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Placebo use in pain management: a mechanism-based educational intervention enhances placebo treatment acceptability

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Abstract

Healthcare providers use treatments whose effectiveness's derive partially or completely from 'non-specific' factors, frequently referred to as placebo effects. While the ethics of interventional placebo use continues to be debated, evidence suggests that placebos can produce clinically meaningful analgesic effects. Burgeoning evidence suggest that patients with chronic pain may be open to placebo treatments under certain contexts despite limited knowledge of their well-established psycho-neurobiological underpinnings. This investigation sought to examine the effects of a brief, mechanism-based placebo analgesia educational intervention on aspects placebo knowledge and acceptability. Participants with chronic musculoskeletal pain completed a web-based survey where they rated their knowledge of placebo analgesia; assessed placebo acceptability across different medical contexts; and evaluated six unique patient-provider treatment scenarios to assess the role of treatment effectiveness and deception on patient/provider attributions. Using a pre-post design, participants were randomized to receive either a placebo educational intervention or an active control education. Results demonstrated that the educational intervention greatly improved perceptions of placebo knowledge, effectiveness, and acceptability, even in deceptive treatment contexts. This is the first study of its kind to demonstrate the value of an educational intervention in increasing openness to and knowledge of placebo analgesic interventions among patients with chronic musculoskeletal pain.

Keywords

Placebo; placebo analgesia; placebo acceptability; education intervention; musculoskeletal pain

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INTRODUCTION

Several studies show that physicians and other healthcare providers use treatments whose effectiveness's derive from 'non-specific' factors, frequently referred to as placebo effects [9,10,13,25]. While the use of 'pure' placebos (e.g., sugar pills, saline injections) is rare outside the clinical trial context, providers commonly use 'impure' placebos – the use of an intervention to manage a condition that the treatment has no demonstrated efficacy for (e.g. antibiotics to treat a viral infection). Interventional placebo use remains controversial due its association with deception [27]; the presumed negative consequences of deceptive means on the provider-patient relationship [7]; and placebo's historical place as representing a 'null' or 'insignificant' treatment effect.

Conceptualizations of placebos and related effects have changed dramatically over the past 25 years in concert with scientific advances. The placebo effect is a term used to describe a multitude of responses with different magnitudes, biological substrates, and mechanisms dependent on the outcome and context of administration[31]. Placebo for pain relief is perhaps the most well-understood placebo model, with clearly defined neurobiological mechanisms (e.g. endogenous opioids and cannabinoids) and psychological mechanisms (e.g., expectation, classical conditioning) [6,11]. Placebo analgesic effects have demonstrated large effects sizes when targeting these mechanisms, at times comparable to established treatments for pain [21,22,29,35,37,38]. As such, there has been a recent shift towards investigating ways in which placebo effects can be ethically and acceptably applied to improve patient health outcomes.

A burgeoning literature illustrates that patients may be open to placebo treatments despite having limited knowledge about their underlying mechanisms [4,5,14,17]. One study demonstrated that a placebo treatment could be delivered with limited deception and still produce clinically meaningful symptoms relief [15]. A recent study by our research group explored placebo analgesia knowledge and acceptability for patient with chronic pain [16]. Consistent with the extant literature, patients were open to placebo analgesic treatments under certain medical contexts, such as when they are explicitly used to compliment another treatment. However, these patients likely had limited knowledge of the underlying factors that drive placebo analgesic effects, which may have attenuated their openness to this treatment modality. Moreover, knowledge of treatment mechanisms has been shown to be significant contributing factor in pain treatment outcomes [12,23,24,28].

The present investigation sought to examine the effects of placebo education on patient's knowledge of and acceptability towards a placebo analgesic intervention. Specifically, we sought to determine whether: 1) a greater understanding of both neurobiological and psychological mechanisms would improve patient's willingness's to receive a placebo treatment; and 2) explore whether this knowledge would mitigate presumed negative consequences of deceptive placebo administration on patient mood and prescribing provider attributions. We hypothesized that, given a paucity of lay knowledge concerning placebo analgesia mechanisms, a brief educational intervention would significantly improve placebo acceptability across a variety of treatment contexts.

METHODS

Subjects

Participants were recruited with flyers posted in the surrounding community as well as directly recruited from two university outpatient medical clinics. Subjects comprised 57 adults with chronic musculoskeletal pain (17 males, 40 female; M age = 42.12, SD = 19.16). Inclusion criteria were as follows: the presence of musculoskeletal pain that has lasted at least three months; internet access to complete the study; adults age 18 years or older; and the ability to read English fluently. Exclusion criteria included having any other non-musculoskeletal chronic pain etiology (e.g. neuropathic pain) or diagnosis of cancer.

