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Positive messages may reduce patient pain: A meta-analysis

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ABSTRACT

Introduction. Current treatments for pain have limited benefits and worrying side effects. Some studies suggest that pain is reduced when clinicians deliver positive messages. However, the effects of positive messages are heterogeneous and have not been subject to meta-analysis. We aimed to estimate the efficacy of positive messages for pain reduction.

Methods. We included randomized trials of the effects of positive messages in a subset of the studies included in a recent systematic review of context factors for treating pain. Several electronic databases were searched. Reference lists of relevant studies were also searched. Two authors independently undertook study selection, data extraction, risk of bias assessment, and analyses. Our primary outcome measures were differences in patient- or observer-reported pain between groups who were given positive messages and those who were not.

Results. Of the 16 randomized trials (1703 patients) that met the inclusion criteria, 12 trials had sufficient data for meta-analysis. The pooled standardized effect size was −0.31 (95% confidence interval [CI] −0.61 to −0.01, p = 0.04, I^2 = 82%). The effect size remained positive but not statistically significant after we excluded studies considered to have a high risk of bias (standard effect size −0.17, 95% CI −0.54 to 0.19, *P* = 0.36, I^2 = 84%).

Conclusion. Care of patients with chronic or acute pain may be enhanced when clinicians deliver positive messages about possible clinical outcomes. However, we have identified several limitations of the present study that suggest caution when

interpreting the results. We recommend further high-quality studies to confirm (or falsify) our result.

Keywords: Expectations; Meta-analysis; Positive messages; Context factors; Pain; Healthcare consultations

1. INTRODUCTION

Chronic and acute pain are common, debilitating, and costly conditions. One hundred million people in the United States alone suffer from chronic pain, and treatment costs exceed an estimated $250 billion per year, which is a considerable burden on the US economy in terms of lost productivity [1]. Reliable estimates of the expenditure for acute pain are not available, but the market for pharmacological treatments for acute pain is believed to be large [2]. Analyses of non-steroidal anti-inflammatory drug treatment of pain suggest that, when taken alone, these drugs have very modest effects [3]. Opioids and intra-articular corticosteroids may have more substantial short-term benefits, but are usually accompanied by more serious adverse effects and therefore an unattractive long-term treatment option [4, 5]. The pursuit of safer and more effective pain treatments is fraught with difficulties, but there are promising strategies readily available to enhance our current therapeutic efforts [6].

Increasing evidence from clinical trials suggests that clinicians can enhance pain relief by delivering positive messages that modulate patients' expectations and experience of pain [10, 11, 12]. The efficacy of expectation-inducing interventions was tested in one trial in which the patient was impelled to believe that "the medication was a potent painkiller [and] that their pain was going to subside within a few minutes" [13]. In another trial, patients were induced to believe that the medication they were about to receive was a groundbreaking drug that "recently became available in the Netherlands…[t]his drug, according to my experience, is very effective and will decrease the pain quickly after taking it" [10]. In both trials, patients who received positive messages experienced less pain than those who did not. These results indicate

that expectation-inducing interventions have a considerable effect on the outcome of pain treatments. Specifically, the way practitioners deliver positive messages is a key component of expectation-inducing interventions and is therefore likely to be an important part of multipronged treatment efforts for clinical pain.

The main mechanism explaining how positive messages enhance pain is likely to involve the brain's reward system, which could produce a physiological response to pain that prompts the patient's body to produce endogenous opioid analgesia [15]. Pain relief interventions that use positive messages could be mediated through similar mechanisms to drug interventions. There is compelling evidence to support the role of positive messages in reducing anxiety, a condition closely related to pain [16] and evidence to support the role of expectation-inducing interventions in reducing stress and improving well-being in patients suffering from chronic disease [17]. Crucially, enhancing patients' own pain relief mechanisms may be more effective than administering opiate-related drugs. Expectation-inducing methods of pain relief may provide the additional benefit of reducing side effects of drug treatment, such as withdrawal symptoms, addiction, and drug abuse. Understanding brain and nervous system functioning in the production of pain relief using positive messages is an important step in the scientific understanding of core mechanisms and treatments for pain-related conditions, for which there is no cure.

