

# Harnessing the Placebo Effect: Exploring the Influence of Physician Characteristics on Placebo Response

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**Objective:** Research on placebo/nocebo effects suggests that expectations can influence treatment outcomes, but placebo/nocebo effects are not always evident. This research demonstrates that a provider's social behavior moderates the effect of expectations on physiological outcomes. **Methods:** After inducing an allergic reaction in participants through a histamine skin prick test, a health care provider administered a cream with no active ingredients and set either positive expectations (cream will *reduce* reaction) or negative expectations (cream will *increase* reaction). The provider demonstrated either high or low warmth, or either high or low competence. **Results:** The impact of expectations on allergic response was enhanced when the provider acted both warmer and more competent and negated when the provider acted colder and less competent. **Conclusion:** This study suggests that placebo effects should be construed not as a nuisance variable with mysterious impact but instead as a psychological phenomenon that can be understood and harnessed to improve treatment outcomes.

**Keywords:** expectation, placebo/nocebo effects, patient-physician interactions, social perception, allergies

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Placebo research illustrates how positive expectations can transform substances with no active ingredients into meaningful health outcomes (Finniss, Kaptchuk, Miller, & Benedetti, 2010). For example, when a cream with no apparent medical properties is labeled as a painkiller, it reduces subjective reports of pain (Price et al., 1999). When migraine patients believe that an inert pill is an active drug, it relieves reported pain from headaches (Kam-Hansen et al., 2014). Relatedly, literature on nocebo (negative placebo) effects demonstrates how negative expectations may change the course of medical treatment (Faasse & Petrie, 2013) by increasing experienced pain (Benedetti, Lanotte, Lopiano, & Colloca, 2007; Bingel et al., 2011) and increasing reports of treatment side effects (Mondaini et al., 2007). Expectations about a health-relevant stimulus can affect both psychological and physiological responses to that stimulus (Colloca, Lopiano, Lanotte, & Benedetti, 2004; Crum, Corbin, Brownell, & Salovey, 2011; Crum & Langer, 2007; Crum, Salovey, & Achor, 2013; Price, Finniss, & Benedetti, 2008).

However, the placebo effect appears to be variable. Some meta-analyses of randomized clinical trials have found that placebo effects are less powerful than once assumed (Hróbjartsson & Gøtzsche, 2004; see also Kiene & Kienle, 1997). Other research, including replications of an earlier meta-analysis, provides strong evidence for placebo effects (Wampold, Minami, Tierney, Baskin, & Bhati, 2005) or suggests that placebo interventions influence outcomes in certain settings (Hróbjartsson & Gøtzsche, 2010). Effects are often variable in size, even in well-conducted trials. Thus, it is critical for research to de-mystify this variability by identifying factors that shape whether or not placebo effects occur.

In the current study, we address the puzzle of when placebo/nocebo effects are most likely to occur. We hypothesize that the effect of expectations on physiological health is moderated by the social context in which the expectations are deployed. Our goal is to take a first step toward a more sophisticated understanding of the psychological and social components underlying placebo effects, in order to see whether placebo effects can be understood and managed as an active tool to improve treatment outcomes and reduce unnecessary pain and suffering.

What social or contextual factors are the most likely to influence expectations and to contribute to placebo effects? When forming impressions, humans readily and rapidly determine whether another person's intentions are benevolent (*judgments of warmth*), and whether this person has the ability to enact those intentions (*judgments of competence*; Fiske, Cuddy, & Glick, 2007). These attributes should be particularly relevant in the clinical context and thus likely to impact health outcomes. When a physician seems likable and credible, a patient may be more likely to trust their advice and therefore be more influenced by the expectations the physician sets. Warmth and competence may thus potentiate the impact of positive expectations and improve treatment outcomes. Interestingly however, if a warm and competent physician is not

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optimistic about a course of treatment or expects adverse side effects from a treatment, then the expectations a physician sets may undermine treatment outcomes. When a more credible and likable physician suggests to a patient that they are likely to experience side effects of a treatment, their statements may be more impactful and therefore increase the prevalence and/or severity of the side effects, as suggested by research on nocebo responses (Mondaini et al., 2007; Silvestri et al., 2003; Wells & Kaptchuk, 2012). The warmth and competence of a physician are significant contextual factors because they map on to prominent models of patient–physician relationships, which distinguish whether a physician focuses more on competence-related features (e.g., biomedical information) versus warmth-related features (e.g., discussing feelings and emotions; Roter et al., 1997), making these elements particularly important to understand for health care.

The current study builds on previous research in three significant ways. First, we independently manipulate health care provider warmth and competence to assess the influence of the social context on expectations. Second, we explore the impact of both negative and positive expectations about a treatment. Third, we measure expectations' effects on *physiological* treatment outcomes. To our knowledge, only one previous study has directly manipulated both expectations and the social qualities of the physician who sets them. Patients with irritable bowel syndrome (IBS) received placebo acupuncture treatment either in a neutral encounter, or in the context of a supportive patient–physician interaction (Kaptchuk et al., 2008). In the latter condition, the physician expressed positive expectations about the treatment (e.g., “I have [ . . . ] experience treating IBS and look forward to demonstrating that acupuncture is a valuable treatment”) and developed rapport with the patient by expressing empathy, practicing active listening, interacting with the patient in a warm and friendly manner, and engaging in thoughtful silence. Patients who received the placebo treatment in the context of this supportive interaction reported more improvement than patients who received only the placebo treatment.