Procedure

This investigation was reviewed and approved by the University of Florida Institutional Review Board (IRB). Participant informed consent was acquired electronically. Before participating, subjects were notified that the study would involve assessing their attitudes towards and knowledge of novel treatments for pain, such as placebo, as well as completing questionnaires about pain and appraisals of pain interventions. In addition, participants were informed that the goal of the research was to help develop better ways to manage chronic pain in the future. Participant data was collected between March 2013 and July 2013. Completion of the online study took approximately 45 minutes and all responses were anonymous. Subjects were provided the Internet website for the study in addition to a unique identification username and password to access the study. After completing demographic and pain assessment questionnaires, the remainder of the study constituted a pretest/posttest design comprised of three sections (Figure 1): 1) placebo knowledge section; 2) placebo acceptability section; and 3) treatment scenarios section. Pretest findings have been published [16]. Participants completed the survey twice consecutively; after completing the initial pretest sections, participants were randomly assigned to receive either an educational intervention about placebo analgesia or control educational information about musculoskeletal pain. Participants then proceeded to complete the three survey sections a second time for posttest assessment. N.R.K generated the random allocation sequence, enrolled participants, and assigned participants to treatment groups. Participants were blinded to treatment allocation.

Measures

Visual analogue scale ratings (VAS) were used for all survey measures. VAS ratings produced numerical values between 0 and 100 and have shown to be valid and reliable measures of pain and other subjective experiences [20,32]. For the development of survey sections and measures, please see prior studies by our research group [16–18].

Placebo knowledge, conceptualization, and efficacy—In the Placebo Knowledge Section, subjects provided VAS ratings of the following (Table 1): 1) perceived knowledge of placebo analgesia, 2) conceptualization of placebo, and 3) perceived effectiveness of placebo for reducing pain.

Placebo acceptability—In the Placebo Acceptability Section, the following six questions/VAS ratings were used to assess placebo acceptability across various treatment contexts (Table 1): how acceptable would it be if a physician 1) overtly or 2) covertly administered a placebo treatment for pain; 3) how acceptable would it be if a physician used a placebo as a treatment enhancer or an adjunct treatment; is it acceptable for a medical provider to treat pain with placebo for a condition for which there are 4) other established treatments or 5) for a condition in which there are no other established treatments; and 6) is it acceptable for a medical provider to use a placebo to determine if a patient’s pain complaints are “real.”

Deception, trust, and negative mood—The Treatment Scenarios Section was comprised of six hypothetical scenarios, each portraying a clinical encounter in which a patient visits a physician for pain management and subsequently receives a placebo (Table 2). Our participants were asked to review each hypothetical scenario and to respond as if they were the individual receiving the placebo intervention. After viewing each scenario, participants responded through VAS rating of the following: 1) deceptiveness of the hypothetical clinical encounter/placebo intervention, 2) their level of trust in the prescribing physician, and 3) the amount of negative mood they would experience if they had received the placebo treatment for their pain.

Two factors were manipulated in each scenario: 1) the outcome/effectiveness of the treatment 2) the healthcare provider’s description of the placebo intervention. There were three possible levels for treatment outcome/effectiveness: upon completion of the treatment, our sample of chronic pain individuals read that the placebo intervention either improved, worsened, or had no effect on the pain of the patient depicted in the scenario. For the description of the treatment, two distinct treatment scenarios were intended to be experimental manipulations of deceptiveness: for the “low deception/random assignment” instructions, the patient in the scenario was informed that they will receive either a “standard drug treatment or a placebo treatment” to manage their pain; for the “high deception/enhanced placebo” scenarios, the hypothetical patient in the scenario was informed that they will receive “a treatment that has been shown to be a powerful analgesic in some people.” Prior research has demonstrated that the “enhanced placebo” – once proposed to be an ethically acceptable description of a placebo treatment – is perceived as highly deceptive [18].

Placebo educational intervention and control condition—Approximately half of participants were randomized to receive either a placebo analgesia educational intervention or general information about musculoskeletal pain. The placebo educational intervention (Figure 2) was a brief, five slide prompt highlighting the following topics regarding placebo: 1) efficacy for reducing pain; 2) neurobiological mechanisms of pain relief (i.e., associated with the release of “natural pain relieving chemicals” in the body; “similar effects on the brain as other standard pain treatments”); 3) psychological mechanisms of pain relief (i.e., expectation and classical conditioning); and 4) data illustrating that healthcare providers often prescribe treatments that rely on placebo mechanisms for efficacy. Each educational topic was linked to relevant empirical citations for additional reference. To underscore the

psychological mechanisms of classical conditioning, an example of a Pavlovian conditioned hunger response was described and related to a classically conditioned analgesic response.

The control condition (Figure 3) was similar in length to the educational intervention and included information about the following: 1) the prevalence of pain in the United States; 2) the economic costs of pain; 3) gender and age differences in musculoskeletal pain; and 4) risk factors for the development of musculoskeletal pain.

