 93%, Q (df = 2) = 30.6, p < 0.01, respectively. Both groups exhibited high heterogeneity, as shown in Figure 9.

Meta-regression analysis of the VAS back pain score dynamics at a 3-month follow-up by year of publication did not reveal significant changes in effect sizes over time, as depicted in Figure S10. Sensitivity analysis was used to assess the robustness of the pooled estimates. The influence diagnostics of the VAS back pain score dynamics at the 3-month follow-up revealed that Kristin Comella, 2017 (23) (study #6) was an outlier (pooled average mean VAS back pain score = 4.20, 95% CI [2.85; 5.55]), as shown in Figure S11. A visual inspection of the funnel plot for VAS back pain score dynamics at 3 months suggested an asymmetric distribution of study results around the estimated effect size, which was confirmed by significant Egger's test (p = 0.0003) (Figure S12).

Discussion

This systematic review and meta-analysis aimed to explore how depression and pain change in patients with LDDD from baseline to three months after treatment. Our findings offer several important insights into the relationship between depression and pain in these patients, which carry significant clinical implications. Our meta-analysis, using a random-effects model, showed a modest decrease in the mean BDI scores from 11.51 at baseline to 9.18 at three months post-treatment. In contrast, we observed a substantial reduction in the mean VAS back pain scores, dropping from 6.72 at baseline to 2.62 after three months. This suggests that while treatment for LDDD may effectively lower pain levels in the short term, its impact on depression is less pronounced.

Additionally, our study found that patients receiving conservative treatment had higher depression rates both at baseline (12.32) and at the three-month follow-up (9.45) compared to those undergoing operative treatment, who had depression scores of 11.23 at baseline and 8.57 at follow-up. Regarding pain,

patients in the conservative treatment group reported lower pain scores at baseline (6.14) but higher scores at the three-month follow-up (3.53) compared to the operative treatment group, which had baseline scores of 7.68 and follow-up scores of 1.45. Our findings align with previous research that indicates a high prevalence of depression among patients with LDDD and underscores the bidirectional relationship between depression and pain. Studies have demonstrated that mental health-related quality of life significantly impacts the subjective experience of pain; specifically, the severity of depression correlates with the severity of pain and the clinical severity of lumbar disease (25–27). Moreover, a meta-analysis on the prognostic value of fear-avoidance beliefs in LDDD patients shows that high fear-avoidance beliefs predict less improvement in postoperative pain intensity and back-specific function, and this effect is sustained for more than 12 months after surgery (28). Our findings also align with existing research, emphasizing the psychological burden of chronic pain in conservative management (29).

In patients with LDDD, chronic pain and depression affect more than just quality of life and disability, impacting social and economic aspects as well, as evidenced by increased opioid use and greater utilization of healthcare resources (30). Research on opioid use in patients undergoing lumbar surgery for degenerative lumbar spine conditions reveals that preoperative and perioperative opioid intake, the presence of degenerative disc disease, multiple prescribers, and depression are significant predictors of prolonged and intensive opioid use post-surgery (31).

One limitation of our study was the high heterogeneity observed among the included studies, which may have affected the robustness of our findings. Additionally, the three-month follow-up period may be insufficient for capturing the long-term changes in depression and pain levels. Another meta-analysis conducted by the authors of the present analysis, which assesses long-term postoperative outcomes of minimally invasive transforaminal interbody fusion in spondylolisthesis patients, indicates that improvements in pain and functional disability tend to decline over time (32).

Future research should focus on investigating the long-term effects of LDDD treatment on depression and pain. Additionally, studies exploring the mechanisms underlying the relationship between depression and pain in patients with LDDD may provide valuable insights into novel treatment approaches.

In conclusion, this systematic review and meta-analysis provide valuable insights into the dynamics of depression and pain in patients with LDDD. Our findings underscore the need for integrated treatment approaches that address both depression and pain to improve the outcomes of patients with LDDD. Although pain reduction is achievable, the management of depression remains a challenge. Future research should explore multidisciplinary approaches and long-term outcomes to optimize patient care.

Author Contribution Statement: IK: Conceptualization, Methodology, Investigation, Formal Analysis, Visualization, Writing – original/draft preparation, Writing–Review and Editing. YK: Resources, Software, Data curation, Supervision, Writing – original/draft preparation, writing–review and editing. MI: Validation, Writing - Review, and Editing. BT: Writing – original/draft preparation, Supervision, Project Administration, Investigation. SM: Writing–Review and Editing, Project Administration.

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Availability of Data: The data used for the analysis in this study are available from the corresponding author upon reasonable request.

Study Registration: The study protocol was registered in the PROSPERO database (Reference: CRD42024561303).

Ethics Statement: The Ethics Commission of Kazakhstan Medical University "KSPH" approved this study under study number #IRB-164-2024, dated 02.05.2024.

Conflict of Interest: The authors declare no conflict of interest regarding this article.

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Correspondence:
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Yerzhan Kuanyshbekov, MD
Department of Spinal Neurosurgery and Peripheral Nervous System Pathology, National center for Neurosurgery, Astana, Kazakhstan, 010000
E-mail: erjan_k96@mail.ru
ORCID: 0009-0007-5142-833X.

