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Bibliographic Data	
Authors	Kamper SJ, Apeldoorn AT, Chiarotto A, and et al.
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Other information if relevant	

Methods	
Aim of study	To review the evidence on the effectiveness of multidisciplinary biopsychosocial rehabilitation (MBR) for patients with chronic low back pain (LBP) compared with usual care and physical treatments measuring outcomes of pain, disability and work status, particularly in the long term.
Design	Meta-analyses of randomized clinical trials

PICOS	
Population from which participants are drawn	Adults older than 18 years of age reporting non-specific chronic LBP that persisted for 12 weeks or more and was not associated with pathological entities.
Intervention being evaluated	MBR is defined as an intervention that involves a physical component (e.g. an exercise program) and at least one other element from the biopsychosocial model such as psychological, social or occupational. The MBR intervention program has to be delivered by healthcare professionals from a minimum of 2 different disciplines or professional backgrounds.
Comparison or control intervention	Primary comparisons were usual care and physical treatment. Secondary comparisons were surgery or waiting list.
Outcomes	Primary outcomes were pain, disability or functional status, and return to work. The primary outcome follow up time point was long-term follow up at 12 months or more. Secondary outcomes included quality of life, healthcare utilization, global improvement, and psychological/cognitive function and outcome time points at 3 and 6 months.
Study types	Only RCTs published in full in peer-reviewed journals

Study selection	
Search date of literature review	March 2014
Databases in literature search	Cochrane Back Review Group Trials Register, CENTRAL, MEDLINE, EMBASE, CINAHL, and PsycINFO
How authors assessed study quality (risk of bias and other considerations	Cochrane risk of bias tool using the 12 criteria recommended by the Cochrane Back Review Group. A low risk of bias was defined as studies fulfilling 6 or more of the 12 internal validity criteria. GRADE (Grades of Recommendation, Assessment, Development and Evaluation) profiles were used to evaluate the overall quality of the evidence and the strength of the recommendations. GRADE factors that may decrease the quality of the evidence were: study design and risk of bias, inconsistency of results, indirectness, imprecision, and other factors (e.g. reporting bias). The quality of the evidence for a specific outcome was reduced by a level according to these 5 factors. The quality of evidence was downgraded by one level for risk of bias in studies that did not meet the threshold of 6 items on the risk of bias scale, for an I^2 statistic greater than 60%, and for less than a total of 400 participants in the comparison.
Additional information if relevant	Subgroup analyses were conducted on symptom/functional intensity, and intervention intensity. Sensitivity analyses were performed including only evidence from studies with a low risk of bias.

Results	
Number of studies screened	6189 RCTS were screened from the electronic searches and checking reference lists
Number of studies selected for analysis of results	31 RCTS were selected and all 10 studies from the 2006 previous Cochrane were added in this current Cochrane for a total of 41 studies with 6858 participants. Included studies were published between 1989 and 2013. Thirty-three of the included studies were conducted in Europe. Sample sizes ranged from 20 to 542.
Whether authors elected to perform meta-analysis to pool study results statistically and type of meta-analysis done (fixed effect or random effects, heterogeneity, etc)	Clinical homogeneity regarding the control intervention, outcome measure and timing of measurement was assessed prior to pooling. Random-effects models were used to quantify pooled treatment effect sizes. Studies included in the meta-analyses: 16 studies reported on a comparison of MBR with usual care, 19 with physical treatment, 2 with surgery, and 4with a wait list. Each pooled analysis contained between 2 and 13 studies. Standard mean differences (SMDs) or mean differences (MD), odds ratios, and 95% confidence intervals (CIs) were calculated for each analysis. Heterogeneity was high in some comparisons with I^2 values ranging between 0% and 94%. I^2 statistics were not used to determine whether or not to perform a meta-analysis, but were taken into account during the GRADE assessment.

Quality of studies as assessed by authors	Thirteen studies (32%) had a low risk of bias, meeting 6 or more of the criteria. Only 29 studies used a clearly described and adequate randomization procedure, and 23 an adequate concealment of treatment allocation. Only one study was free of selective reporting. By the nature of the interventions, blinding was not possible. A total of 26 studies reported outcome data that met the criteria for completeness, and 16 studies reported an intention-to-treat analysis. Treatment compliance was assessed as adequate in 7studies. No evidence of publication bias was observed from the funnel plots. Out of 10 comparisons, 6 had only low quality evidence to support the results, and 4 contained moderate quality evidence.
Effect sizes reported for primary outcomes (mean differences, standardized mean differences, response ratios, etc)	- **There was moderate quality evidence from 7 studies (821 participants) that showed that MBR was significantly more effective than usual care for long-term pain relief for patients with chronic LBP (SMD -0.21, 95% CI -0.37 to -0.04). This equates to a small effect size that may be clinically relevant.** - **There was moderate quality evidence from 6 studies (722 participants) that showed that MBR was significantly more effective than usual care for disability improvement in the long-term for patients with chronic LBP (SMD -0.23, 95% CI -0.40 to -0.06). This equates to a small effect size that may be clinically relevant.** - There was moderate quality evidence from 7 studies (1360 participants) that showed that MBR was not significantly more effective than usual care for return to work in the long-term (OR 1.04, 95% CI 0.73 to 1.47). This difference is not statistically or clinically relevant.