These results are suggestive of the power of physician social behavior in shaping placebo responses. However, this previous study's augmented placebo condition varied several features of the patient–physician encounter, including more physician competence and experience, physical contact, and time spent with the patient. In the current study, we refine this initial research by experimentally manipulating health care provider warmth and competence independently. We test whether placebo effects will arise as a result of expectations (Stewart-Williams & Podd, 2004) and whether these expectations can be swayed by these precise elements of the social context. In addition, the study with IBS patients investigated how a provider's behavior amplified positive expectations about treatment, but not negative expectations. Physicians are often tasked with delivering negative expectations, for instance warning patients of potential adverse side effects of treatment. The role of negative expectations during treatment is important to understand alongside positive expectations. We therefore explore how elements of the social context may affect negative, as well as positive, expectations. Finally, the outcomes measured in the study with IBS patients were solely self-report (e.g., self-reported relief of symptoms and symptom severity) rather than objective physiological markers. Whether placebo responses influence objective physiological functioning as well as subjective

health outcomes remains an important, underresearched question. We examine the effect of expectations on physiological treatment outcomes, in this case measured by allergic reactions.

We expect that, in response to a mild allergic reaction induced by a histamine skin prick test (SPT), participants who believe that a cream (with no active ingredient) will decrease their allergic reaction will respond by showing decreased reaction size (*anticipated placebo effect*), and participants who believe that the cream will increase their reaction will respond by showing increased reaction size (*anticipated nocebo effect*). However, and most critically, we predict that placebo and nocebo effects will affect physiological responses to an allergy SPT when set by a high-warmth and high-competence provider, but will *not* affect physiological responses to an allergy SPT when set by a low-warmth, low-competence provider. That is, a credible and likable provider who delivers positive expectations will increase the strength of positive expectations, but a credible and likable provider who delivers negative expectations should increase the strength of negative expectations. And when a provider is neither credible nor warm, expectations should carry little to no potency in either direction. We expect that providers who demonstrate either only warmth or only competence may demonstrate some effect of expectations, but we do not expect that these effects will be as potent as when the provider appears both warm and competent.

## Methods

For our experiment, we recruited 164 healthy adult participants for a study ostensibly about novel food preferences (five are omitted from analyses as a result of missing demographic information used as control variables). We set an a priori recruitment goal of approximately 160 participants (20 per cell), as this would provide us with adequate power (>85%) to detect a medium effect size for our  $2 \times 2 \times 2$  between-subjects study design, which we calculated using the G\*Power tool (Faul, Erdfelder, Lang, & Buchner, 2007).

Participants were told that, in order to participate in the food study, they first would need to undergo a health screening. To test the impact of expectations and provider interaction style on physiological outcomes, we use allergic reactions to histamine administered in a skin prick test. Allergy skin prick testing is the most widely used method worldwide for diagnosing allergies (Demoly, Romano, & Bousquet, 2008) and induces measurable physiological reactions in a short period of time. During a SPT, physicians introduce a small amount of suspected allergens by slightly pricking a patient's skin with a device soaked in the allergen, and measure the reaction on the skin. The reaction consists of a wheal (raised bump) and flare (redness surrounding the bump). The skin's responses to these suspected allergens are compared to reactions to histamine, the positive control in allergy skin prick testing, which causes a reaction in all individuals.

Past research on allergic reactions suggests that this protocol is well-suited for exploring placebo and nocebo effects. Some research demonstrates that expectations affect the onset of allergic responses. For example, in one study, a group of participants received an injection that contained a suspected food allergen. Participants in the control condition received a normal saline solution but were told that it contained a suspected food allergen. The study found that control condition participants reported symp-

toms as frequently as the active condition participants (Jewett, Fein, & Greenberg, 1990), therefore suggesting that allergic reactions are malleable and may be increased by negative expectations. Other research has found that expectations can affect allergic responses to histamine skin prick tests specifically. One study found that exposure to advertisements for the antihistamine medication Claritin, compared to exposure to those for a competing antihistamine, boosted the effectiveness of the drug and reduced wheal size in response to a histamine skin prick test (Kamenica, Naclerio, & Malani, 2013). This study provides preliminary evidence that expectations about a drug's effectiveness, evoked through advertising, can affect allergic responses. Our protocol extends this past research by exploring how both positive and negative expectations about a placebo treatment influence allergic reactions as well and how a provider's social behavior can strengthen or weaken those effects.