An early systematic review and meta-analysis of clinical studies investigated the extent to which positive messages can induce pain relief in patients [18]. However, several new trials have been published since this study was published, including a recent extensive review by Mistiaen et al. [19]. However, Mistiaen et al. chose not to

pool the results of expectation-inducing interventions and therefore did not address the magnitude of response to verbal suggestions by generating an effect size. Quantitative synthesis of data is required to generate a pooled estimate and confidence intervals (CIs) for treatment effects of interventions, even in cases where the pooled effect needs to be interpreted with caution owing to moderate heterogeneity (which was judged to be the case by Mistiaen et al. [19]). However, data pooling is important to generate power calculations for future high-quality trials that may resolve heterogeneity issues [20, 21]. This allows the possibility of investigating the mechanisms that contribute to variability in study results [22]. Thus, building on the Mistiaen et al. review [19], the present study attempts to provide a quantitative assessment and a meaningful interpretation of the efficacy of positive messages for clinically relevant pain.

Another review conducted by Peerdemann et. al. investigated the potential benefits of positive messages or imagery or conditioning and found a positive effect. [14] However the Peerdeman study included experimental pain, they included studies with a high risk of bias, and they combined positive messages with other treatments (conditioning and imagery). Hence the aims of the Peerdeman et al. study were different and it does not provide an unbiased estimate of the effects of practitioner positive messages, whereas ours does.

1.1. Aims and Objectives

We aimed to provide a pooled estimate of the effect of delivering positive messages on patient pain.

2. METHODS

2.1. Eligibility criteria

We included randomized trials of the effects of positive messages in a subset of the studies included in a recent systematic review of context factors for treating pain [19]. The review did not pool the results and was also potentially confounded by the inclusion of non-randomized studies. The protocol, eligibility criteria, information sources, and study selection were reported previously [19]. Reflecting the variety of communication styles within clinical practice, we included trials comparing the effects of positive messages with neutral or negative control [23].We also included studies comparing a neutral message (as would be provided as part of standard care) with a negative message, since these were relatively positive. However we excluded these in a sensitivity analysis. Trials were excluded if an interpreter or translator was used to induce the positive message or if the interaction between patients and care providers was not face-to-face.

2.2. Search strategy

The following electronic databases were searched from their start date to June 2015: CINAHL, Controlled-trials.com, EMBASE, LILACS, OpenGREY, PROQUEST

Dissertations, PsycINFO, PubMed, Sociological Abstracts, the Cochrane Central Register of Controlled Trials, Web of Science. Reference lists of relevant included studies were also searched.

2.3. Outcome measures: primary outcome

Our primary outcome measures were patients' self-reported pain scores, most commonly patients' perception of pain intensity reported on a visual analogue scale (VAS), and (to a lesser extent) observer-reported outcomes (such as physiological changes or observer-reported perceived pain) [24, 25]. We only identified one eligible study with dichotomous outcomes.

We used the primary outcome chosen by study authors where possible. If there was more than one primary outcome, or it was unclear, we chose the one most relevant to patients and provided a rationale for our choice. For example, longer-term follow-up (weeks rather than hours) is more likely to be clinically relevant. We contacted authors by email if data required for pooling was not included in published reports.

2.4. Data extraction and management

We did additional data extraction as there was insufficient data extracted from the Mistiaen et al. review [19]. Because it was crucial to our analysis we also confirmed the risk of bias assessments by re-conducting the risk of bias. Two authors (from JH, AM, and TF) independently extracted data and assessed the risk of bias in accordance with the Cochrane Handbook guidelines [26]. Discrepancies were resolved by

discussion with another author (PM). The extracted data included study design, types of participant, description of intervention and intervention components, description of comparison group, completeness of outcome data, outcome measures, country, and funding source. To investigate possible bias, we recorded data on random sequence generation, allocation sequence concealment, blinding of participants and personnel, blinding with respect to outcome assessment, completeness of outcome data, selective outcome reporting, and other sources of bias.

2.5. Impact of bias

Studies were deemed to have a high risk of bias if they were scored as having a high or unclear risk of bias for either sequence generation or allocation concealment. This is because empirical studies have shown that these characteristics influence outcomes [27, 26]. To assess publication bias, we used a funnel plot and investigated funnel plot asymmetry using the trim-and-fill method [28, 29].

2.6. Synthesis of results

For continuous measures, we analyzed data based on the mean, standard deviation, and number of participants. Where data were not reported in a format suitable for pooling, we reported outcomes narratively. Where possible, we made assumptions to allow the data to be included in the analysis, such as assuming a normal distribution, using the median to estimate the mean, and estimating the standard deviation as 0.75 times the inter-quartile range. For studies that did not report the number of individuals randomized to each group, we assumed that an equal proportion of participants were

randomized to each group. If the standard deviation at follow-up was not reported, we used the standard deviation at baseline. We used GRABIT software to extract data presented in graphical form (Matlab Central, 2015). Because of the variety of pain measures used, we calculated standardized mean differences (SMDs), using 95% CIs and *P*-values for the difference between groups. All analyses used a random effects model.