Statistical analyses

Sample Size—Power analyses were used to determine the number of participants needed to detect sizable effects for deception, health provider trust, negative mood, and placebo acceptability. A variety of methods used to estimate the needed sample size based upon prior iterations of this survey. Based upon repeated measures analyses of variance (ANOVA) partial eta squared main effect effect sizes for deception (.69 and .09) trust in prescribing provider (.50 and .46), and negative mood (.43 and .60), and a negative mood interaction effect size (.08) [17,18], it was estimated that a sample size of 42 patients would be sufficient to detect effects at a power of 0.80 and alpha level 0.05. Based upon repeated measures ANOVA partial eta squared effects sizes for placebo acceptability contexts (.22, .09, .35 and .28) and one-way ANOVA acceptability subgroups Cohen's d effect sizes (.74, .74 and .68) (N. R. Kisaalita & Robinson, 2012), it was estimated that a sample size of 21 patients would be sufficient to detect effects at a power of 0.80 and alpha level 0.05. The final sample size is based on the most conservative value needed to optimally power the study, plus 20 percent more patients to buffer for potential participant drop out. Thus, based upon previously published placebo acceptability studies, recruitment of 50 pain patients was deemed sufficient to adequately power the study. Seven additional participants completed the study after recruitment ended and were thus included in the final sample. Details of sample size estimates have been previously published (N. Kisaalita et al., 2014).

Survey Analyses—IBM SPSS version 20 (IBM, Armonk, New York) was used for all survey analyses. Descriptive statistics (means, standard deviations) were calculated for all pretest and posttest VAS measures. Frequencies were calculated for all categorical outcomes. To examine the effects of the placebo education on placebo knowledge, conceptualization, and effectiveness VAS outcomes, univariate ANOVAs were used to compare treatment group differences on respective posttest outcomes. To examine the effects of placebo education on placebo acceptability, a 2×6 (educational intervention x acceptability) mixed-model ANOVA was conducted for the six-posttest acceptability outcomes. To examine the effects of the educational intervention on deception, provider trust, and negative mood outcomes, three $2 \times 3 \times 2$ (treatment instructions x treatment outcome x educational intervention) mixed-model ANOVA's were conducted on the three respective posttest survey outcomes. Significant omnibus F tests were further examined with simple contrasts or post hoc comparison for ANOVA analyses.

RESULTS

Sample demographics and pain characteristics

Ninety-five participants expressed interest in the study, were successfully screened, and were provided unique login information to access the study online. Thirty-eight participants did not complete the study. Total sample demographic for study completers ($n = 57$) have been previously reported [16]. Ethnic/racial breakdown of the total sample was as follows: 75.4% Caucasian; 7% African American/black; 7% Asian or Pacific Islander; 3.5% Indian; 3.5% Hispanic; and 3.5% other. Average annual income for participants was \$31,121 ($SD = \$41,081$), with income ranging from \$0 to \$220,000. More than half of the sample had either some college education (35.1%) or a college degree (21.1%). The majority of participants reported their relationship status as single (45.6%) or married (42.1%). Demographics information by intervention and control group is displayed in Table 3.

The average rating of current pain intensity was 41.89 ($SD = 25.84$) and participants reported having chronic pain for an average of 6.34 years ($SD = 7.34$). A variety of pain diagnoses were endorsed, with many participants reporting multiple diagnoses: 63.2% endorsed low back pain (LBP), 22.8% endorsed fibromyalgia, 19.3% endorsed osteoarthritis, and 15.8% endorsed IBS. 40.4% of participants also endorsed additional diagnoses, such as temporomandibular joint disorder (TMJ), scoliosis, and herniated disk. Chronic pain characteristics by intervention and control group are displayed in Table 3.

Treatment groups

Twenty-nine participants were randomly assigned to the educational intervention group and 28 participants were randomly assigned to the control group. There were no significant differences in pretest scores between groups for Placebo Knowledge, Placebo Acceptability, and Treatment Scenario Section outcomes.

Placebo knowledge, conceptualization, and effectiveness

The educational intervention had a significant main effect on placebo efficacy and placebo knowledge ratings (Table 4). Patients receiving the educational intervention had higher ratings of placebo knowledge ($p < .001$, $\eta^2 = .245$) and conceptualized a placebo as more “active” ($p < .001$, $\eta^2 = .207$). In addition, the intervention group viewed placebo as a more effective treatment for pain ($p = .006$, $\eta^2 = .129$).

Placebo acceptability

There were significant main effects for both the educational intervention and placebo acceptability contexts, though the acceptability x education interaction was not significant ($p = .158$). Those receiving the educational intervention rated placebo treatments more acceptable across multiple scenarios (Table 5)(Figure 4) ($p < .001$, $\eta^2 = .188$). Comparable to pretest findings [16], significant differences in acceptability were also found across the different treatment contexts ($p < .001$, $\eta^2 = .291$). For example, large differences in acceptability were seen when comparing both explicit placebo use and adjunct placebo use with both deceptive use and placebo use when other established treatments for pain were available.