In a  $2 \times 2 \times 2$  between-subjects study design, we experimentally manipulated provider warmth (high or low), provider competence (high or low), and expectations about a cream with no active substance (positive or negative). We trained a female health care provider to act in one of four ways toward the participant during this health exam and randomized participants into these four conditions: (1) high warmth/high competence, (2) high warmth/low competence, (3) low warmth/high competence, and (4) low warmth/low competence. The provider followed a detailed script in each condition (see the supplemental material available online for additional description). In addition, we varied environmental cues to further enhance or diminish a sense of warmth and competence (see Table 1). This protocol was approved by the Stanford University Institutional Review Board.

The provider first asked the participant about their health background, took basic health measurements and collected saliva samples, and then conducted the allergy SPT. The test was conducted with histamine, to which all participants responded by experiencing itch

and developing a raised bump of itchy skin (a "wheal") surrounded by redness (a "flare"). During the allergy SPT, the provider placed an unscented hand lotion on the wheal of the reaction and then verbally communicated either positive expectations (i.e., that the cream would reduce the reaction and itching) or negative expectations (i.e., that the cream would increase the reaction and itching). The provider measured participants' reactions using a standard ruler for allergy testing at five time-points throughout the exam ( $T1 = 3$  min post-SPT,  $T2 = 6$  min post-SPT and cream administered directly afterward,  $T3 = 9$  min post-SPT and 3 min postcream,  $T4 = 12$  min post-SPT and 6 min postcream,  $T5 = 15$  min post-SPT and 9 min. postcream). We ended the measurements of the skin prick test after 15 min, because the reactions to histamine have been shown to reach their peak at about 6 min and diminish by 15 min (Oppenheimer & Nelson, 2006), making that an ideal timecourse for the study. The endpoint of the reaction was recorded by having the provider trace the reaction in surgical marker, lifting the tracing off the skin with transparent tape, and transferring the reaction to a paper record. These tracings were then measured by a research assistant who was blind to study condition and hypotheses. During the exam, participants rated how itchy their skin felt and how comfortable/anxious they felt (1 = *not at all* to 5 = *extremely*). Afterward, the participant filled out questionnaires about their experience, including rating the provider on items assessing perceived warmth and competence (1 = *strongly disagree* to 7 = *strongly agree*). All data have been made publicly available on the Open Science Framework at <http://osf.io/fajqa>

## Results

### Manipulation Checks

Participant self-reports of provider warmth and competence indicated that our manipulations were effective in creating perceptions of high and low likability and credibility. The health care provider was

Table 1  
*Manipulations of Warmth and Competence in the Study, by Study Condition*

Physician characteristics	Low competence	High competence
Low warmth	VERBAL CUES Did not ask for name or introduce self Used filler words (e.g., um) NONVERBAL CUES Minimized eye contact and faced computer, did not smile, maintained physical distance Put blood pressure cuff on wrong, forgot timer ENVIRONMENTAL CUES Nametag: student doctor No posters on wall Room disorganized, papers scattered on floor	VERBAL CUES Did not ask for name or introduce self Used clear, confident tone NONVERBAL CUES Minimized eye contact and faced computer, did not smile, maintained physical distance Made no mistakes in procedure ENVIRONMENTAL CUES Nametag: Fellow, Allergy Research Center No posters on wall Room organized, neat and clean
High warmth	VERBAL CUES Called person by name and introduced self Used filler words (e.g., um) NONVERBAL CUES Made more eye contact, smiled, sat closer during exam Put blood pressure cuff on wrong, forgot timer ENVIRONMENTAL CUES Nametag: student doctor Posters with warm images Room disorganized, papers scattered on floor	VERBAL CUES Called person by name and introduced self Used clear, confident tone NONVERBAL CUES Made more eye contact, smiled, sat closer during exam Made no mistakes in procedure ENVIRONMENTAL CUES Nametag: Fellow, Allergy Research Center Posters with warm images Room organized, neat and clean

rated as more competent in the two high-competence conditions than the two low-competence conditions,  $M_{\text{High Competence}} = 6.48$ ,  $SD = .59$ ,  $M_{\text{Low Competence}} = 6.11$ ,  $SD = .98$ ,  $t(153.77) = 2.97$ ,  $p = .004$ .<sup>1</sup> The health care provider was rated warmer in the two high-warmth conditions than in the two low-warmth conditions,  $M_{\text{High Warmth}} = 6.25$ ,  $SD = .97$ ,  $M_{\text{Low Warmth}} = 3.94$ ,  $SD = 1.60$ ,  $t(133.76) = 11.17$ ,  $p < .001$ .

We conducted a factor analysis of the items on which participants rated the health care provider after the exam and as expected two factors related to warmth ( $\alpha = .92$ ) and competence ( $\alpha = .89$ ) emerged. The health care provider was rated higher on this composite measure of competence in the two high-competence conditions than in the two low-competence conditions,  $M_{\text{High Competence}} = 6.35$ ,  $SD = .65$ ,  $M_{\text{Low Competence}} = 6.01$ ,  $SD = .80$ ,  $t(161) = 2.97$ ,  $p = .004$ . The health care provider was rated higher on this composite measure of warmth in the two high-warmth conditions than the low-warmth conditions,  $M_{\text{High Warmth}} = 6.40$ ,  $SD = .68$ ,  $M_{\text{Low Warmth}} = 4.82$ ,  $SD = 1.25$ ,  $t(124.90) = 9.97$ ,  $p < .001$ . See Figure 1 for a graphical depiction of these results. Taken together, this evidence suggests that our manipulations of warmth and competence via the health care provider's behavior were effective in shaping perceptions of warmth and competence.