2.7. Assessment of heterogeneity

We anticipated heterogeneity in terms of intervention modalities, conditions, outcome measures, patients, and effect sizes, and therefore used a random effects model for the meta-analysis. Where studies were sufficiently similar to allow pooling of data, quantified heterogeneity was assessed using the I^2 statistic; an I^2 value of 50% or more was interpreted as indicating a substantial level of heterogeneity. Because of the study aims was to quantify the efficacy of positive messages to estimate potential benefits and make comparisons with other treatments, we pooled data despite substantial heterogeneity and noted the limitations of relying on the estimate (Higgins and Green, 2011).

2.8. Subgroup /sensitivity analyses

We conducted one pre-planned subgroup analysis that excluded studies with a high risk of bias. This was to establish the least biased estimate possible. We also conducted several exploratory subgroup analyses that were not pre-planned:

1. Exclusion of studies for which we had to make assumptions about the data to obtain poolable data, to test whether our assumptions affected the results.
2. Isolation of studies that measured the effects of expectations on chronic and acute pain, to detect differences in the effects of positive messages on different types of pain.
3. Examination of the effects of positive messages in specific conditions (those that had more than one study investigating them), to detect differences in the effects of positive messages on different types of pain.
4. Exclusion of studies that measure pain as part of a composite outcome, to detect differences in the effects of positive messages on different types of pain outcomes.
5. Exclusion of studies that compared neutral vs. negative or positive vs. negative messages, to detect differences in the effects of positive messages in different types of studies.
6. Exclusion of outlier studies, to detect an effect size that was not unduly influenced by an anomalous result.

2.9. Statistical software used

Analysis was carried out with the 'meta' package in R. (Schwarzer, 2014, R Core Team, 2014)

3. RESULTS

Sixteen studies (1703 patients) within the systematic review met our inclusion criteria [33, 13, 10, 34, 35, 36, 12, 37, 38, 39, 40, 25, 41, 42, 43]. These studies included a variety of interventions (see Tables 1 and 2). Twelve of these (1426 patients) had sufficient data for meta-analysis [13, 10, 34, 35, 37, 38, 40, 25, 41, 42, 43]. One study report [13] conveyed results for two trials, which were treated separately.

[Tables 1 and 2 about here]

We could not extract suitable data for meta-analysis from four studies [33, 36, 12, 39], mostly because no measure of variability of the primary outcome was reported (and attempts to obtain this data from the authors failed). The risk of bias was judged as high in 10 of the 16 studies included (see Figure 1) [33, 13, 10, 34, 35, 36, 37, 39, 40]. Pain intensity was measured directly using a VAS in most of the studies, and as part of a composite outcome in two studies [37, 38].

[Figure 1 about here]

3.1. Continuous outcomes

For the continuous outcome measures, the pooled estimate of the SMD was −0.31 (95% CI −0.61 to −0.01, $P = 0.04$), indicating a beneficial effect of delivering positive messages to patients. Statistical heterogeneity was high ($I^2 = 82\%$, $P < 0.001$) (see Figure 1). A pre-planned subgroup analysis was conducted excluding studies with a high risk of bias. Based on the six remaining studies eligible for meta-analysis [34, 38, 25, 41, 42, 43] with a low risk of bias and data suitable for pooling, the pooled

estimate of the SMD was positive but not statistically significant: −0.17 (95% CI −0.54 to 0.19, $P = 0.36$, $I^2 = 84\%$).

[Figure 2 about here]

3.2. Subgroup analysis

Excluding studies for which we had to make assumptions about the data to pool results, [13, 10, 34, 35, 37, 42, 43] the effect was −0.15 (95% CI −0.31 to 0.02, $P = 0.08$, $I^2 = 0\%$). Excluding studies that measured pain as part of a composite outcome [37, 38], the pooled estimate was −0.32 (95% CI −0.68 to 0.04, $P = 0.08$, $I^2 = 85\%$). Excluding studies that compared neutral versus negative [13, 34] or positive versus negative suggestions [42], the pooled estimate was −0.14 (95% CI −0.43 to 0.14, $P = 0.33$, $I^2 = 72\%$). For studies that measured chronic pain, the effect size was −0.10 (95% CI −0.25 to 0.05, p=0.18, $I^2 = 0\%$) and in studies measuring acute pain, it was −0.49 (95% CI −1.04 to 0.07, $P = 0.08$, $I^2 = 89\%$). For studies of a single condition (postoperative pain), the effect was positive but not statistically significant: [13, 43] −0.79 (95% CI −2.31 to 0.72, $P = 0.30$).