ANNEX

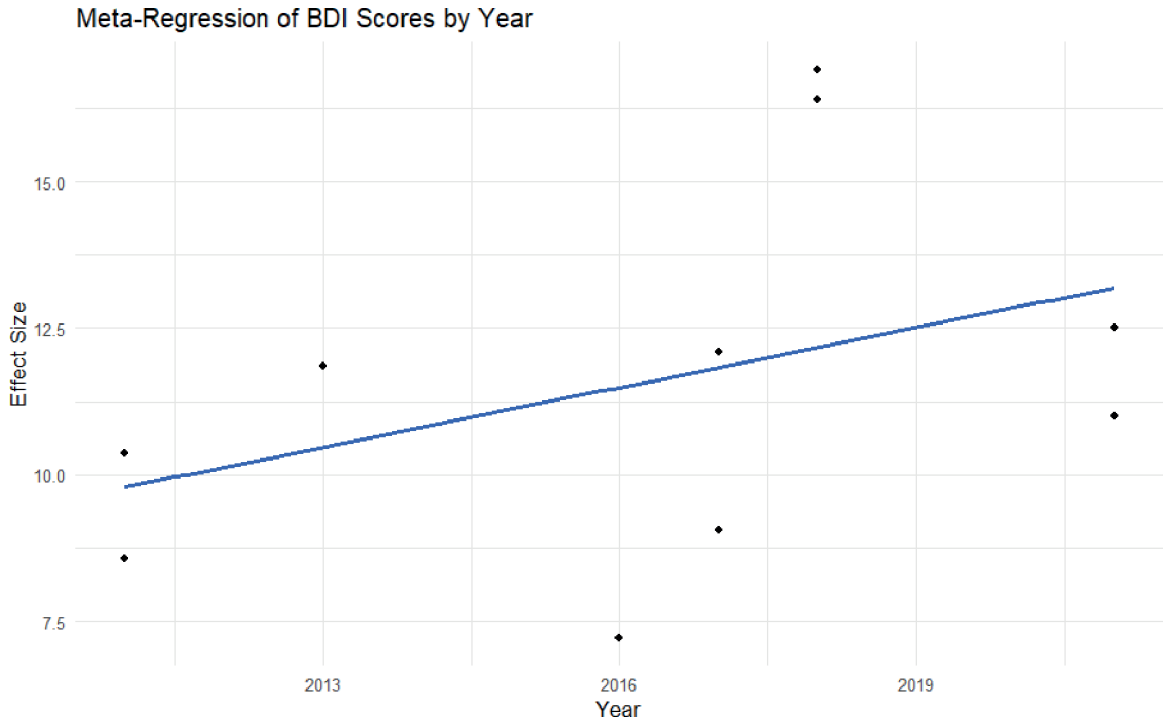

Figure S1. Meta-Regression Analysis of the BDI Score at Baseline in Patients with LDDD by Year of Publication.
Abbreviations: BDI: Beck Depression Inventory; LDDD: Lumbar Degenerative Disk Disease.