### Analytic Strategy for Physiological Results

Using multilevel longitudinal modeling, we examined changes in the size of participants' allergic reaction to the SPT, in the 6-min period immediately after they received a placebo cream and were given expectation information about the cream's potency. As is common in allergy skin prick testing (Brockow et al., 2002), we analyzed the wheal and the flare separately beginning at 3 min after the application of the cream, and then again at 6 and 9 min after the cream application. Here we discuss the results concerning the wheal, as it was the site on which the cream was applied and is often the focus of research on allergic reactions (Booth, Petrie, & Brook, 1995; Eigenmann & Sampson, 1998; Torres et al., 2003). The results on the flare of the reaction were mostly similar (see the supplemental material available online). In each analysis we controlled for participants' gender and race and the average size of the wheal reaction at two time-points prior to the application of the cream (Time 1 and Time 2). The key parameter of interest was the coefficient associated with the final Time 5 difference in means between conditions, 6 min following application of the cream. Where relevant, we also discuss condition differences in the initial means (Time 3, 3 min after cream application) and the rate of change over time (slope from Time 3 to Time 5, from 3 to 9 min after cream application).

### Do Expectations About an Inert Cream Shape Allergic Reactions?

First, we examined whether having different expectations about the inactive cream would influence participants' physiological response. We expected having positive expectations would decrease skin reactions to the SPT (a smaller wheal/flare) indicating a placebo response, while having negative expectations would increase them (a larger wheal/flare), indicating a nocebo response. As predicted, at Time 5, participants who were told the cream would have a positive effect (by decreasing the reaction) had a

smaller wheal size than participants who were told the cream would have a negative effect ( $M_{\text{adj}} = 4.714$  vs. 5.093 mm;  $B = -0.379$  mm,  $z = -3.91$ ,  $p < .001$ ,  $d = -0.55$  SD), as shown in Figure 2A. This effect emerged over time (see Figure 2B), indicating that expectations for the cream had a significant effect on the slope of the wheal trajectory ( $B = -0.050$  mm/min,  $z = -3.59$ ,  $p < .001$ ,  $d = -0.07$  SD/min), but not on initial levels (Time 3) at the first measurement taken at three minutes after the cream was applied ( $B = -0.081$  mm,  $z = -0.98$ ,  $p = .326$ ,  $d = -0.12$  SD).

### Does a Positive Interaction Enhance the Effect of Expectations on Allergic Reactions?

Second, we examined whether a positive interaction, as indicated by the presence of warmth and/or competence on the part of the provider, would amplify the effect of expectations for the placebo cream on the histamine response (see Figure 3). As predicted, at Time 5, there were no differences in wheal size as a function of expectations, for participants in the condition where the provider was neither warm nor competent ( $M_{\text{adj}} = 4.972$  mm vs. 5.052 mm;  $B = -0.079$  mm,  $z = -0.41$ ,  $p = .683$ ,  $d = -0.12$  SD). When the provider was both warm and competent, by contrast, participants in the positive expectation condition had significantly smaller wheal size at Time 5 than participants in the negative expectations condition ( $M_{\text{adj}} = 4.326$  mm vs. 5.046 mm;  $B = -0.720$  mm,  $z = -3.63$ ,  $p < .001$ ,  $d = -1.05$  SD; see Figure 3A). This effect emerged over time (see Figure 3B). Compared to the "both low" condition, in this "both high" condition, positive expectations significantly decreased the slope of the wheal trajectory ( $B = -0.081$  mm/min,  $z = -2.85$ ,  $p = .004$ ,  $d = -0.12$  SD/min) but did not affect the size of the wheal at the first measurement, taken at three minutes after the cream was applied ( $B = -0.236$  mm,  $z = -1.41$ ,  $p = .159$ ,  $d = -0.34$  SD).

The two hybrid conditions, in which the provider was high on one quality but low on the other, yielded intermediate effects. In the high competence/low warmth condition, the wheal size at Time 5 was significantly smaller when participants had positive expectations than when they had negative expectations ( $M_{\text{adj}} = 4.737$  mm vs. 5.163 mm;  $B = -0.427$  mm,  $z = -2.24$ ,  $p = .025$ ,  $d = -0.62$  SD). However, neither the effect of expectations on the size of the wheal at the first measurement taken at three minutes after the cream was applied ( $B = -0.184$  mm,  $z = -1.14$ ,  $p = .253$ ,  $d = -0.27$  SD) nor slope compared to the "both low" condition ( $B = -0.040$  mm/min,  $z = -1.48$ ,  $p = .138$ ,  $d = -0.06$  SD/min) reached significance. In the high warmth/low competence condition, the wheal size at Time 5 was also smaller for positive expectations than for negative expectations ( $M_{\text{adj}} = 4.819$  mm vs. 5.111 mm), but was nonsignificant ( $B = -0.292$  mm,  $z = -1.51$ ,  $p = .131$ ,  $d = -0.43$  SD). Yet in this condition (high warmth/low competence), positive expectations did significantly lower the slope relative to negative expectations compared to the "both low" condition [ $B = -0.066$  mm/min,  $z = -2.39$ ,  $p = .017$ ,  $d = -0.10$  SD/min].