Deception, trust in healthcare provider, and negative mood

There were no significant main effects or interactions for the educational intervention for any Treatment Scenario dependent variables (Table 6). However, there were significant main effects of treatment instructions on deception, and significant main effects for treatment instruction and treatment outcome on provider trust and negative mood dependent variables. Posttest intervention findings regarding the influence of treatment instructions and outcomes were nearly identical to previously published pretest findings (Kisaalita et al. 2014). Specifically, high deception/enhanced placebo instructions were rated significantly more deceptive than random assignment institutions ($p < .001$, $\eta^2 = .488$) with no significant effects found for treatment outcome ($p = .327$); trust ratings were significantly higher for improved treatment outcomes ($p < .001$, $\eta^2 = .320$) and random assignment instructions ($p < .001$, $\eta^2 = .323$); and negative mood ratings were significantly greater as treatment outcomes worsened ($p < .001$, $\eta^2 = .399$) and when patients received enhanced placebo instructions ($p < .001$, $\eta^2 = .323$).

DISCUSSION

Interventional placebo use remains a debated topic among ethicists, providers, and researchers; nevertheless, scientific advances elucidating placebo's neurobiological and psychological mechanisms, as well as potential efficacy for alleviating pain, have reinforced continued exploration of acceptable placebo applications to improve patient health outcomes. The objective of this line of empirical inquiry was to further the placebo treatment literature through use of a patient-centered methodology. Given evidence that lay individuals may be open to placebo analgesic interventions despite limited knowledge of contributing factors related to treatment efficacy, we sought to examine whether a mechanism-based educational intervention would improve aspects of placebo knowledge, treatment efficacy and acceptability.

To our knowledge, this is the first study to demonstrate the utility of an educational intervention in increasing patients' knowledge of and openness to placebo analgesic treatments. The intervention successfully improved patient's knowledge of placebo and its effects ($\eta^2 = .245$) and increased placebo conceptualizations to reflect more of an "active" as opposed to "inert" ($\eta^2 = .207$) treatment; this serves as one validly check for our intervention. In addition, those receiving the educational intervention also rated placebo analgesic treatments as more effective ($\eta^2 = .129$). Our educational intervention had a moderate to large effect on placebo acceptability, accounting for nearly 19% of the variance in acceptability contexts. Those receiving the educational intervention rated placebo treatments as relatively more acceptable in nearly all contexts, including deceptive/covert use (Figure 4). The only scenario that was not significantly more acceptable between the intervention and control group was diagnostic placebo use. This finding represents a second validly check for the educational intervention, as diagnostic placebo use is an area in which informed providers can reasonably agree constitutes unacceptable use [34]. Similar to previous research, a large portion of the variance in placebo acceptability was accounted for by contextual factors ($\eta^2 = .291$). In other words, independent of educational intervention group assignment, certain treatment contexts (e.g., when placebo is used as a treatment

enhancer/adjunct treatment, when healthcare providers were open in disclosing their use of a placebo, and when placebo is used when no other established treatments are available) were perceived as more acceptable than other contexts (e.g., covert/deceptive placebo use, placebo use when other established treatments for pain were available, and when placebo was used diagnostically to determine whether a patient's pain was "real").

The educational intervention did not have an effect on deception, trust, or negative mood ratings in the Treatment Scenarios. Consistent with pretest findings [16], the deceptiveness of the placebo intervention was entirely determined by the explicitness of the treatment instructions, accounting for nearly half the variance in treatment deceptiveness ($\eta^2 = .488$). The "enhanced placebo" instruction – a vague (yet technically accurate) interpretation of a placebo intervention – has been shown to be highly deceptive [18]. Once touted as an ethically permissible placebo treatment description [30,36,37], our findings demonstrate that this is not the case, even when participants were informed of placebo's underlying mechanisms. Regarding trust and negative mood, provider trust and patient negative mood were similarly influenced by the explicitness of treatment instructions ($\eta^2 = .323$ and $.323$, respectively) and improved pain outcomes ($\eta^2 = .320$ and $.399$, respectively). This suggests that, in concert with prior research [14], patients are rather pragmatic when appraising placebo interventions for pain, independent of their knowledge of placebo mechanisms.

Implications

The educational information had the effect of increasing placebo treatment acceptability – arguably one of the most important factors (along with efficacy) in evaluating the appropriateness of this treatment modality [26]. Educating patients about the role of endogenous opioids, expectancy, and classical conditioning improved perceptions of treatment acceptability, even in highly deceptive scenarios. Our results also confirmed prior findings highlighting treatment contexts most amenable for placebo treatments, including when used in conjunction with existing pain interventions to improve overall treatment effectiveness. Findings suggest that medication dose-extender models using different reinforcement schedules [2], similar to what has been used in treatments of psoriasis [1] and attention deficit disorder [33], may warrant further exploration for analgesics medications.