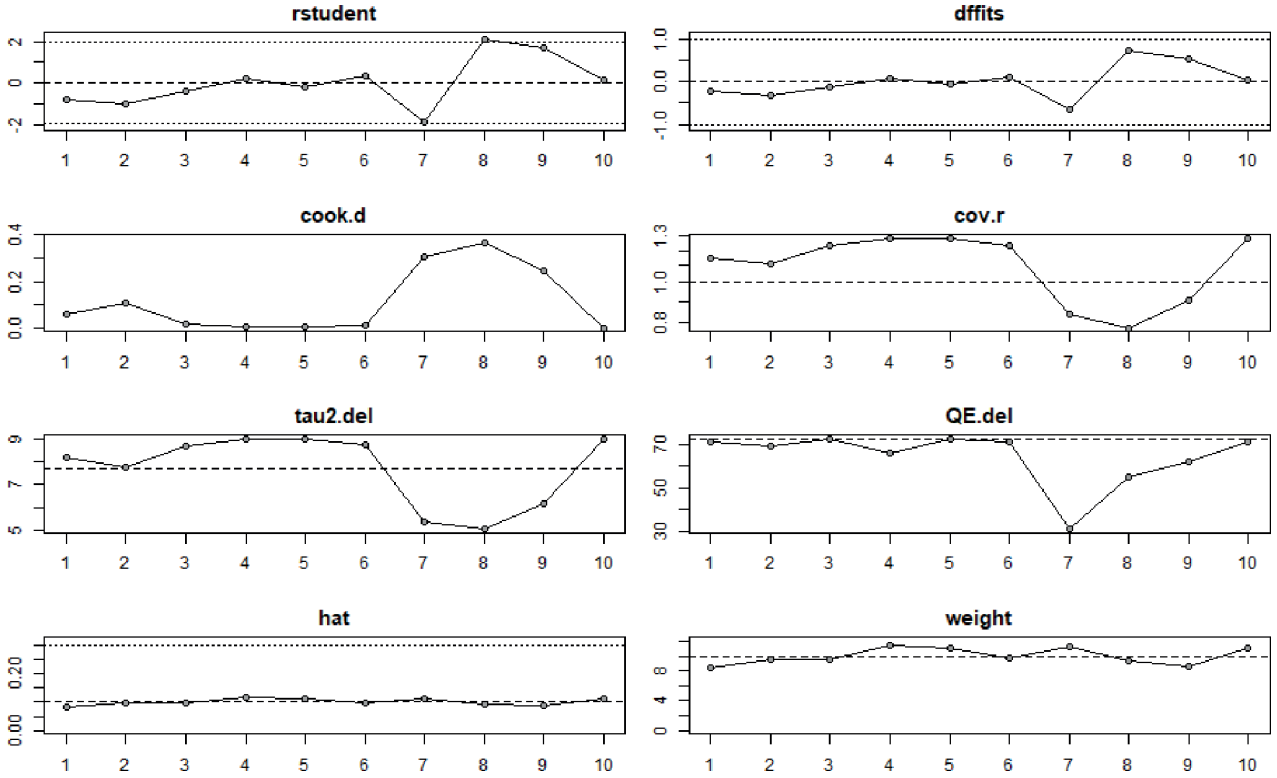

Figure S2. Influence Diagnostics for BDI Score at Baseline in Patients with LDDD.
Abbreviations: BDI: Beck Depression Inventory; LDDD: Lumbar Degenerative Disk Disease.

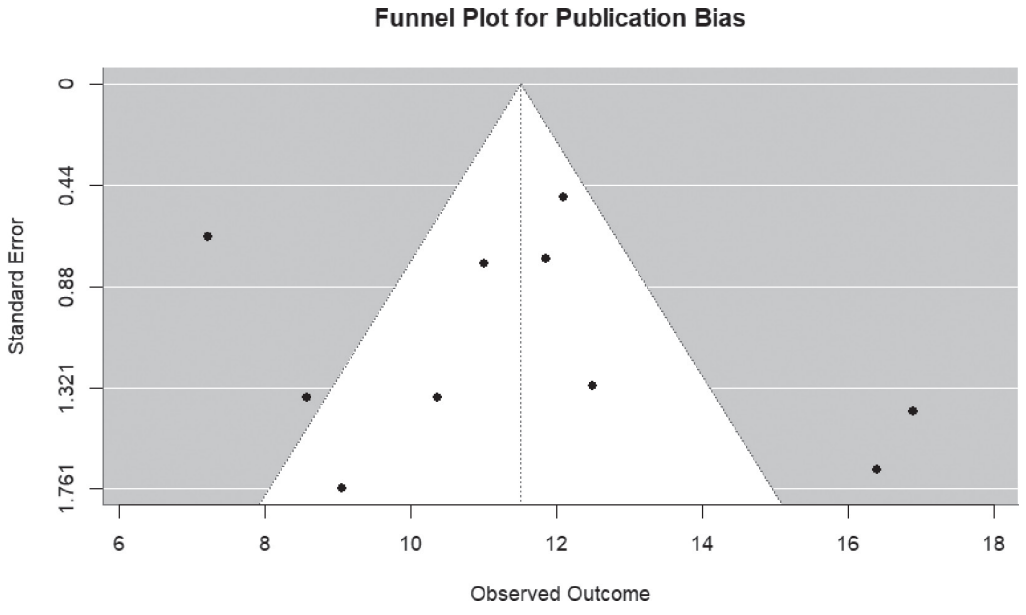

Figure S3. Publication Bias Assessment for the BDI Score at Baseline in Patients with LDDD.
Abbreviations: BDI: Beck Depression Inventory; C.I.: confidence interval; LDDD: Lumbar Degenerative Disk Disease; SD: standard deviation.

