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Article

Effects of Multidisciplinary Biopsychosocial Rehabilitation on Short-Term Pain and Disability in Chronic Low Back Pain: A Systematic Review with Network Meta-Analysis

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Abstract: Chronic Low Back Pain (CLBP), defined as pain persisting for at least 12 weeks, is a significant public health issue, with prevalence intensifying due to an ageing global population, amassing approximately 619 million cases in 2020 and projected to escalate to 843 million by 2050. Given the multitude of therapeutic modalities available for CLBP, this research sought to ascertain their respective efficacies in ameliorating pain and disability. We specifically scrutinized Multidisciplinary Biopsychosocial Rehabilitation (MBR) among adults enduring non-specific low back pain for over 12 weeks, excluding acute pain conditions and pre-study surgical interventions. MBR is an approach encompassing various modalities, including exercise, behavioral therapies, educational programs, and work conditioning aspects, necessitating a comprehensive Network Meta-Analysis (NMA) to fully grasp the extensive scope of its impact. The constructed network comprised diverse MBR modalities (behavioral, educational, and work conditioning) alongside exercise therapy (ET), minimal intervention, and usual care, serving as controls with pain and disability as outcomes. Through the analysis of 4,619 initially identified studies, 93 were included, encompassing a total of 8,059 participants. The NMA conducted substantiated that both ET and MBR modalities were notably effective in alleviating CLBP, with education-oriented MBR emerging as the most efficacious for pain mitigation and behavior-focused MBR for disability reduction. Nevertheless, the discerned differences amongst the treatments were minimal and uncertain, highlighting that no modality was definitively superior to the others. The analysis revealed low global and local inconsistency within the network, underscoring the reliability of the observed outcomes. Given the intricate nature of CLBP, embodying various facets, our findings advocate for a combined therapeutic approach to optimize treatment efficacy. Nonetheless, the presence of high study heterogeneity and potential biases necessitates cautious interpretation of the results, prompting future research.

Keywords: chronic low back pain; multidisciplinary biopsychosocial rehabilitation; exercise therapy; network meta-analysis

1. Introduction

Chronic low back pain (CLBP) is characterized by pain and discomfort localized below the inferior margin of the 12th ribs and above the inferior gluteal folds, persisting for a duration of at least 12 weeks, usually without a specific cause of the pain [1]. In contrast, acute low back pain is often transient and has a clear underlying cause, such as mechanical injury while the etiology of CLBP is often multifactorial, encompassing structural, biomechanical, neurological, psychological, and social elements. While the general prognosis is good, the high prevalence rate is what makes CLBP a major

public health issue, especially given that CLBP prevalence increases linearly with age [2] and the global population is ageing [3]. In 2020 number of low back pain cases was estimated to be 619 million (95% Uncertainty Intervals (UI) 554-694), with a projected number of cases rising to 843 million (95%: UI 59-933) by year 2050 [4]. Globally pooled, overall cost, per patient, per annum was estimated at 10,100 (95% CI 6,100\$-14,200\$) [5].

According to clinical guidelines, exercise therapy (ET) is broadly recommended as the first line of treatment for reducing pain and disability with no clear evidence supporting any specific modality over the others [6]. Given the multifactorial nature of CLBP causes, as well as the influence of psychosocial patient aspects of pain and disability [7], exercise therapy is often paired with various other forms such as pharmacotherapy (paracetamol, nonsteroidal anti-inflammatory drugs), patient education, psychosocial interventions, work hardening, and multidisciplinary rehabilitation. Alternatively, invasive treatments, such as surgery, spinal injections, and radiofrequency denervation are also used [6,8,9]. An updated overview that collected national clinical practice guidelines identified that 9 out of 11 guidelines recommend multidisciplinary rehabilitation [8].

Multidisciplinary biopsychosocial rehabilitation (MBR) is a comprehensive approach to the management of conditions like chronic low back pain (CLBP). It is rooted in the biopsychosocial model, which posits that biological, psychological, and social factors all play significant roles in human functioning in the context of disease or illness [10]. Key to the MBR approach is that the intervention program should be delivered by a team of healthcare professionals from different backgrounds. This team may include physicians, psychologists, physiotherapists, social workers, occupational therapists, and others. At least two professionals from different backgrounds should be involved in the intervention delivery [11]. It's vital that the various components of the intervention are integrated and that there is active communication between the providers responsible for different aspects of the patient's care.