Treatments whose efficacies rely on placebo effects/factors are utilized in modern medicine, often unbeknownst to patients. Providers' motivations for using placebos are varied [10], and may include a desire to appease the patient and/or not wanting the patient to leave a clinical setting "empty-handed." It is possible that if physician's understood the mechanisms underlying their placebo treatments, they may be more open with their patients when using this treatment modality. More research is needed in understanding the effects of placebo education for both patients and healthcare providers. While our findings are meaningful given documented frequently of placebo use, it is also important to note that there are alternative methods/means to utilize the benefits of placebo factors without using placebos and/or deception. These include accurately increasing treatment expectation, improving patient provider communication, and explaining the mechanisms underlying a treatment [3,19].

The educational intervention did not improve aspects of perceived deceptiveness, provider trust, nor negative mood in hypothetical placebo treatment scenarios. One potential interpretation is that this the notion that placebos are inherently deceptive when used clinically, regardless of the information provided to the patient. However, we would argue against this view given the instructions used. The “enhanced placebo” instructions, while technically describing a placebo by stating “*what you have been given has been shown to be a powerful pain reliever in some people,*” may be considered deceptive because the use of placebo is not explicitly stated (i.e. “*powerful pain reliever*” could describe a variety of treatments). While a point could be made that non-significant effects on deception, mood, and provider attributions reflect a failure of the educational intervention (i.e., patients were not convinced that a placebo was “not nothing”), we would argue that our overall significant results (e.g., regarding placebo acceptability, efficacy) suggests otherwise. Thus, a more plausible alternative is that educated patients do in fact perceive placebo treatments as “real,” but are still object to their deceptive use. Future studies are needed to determine which descriptions of placebo most accurately enhance expectations and subsequent placebo responses. For example, we would hypothesize that those receiving the educational intervention would have found the following edited descriptions as non-deceptive: “*the placebo/expectation intervention/conditioning intervention that you have been given has been shown to be a powerful pain reliever in some people.*” However, ultimately the most important signifier of applied placebo “ethics” is treatment acceptability - not perceived deceptiveness - and our findings suggest that placebo education improved the acceptability of even the most deceptive treatment contexts.

While our findings provide a significant contribution to the placebo acceptability/ethics literature, additional studies are warranted. While the educational intervention produced sizable effects, more research is needed on how to optimize the educational prompt. It is possible that a slightly longer intervention may yield greater effects, or that comparable effects could be seen with an even briefer prompt. Additionally, the exact mechanisms underlying the efficacy of the educational interventions remain unclear. It’s possible that knowledge of each individual mechanism (i.e., endorphins, expectancy, and classical conditioning) may differentially contribute to acceptability. As our understanding of placebo analgesia mechanisms increases, new information may be incorporated into the educational intervention, such as highlighting treatment effect sizes and placebo effects on the spinal cord [8]. In addition, more studies are needed to examine how the delivery of the placebo information (e.g., written, verbal, video presentation) may differentially influence acceptability.

Limitations

The generalizability of our findings may be limited by the sample, as participants without knowledge of or access to the Internet could not participate. We also acknowledge that there are some limitations in relying purely on self-report measures in any study design, and that there is potential for error when utilizing participant self-selection for study enrollment. Additional studies are needed to examine placebo acceptability in other pain populations, as finding from this musculoskeletal population may not generalize to patients with acute pain or other chronic pain conditions. The random assignment instructions (used as a

manipulation of deception) are perhaps a better reflection of deception in a clinical trial setting as opposed to a traditional clinical encounter; future studies should include instructions that are equally non-deceptive and also more representative of traditional clinical encounters. While our findings are promising, more studies are needed to clarify the strength and duration of placebo analgesic effects before they can be consistently utilized in clinical practice. Finally, we acknowledge that it may be difficult to interpret responses of participants who reported having no knowledge (i.e., “0” on a “0 – 100” VAS) of placebo. However, this occurred for only 3 participants. As all participants were informed in study advertisements, during screening, and through informed consent that they would have to answer questions regarding placebo, it is assumed that participants had some base knowledge. These participants were kept in the final analyses as their exclusion still produced identical results.

Conclusions

The observations from this study suggest that a mechanism-based placebo educational intervention greatly improved perceptions of placebo treatment knowledge, efficacy, and acceptability compared to an active control intervention. We hope that these findings and future research will continue to generate testable hypotheses to explore the role of placebo education and other contextual factors in to improve treatment outcomes for chronic pain patients.

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Perspective

This article highlights how patients with chronic pain may be open to placebo interventions, particularly adjunct/complementary treatments, when provided education on the neurobiological and psychological mechanisms underlying placebo effects. Study findings highlight ethically acceptable ways to potentially utilize placebo factors to enhance existing pain treatments and improve patient health outcomes.

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Manuscripts Highlights

- Research suggests that placebo analgesic effects can be large and clinically meaningful.
- Survey assessed patient knowledge of and acceptability towards placebo treatments.
- Patients were conditionally willing to receive placebo interventions for pain.
- Placebos used as complementary treatments were rated as highly acceptable.
- Providing education on placebo mechanisms greatly enhanced placebo acceptability.

Figure 1.

Study Flow Chart. Flow diagram of the participants' progress through the study including enrollment, randomization, survey sections, and treatment allocation.