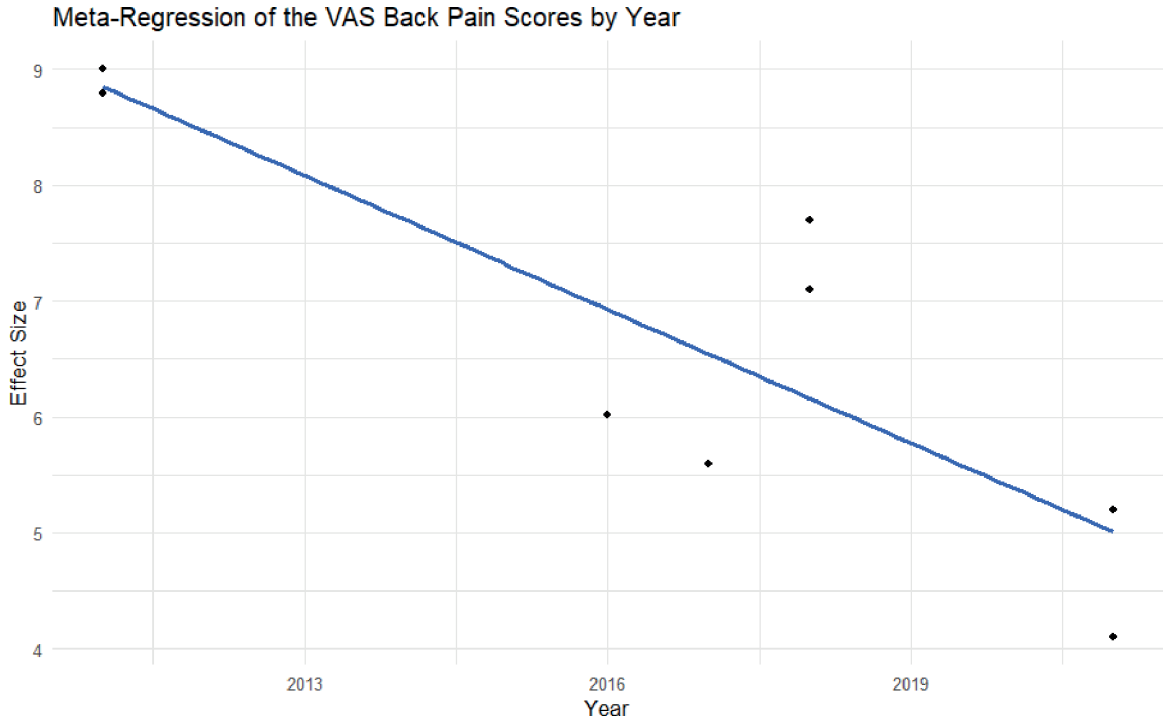

Figure S4. Meta-Regression Analysis of the VAS Back Pain Score at Baseline in Patients with LDDD by Year of Publication.

Abbreviations: LDDD: Lumbar Degenerative Disk Disease; VAS: Visual Analogue Scale.

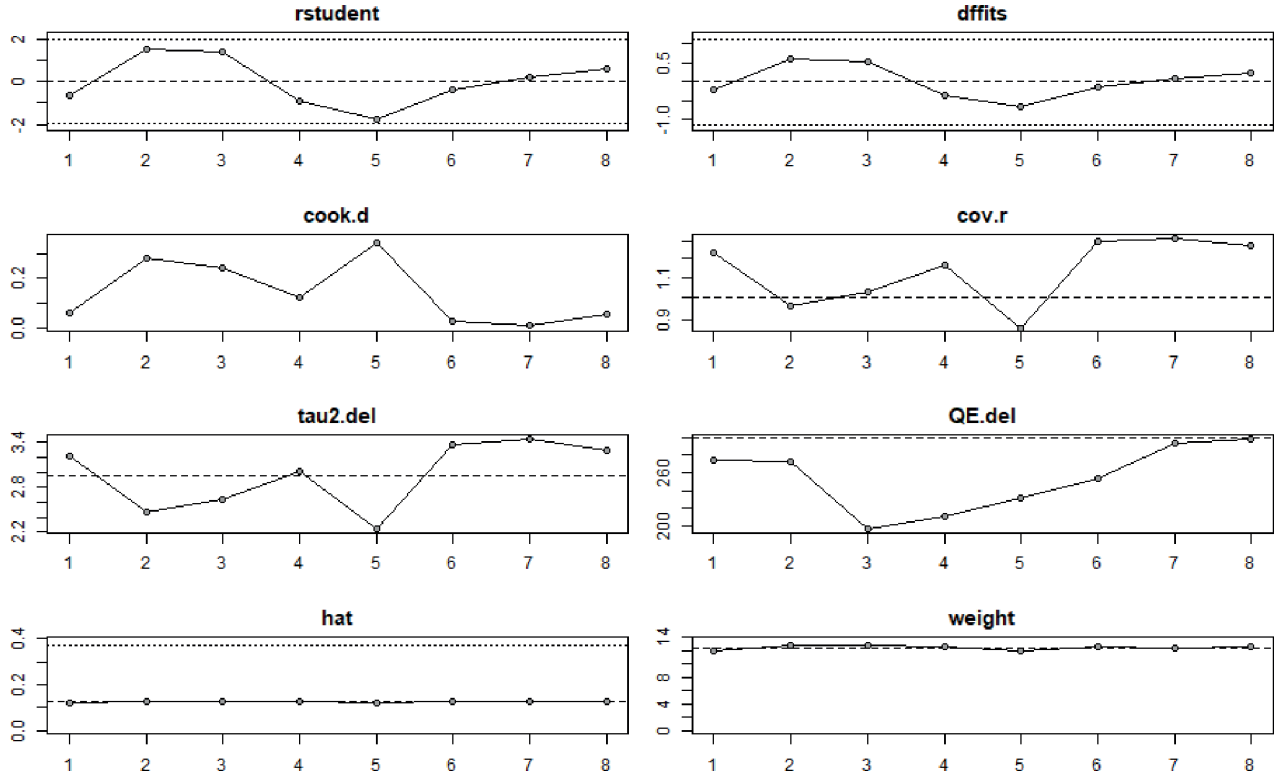

Figure S5. Influence Diagnostics for VAS Back Pain Score at Baseline in Patients with LDDD.

Abbreviations: LDDD: Lumbar Degenerative Disk Disease; VAS: Visual Analogue Scale.