Effect sizes reported for additional outcomes (mean differences, standardized mean differences, response ratios, etc)	- **There was low to moderate quality evidence from 6-9 studies (740 to 879 participants) that showed that MBR was significantly more effective than usual care for short (SMD -0.55, 95% CI -0.83 to -0.28) and medium term (SMD -0.60, 95% CI -0.85 to -0.34) pain relief for patients with chronic LBP. These equate to medium effect sizes that are clinically relevant. This evidence was downgraded from moderate to low due to heterogeneity that was > 60%. Short term I^2 was 72% and medium term was 63%.** - **There was moderate quality evidence from 6-9 studies (786 to 939 participants) that showed that MBR was significantly more effective than usual care for short (SMD -0.41, 95% CI -0.62 to -0.19) and medium term (SMD -0.43, 95% CI -0.66 to -0.19) disability improvement for patients with chronic LBP. These equate to small effect sizes that may be clinically relevant.** - The pooled effects for MBR versus usual care on work outcomes ranged from 1.04 to 1.60 (OR) and were not statistically significant at any time point. - For the sensitivity analyses, the inclusion of low quality studies in the meta-analyses did not appear to result in a bias towards overestimation of the effect of MBR versus usual care or versus physical treatment. - For the subgroup analyses, the intensity of the intervention appeared to have little influence on the effect of MBR versus usual care. - **There was moderate quality evidence from 9 studies (511 to 531 participants) that showed that MBR was significantly more effective than physical treatment in the medium term for pain relief (SMD -0.28, 95% CI -0.54 to -0.02),** but not for disability improvement (SMD -0.21, 95% CI -0.48 to 0.06) in patients with chronic LBP. These equate to small effect sizes. - **There was moderate quality evidence from 8 studies (1006 participants) that showed that MBR was significantly more effective than physical treatment for return to work in the long-term (OR 1.87, 95% CI 1.39 to 2.53). This estimate indicates that people receiving a MBR intervention had approximately twice the odds of those receiving a purely physical treatment of being at work 12 months after the intervention.**
Additional information if relevant –summary of results	

Authors' Conclusions		
Key conclusions of study authors	- This review found that when compared with usual care, MBR decreased pain and disability to a moderate degree, but had little to no effect on work outcomes. When compared with physical rehabilitation, MBR showed moderate effects on pain, disability and work outcomes. Although the quality of the evidence was moderate or low depending on the comparison, the overall size of the effects of MBR was quite consistently small. These small effects translate to an average difference in pain of about 1 to 2 points on a 10-point scale, and an average difference in disability of 2 to 4 points on the 24-point Roland Morris questionnaire. The improvement of work outcomes with MBR when compared to physical rehabilitation translates to about double the odds of being at work 12 months later. - Choosing an MBR intervention over usual care or a physical treatment program for chronic low back pain is likely to result in a positive effect on pain and disability outcomes. It is also likely that MBR will have a beneficial effect on work outcomes compared to physical treatment. However, given the moderate size of these effects and the potentially high cost of an intensive intervention, in terms of both the monetary and time burden, the decision to refer to MBR requires some consideration. - The results of this review are in line with those of others in the low back pain field in that small effects are observed between the treatment and the control interventions. It is important to consider whether these small effects are clinically worthwhile and cost-effective. The resources, time, and costs associated with delivering MBR programs should be considered and weighed against those of usual care or physical training regimens. MBR in 15 of the included studies required more than 100 face-to-face hours of patient training. - For the main comparisons, pooled effects do not appear to have been overestimated due to inclusion of low quality studies. - The sensitivity analyses did not indicate that inclusion of lower quality studies resulted in overestimation of the effect. This, along with the consistency of the size of the pooled effects on pain and disability, gives confidence that the reported estimates for the primary outcomes are robust. - Unfortunately, data were not reported in a comparable manner, thus limiting the ability to estimate the true effect of MBR for the critical outcomes of return to work and healthcare utilization. - The quality of the evidence regarding the primary outcomes is at best moderate, although consistent in terms of effect size. Despite this, the volume of evidence is substantial and conducting further, similar studies is unlikely to greatly change the estimate of the effectiveness of MBR versus usual care or physical treatment.	