We conducted an exploratory analysis that excluded outliers in which we repeated the meta-analysis after removing each study separately [44]. This produced point estimates of the effect size that varied from −0.22, 95% CI −0.50 to 0.07 (omitting [13]) to −0.39, 95% CI −0.68 to −0.10 (omitting [43]); the corresponding *P*-values varied between 0.13 to 0.009. As expected from Figure 1, the studies that appeared to

have the most influence on the pooled estimate were [13, 45, 42, 43]. However, we found no substantive reason to exclude any of these studies from our primary analysis.

3.3. Assessment of risk of bias within studies

When studies with a high risk of bias were excluded, the effect of positive messages remained positive but not statistically significant. The nature of the intervention makes it difficult to blind practitioners, but it is possible to blind patients. Four studies had a low risk of bias for blinding participants [10, 36, 25, 43]. Ten of the included studies had a low risk of bias for blinding outcome assessors [24, 10, 34, 35, 12, 37, 38, 41, 42, 43]. Seven studies were ranked as having a high or unclear risk of bias for incomplete outcome data [36, 12, 38, 39, 40, 41, 43]. Only one study had a high risk of bias for selective reporting [40]. Other sources of bias included inadequate description of methodology [13] and "floor effects" leading to inability to detect treatment effects [39].

3.4. Publication bias

Visual inspection of the funnel plot indicated the possibility of publication bias, with two smaller studies having the largest effect sizes [45, 13]. Investigation of funnel plot asymmetry using the trim-and-fill method [46] led to a small attenuation in the pooled estimate, to −0.22, 95% CI −0.53 to 0.09, $P = 0.17$, with the method indicating the possibility of a missing study with a large positive effect size (effectively balancing the result of one of Benedetti's studies). Egger's test of funnel plot asymmetry gave a non-significant *P*-value of 0.31 [29]. Although we note the

relatively large effect size observed in the two Benedetti studies, considering both these results and the visual inspection of the funnel plot, we did not find compelling evidence of publication bias. However, publication bias is a potential problem with all evidence syntheses [47, 48].

5. DISCUSSION

5.1. Summary of evidence

This is the first meta-analysis of randomized trials of positive messages for patient pain. Although the effects of positive messages are generally encouraging, contrary to what has been reported in previous systematic reviews [49, 18], they are not unambiguously so. When non-randomized trials are excluded from analysis, the effects are small. Our subgroup analyses (in which we excluded studies with a high risk of bias, investigated chronic and acute pain individually, and investigated postoperative pain individually) showed that the benefits of positive messages persisted but were not always statistically significant. Our meta-analysis is also the first to provide a likely effect size which could be used to make power calculations for future, more definitive (higher quality) randomized trials. Assuming a typical standard deviation of between 1 and 2 units, our review demonstrated a pooled effect size estimate of approximately half of 1 point on a 10-point VAS. This falls short of the 1 to 2-point reduction deemed to be clinically relevant [50]. We found no reason to believe that the effects of positive messages are only beneficial in the short term.

5.2. Consistency with existing evidence

Several systematic reviews of placebos (which can include positive messages) have shown placebo to be effective in treating pain [51, 52, 53, 54]. However, the delivery of placebo interventions includes more than positive messages; they also include the effects of a sham intervention [55] and classical conditioning [56].

5.3. Comparison of positive messages with drug effects

Although some drugs have a substantial clinical analgesic effect [57] others do not. Some drug interventions for treating dental pain [58, 59], a condition investigated in three of the included studies [24, 36, 37], knee pain [60], neuropathic pain, and low back pain [61] revealed effect sizes similar to those found in our study. Pharmacological interventions may be more likely than positive messages to have adverse side effects [62, 61]. Although our preliminary analysis suggests that they are similar, at this stage, a robust comparison of positive messages with drug effects is not possible.