While research into MBR as a treatment option for CLBP has shown [10,12] its viability, similarly to ET there are no recommendations as to what modality of MBR has the largest effect on pain and disability, nor how does ET, a first-line treatment, compare with various modalities of MBR. A network meta-analysis, which simultaneously compares multiple treatment modalities, is potentially more effective for comparing treatment options. The research question posed in this systematic review is:

How do the modalities of multidisciplinary biopsychosocial rehabilitation (MBR) compare to exercise therapy (ET), usual care (UC), and minimal intervention (MI) in terms of efficacy for short-term pain and disability relief in individuals with chronic low back pain?

2. Materials and Methods

2.1. Protocol and registration

This meta-analysis was carried out following the PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions [13] and is registered with PROSPERO (CRD42022321892) [14].

2.2. Eligibility criteria

Study characteristics adhered to the PICOS framework:

Population: The systematic review focused on adult individuals (18+ years old) with non-specific low back pain persisting for longer than 12 weeks. Studies examining individuals with serious medical conditions that mimic CLBP symptoms such as trauma injury, compressive vertebral fracture, disc herniation, spinal stenosis, rheumatic disease, and cancer were excluded. Conditions like disc degeneration, bulging disc, and osteoarthritis of facet joints were included, given their commonality and often non-severe symptoms. In terms of context, studies in outpatients' clinics and other clinical settings were included. No context-related exclusion criteria were identified.

Intervention: In the context of this systematic review, MBR was characterized as an intervention that includes a physical component, such as an exercise program or similar physiotherapy

intervention, combined with at least one other component drawn from the psychological or social and occupational domains of the biopsychosocial model. We initially considered studies examining four modalities: behavioral (MBR-BE), biofeedback, work/physical conditioning programs (MBR-WR), education programs (MBR-ED) based on previous systematic reviews [10,15].

Studies where surgical intervention was undertaken at any point before intervention were excluded, but studies that used pharmacotherapy along investigated therapeutic modalities were included.

Comparator: Three comparators were used for the network. Exercise therapy (ET), and two Controls - minimal intervention (MI) or usual care (UC). Comparator was classified as MI if the study stated explicitly that no therapy was provided for the participants. This includes participants on waiting lists and participants who were instructed how to generally manage CBLP but were never given any specifics on exercise or how to modify their activities. UC received standard care for CLBP, usually including some form of physiotherapy and/or general exercises for lower back issues. Studies featuring surgical intervention before ET, MI, or UC as comparators were excluded.

Outcome: The main outcomes were pain and disability. Pain was primarily measured via the Visual Analogue Scale, McGill Pain Questionnaire, Numerical Rating Scale, while disability was measured via the Roland Morris Disability Questionnaire, Quebec Back Pain Disability Scale, Oswestry Low Back Pain Disability Questionnaire, Pain Disability Index, and Hannover Functional Ability Questionnaire. For inclusion, only outcomes measured immediately after intervention were considered for this study.

Study Design: Only randomized controlled trials (RCT) were included in the systematic review.

2.3. Information sources & Search strategy

Information sources included the following electronic databases: MEDLINE, PEDro, EMBASE, CINAHL, CENTRAL, and PsycINFO. The literature search included studies up to March 4, 2022. No gray literature, clinical trial registries or regulatory agencies websites were searched. Authors of included studies were contacted if any clarification or additional data was needed for their studies. The complete search strategy is available in supplement materials (Document S1).

2.4. Study selection

Studies were screened by title and abstract independently by two researchers (KD & LE). Any disagreements were resolved by a third researcher (IJ). Full text selection was conducted by the same researchers. Studies were considered eligible if they compared any combination of ET, MBR, and either Control (MI or UC). Studies were excluded if the pain experienced by the participants was explicitly stated to be specific and acute. If no such statements were made, we examined the inclusion criteria for specific diagnoses and reviewed the sample description for reported pain duration to determine whether the underlying cause of the pain was nonspecific. Studies were also excluded if they did not measure pain or disability. The review process utilized the Covidence review management system [16].