<sup>1</sup> For several of the following analyses (in which degrees of freedom are not integers), we use Welch two sample *t* tests, since Bartlett tests of homogeneity of variances indicated unequal variances across conditions (all Bartlett's *K*-squared > 19.07, all *p*s < .001).

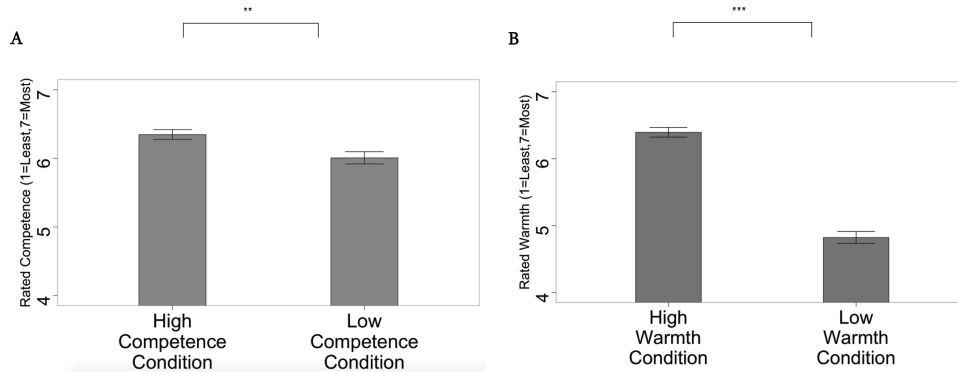


Figure 1. Participants' postexam ratings of health care provider warmth and competence. Panel (A) displays rated competence (collapsing across warmth condition), showing a main effect such that participants rated the health care provider as more competent in the high competence condition. Panel (B) displays rated warmth (collapsing across competence condition), showing a main effect such that participants rated the health care provider as warmer in the high warmth condition. All questions related to warmth and competence were statements (e.g., "The medical assistant was warm," with response options from 1 = *strongly disagree* to 7 = *strongly agree*). Standard errors represent  $\pm 1 SE N = 159$ . \*\*  $p < .01$ . \*\*\*  $p < .001$ .

### Does a Positive Interaction Enhance the Strength of Positive or Negative Expectations?

Provider interaction style could have moderated the effect of expectations by increasing the strength of positive expectations, increasing the strength of negative expectations, or both. To answer this question, we compared each provider interaction condition with the average of all warmth/competence cells within an expectation condition. This aggregate condition is the best possible representation of the effects of positive or negative expectations under "neutral" or "average" warmth and competence, and therefore isolates the effect of expectation alone for both of these expectation conditions. If a positive interaction strengthened positive expectations, the wheal size in conditions where the provider had high warmth and/or competence should be *smaller* than the wheal size corresponding to the average for participants with

positive expectations. Similarly, if a positive interaction strengthened negative expectations, the wheal size in conditions where the provider had high warmth and/or competence should be *larger* than the wheal size corresponding to the average for participants with negative expectations. For this analysis, we focus on the condition with the most positive provider interaction (both high-warmth and high-competence) relative to the average. Figure 4 displays this analysis. To test our hypotheses about how specific condition means or slopes compared to the average for a given provider interaction style, we used general linear hypothesis tests (denoted by chi-square statistics) within the full longitudinal model (Singer & Willett, 2003).

These results demonstrate that the provider qualities of warmth and competence moderated the effect of cream expectations by strengthening *positive* expectations, but not negative expectations.