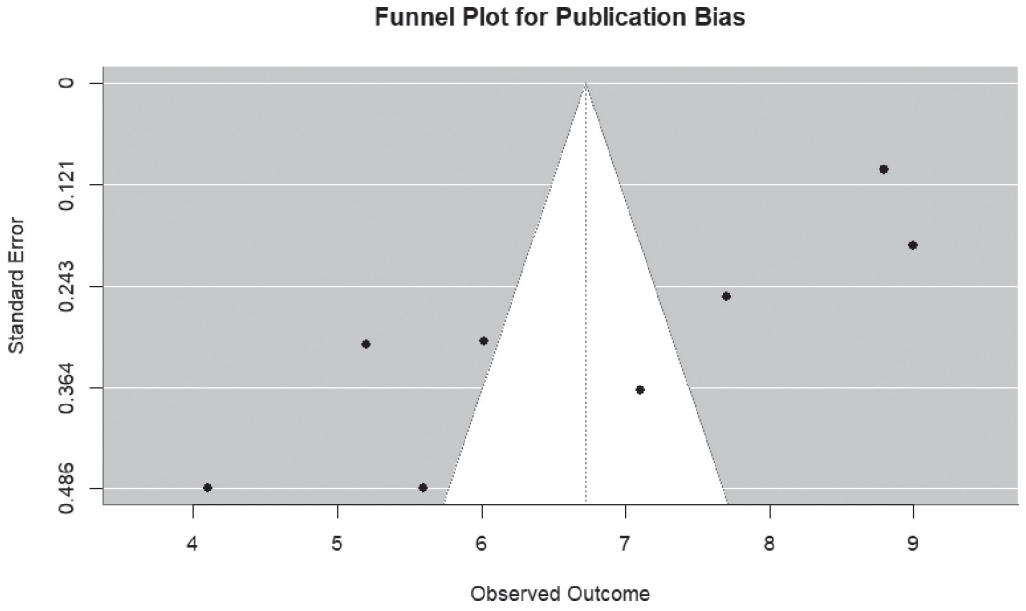

Figure S6. Publication Bias Assessment for the VAS Back Pain Score at Baseline in Patients with LDDD.
Abbreviations: LDDD: Lumbar Degenerative Disk Disease; VAS: Visual Analogue Scale.

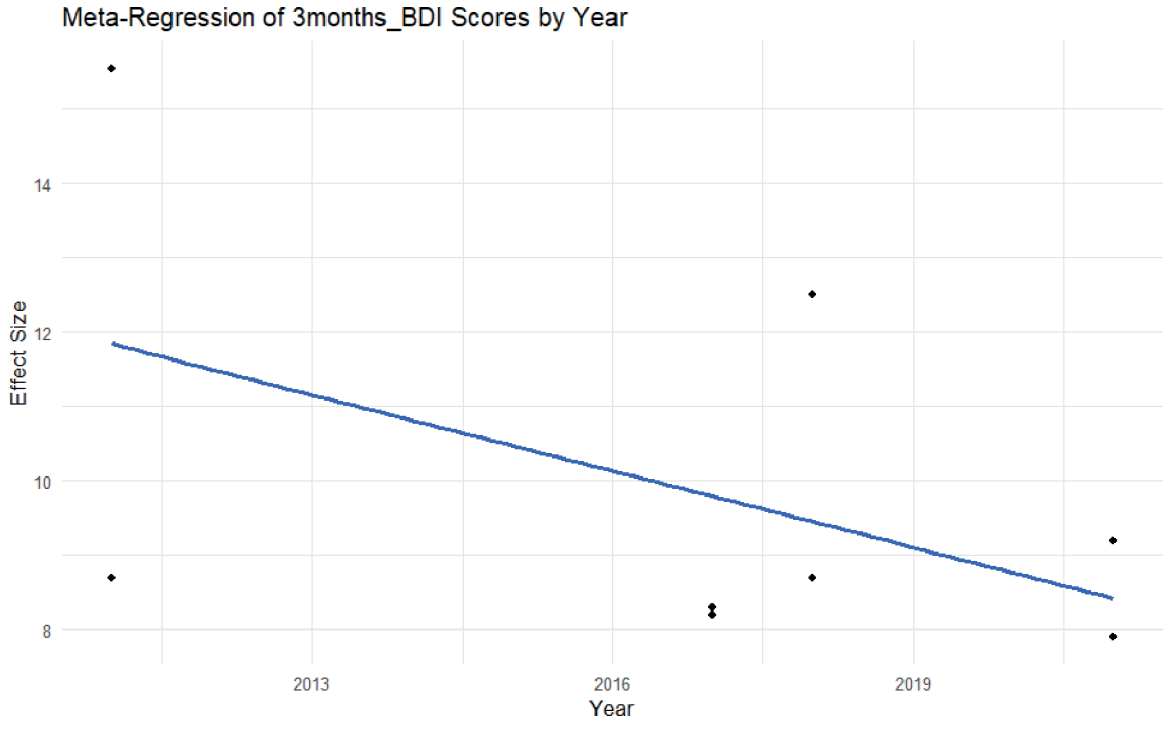

Figure S7. Meta-Regression Analysis of the BDI Score Dynamics at a 3-Month Follow-up in Patients with LDDD by Year of Publication.
Abbreviations: BDI: Beck Depression Inventory; LDDD: lumbar Degenerative Disk Disease.