Figure 2.

Placebo Education. Placebo educational intervention defining placebo analgesia and describing its psychological and neurobiological mechanism.

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<p>Pain in the United States</p> <ul style="list-style-type: none"> • Pain is one of the most common symptoms leading patients to seek healthcare in the US¹ • 50% of Americans visit a doctor with a main complaint of pain each year²
<p>Prevalence and Costs of Chronic Pain</p> <ul style="list-style-type: none"> • Approximately 25% of the adult population suffers from chronic or recurrent pain³ • Pain is expensive because:⁴ <ul style="list-style-type: none"> – It gets in the way of one's ability work and function in society – It often requires medical treatment • Chronic pain costs the US economy between \$560 and \$635 billion each year⁴ <ul style="list-style-type: none"> – This is greater than yearly cost of diabetes, heart disease, and cancer
<p>Musculoskeletal Pain</p> <ul style="list-style-type: none"> • Musculoskeletal pain is pain that affects the muscles, ligaments, tendons and bones • At any one time, it is estimated that <ul style="list-style-type: none"> – 12-33% of adults may experienced low back pain⁵ – 15-20% of adults may experience neck and shoulder pain⁶ – 0.5 - 4% of adults may experience Fibromyalgia pain¹⁰
<p>Age and Gender</p> <ul style="list-style-type: none"> • Musculoskeletal pain problem tend to vary by age and sex <ul style="list-style-type: none"> – Women report more musculoskeletal problems than men in the neck, shoulders, upper limbs and hips¹¹ – Osteoarthritis and fibromyalgia are more prevalent among women¹¹ – Knee pain from osteoarthritis is highly common in the elderly but is much less common in younger persons¹²
<p>Risk factors for Musculoskeletal Pain</p> <ul style="list-style-type: none"> • The following are risk factors that may increase an individual's chances of developing musculoskeletal pain <ul style="list-style-type: none"> – Stress, anxiety, depression, and other psychological factors⁷ – Repetitive use and disuse of musculoskeletal units (e.g., in tendons, muscles, bones etc)^{8,9}

Figure 3.

Musculoskeletal Pain Education. Control condition providing basic information about musculoskeletal pain.

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Figure 4. Placebo Acceptability. The effect of the placebo educational intervention on placebo acceptability contexts ratings. * = significant main effect ($p < .05$); error bars are 95% confidence intervals.

Table 1

Participant Demographics and Chronic Pain Characteristics (n = 57)
 Posttest placebo knowledge, effectiveness, and acceptability outcomes

Factor/Survey Question	VAS Anchors (0 – 100)	Abbreviation	M (SD)	
			Con Grp	Inter Grp
Knowledge				
Overall, is a placebo something “inert/incapable of producing an effect” or something “active/capable of producing an effect?”	Completely inert; Completely active	Placebo Conceptualization	28.64 (24.89)	58.03 (33.00)
How much knowledge do you have about placebo for pain relief?	No knowledge of placebo for pain relief; Most knowledge of placebo for pain relief imaginable	Placebo Knowledge	33.32 (30.43)	64.72 (25.55)
Effectiveness				
How effective would placebo be for your pain?	Completely ineffective; Completely effective	Placebo Effectiveness	18.68 (18.32)	35.83 (26.21)
Acceptability				
How acceptable would it be if your physician used a placebo treatment to reduce your pain without telling you?	Completely unacceptable; Completely acceptable	Deceptive Placebo Acceptability	18.21 (32.24)	40.41 (31.63)
How acceptable would it be if your physician told you that he/she was going to use a placebo treatment to reduce your pain?	Completely unacceptable; Completely acceptable	Explicit Placebo Acceptability	38.96 (33.72)	65.28 (31.03)
How acceptable would it be if your physician told you that he/she was going to use a placebo treatment that may enhance the effectiveness of your usual pain treatments?	Completely unacceptable; Completely acceptable	Treatment Enhancer Placebo Acceptability	47.86 (33.20)	72.07 (23.82)
How acceptable would it be if your physician treated your pain with placebo when other established treatments were available?	Completely unacceptable; Completely acceptable	Placebo Acceptability when other EBTs are available	20.07 (21.21)	48.34 (25.21)
How acceptable would it be if your physician treated pain with placebo when NO other established treatments were available?	Completely unacceptable; Completely acceptable	Placebo Acceptability when NO other EBTs are available	55.14 (35.77)	74.21 (28.22)
How acceptable would it be if your physician used a placebo to see if your pain is “real”?	Completely unacceptable; Completely acceptable	Diagnostic Placebo Acceptability	35.71 (36.66)	42.55 (38.48)

Note: M, mean; SD, standard deviation.