2.5. Data collection process & Data items

Raw data were extracted to a prepared data extraction form from eligible studies by two researchers (KD & LE). A third researcher (IJ) extracted data that needed recalculation (i.e., standard errors (SE) to standard deviations (SD), or medians to means), or if only the graphically presented data were available. If it was not possible to extract the data, authors of the original studies were contacted twice to supply their data. The last step was to check whether the extracted data matched the data used in previous similar systematic reviews and meta-analyses [10,17]. As a final measure, due to strong relationships between means and SDs of all studies, the SDs for two studies with missing data were imputed using a linear regression model.

Along with the intervention groups, mean, SD and sample size, the following variables of interest were extracted with the purpose of inclusion in the analysis: specific measures used for both

pain and disability outcome assessment, number of male and female participants per intervention group, mean duration of therapeutic intervention in weeks, mean length of therapeutic interventions in hours per week, mean age, mean BMI, mean duration of symptoms in months.

2.6. Geometry of the network

The network incorporates multidisciplinary biopsychosocial rehabilitation with following modalities: behavioral (MBR-BE), education programs (MBR-ED), work/physical conditioning (MBR-WR), and exercise therapy (ET). Finally, Usual Care (UC) and Minimal Intervention (MI) were also included as nodes. Minimal intervention was used as the reference treatment. Geometry of the network is represented in network diagram (Figure 1).

2.7. Risk of bias within individual studies and across studies

Risk of bias was assessed at the study level by Cochrane's Risk of Bias 2 tool [18]. Studies were categorized by their Overall Risk of Bias into low bias, some concerns and high bias categories. The Overall Risk of Bias in our network meta-analysis was determined by an algorithm that considered the importance and level of bias across different domains. We identified D1, D3, and D4 as the most impactful domains for the bias assessment due to their inherent attributes in study design and data management. Rob 2 algorithm for Overall Risk of Bias is detailed in the supplement materials (Document S2). Rob 2 was visualized by *robvis* tool [19].

The possible presence of publication bias was evaluated using funnel plots and Egger's test.

2.8. Summary measures

Data collection and analysis were performed based on outcomes and specific data points. Diverse visual analogue scales for pain outcomes were rescaled to 0-100, employing a similar approach as in the most recent Cochrane review on a related topic [17]. As for disability outcomes, multiple scales were also utilized. These Health-Related Quality of Life Questionnaires (HRQoL), which are inherently more complicated than visual analogue scales, were maintained as raw data for the calculation of Hedges' *g* standardized mean difference (SMD) effect size estimators [20].

Since we are primarily interested in modalities of MBR, if a particular study had more than one ET modalities, their means and SDs were pooled together according to procedures for pooling groups descried in Cochrane's manual [21].

2.9. Planned methods of analysis

All statistical analyses were conducted using the R statistical software (version 4.3.1), utilizing the *netmeta* package for network meta-analysis (NMA) [22].

For the analysis, a frequentist random-effects NMA was conducted, and multi-arm studies were integrated into the network. The non-independence of these multi-arm studies was addressed by reweighting all comparisons within each study.

2.10. Assessment of Heterogeneity & Inconsistency

Due to high expected heterogeneity, the restricted maximum-likelihood estimator (REML) was used for calculating between-study variance (tau²), with Q-profile for calculating the confidence interval of tau² and tau. Treatment rankings were determined using P-scores, which are the frequentist counterparts of SUCRA values [20]. Global inconsistency was evaluated using the Q statistic based on full design-by-treatment interaction random effects model (DBT model), whereas local inconsistencies were assessed through node-splitting analysis.

2.11. Additional analyses

Given that we expected high heterogeneity and inconsistency, a Bayesian network metaanalysis, using the same dataset and non-informative priors, employing Markov Chain Monte Carlo

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simulation with 10⁵ iterations and a burn-in period of 5,000 iterations was performed as a sensitivity analysis to better assess uncertainty and to perform a network meta-regression analysis using RoB 2 as a covariate. Treatment rankings by surface under the cumulative ranking curve (SUCRA) values were compared to rankings by frequentist P-value rankings.