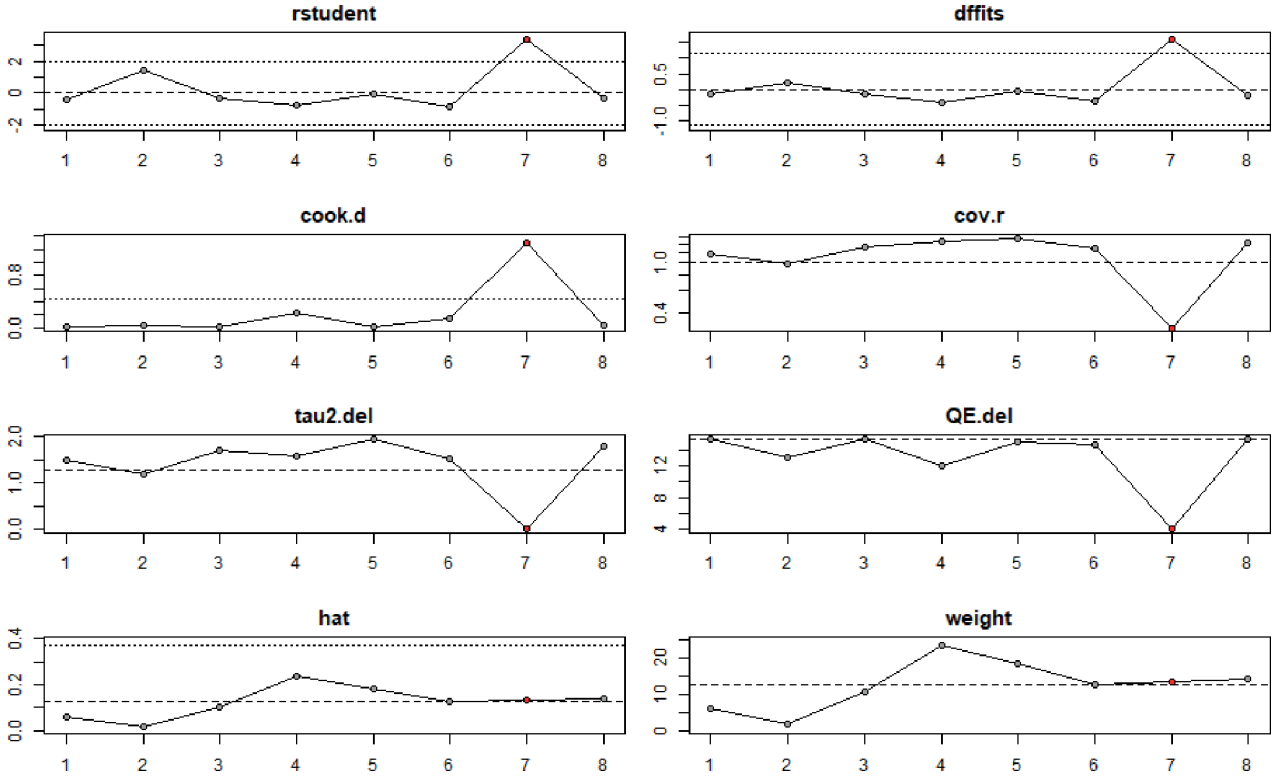

Figure S8. Influence Diagnostics for BDI Score Dynamics at a 3-Month Follow-up in Patients with LDDD.
Abbreviations: BDI: Beck Depression Inventory; LDDD: Lumbar Degenerative Disk Disease.

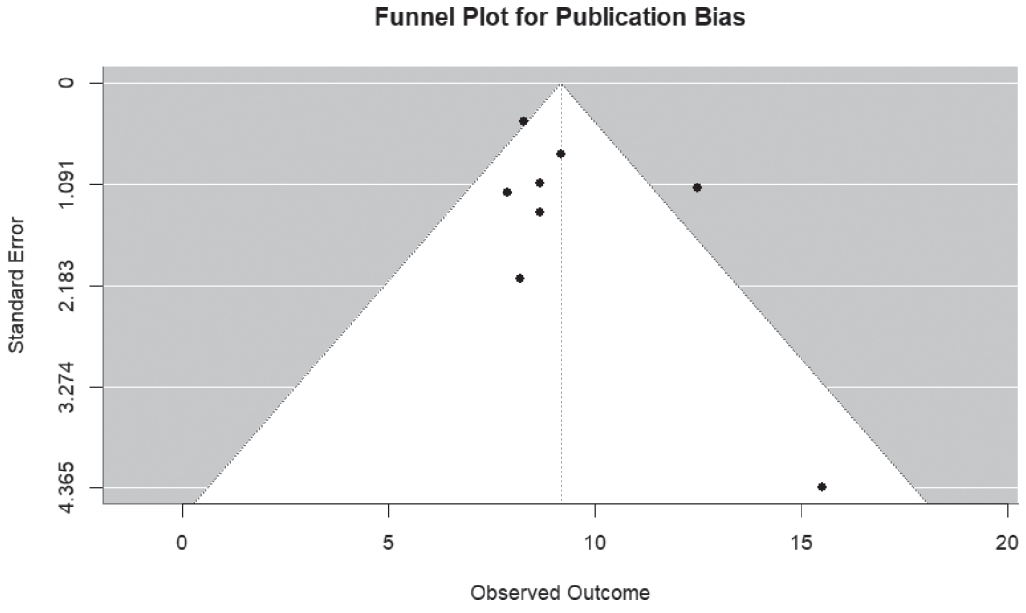

Figure S9. Publication Bias Assessment for the BDI Score Dynamics at a 3-Month Follow-up in Patients with LDDD.
Abbreviations: BDI: Beck Depression Inventory; LDDD: Lumbar Degenerative Disk Disease.