Table 2

Posttest Placebo Knowledge, Effectiveness, and Acceptability Outcomes
Posttest deception, trust, and negative mood outcomes

Survey Treatment Scenarios	Scenario Abbreviation	<i>M (SD)</i>				Rate the level of negative mood you would experience			
		How deceptive would this be?		Rate your level of trust in this physician		Rate the level of negative mood you would experience		Rate the level of negative mood you would experience	
		Con Grp	Inter Grp	Con Grp	Inter Grp	Con Grp	Inter Grp	Con Grp	Inter Grp
Imagine that you are seeing a physician to manage your pain. The doctor provides you with a prescription for your pain, and states that what you have been given has been shown to be a powerful pain reliever in some people. Two weeks after the treatment, you report that your condition has improved. You received a placebo.	Enhanced placebo instructions used and pain improves	62.18 (29.91)	44.83 (33.97)	37.68 (31.02)	55.76 (28.68)	30.46 (25.99)	26.38 (28.04)		
Imagine that you are seeing a physician to manage your pain. The doctor provides you with a prescription for your pain, and states that what you have been given has been shown to be a powerful pain reliever in some people. Two weeks after the treatment, you report that there is no change in your condition. You received a placebo.	Enhanced placebo instructions used and pain is unchanged	59.39 (33.95)	53.24 (35.31)	27.07 (26.74)	41.00 (29.26)	52.32 (25.48)	45.83 (30.69)		
Imagine that you are seeing a physician to manage your pain. The doctor provides you with a prescription for your pain, and states that what you have been given has been shown to be a powerful pain reliever in some people. Two weeks after the treatment, you report that your condition has gotten worse. You received a placebo.	Enhanced placebo instructions used and pain worsens	67.00 (34.25)	55.00 (37.37)	24.53 (26.47)	30.66 (30.75)	62.61 (34.86)	56.45 (33.45)		
Imagine that you are seeing a physician to manage your pain. The doctor tells you that you will randomly receive either a standard drug treatment or a placebo treatment for your pain. Two weeks after the treatment, you report that your condition has improved. You received a placebo.	Randomly assigned and pain improved	24.32 (32.20)	18.21 (22.05)	62.71 (29.25)	65.97 (29.20)	17.68 (21.88)	18.55 (25.86)		
Imagine that you are seeing a physician to manage your pain. The doctor tells you that you are going to randomly receive either a standard drug treatment or a placebo treatment for your pain. Two weeks after the treatment, you report that there is no change in your condition. You received a placebo.	Randomly assigned and pain is unchanged	25.50 (30.47)	25.45 (31.49)	50.75 (29.56)	47.97 (34.50)	35.50 (22.73)	30.93 (26.70)		
Imagine that you are seeing a physician to manage your pain. The doctor tells you that you will randomly receive either a standard drug treatment or a placebo treatment for your pain. Two weeks after the treatment, you report that your condition has gotten worse. You received a placebo.	Randomly assigned and pain worsens	23.53 (28.12)	16.66 (24.44)	40.53 (32.84)	49.97 (32.97)	52.32 (33.02)	38.44 (32.04)		

Note: *M*, Mean; *SD*, Standard Deviation; Deception VAS anchors = "Not at all deceptive" – "Completely deceptive"; Trust VAS anchors = "No trust" – "Most trust imaginable"; Negative mood VAS anchors = "No negative mood" – "Most negative mood imaginable."

Table 3

Posttest Deception, Trust, and Negative Mood Outcomes
Participant demographics and chronic pain characteristics (n = 57)

Demographics/pain characteristics	Control Group (n= 28)		Intervention Group (n = 29)	
	<i>M(SD)</i>	<i>n</i>	<i>M(SD)</i>	<i>n</i>
Age (years)	43.75 (18.89)		46.45 (19.65)	
Income (\$ thousands)	33.10 (48.70)		29.21 (32.87)	
Sex	-		-	
Female	-	19	-	21
Male	-	9	-	8
Ethnicity	-		-	
Caucasian	-	22	-	21
African American/black	-	2	-	2
Indian	-	2	-	0
Hispanic	-	1	-	1
Asian or Pacific Islander	-	1	-	3
Other	-	0	-	2
Education	-		-	
No high School Education	-	0	-	1
High School Diploma/GED	-	7	-	0
Some College Education	-	6	-	14
College Degree	-	5	-	7
Some Graduate Education	-	3	-	1
Graduate School Degree	-	7	-	6
Marital Status	-		-	
Single	-	12	-	14
Living With Partner	-	3	-	1
Married	-	12	-	12
Divorced	-	1	-	1
Separated	-	0	-	1
Current Pain Intensity (VAS 0 = “no pain”; 100 = “worst pain imaginable”)	38.75 (22.70)	-	44.93 (28.63)	-
Usual Pain Intensity (VAS 0 = “no pain”; 100 = “worst pain imaginable”)	48.86 (19.97)	-	53.41 (27.24)	-
Years experiencing chronic pain	5.63 (5.52)	-	7.01 (8.80)	-
Pain Diagnoses				
Fibromyalgia		7		6
LBP		16		20
IBS		3		6
Osteoarthritis		5		6
Other Diagnosis		12		11

Note: VAS, Visual Analogue Scale; *M*, mean; *SD*, Standard Deviation, *n*, sample size; %, percentage.