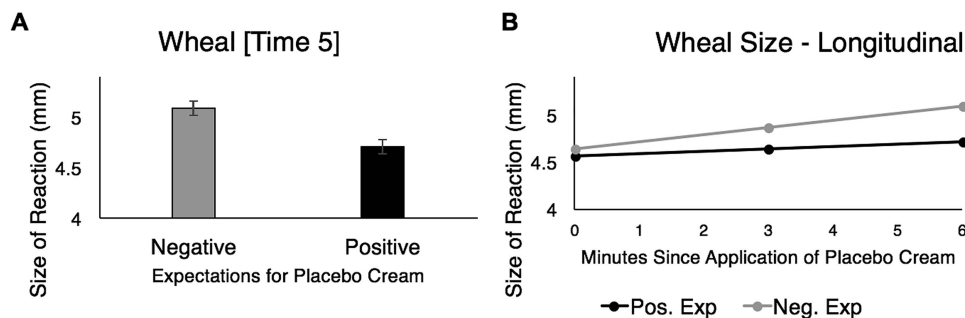


Figure 2. Difference in the size of the wheal as a function of expectations about the effects of a placebo cream delivered just before Minute 0 (Time 3), 9 min after the skin prick test. Panel (A) displays adjusted means at Time 5, 6 min after the application of the placebo cream and 15 min after the skin prick test. Nonoverlapping error bars indicate reliable differences at the  $p < .05$  level. Panel (B) displays the longitudinal trajectory of wheal size from Time 3 to Time 5 for participants given positive expectations and negative expectations. The difference between the slopes is significant at the  $p < .05$  level. All adjusted means are derived from the same multilevel longitudinal model, which controls for participants' gender ( $-1 = \text{male}$ ,  $+1 = \text{female}$ ), ethnicity ( $-1 = \text{white}$ ,  $+1 = \text{nonwhite}$ ), and average wheal size at Times 1 and 2 (3 and 6 min after the skin prick test, respectively), grand-mean centered. Standard errors represent  $\pm 1 SE N = 159$ .

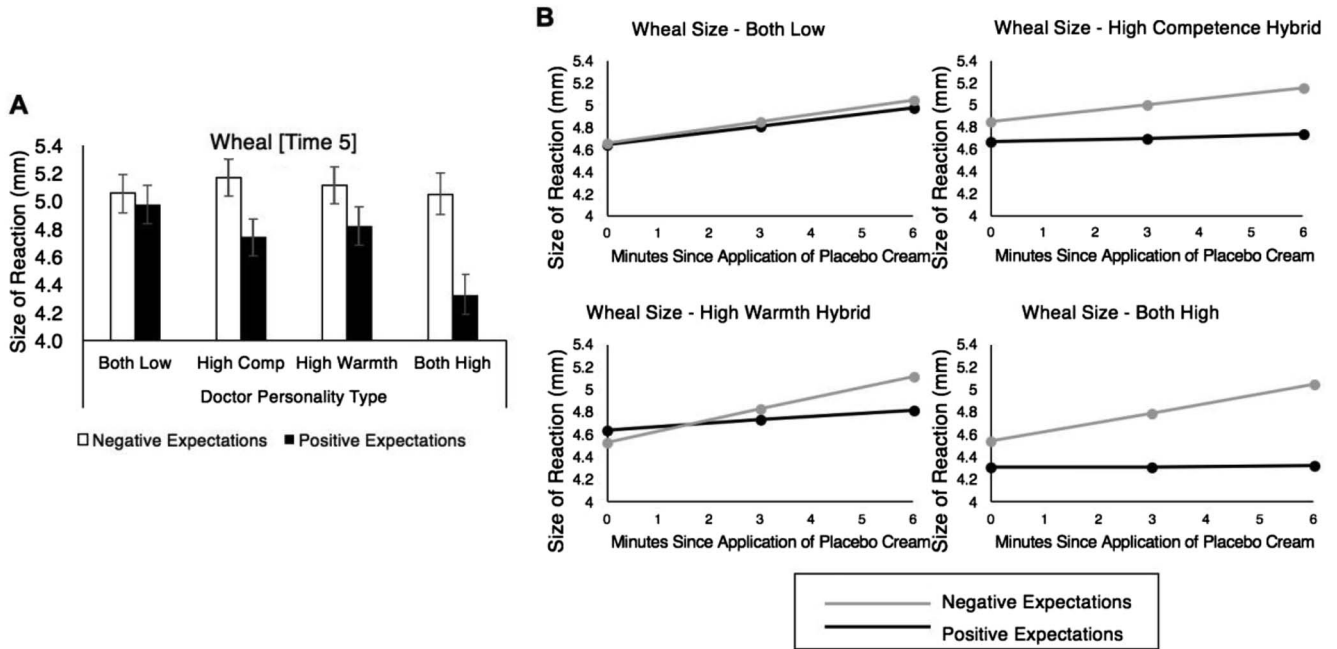


Figure 3. Difference in wheal size as a function of positive and negative expectations, within each of the four health care provider interaction styles defined according to two dimensions: high or low warmth, and high or low competence. Panel (A) displays adjusted means at Time 5, 6 min after the application of the placebo cream and 15 min after the skin prick test. Nonoverlapping error bars indicate reliable differences at the  $p < .05$  level. Panel (B) displays the longitudinal trajectory of wheal size from Time 3 to Time 5. The difference between the slopes in the high-warmth, high-competence condition compared to the both low condition is significant at the  $p < .05$  level. All adjusted means are derived from the same multilevel longitudinal model, which controls for participants' gender ( $-1 = \text{male}$ ,  $+1 = \text{female}$ ), ethnicity ( $-1 = \text{white}$ ,  $+1 = \text{nonwhite}$ ), and average wheal size at Times 1 and 2 (3 and 6 min after the skin prick test, respectively), grand-mean centered. Standard errors represent  $\pm 1 SE N = 159$ .