3. Results

3.1. Study selection & Included studies charateristics

Initial databases search identified 4619 references and 4616 studies. Automated duplication screen removed 1836 as duplicates. Title and abstract screening phase removed 2308 studies and 380 additional studies were removed during full-text screening phase. Two thirds (66.8%) of the removed studies compared interventions that were of no interest for this systematic review and subsequent meta-analysis. Finally, 93 (87 for pain outcomes and 74 for disability outcomes) studies were marked for data extraction and analysis [23–115]. PRISMA flow diagram can be found in supplement materials (Figure S1).

For screening, the inter-rater reliability, assessed using Cohen's kappa, demonstrated moderate agreement in title and abstract screening (κ = 0.542), and fair agreement during the full-text screening phase (κ = 0.357).

Table 1 summarizes the basic parameters of population in the included studies. In our study, we included a total of 93 trials with a combined participant count of 8,059 individuals.

Population characteristics	Mean (min, max)	# of studies	Sample size
Male [%]	31.18%	72	6476
Age [years]	44.61 (21.4 to 73.63)	88	7432
BMI	25.89 (20.77 to 35)	61	5075
Symptom duration [months]	53.6 (5.3 to 222)	40	4101
Intervention duration [weeks]	9.01 (1 to 24)	84	7163
# of hours per week	2.3 (0.12 to 30)	80	6867

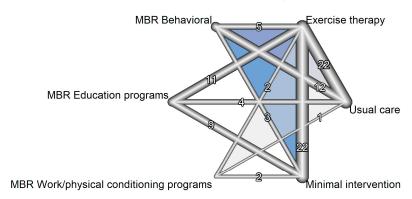
Table 1. Characteristics of included trials population.

Most of the included studies (84 studies, 96.55%) employed the Visual Analogue Scale (VAS) as the primary instrument to gauge pain outcomes, with values ranging from 0-10 or 0-100. A few other scales, like McGill Pain Questionnaire (MGPQ, 2 studies, 2.3%), and Pain Rating Chart (PRC, 1 study, 1.15%), were also used. Regarding disability outcomes, the Roland-Morris Disability Questionnaire (RMDQ, 41 studies, 47.13%) and the Oswestry Disability Index (ODI, 30 studies, 39.19%) were the most utilized. Other scales used include the Quebec Back Pain Disability Scale (QBPDS, 3 studies, 4.05%) and Physical Disability Index (DI, 1 study, 1.35%). Table of study characteristics of pain and disability outcomes, comparisons, and number of participants per study is available in supplement materials (Table S1).

3.2. Presentation of network structure & summary of network geometry

Figure 1 shows a network structure for pain and disaiblity outcomes respectively. Blue, light blue and gray tringles show presence of multi-arm studies in these particular comparisons of nodes. Unsurprisingly, Exercise therapy in general, followed by minimal intervention and usual care are the most connected nodes to the network, while MBR modalities have fewer connections. There was only one included study evaluating biofeedback and it was merged into behavioral MBR group (MBR-BE) as these modalities are more closely related than the others.

Network structure of pain outcome



Network structure of disability outcome

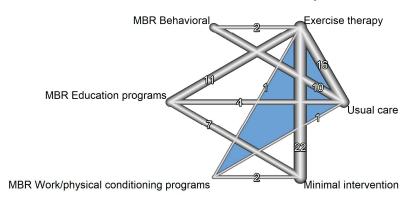


Figure 1. Network structure of pain & disability outcomes.

3.3. Risk of bias within studies

Summary of the risk of bias, using Risk of Bias 2 tool is presented in Figure 2. In evaluating the risk of bias in our collected studies on chronic low back pain treatment we observed variability in quality. The risk of bias arising from the randomization process was generally low or of some concern, indicating satisfactory randomization procedures. Bias due to deviations from intended interventions varied, with some studies flagged for high bias, suggesting potential implementation discrepancies. Most studies maintained solid data integrity, indicated by the predominantly low bias due to missing outcome data. Conversely, we noted substantial variations in bias in the measurement of outcomes and in the selection of reported results, with several studies presenting high bias. Ultimately, the overall bias ranged broadly across studies. These variances underscore the necessity for caution and rigorous interpretation in interpretation of analysis. Complete risk of bias figure for included studies can be found in supplement documents (Figures S2–S5).