Comparisons between the effects of positive messages with drugs must be treated with caution. This is because recent estimates of analgesic efficacy use the Oxford League Table [63], which is not straightforwardly translatable to the continuous VAS measures typical of studies in this review. Our effect size comparisons are based on older effect estimates of analgesic drugs compared with placebo.

5.4. Strengths and limitations

This is the first study that quantifies the efficacy of positive messages for treating pain. There are several limitations to this meta-analysis. The risk of bias was high in many of the studies and the effect size estimate was reduced in subgroup analyses that excluded these studies. There was also some evidence of publication bias. The included studies were also heterogeneous, both statistically and in terms of the interventions. Statistical heterogeneity remained in most cases even after subgroup analyses. This was expected owing to the wide range of interventions, patients, settings, and practitioners. Our use of a random effects model partly addressed this problem.

Heterogeneity of the control interventions could have influenced the effect in either direction. As the effects of positive messages were estimated by subtracting the effects in the control groups from effects in the treatment groups, Hawthorne effects in the control group might have reduced the effect size. A recent systematic review suggested that "untreated" (neutral) control groups in clinical trials benefit from Hawthorne effects [64]. If so, then the effects of positive messages revealed by our study are an underestimate. Our decision to pool studies with different types of controls reflects clinical practice, in which caregivers have a range of consultation styles. The decision to pool results despite the high heterogeneity was also justified because all but one of the studies [23] revealed results consistent with a positive effect.

Reporting bias in the individual studies might have arisen because of the difficulty of blinding caregivers and participants. However, outcomes were assessed by blind observers in two of the included studies [33, 25] and the effects of positive messages were statistically significant in both of these.

Finally, two dangers may arise when implementing the results of these studies. First, if there is a large discrepancy between the patient's experience of pain and what the doctor tells the patient they will feel, the patient may adjust their beliefs to develop a negative expectation (and a subsequent "nocebo" effect) [65]. Delivering an overly positive message that does not match the patient's experience may also threaten the patient/doctor relationship, as the patient may perceive that the doctor is deceiving them [66]. Hence future trials in this area must consider likely realistic prognoses and ensure that any positive messages delivered by clinicians are realistic and non-deceptive.

5.5. Conclusions and implications

Positive messages appear to be moderately effective for treating pain. Patients are likely to benefit from positive messages, either alone or together with other treatments. Limitations to the study, most notably heterogeneity, warrant caution when interpreting the results. However, given the lack of serious harms, the ease of implementation, and the potential benefit to the many patients suffering from pain, clinicians are warranted in implementing the results of this review by delivering (realistic and non-deceptive) positive messages to their patients. Future research is now required to investigate the most efficient, ethical and cost-effective strategies for clinicians to maximize the benefits of positive framing for treating pain. Further work is also required to investigate independent and interactive effects of positive messages and treatments.

Conflicts of interests

There are no conflicts of interest to declare.

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Table 1. Description of included studies

Study	Country	Participants	No. Participants	Mean age	Male Sex, %	Interventions	Intervention timing	Method for assessing pain intensity*
Anderson 1991	United States	Dental patients needing at least 2 fillings	34	26	42	Positive suggestion	After dental filling procedure	VAS**
Benedetti 2003a	Italy	Patient having undergone thoracotomy	42	55	57	Open administration of treatment with positive suggestion	1 hour after operation	VAS
Benedetti 2003b	Italy	Patient having undergone thoracotomy	36	55	57	Open administration of treatment with positive suggestion	1 hour after operation	VAS
De Craen 2001	The Netherlands	Patients with chronic pain attending an outpatient clinic for a routine visit	111	52	32	Open administration of treatment with positive suggestion	1 hour after administration of experimental pain	VAS
Dutt-Gupta 2007	Australia	Unpremedicated patients requiring placement of an intravenous cannula	101	46	19	Negative suggestion	Within 2 minutes of cannula placement	VAS
Goodenough 1997	Australia	Children aged 3–17 years requiring venepuncture	117	10	62	Placebo with positive suggestion	Immediately after venepuncture	Faces pain scale
Kincheloe 1991	United States	Dental patients requiring injection	128	n/a	46	Positive suggestion	Immediately after injection	VAS
Knipschild 2005	The Netherlands and Belgium	Patients in general practice with pain complaints	77	n/a	n/a	Positive message	Between 7 and 100 days	VAS
Litt 1993	United States	Dental patients undergoing molar extraction	34	26	39	Positive message	Immediately after oral surgery	VAS
Little 2001	United Kingdom	Patients with low back pain	122	42	43	Positive message	1 week after visit to doctor	Combined pain/function score with numerical rating scale
Petersen 2012	Denmark	Patient having undergone thoracotomy	38	62	63	Positive message	Immediately after treatment	VAS
Petersen 2014	Denmark	Patients with chronic neuropathic	36	57	55	Open administration	Immediately after	Mechanical VAS