Among participants told information designed to create positive expectations, wheal size in the “both high” condition was significantly smaller relative to the average ( $M_{\text{adj}} = 4.326 \text{ mm}$  vs.  $4.714 \text{ mm}$ ;  $\chi^2(1) = 10.55$ ,  $p = .0010$ ). This effect emerged at the first measurement taken at three minutes after the cream was applied, as indicated by a significant difference in reaction size at Time 3 ( $\chi^2(1) = 6.64$ ,  $p = .01$ ). This initial effect was then maintained

over time; there was no difference in slope between the “both high” condition and the average ( $\chi^2(1) = 1.56$ ,  $p = .211$ ). By contrast, provider warmth and competence did not appear to strengthen negative expectations. Among participants told information designed to create negative expectations, wheal size in the “both high” condition was no different than the average ( $M_{\text{adj}} = 5.046 \text{ mm}$  vs.  $5.093 \text{ mm}$ ;  $\chi^2(1) = 0.15$ ,  $p = .703$ ). There was also

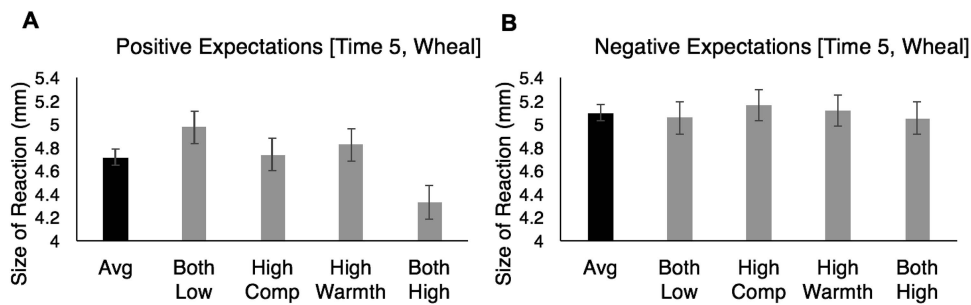


Figure 4. Difference in wheal size of each provider interaction style relative to the average wheal size, controlling for expectations. Panel (A) displays the relevant comparisons for the placebo effect. Nonoverlapping error bars indicate reliable differences at the  $p < .05$  level. Panel (B) displays the relevant comparisons for the nocebo effect. Both figures display adjusted means from the same longitudinal model as for Figures 1 and 2. Standard errors represent  $\pm 1 SE N = 159$ .

no difference relative to the average on initial levels at Time 3, the first measurement taken at three minutes after the cream was applied ( $\chi^2(1) = 1.01, p = .315$ ) or the slope ( $\chi^2(1) = 0.30, p = .585$ ).

### Comparing to a No Expectations Condition

Comparing the trajectory of the allergic reactions under positive and negative expectations allows us to test the difference between positive and negative expectations in the context of different interaction styles and revealed that positive and negative expectations did not create differences in allergic reactions in low-warmth, low-competence interactions, but did shape outcomes in high-warmth, high-competence interactions. Comparing the allergic reaction in the high-warmth, high-competence condition to the average wheal size of all the conditions allowed us to test whether positive or negative expectations drove these differences in trajectories, and suggested that positive, but not negative, expectations were enhanced by the presence of a high-warmth and high-competence provider. Neither of these comparisons, however, enabled us to test whether placebo and nocebo effects emerged relative to a condition in which no expectations are set. Therefore, to examine this important question, we ran 30 new participants through the high-warmth and high-competence protocol but this time gave no expectation information about the effect of the inert cream (no-expectations condition). By doing so, we are able to compare the effect of positive and negative expectations to no expectations within the high-warmth, high-competence condition. This comparison revealed that the Time 5 wheal size for the no expectations condition ( $M_{\text{adj}} = 4.617$  mm) was smaller than for the negative expectations condition ( $M_{\text{adj}} = 4.904$  mm;  $B = -0.29$  mm,  $z = 1.42, p = .155, d = -0.42$  SD) and larger than for the positive expectations condition ( $M_{\text{adj}} = 4.287$  mm;  $B = 0.33$  mm,  $z = -1.67, p = .095, d = 0.48$  SD; see the supplemental material available online and Figure S1). These results are consistent with the hypothesis that, although the increased allergic reactions prompted by negative expectations were not worsened when interacting with a warm and competent provider (as compared to a low-warmth and low-competence provider), both placebo and nocebo effects surface in interactions with a high-warmth, high-competence provider.

### Discussion

This study makes two major contributions. First, this study continues a critical process of unpacking the active ingredients underlying placebo effects and helps to shed light on a longstanding puzzle, providing a potential reason why placebo effects sometimes appear potent, and sometimes appear ineffectual. This study suggests that the placebo effect can be boosted or diminished by the social context, in this case marked by the warmth and competence of the health care provider. Positive expectations, when delivered by a warm and competent provider, diminished participants' allergic responses. However, when delivered by a provider that was less warm and less competent, neither positive nor negative expectations had influence. This study demonstrates that the effects of expectations on a medical treatment are not as simple as may previously have been thought, because they are moderated by warmth and competence.