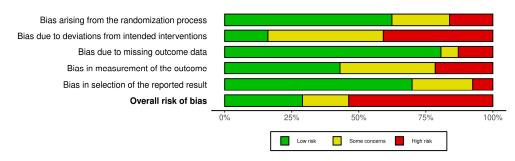


Figure 2. Summary of risk of bias of included studies.

The league table (Table 2) summarizes the comparative effects of different interventions on pain outcomes, with Minimal Intervention (MI) serving as the reference therapy. In this table, the lower triangle presents the network meta-analysis (NMA) estimates, which integrate both direct and indirect evidence to provide comprehensive comparisons between interventions. Conversely, the upper triangle showcases direct comparisons derived solely from head-to-head trials between the specific interventions. A positive mean difference indicates that the row intervention is more effective than the column intervention by the stated amount.

14.56 14.03 9.96 14.06 MI (10.41; 18.71)(-0.59; 28.65) (-1.68; 21.59)(7.43; 20.68)4.81 9.08 0.20 11.43 11.26 UC (0.02; 9.60)(1.62; 20.90)(4.90; 13.27)(-17.86; 18.26)(5.59; 17.28)12.38 7.57 1.53 10.27 9.99 ET (8.83; 15.94)(3.95; 11.20)(11.59; 14.64)(1.78; 18.77)(4.17; 15.80)12.65 7.84 0.27MBR-WR (3.09; 22.21)(-1.99; 17.68)(-9.19; 9.73)12.36 17.17 4.79 4.52 MBR-BE (11.34; 22.99)(7.52; 17.20)(-0.36; 9.93)(-6.02; 15.05)18.29 13.49 5.91 5.64 1.13 MBR-ED (13.70; 22.89)(8.42; 18.55)(1.67; 10.16)(-4.49; 15.77)(-5.19; 7.44)

Table 2. League table with direct comparison and NMA estimates of pain outcomes.

Legend: [values: mean difference (95% CI)]; **MI** = Minimal intervention; **UC** = Usual care; **ET** = Exercise therapy; MBR-**WR** = MBR Work conditioning/hardening; MBR-**BE** = MBR Behavioral; MBR-**ED** = MBR Education.

Looking at NMA estimations, MBR education (ED) demonstrated the largest mean difference in reducing pain outcomes, with a value of 18.18 (95% CI: 13.06 to 23.30). This was closely followed by MBR behavioral (BE) with a mean difference of 16.96 (95% CI: 10.47 to 23.46). MBR work conditioning/hardening (WR) showed a mean difference of 12.72 (95% CI: 2.05 to 23.39) in pain reduction, while exercise therapy (ET) exhibited a mean difference of 12.37 (95% CI: 8.40 to 16.34). It's noteworthy that some comparisons included negative lower limits in their confidence intervals, indicating nonsignificant effect. Table of mean differences and standard errors of pain and disability outcomes by study, is available in supplement materials (Tables S2 and S3).

Table 3 shows the direct comparison and NMA estimates concerning disability outcomes across varying interventions. A positive, higher value of standardized mean difference indicates that the row intervention is more effective than the column intervention by the stated amount. Looking at indirect estimations and using minimal intervention (MI) as the reference, MBR behavioral (MBR-BE) exhibited largest SMD of 0.88 (95% CI 0.46 to 1.30) with no direct comparison available.

	8	1		J	
MI		0.55 (-0.24; 1.35)	0.66 (0.42; 0.89)	0.28 (-0.12; 0.68)	
0.07 (-0.24; 0.37)	UC	-0.11 (-1.15; 0.92)	0.44 (0.17; 0.71)	0.73 (0.17; 1.30)	0.81 (0.46; 1.16)
0.43 (-0.18; 1.03)	0.36 (-0.28; 0.99)	MBR-WR	-0.05 (-1.10; 0.99)		
0.53 (0.32; 0.74)	0.46 (0.23; 0.70)	0.10 (-0.51; 0.72)	ET	0.36 (0.03; 0.69)	0.37 (-0.36; 1.10)
0.67 (0.40; 0.94)	0.60 (0.29; 0.91)	0.24 (-0.40; 0.89)	0.14 (-0.11; 0.39)	MBR-ED	
0.88	0.81	0.45	0.35	0.21	MBR-BE

Table 3. League table with direct comparison and NMA estimates of disability outcomes.

