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| **Supplementary table**  Intervention of each study included in the meta-analysis | | | | |
| **Study** | **Ashar et al. 2024** | **Borgmann et al. 2019** | **Carvalho et al. 2016** | **Ikemoto et al. 2020** |
| **Brief name** | Open-Label Placebo Injection for Chronic Back Pain. | Open-label placebo on pain, functional  disability, and spine mobility in patients with  chronic back pain | Open-Label Placebo Treatment for Chronic Low Back Pain. | Open-Label Placebo administration combined with Treatment as Usual for chronic low back pain. |
| **Why** | The intervention is based on the understanding that placebos can produce significant therapeutic effects even when patients are aware they are receiving an inert treatment. The rationale is that the OLP can engage the body's natural healing processes and endogenous opioid release, potentially leading to pain relief and improved psychological outcomes. | The rationale behind the OLP intervention is based on the understanding that even when patients are aware they are receiving a placebo, it can still produce significant therapeutic effects, particularly in managing chronic pain conditions. The objective is to explore the potential benefits of OLP in reducing pain intensity and functional disability in patients with chronic low back pain | The objective of the intervention was to investigate whether adding OLP to usual treatment could benefit patients with chronic low back pain by ethically harnessing placebo effects. The underlying theory is that transparency and positive expectation can enhance treatment efficacy. | The intervention aimed to investigate the effectiveness of OLP in alleviating pain and improving functional outcomes in Japanese patients with CLBP. The rationale was based on previous studies suggesting that non-deceptive placebos could provide therapeutic benefits even when patients are aware they are receiving a placebo. |
| **What: materials** | Participants received informational materials that included videos explaining the nature of the placebo, its potential effects, and the rationale behind the treatment. They also had a structured conversation with the treating physician, which aimed to reinforce the understanding of the placebo's effects. | The physical material used in the intervention consisted of capsules containing microcrystalline cellulose, which were administered to participants. Additionally, participants were provided with standardized information about the placebo effect and recent research findings on the potential benefits of OLP before randomization. | Participants received placebo pills, which were provided by Bial (Porto, Portugal). Additionally, information about the treatment and the nature of the placebo was communicated to participants to ensure understanding and informed consent. | The physical material included OLP capsules containing 450 mg of lactose. Participants were provided with information explaining the placebo effect, which included key points about the efficacy of placebos, the body's automatic response, the importance of a positive attitude, and the necessity of regular capsule intake. |
| **What: procedures** | The intervention involved a single subcutaneous injection of saline at the site of greatest back pain. Participants were informed about the treatment and its expected effects, and they continued any ongoing usual care for their back pain. | Participants in the OLP group received the capsules twice daily for three weeks. The intervention included monitoring and assessing pain intensity, functional disability, and other relevant outcomes at baseline and after the treatment period. | Participants were randomized to receive OLP in addition to TAU. OLP was administered over 3 weeks, with participants informed about the nature of the treatment and encouraged to report their experiences of pain and functionality. | Participants in the OLP + TAU group were instructed to take two OLP capsules daily for 12 weeks. They also received advice to remain active and engage in exercises as part of the TAU. The intervention included assessments using the RMDQ, NRS for pain intensity, and the TUG test at baseline, week 3, and week 12. |
| **Who provided** | The intervention was administered by a physician trained in delivering the OLP treatment. Specific training included understanding the psychological aspects of placebo effects and how to communicate effectively with patients about the treatment. | The study involved trained neurologists who screened participants for eligibility and provided information about the study. Specific training details for the personnel conducting the intervention were not explicitly mentioned in the study. | The intervention was conducted by healthcare professionals, including doctors and psychologists, who were familiar with administering placebos and the ethics involved. Specific training details were not provided, but the team was guided on the importance of clear communication and building positive expectations. | The intervention was conducted by healthcare professionals from the Department of Orthopedic Surgery and the Multidisciplinary Pain Center. Specific training details for the personnel involved in administering the OLP were not provided in the study. |
| **How** | The intervention was provided in person at a private orthopedic medical center. Each participant received the OLP treatment individually during a clinical visit. | The intervention was delivered in person, with participants receiving the OLP capsules during the study period. It was conducted individually, as each participant received their treatment regimen. | The intervention was provided in person, with participants receiving placebo pills and interacting with healthcare professionals during treatment. The intervention was conducted individually. | The intervention was delivered in person, with participants receiving instructions and the OLP capsules directly from the healthcare providers. It was conducted individually. |