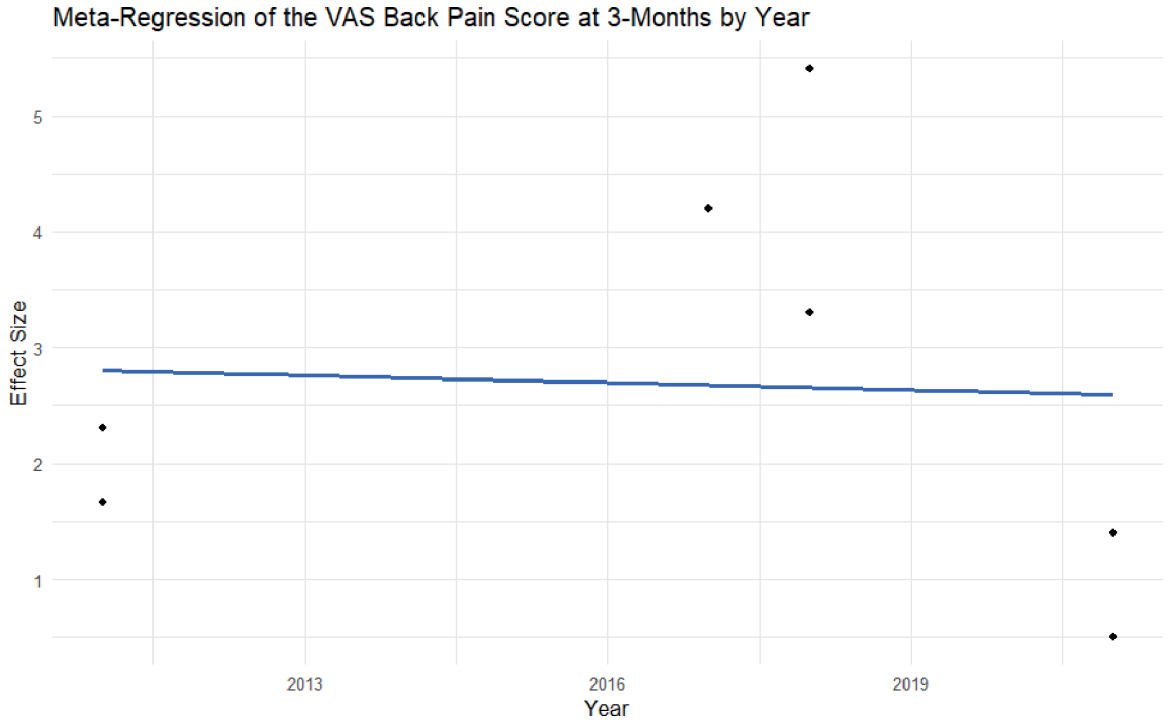

Figure S10. Meta-Regression Analysis of the VAS Back Pain Score Dynamics at a 3-Month Follow-up in Patients with LDDD by Year of Publication.

Abbreviations: BDI: Beck Depression Inventory; LDDD: lumbar Degenerative Disk Disease.