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(0.46; 1.30)	(0.49; 1.13)	(0 24, 1 15)	(-0.02; 0.72)	(-0.21; 0.64)	
(0.40, 1.30)	(0.49, 1.13)	(-0.24; 1.15)	(-0.02, 0.72)	(-0.21, 0.04)	

Legend: [values: standardized mean difference (95% CI)]; MI = Minimal intervention; UC = Usual care; ET = Exercise therapy; MBR-WR = MBR Work conditioning/hardening; MBR-BE = MBR Behavioral therapy; MBR-ED = MBR Education.

MBR education (MBR-ED) displayed a significant reduction in disability with a standardized mean difference (SMD) of 0.67 (95% CI: 0.40; 0.94) while exercise therapy (ET) showed a relatively similar efficacy with an SMD of 0.53 (95% CI: 0.32; 0.74) in comparison to MI. The range of the associated 95% CIs underscores the variability and uncertainty in some of these estimates, making it crucial to interpret results with caution.

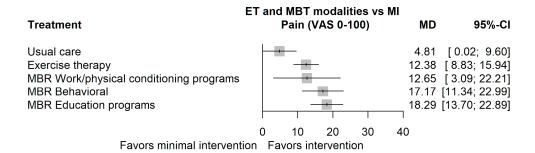
In the assessment of pain and disability outcomes, the treatments ranked based on their probabilities that a particular treatment is better than another treatment chosen at random (P-scores) revealed distinct hierarchies (Table 4). For pain outcomes, the MBR-ED took precedence with the highest P-score of 0.899, followed closely by MBR-BE at 0.826, and MBR-WR at 0.559. Parallel trends were observed in disability outcomes. MBR-BE led with a P-score of 0.940, MBR-ED was second at 0.761.

Pain outcome		Disability outcome			
Rank	Treatment	P-score	P-score	Treatment	Rank
1	MBR-ED	0.899	0.940	MBR-BE	1
2	MBR-BE	0.826	0.761	MBR-ED	2
3	MBR-WR	0.559	0.559	ET	3
4	ET	0.503	0.496	MBR-WR	4
5	UC	0.207	0.161	UC	5
6	MI	0.006	0.082	MI	6

Table 4. Rankings of P-score scores for pain & disability outcomes.

Minimal intervention; UC = Usual care; ET = Exercise therapy; MBR-WR conditioning/hardening; MBR-BE = MBR Behavioral therapy; MBR-ED = MBR Education.

Modalities ranked 1st and 2nd for pain outcomes have very similar probabilities, which decline more sharply for the 3rd ranked modality in both outcomes. While examining rankings provides an approximation of the most useful therapeutic modality, it doesn't paint the full picture. Although the calculation of P-scores accounts for variance, visually inspecting a forest plot with effect size estimates against a common reference therapy reveals the confidence surrounding the point estimate, and consequently, confidence in the rankings. Figure 3 summarizes MD/SMD for pain and disability when compared to minimal intervention. From the figure, for pain outcomes, MBR-ED appears the most successful, with MBR-BE as a close runner-up. Evaluating the SMDs and 95% CIs for disability outcomes, the first three modalities: MBR-BE, MBR-ED, and ET are all quite similar. While MBR-BE has the largest effect size, it's reasonably uncertain which one is truly the most effective.



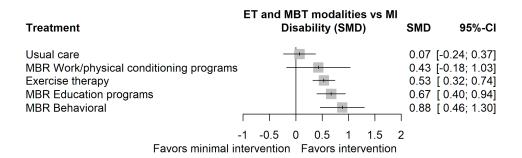


Figure 3. Exercise therapy and MBR modalities vs minimal intervetion in pain outcomes.

3.5. Exploration for heterogeneity & inconsistency

For the network assessing pain outcomes, the total Q statistic of 920.85 with 85 degrees of freedom (df) signifies considerable heterogeneity within the network (p<0.001). This heterogeneity can be partitioned into two parts: within-designs and between-designs. Significant heterogeneity was observed both within designs (Q=628.07, df=74, p<0.001) and between designs (Q=292.78, df=11, p<0.001). Under the assumption of a full design-by-treatment interaction random effects model, the Q statistic was non-significant (Q = 14.39, df=11, p=0.2124), suggesting no notable inconsistency between designs. Local inconsistency assessments highlighted two significant inconsistencies. Specifically, the comparisons 'exercise therapy vs MBR education' and 'exercise therapy vs minimal intervention' were found inconsistent with p-values of 0.044 and 0.046, respectively. Other therapeutic comparisons did not demonstrate significant inconsistency.