| **Where** | The intervention took place at a private orthopedic medical center in Golden, Colorado. The facility was equipped to provide medical treatments and had the necessary infrastructure for patient care. | The intervention took place at the University Hospital Essen, specifically within the Chronic Pain Center. The infrastructure included facilities for patient assessment and treatment administration. | The intervention took place in an outpatient pain unit of a public hospital in Lisbon, Portugal. Necessary infrastructure included offices for consultations and the administration of pills. | The intervention took place at Aichi Medical University and associated healthcare facilities in Nagakute, Japan. The necessary infrastructure included clinical settings for patient assessments and follow-ups. |
| **When and how much** | The OLP intervention was conducted once, with a single injection administered during the participant's visit. The entire process, including the informational session and injection, occurred during one appointment. | The OLP intervention was conducted over a period of three weeks, with participants receiving the treatment twice daily. This resulted in a total of 42 doses (2 doses per day for 21 days). | The intervention was conducted over 3 weeks, with participants receiving OLP daily. The exact number of sessions was not specified, but the administration of the placebo occurred daily during the period. | The OLP intervention was conducted over a period of 12 weeks, with participants taking two capsules daily. Assessments were made at baseline, week 3, and week 12. |
| **Tailoring** | The intervention was not specifically tailored to individual participants but was standardized across the study. However, the physician's conversation with each participant allowed for some degree of personalization based on individual concerns and questions. | The intervention was not specifically individualized for each participant; however, all participants were informed about the nature of the placebo treatment and its potential effects. | The intervention was not specifically individualized, but participants were informed about the treatment and encouraged to report their experiences, allowing for some adaptation in communication and support. | The intervention was not specifically tailored to individual participants but was standardized for all patients receiving OLP + TAU. The rationale for this approach was to maintain consistency in treatment delivery. |
| **Modifications** | There were no reported modifications to the intervention during the execution of the study. The protocol was followed as planned. | There were no reported modifications to the intervention during the study execution. The protocol was followed as planned. | No significant modifications to the intervention were mentioned during the study. The OLP approach was maintained as planned. | There were no reported modifications to the intervention during the study execution. |
| **How well: planned** | Adherence to the intervention was monitored through participant feedback and follow-up assessments. The study design included measures to ensure fidelity, such as standardized training for the administering physician and structured informational materials. | No detailed information | Adherence to the intervention was monitored through participant reports on the administration of placebo pills. | No detailed information |
| **How well: actual** | The intervention was implemented as planned, with all participants receiving the OLP injection and the accompanying informational session without deviations from the protocol. | No detailed information | The extent of the intervention's execution was assessed through participant follow-up.The expectation was that participants would follow the protocol for daily administration of the placebo. | No detailed information |
| OLP = Open label placebo; TAU = treatment as usual; CLBP = Chronic low back pain; RMDQ = Roland-Morris Disability Questionnaire; NRS = Numerical Rating Scale; TUG = Timed-Up-and-Go.    **Brief Name**: Name or phrase that describes the intervention. This is a concise title that summarizes the intervention clearly.  **Why**: Rationale or justification for the intervention. Explains the reason the intervention was developed and the problem it aims to address.  **What**: Description of the materials used in the intervention. Includes information about the materials and resources provided to participants.  **Procedures**: Description of the procedures of the intervention. Details how the intervention was implemented, including specific steps and activities.  **Who Provided**: Information about who delivered the intervention. Describes the training and expertise of the intervention providers, such as psychologists or nurses.  **Where**: Location where the intervention took place. Indicates the specific sites where the intervention occurred, such as clinics or community settings.  **Tailoring**: Personalization of the intervention. If the intervention was adapted for different participants, describes how and why these adaptations were made.  **When and How Much**: Frequency and duration of the intervention. Details the number of sessions, the schedule, and the total duration of the intervention.  **Modifications**: Modifications made during the study. If the intervention was altered, describes what was changed, why, and how.  **How Well (Planned)**: Assessment of planned adherence or fidelity. Describes how adherence to the intervention was monitored and what strategies were used to maintain fidelity.  **How Well (Actual)**: Assessment of actual adherence or fidelity. Reports the extent to which the intervention was actually delivered as planned. | | | | |