Table 4

Posttest Placebo Knowledge, Trust and Efficacy Univariate ANOVAs

<i>Dependent Variables/Main effects and contrasts</i>	<i>F</i>	<i>P</i>	<i>ES (η^2)</i>
Placebo Knowledge	$F(1, 55) = 17.85$	<.001**	.245
Education > Control	-	<.001**	.245
Placebo Conceptualization	$F(1, 55) = 14.34$	<.001**	.207
Education > Control	-	<.001**	.207
Placebo Efficacy	$F(1, 55) = 8.14$	.006*	.129
Education > Control	-	.006*	.129

Note: *F*, *f* statistic; *P*, *p*-value; *ES* (η^2), partial eta squared effect size.

Table 5Posttest placebo acceptability mixed-model (6×2) ANOVA

Main effects and post hoc analyses	<i>P</i>	ES (ηp^2)
Education	.001 *	.188
Intervention > Control	.001 *	.188
Acceptability Contexts	<.001 **	.291
Deceptive Placebo < Explicit Placebo	<.001 **	.305
Deceptive Placebo < Treatment Enhancer	<.001 **	.506
Deceptive Placebo – When other EBTs are available	.1.00	.031
Deceptive Placebo < when NO other EBTs are available	<.001 **	.503
Deceptive Placebo - Diagnostic Placebo	.412	.085
Explicit Placebo - Treatment Enhancer	.274	.097
Explicit Placebo > when other EBTs are available	<.001 **	.322
Explicit Placebo - when NO other EBTs are available	.064	.139
Explicit Placebo – Diagnostic Placebo	.237	.101
Treatment Enhancer > When other EBTs are available	<.001 **	.449
Treatment Enhancer – when NO other EBTs are available	1.00	.046
Treatment Enhancer < Diagnostic Placebo	.001 *	.245
When other EBTs are available < when NO other EBTs are available	<.001 **	.516
When other EBTs are available – Diagnostic Placebo	1.00	.019
When NO other EBTs are available > Diagnostic Placebo	<.001 **	.283
Education x Acceptability	.158	.028

Note: *P*, p-value; ES (ηp^2), partial eta squared effect size;*, Indicates significant difference ($p < .05$);**, Indicates significant difference ($p < .001$); Bonferroni alpha correction used for post hoc analyses

Table 6Posttest deception, trust, and negative mood mixed-model ($2 \times 3 \times 2$) ANOVAs

Dependent variable/main effects, interactions, and contrasts	<i>F</i>	<i>P</i>	ES (ηp^2)
Deception			
Education	$F(1, 55) = 2.27$	.138	.040
Instructions	$F(1, 55) = 52.47$	<.001**	.488
Enhanced Placebo > RA	-	<.001**	.488
Instructions x Education	$F(1, 55) = .612$	.438	.011
Tx Outcome	$F(2, 110) = 1.13$	.327	.020
Tx Outcome x Education	$F(2, 110) = 1.51$	.226	.027
Instruction x Tx Outcome	$F(2, 110) = 2.28$	.108	.040
Instruction x Tx Outcome x Education	$F(2, 110) = .21$	.814	.004
Trust in Healthcare Provider			
Education	$F(1, 55) = 1.77$	.188	.031
Instructions	$F(1, 55) = 26.22$	<.001**	.323
RA > Enhanced Placebo	-	<.001**	.323
Instructions x Education	$F(1, 55) = 2.04$	.159	.036
Tx Outcome	$F(2, 110) = 25.85$	<.001**	.320
Improved > No Change	-	<.001**	.287
Improved > Worsened	-	<.001**	.415
No Change > Worsened	-	.017*	.099
Outcome x Education	$F(2, 110) = .433$	.650	.008
Instruction x Outcome	$F(2, 110) = .169$	.845	.003
Instructions x Outcome x Education	$F(2, 110) = 2.87$	.060	.050
Negative Mood			
Education	$F(1, 55) = 1.08$	.304	.019
Instructions	$F(1, 55) = 26.28$	<.001**	.323
Enhanced Placebo > RA	-	<.001**	.323
Instructions x Education	$F(1, 55) = .00$	.958	.000
Tx Outcome	$F(1.61, 88.47) = 36.52$	<.001**	.399
Improved < Worsened	-	<.001**	.463
Improved < No Change	-	<.001**	.400
No Change < Worsened	-	<.001**	.207
Outcome x Education	$F(2, 110) = .75$	.476	.013
Instruction x Outcome	$F(2, 110) = 1.12$	.328	.020
Instructions x Outcome x Education	$F(2, 110) = 1.52$	.223	.027

Note: RA, Random assignment; *F*, *f* statistics; *P*, *p* value; ES, effect sizes; ηp^2 , partial eta squared;*, Indicates significant deviation ($p < .05$);**, Indicates significant deviation ($p < .001$).