For the network assessing disability outcomes, significant heterogeneity was present, as indicated by a total Q statistic of 316.89 (df=70, p<0.001). The heterogeneity within designs was substantial (Q=282.52, df=65, p<0.001), and between designs, it was also significant (Q=34.37, df =5, p<0.001). Under the presumption of a full design-by-treatment interaction random effects model, the Q statistic for between designs was 9.53 (df=5, p=0.090), indicating possible inconsistency. When focusing on specific comparisons, three stood out. The comparisons 'exercise therapy vs minimal intervention', 'MBR education vs minimal intervention', and 'exercise therapy vs MBR education' were statistically significant with p-values of 0.021, 0.008, and 0.045, respectively. All other comparisons were non-significant.

Comprehensive details regarding the heterogeneity and inconsistency of both network metaanalysis models are provided in the supplementary materials (Tables S3–S6, Figures S6 and S7).

3.6. Risk of bias across studies

For pain outcome Egger's test showed no statistically significant results (p = 0.124). Visual inspection of the plot suggested a potential asymmetry, indicating the possibility that studies demonstrating non-positive effects of the experimental therapeutic modalities as opposed to Minimal intervention may be underrepresented in the published literature. While it is important to note that Egger's test, despite its widespread use, is known to have low power and can fail to detect bias [116], funnel plot shows no significant symmetry deviation.

For disability outcomes both Egger's test (p=0.003) and visual assessment of funnel plot suggest a possibility of publication bias. Funnel plots for both outcomes are available in the supplement materials (Figures S8 and S9).

3.7. Results of additional analyses

The results of the Bayesian network meta-analysis (BNMA), employing a non-informative prior distribution, largely corroborated the findings from the frequentist network meta-analysis (NMA). For pain-related outcomes, node-splitting analysis revealed no statistically significant inconsistencies among the comparisons. Notably, the therapeutic modalities were ranked according to SUCRA scores in a manner consistent with the frequentist ranking.

Similar outcomes were observed for disability-related endpoints. As in the frequentist NMA, the results exhibited substantial consistency, with the only inconsistency identified occurring in the comparisons between exercise therapy (ET) and minimal intervention (MI), as well as between ET and MBR-ED (MBR education), and between MBR-ED and MI. Table 5 presents the SUCRA scores for both pain and disability outcomes, demonstrating that the rankings of therapeutic modalities align with those derived from the P-scores.

Within the Bayesian framework, we conducted a network meta-regression employing the RoB 2 Overall domain as a moderator. Interestingly, this model did not provide any meaningful explanations for inconsistencies within the network. Furthermore, there were no significant differences in effect sizes when considering the grouping of studies into 'low risk,' 'some concerns,' and 'high risk' categories for both pain and disability outcomes. However, it is worth noting that effect sizes generally appeared more substantial in 'low risk' studies. For a comprehensive BNMA analysis of both outcomes, refer to the supplementary materials (Figures S10–S15).

4. Discussion

The aim of the research was to discern the efficacy of multidisciplinary biopsychosocial rehabilitation (MBR) modalities relative to exercise therapy (ET) for short-term pain and disability relief in chronic low back pain sufferers.

Our results support the previous research in regards the efficacy of ET and MBR modalities versus minimal intervention and usual care. The efficacy of ET versus minimal intervention or usual care is well established [17]. The MBR approach has less evidence to support its efficacy, but previous studies do show promise when compared to usual care [12] or exercise therapy [10]. When indirectly compared hierarchy emerged in the P-scores of the pain outcomes, with MBR-ED leading, followed by MBR-BE. Parallel to the findings on pain outcomes, a P-score ranking for disability outcomes positioned MBR-BE at the top rank, followed by MBR-ED. Both MBR-ED and MBR-BE showed larger effects on pain and disability than ET and MBR-WR which in turn, expectedly, showed larger effects than UC and MI. This demonstrates that better outcomes are associated with modalities that have enhanced physiotherapy interventions with a cognitive aspect, either through behavioral or educational modalities.