		pain				of painkiller	treatment	
Ronel 2011	Germany	Patients 18–80 presenting with biomarker-negative chest pain	28	64	83	Positive message	1 minute after angiogram	VAS
Suarez-Almazor 2010	United States	Age 50+, patients with painful knee osteoarthritis	418	64	36	Positive message	3 months after treatment	VAS
Varelmann 2010	United States	Healthy patients at term requesting labor epidural analgesia / nonlaboring parturients presenting for elective cesarean delivery under spinal anesthesia	140	33	0	Positive message	Immediately after injection	VAS
Wang 2008	China	Abdominal hysterectomy patients, aged 18–65	241	44	0	Positive or neutral/negative suggestions	6 hours after operation	VAS

* Was pain intensity unless otherwise stated
**Visual analog scale

Table 2. Positive message delivered in trial

Study	Description of positive message delivered to participants in the intervention group
Anderson 1991	Patients were told; "a procedure involving music has been effective in suppressing pain in 5000 dental operations." They were then given music and told: "This new procedure is quite simple. We let you listen to music tapes you particularly like over headphones, and most crucial, we let you make changes in the volume any time you feel any particular increase in tension, discomfort, anxiety, or pain. You do this by moving a dial we've located on your chair up and down." Turning the dial actually moderated the volume slightly, and patients were told that variations in volume would help them attend to the music.
Benedetti 2003a	The open administration of morphine was performed at the bedside by a doctor, who told the patients that the medication was a potent painkiller, according to routine clinical practice. In other words, the patients were informed that their pain was going to subside within a few minutes.
Benedetti 2003b	The open administration of morphine was performed at the bedside by a doctor, who told the patients that the medication was a potent painkiller, according to routine clinical practice. In other words, the patients were informed that their pain was going to subside within a few minutes.
De Craen 2001	"This is a medication that recently became available in the Netherlands. This drug, according to my experience, is very effective and will decrease the pain quickly after taking it."
Dutt-Gupta 2007	"I am going to apply the tourniquet on the arm. As I do this many people find the arm becomes heavy, numb and tingly. This allows the drip to be placed more comfortably."
Goodenough 1997	"We are trying out a new special cream. I am going to put some cream on your arm that might make it (the needle) hurt less.
Kincheloe 1991	Patients were instructed that the topical aesthetic (in fact a placebo) would numb them and make the injection a lot less painful.
Knipschild 2005	(After ascertaining there was no serious disease) patients were told: "You will be better within a week or so."
Litt 1993	Patients were told that their relaxation efficacy was high by the experimenter. The experimenter's positive suggestion was reinforced by (false) biofeedback which appeared to confirm the patients' ability to relax.
Little 2001	A booklet provided to patients gave positive messages: "you can ease your pain" and "most people do get better within 4 weeks."
Petersen 2012	Participants were told: "An active medication that has been shown to be effective for some types of pain will be tested." The active medication was given in full view of the patients, and the patients were told: "The agent you have just been given is known to powerfully reduce pain in some patients."
Petersen 2014	The intervention (placebo or treatment) was administered openly (as opposed to covertly for the control patients).
Ronel 2011	"Mrs./Mr. XYZ, we are now injecting a drug through the catheter which will widen your coronary vessels. This procedure will improve the blood flow in your heart. This drug is very effective and starts its action immediately. It is possible that you might feel some agreeable warmness or formication after only a few seconds."
Suarez-Almazor 2010	"I think this will work for you," "I've had a lot of success with treating knee pain," and "Most of my patients get better."
Varelmann 2010	"We are going to inject the local anesthetic that will numb the area where we are going to do the epidural/spinal anesthesia and you will be comfortable during the procedure."
Wang 2008	"The PCA pump was great in treating pain, especially for people who like you underwent abdominal surgeries", "You took a correct decision on using a PCA pump for your postoperative pain", and "The PCA pump was very effective in removing the postoperative pain affliction."

Figure 1 [previously Figure 2]: Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

Figure 2 [previously Figure 3]: Forest plot of comparison: Effects of positive suggestions vs usual care.