The second major contribution is a methodological contribution. In this study, we test a novel protocol, the application of an inactive cream after a histamine skin prick test, which may be adapted by other researchers in order to study how placebo and nocebo effects impact allergic responses. There is a relative dearth of research examining what providers and patients can do to actively harness placebo and nocebo effects in health care. The design of this study allows us to unpack the variables that underlie the placebo effect, including expectations and social context, and examine their relative impact. Although the immediate application of this knowledge should be taken with caution, as this was a laboratory study conducted with healthy participants on only one outcome (allergic response), our findings begin the process of revealing some useful and important clinical implications with respect to what health care providers can do to boost the ultimate impact of treatment. The design of this study moves placebo and nocebo effects from a nuisance variable with mysterious impact to something that can begin to be understood and harnessed to enhance healing, and encourages future research in clinical contexts.

In this study, positive, but not negative, expectations were strengthened when a provider was both likable and credible. This runs contrary to our hypothesis that both positive and negative expectations would be strengthened when a provider was both likable and credible. There are several possible explanations why. Allergic reactions should decrease naturally over time. Whereas positive expectations complemented this already-occurring process, negative expectations essentially countered it. In addition, negative expectations were set regarding a relatively uninvolved process. Whether negative expectations about other, more serious, treatments (e.g., side effects of surgery, medication, etc.) might be enhanced by a positive patient-provider interaction is an open question and one that deserves further research, particularly in clinical contexts. It is notable that negative expectations did impact physiological outcomes in the high-warmth, high-competence interaction compared to a neutral expectations condition. Thus, although negative expectations were not strengthened by warmth and competence in the current study, it is important to further explore whether a physician's social behavior can influence the strength of nocebo effects in other contexts. Future research should continue to explore the most effective ways that physicians may discuss negative expectations (e.g., side effects) with their patients to avoid adverse consequences of discussing negative expectations with patients.

This study has a few limitations that should be noted. First, because the provider in this study was a woman, further research is needed to explore whether similar effects emerge for male providers. Second, our manipulation of competence produced a statistically significant, but not particularly large, difference in ratings of perceived competence. Even in the "low competence" condition, patients rated the provider as highly competent (the mean was 6.01 out of a 7-point scale). Although these differences likely match reality (most physicians are seen as competent), future research should explore the effect of larger differences in provider competence and think carefully about how to manipulate perceived competence in study design. Third, the timescale of the study was relatively short. Future research could explore these effects in other contexts where results unfold over a greater course of time, as well as in repeated interactions with clinicians rather

than single interactions (e.g., repeated placebo acupuncture treatments). Finally, given the moderate results in both the hybrid conditions (high warmth, low competence and low warmth, high competence), additional research is still needed to disentangle the respective roles of warmth and competence in inspiring patients to respond to expectations about treatment. While in this study both warmth and competence appeared necessary for eliciting expectation effects, literature on social perception suggests that warmth may be particularly crucial in social interactions (Cuddy, Fiske, & Glick, 2008). Future research exploring how verbal, nonverbal, and contextual elements underlying perceptions of warmth and competence are perceived by patients with varying personalities and preferences is needed. In addition, future research could elaborate on the precise mechanisms through which expectations impact physiology. For example, the manipulation of positive and negative expectations in this study could have served to decrease or increase patient anxiety, prompted cognitive reappraisals of the treatment, and/or changed where participants directed their attention during the medical procedure. We look forward to studies that explore these and other intriguing possibilities.

While this study was conducted in a laboratory setting with healthy participants, it has intriguing implications for the practice of medicine. These possibilities could be elaborated on in future research in clinical contexts. First, this research suggests that cultivating both warmth and competence may improve medical care by strengthening the impact of a treatment. In this case, even when the treatment involved only an inert cream, warmth and competence shaped whether this cream relieved participants' allergic reactions. Among the many demands of a career in medicine, physicians have been increasingly directed to build rapport with their patients (e.g., by exhibiting empathy). This research suggests a compelling reason for why physicians should pay attention to these psychological and social forces: They can impact physiological health outcomes. Second, as evidence for the role of expectations in improving medical treatment grows, physicians may be searching for ways to boost patient health outcomes by fostering positive expectations. This study suggests that, if physicians have a reason to hold positive expectations about a particular treatment, perhaps because it has a good record of success in the field, physicians may amplify the power of positive expectations by demonstrating warmth (likability) and competence (credibility) in their interactions with their patients. Future research should explore these effects with patients with varying clinical conditions, and should also continue to explore the boundaries of positive expectations' benefits. Of course, positive expectations are not a panacea for health care, and there are open questions about their limits, such as whether positive expectations may backfire if they are overly optimistic.

Medical procedures are always embedded in a multifaceted social context. Here we have isolated and explored critical elements of this context—the warmth and competence of the health care provider who delivers expectations about a procedure. This research calls attention to how critical it is to take these psychosocial forces into account when assessing the impact of a medical procedure. The same treatments, and even the same expectations about treatments, are not always equally influential. Instead, a complete picture of health care must consider not only the diagnoses and treatments themselves, and not simply how expectations

influence these diagnoses and treatments, but also how these expectations are delivered.

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