This should be examined through the multifactorial nature of chronic low back pain (CLBP). A recent systematic review [117] found that increased pain intensity, elevated body weight, lifting heavy objects at work, challenging work postures, and depression are the most commonly observed risk predictors for CLBP. Additionally, behaviors that aren't adaptive, general anxiety, functional limitations during the episode, and particularly physically demanding work are distinctly linked to the persistence of symptoms. The most frequently identified protective factor against CLBP was regular physical activity. Given this variety of risk factors, it stands to reason that effectively addressing CLBP requires a multifaceted approach, as suggested by our results.

Defining which of these MBR approaches is superior is much more challenging. To our knowledge there is no previous attempt to try to assess different types of MBR against each other. While the results produced rankings, giving MBR-ED and MBR-BE highest rank of pain and disability outcomes, respectively, there is a high degree of uncertainty within the results, evidenced by wide confidence intervals, significant heterogeneity, and some local inconsistency within the

network. This was generally anticipated, given similar findings in other studies [10,12,17] and because, by design, studies were broadly included and categorized to be relevant to clinicians, researchers, and policymakers, but such high heterogeneity is a deterrent to producing confident results. Even though ranking treatments favored MBR-ED for pain and MBR-BE for disability outcomes, the differences between the various MBR modalities are too minimal and uncertain to be clinically significant. Furthermore, for disability outcomes, ET cannot be reliably differentiated from its MBR counterparts.

4.1. Limitations

High heterogeneity, especially within designs, was present. Although consistency assessed under the assumption of a full design-by-treatment interaction random effects model was non-significant, three comparisons also showed local inconsistency. Employing the RoB 2 Overall domain as a moderator in the Bayesian framework, however, did not yield any significant results in explaining network heterogeneity and inconsistency. Regarding the exploration of heterogeneity, lack of sample characteristics data in many studies, such as age, male to female ratio, BMI, duration of symptoms, and use of medications prevented us from exploring the effects of study modifiers.

Additionally, in this analysis we did not analyze different forms of ET, which may help to narrow down the effect modifiers and differences in the effect sizes.

There is some evidence of publication bias in disability outcomes. The results of Egger's test for pain outcomes were non-significant, the test's low power warrants caution in its interpretation, potential underrepresentation of studies showing non-positive effects compared to Minimal intervention must be considered.

Furthermore, the inclusion of a diverse range of scales to measure disability outcomes introduces challenges in direct comparisons and synthesis of results.

Finally, like other systematic reviews, the undocumented use of pain medications might have influenced the results of the primary studies, thus making our estimates possibly biased.

4.2. Recommendations for stakeholders

Clinicians: Recognizing the multifaceted etiology of CLBP, while exercise therapy (ET) remains a mainstay, it might be prudent to augment ET with educational sessions. These sessions could elucidate potential pain triggers, preventive measures, and coping strategies for disability. Additionally, clinicians should remain attuned to patients' psychological well-being, and, when deemed necessary, consider referrals for behavioral interventions to broadly address CLBP's dual physical and emotional facets.

Researchers: The strength of network meta-analysis (NMA) lies in its ability to discern comparative effectiveness across a spectrum of treatments. However, ensuring that the results remain unbiased mandates careful attention to potential sources of heterogeneity and inconsistency within the network. Delving deeper into patient characteristics like age, gender distribution, BMI, clinical setting, intervention duration, and intensity could shed light on these disparities. Moreover, recognizing the intricacies of CLBP, it's advisable to blend various interventions, encompassing educational components, behavioral modifications, and pain management tactics with ET in experimental designs to discern the optimal therapeutic combination.

Policy-Makers: CLBP's impact transcends individual suffering, translating into significant socio-economic ramifications. Notably, MBR modalities, by virtue of involving multiple professionals, inherently command higher costs. While preliminary evidence suggests a potential edge in efficacy over ET, it would be counterintuitive to further compound the financial burdens associated with CLBP by advocating for costlier treatments without discernible clinical superiority. Hence, a thorough cost-benefit analysis is warranted to ascertain the most economically viable and clinically efficacious treatment modalities, potentially integrating salient components of MBR into standard ET.

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Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

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