Critique author	**Ed Whitney**

Bibliographic Data	
Authors	Carvalho C, Caetano JM, et al.
Title	Open-label placebo treatment in chronic low back pain: a randomized controlled trial.
PMID	27755279
Citation	Pain. 2016 Dec;157(12):2766-2772.
Other information if relevant	

Methods	
Aim of study	To test the effect of open label placebo in the treatment of uncomplicated low back pain
Design	Randomized clinical trial

Participants	
Population from which participants are drawn	Patients with chronic low back pain
Setting (location and type of facility)	The outpatient pain clinic of a general public hospital in Lisbon, Portugal
Age	44
Sex	59 women, 24 men
Total number of participants for whom outcome data were reported	83
Inclusion criteria	Age over 18 with persistent lower back pain of more than 3 months duration confirmed by a nurse practitioner and a board-certified pain specialist

Exclusion criteria	Medication with opioids in past 6 months, history of refusal to take oral medication, back pain arising from specific causes such as cancer, fracture, infection, prior low back surgery, disc degeneration from age or trauma, paralysis, psychosis, fibromyalgia, rheumatoid arthritis, pregnancy breastfeeding, concurrent legal issues, participation in another clinical study
Other information if relevant	

Intervention Groups

Group 1	
Group name	Open label placebo (OLP)
Number in group	41
Description of intervention	After determining eligibility, patients met with the first author, who explained that a placebo was an inactive substance with no active medication in it, but that the placebo effect may be powerful, that a positive attitude is helpful but not necessary, but that taking the placebo pills faithfully is critical. Patients then received a typical medicine bottle clearly labeled "placebo pills" with instructions to take twice per day. The pills were orange gelatin capsules filled with cellulose On day 11, the patients met with a registered nurse who was blinded to group assignment for a brief conversation in which the patient was reminded of the nature of the placebo effect
Duration of treatment period	3 weeks
Co-interventions if reported	Patients were allowed to continue taking their existing medications, provided that they agreed not to change the dosing or schedule, and agreed not to undertake any lifestyle changes such as diet or exercise for the duration of the study
Additional information if relevant	

Group 2	
Group name	Treatment as usual (TAU)
Number in group	42

Description of intervention	The initial meeting with the first author was the same as that of the OPL group, with the same information about the placebo effect No placebo was issued to the TAU group, but they were promised that at the end of the 3 weeks of the randomized trial, they would be given placebos for 3 weeks if they desired to remain in the study
Duration of treatment period	3 weeks
Co-interventions if reported	Same as for OPL
Additional information if relevant	

Primary outcome	
Outcome name and criteria for definition	Improvement in a 10 point composite pain score (minimum pain, maximum pain, and usual pain) from baseline to followup, analyzed with analysis of covariance, which adjusts improvement scores for baseline scores
Time points measured and/or reported	Baseline and 3 weeks after randomization
Differences between groups	The OPL group had a greater improvement in the composite pain score (1.49 points) compared to TAU (0.24 points), representing a 28% pain response compared to a 5% pain response
Additional information if relevant	

Secondary outcomes	
Outcome name and criteria for definition	Roland-Morris Disability Questionnaire (RDQ)
Time points measured	Baseline and again at 3 weeks after randomization
Differences between groups	The OPL group had a greater improvement in RDQ (1.44 points) than TAU (0.02 points), representing a 29% change versus a 0% change

Additional information if relevant	- A third outcome was the pain bothersomeness score, which did not show a significant difference between groups in degree of improvement - 30 of the TAU patients elected to continue with the study after the end of the 3 week trial, and took placebo capsules for three weeks, after which they had mean improvement in composite pain scores of 1.98 points and improvements in RDQ of 3.22 points

Conclusions	
Key conclusions of study authors	- Adding OLP to TAU resulted in significant reductions in low back pain and disability compared to TAU alone - This benefit is added beyond the benefits of the medications the patients were taking at the time of trial entry - Patients with chronic low back pain could benefit from adding an open label placebo to their current treatment regimen

Risk of bias assessment		
Domain	Risk of bias Low High Unclear	Comments
Random sequence generation *(selection bias)*	Unclear, probably low	Generation of randomization sequence is not specified, but the criterion of allocation concealment appears to have been met, which means that the randomization was adequately done
Allocation concealment *(selection bias)*	Low	Opaque sealed envelopes were opened at the time of the initial meeting with the first authors
Blinding of participants and personnel *(performance bias)*	Irrelevant	The purpose of the study was to examine the effects of open label placebo; having the patients know that they were taking placebo was essential to the execution of the study

Blinding of outcome assessment *(detection bias)*	Irrelevant	See above
Incomplete outcome data *(attrition bias)*	Low	
Selective outcome reporting? *(reporting bias)*	Low	
Other bias		

Sponsorship if reported		
Study funding sources if reported	The Portuguese Foundation for the Science of the Therapeutic Encounter	
Possible conflicts of interest for study authors	None declared	
Notes:		

Comments by DOWC staff

- There was a baseline imbalance not acknowledged by the authors; in the TAU group, 3 of the 42 patients were taking benzodiazepines when the study began, compared to 10 of 42 in the OLP group
- Since the main outcome was improvement from baseline rather than raw pain and disability scores, the amount of bias introduced by this imbalance is probably not a major factor in explaining the differences between groups; the patients were instructed not to change their treatment regimens
- However, the interpretation of the study is far from straightforward; the benefits observed in the OLP group could be partly explained by the fact that taking placebo would enhance the likely benefits of simply participating in a clinical trial; the OLP group had a greater degree of active participation in the trial during the three weeks after randomization than the TAU group
- The patients who volunteered to participate may not be representative of all patients with chronic low back pain, since a total of 239 people completed telephone or e-mail screening, and 118 were either ineligible or unwilling to participate; the participants are likely to have been willing to participate in an unusual experiment in which the very novelty of the intervention may have been an attraction for many participants
- The study meets most criteria for internal validity regarding the comparison of the intervention groups, but the external validity is far from clear
- The interpretation that a randomly selected patient with chronic back pain would benefit from adding open label placebo is speculative
- The article is a proof-of-principle study for a short term response to open label placebo

Assessment by DOWC staff	
Overall assessment as suitability of evidence for the guideline ☐ High quality ☒ Adequate ☐ Inadequate	Supports some evidence that in the setting of uncomplicated low back pain lasting longer than three months, patients who were willing to participate in a trial of capsules clearly labeled as placebo experienced short-term reductions in pain and disability after the principles of the placebo effect had been explained to them.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant
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