Key conclusions of study authors	- In future trials, incorporation of treatment modalities into MBR that specifically focus on re-integration to the work place would be of value. - It is still unknown what type of patients benefit most from MBR. While this review was not able to determine if symptom intensity at presentation influenced the likelihood of success, it seems appropriate that only those people with indicators of significant psychosocial impact are referred to MBR.
Additional information if relevant	

Comments by DOWC staff

- Many of the pooled analyses resulted in substantial heterogeneity at least in part due to differences in the MBR interventions themselves. The MBR interventions evaluated in the included studies differed from each other in a number of ways. There were differences in the number of face-to-face sessions and the intensity of the treatment, differences in the settings, differences in the balance of the interventions in terms of focus on physical, psychological and social factors, and differences in the backgrounds of the clinicians that administered the interventions. This clinical heterogeneity is likely due to varying definitions of MBR. More heterogeneity was also introduced by differences in the control interventions. This review attempted to account for this heterogeneity by using a random-effects model for generating the pooled estimates, and incorporating the I^2 statistic into the evidence quality assessment within the GRADE system.
- For all 4 MBR versus physical treatment comparisons on pain and disability in the short and long-term, substantial heterogeneity was present with I^2 statistics ranging from 80 to 94%. This risk of bias due to inconsistency resulted in the downgrading of the evidence to low quality. One identified study that reported a very large effect, three to five times the size of the effects reported by the other studies (SMD 1.99 to 5.32), was responsible for introducing substantial heterogeneity into the meta-analyses. Removal of this study from the pooled analyses reduced the I^2 values substantially.
- For all MBR versus usual care comparisons on pain and disability, the smallest effects were observed at the long-term follow up compared to larger effects seen at the short and medium follow-up time points.
- This review applied a stringent rule that inclusion of one or more studies at high risk of bias in a meta-analysis meant downgrading the quality of the evidence by one level within the GRADE system. This rule increased our confidence in the results of the review and assured that the quality of the evidence was correctly assessed.
- The proportion of people that experienced a clinically relevant improvement was not typically reported in the RCTs and was not a part of this review. Since we don't have this data, the extent to which the between group difference reflects an important change on behalf of individual participants is unknown.
- The people referred to these MBR programs most often have long-standing symptoms which had not responded to previous treatments. Since a longer duration of symptoms is often an indicator of poor prognosis, a modest improvement in symptom severity compared to another treatment may be significant for this population.
- This review found that MBR was significantly more effective than usual care for both pain relief and disability improvement at all time points for patients with chronic LBP. Even though small effect sizes were found that were statistically significant, it may not be clinically important alone in the treatment of chronic pain. Since few if any chronic pain treatments have specific large effects that meet the threshold for clinically relevant benefits, this does not necessarily mean that there are no effective treatments for chronic pain. It appears that MBR or any intervention in isolation will not be sufficient to adequately reduce chronic pain. This might mean instead that the threshold for clinical relevance is too high for any individual treatment alone, and that a multidisciplinary approach to chronic pain management, with a focus on combining several non-pharmacological therapies is necessary.
- From the results of the meta-analyses, it can be seen that MBR for chronic LBP generally results in small effect sizes. However, as MBR can be considered inherently harmless, small benefits could be considered useful if they prove to be cost-effective.

Comments by DOWC staff

- The variation in outcome measures hampered the comparability between studies in this review. This renders meaningful synthesis of the body of evidence difficult and may also introduce bias as decisions must be made regarding which outcome measures should be included in the pooled effect estimates. Future studies need to determine the appropriate outcomes to use that are the best predictors of disability.
- Only one third of the included trials were at a low risk of bias. None of the comparisons made in this review provided high quality evidence, either for or against MBR. For most of the comparisons made in this review, there was only low or moderate quality evidence to support the results. Due to the low quality studies included in this review, only good evidence, not strong, can be derived from this review.

Assessment by DOWC staff	
Overall assessment as suitability of evidence for the guideline ☒ High quality ☐ Adequate ☐ Inadequate	High quality Cochrane meta-analysis supporting good evidence that multidisciplinary biopsychosocial rehabilitation shows small effects in reducing pain and improving disability compared to usual care, and that MBR was more effective than physical treatment for return to work after 12 months of treatment in patients with chronic low back pain. Patients with a significant psychosocial impact are most likely to benefit.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant

- Guzman J, Esmail R, Karjalainen KA, Malmivaara A, Irvin E, Bombardier C. Multidisciplinary bio-psycho-social rehabilitation for chronic low-back pain. *Cochrane Database of Systematic Reviews* 2006, Issue 2. [DOI: 10.1002/ 14651858.CD000963.pub2]