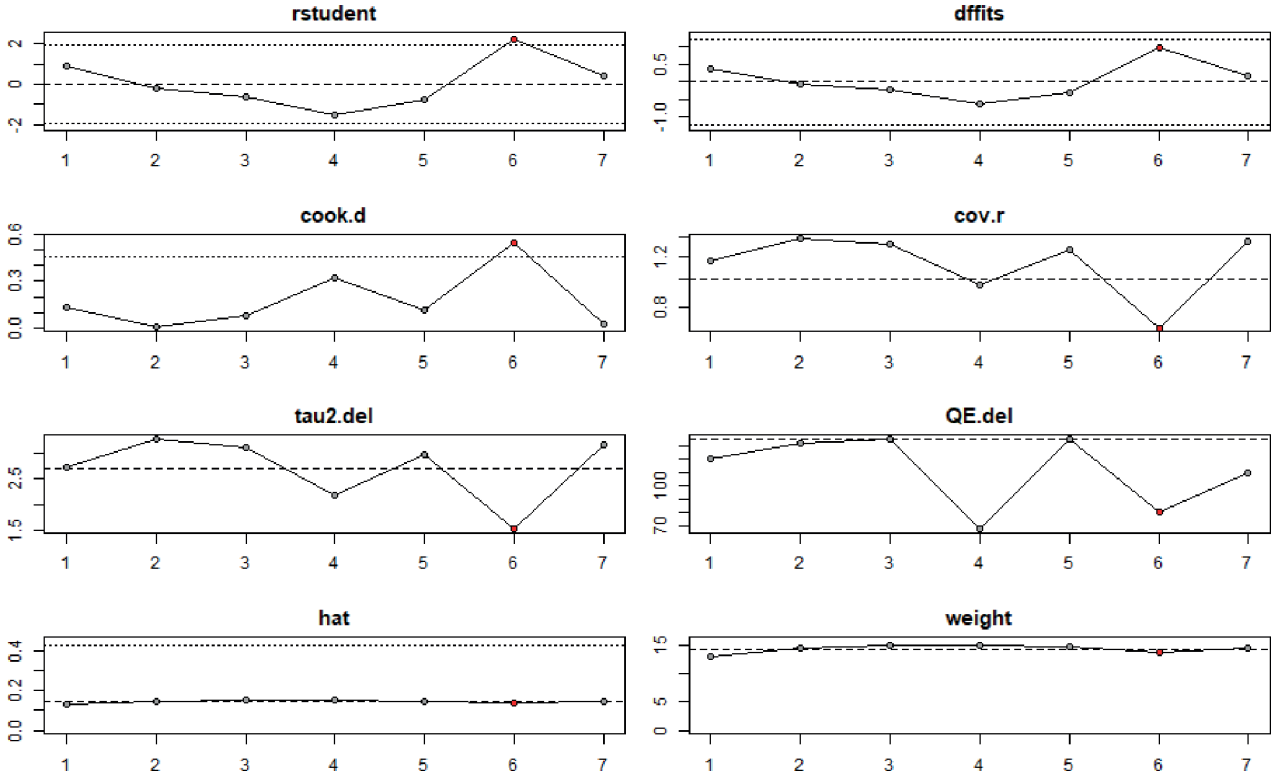

Figure S11. Influence Diagnostics for VAS Back Pain Score Dynamics at a 3-Month Follow-up.
Abbreviations**:** LDDD: Lumbar Degenerative Disk Disease; VAS: Visual Analogue Scale.

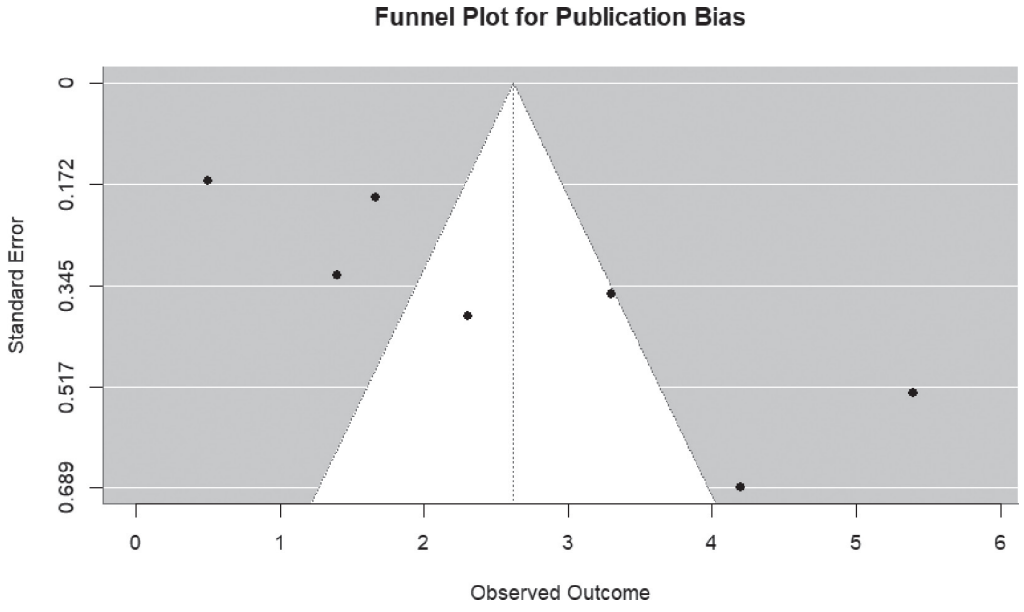

Figure S12. Publication Bias Assessment for the Visual Analogue Scale Back Pain Score Dynamics at a 3-Month Follow-up.

S1 Table. Search strategy of the Systematic Review of the depression and Pain Dynamics in Lumbar Degenerative Disk Disease in LDDD.

Pubmed	Web of Science	Science Direct	Academic Search complete	Google Scholar
Criteria: Search in All Fields. **Filter: none** **Search date:** **January - March 2024** 1. Depression degenerative disk disease 2. Pain degenerative disk disease (English only)	**Criteria: Search in All Fields.** **Filter: include only "Articles"** **Search date:** **January - March 2024** 1. Depression degenerative disk 2. Pain degenerative disk	**Criteria: Search in All Fields.** **Filter: include only Content type: Research Articles. Search date:** **January - March 2024** 1. Depression AND "degenerative disk" 2. Pain AND degenerative disk: search in Title/ abstract or Keywords.	**Criteria: Search in All Fields.** **Filter: include only publications in English, and academic journals. Search: Title/ Abstract** **Search date:** **January - March 2024** • Depression AND "degenerative disk" • Pain AND "degenerative disk"	**Criteria: Search in Abstract.** **Filter: Do not include patents. Do not include citations. Exclude review** **Search date:** **January - March 2024** 1. abstract: Depress* "Degenerative disk" -review -cancer -animal - 86 2. abstract: Pain AND "Degenerative disk" -cancer -animal -review -poster - 30