Commercial Features of Placebo and Therapeutic Efficacy

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In response to Dr Browning, I did not lay the problems of general surgery "at the feet of primary care." Having been involved in an effort to undo the flawed sustainable growth rate system for the past decade, I know that the system is broken. In a rational world, specialties would unite to correct this flawed system, which seems cynically designed to pit specialties against each other.

The calculations for physician compensation used in the cited study of internal medicine reimbursement[3] cut off in 2004 while the increases in evaluation and management codes took place in 2004 through 2007. For example, evaluation and management codes increased in work relative value units from 2006 to 2007 (code 99213: increase from 0.67 to 0.92 [37%]; code 99214: 1.10 to 1.42 [29%]; and code 99215: 1.77 to 2.00 [12.9%]). Furthermore, this article has been rebutted.[4] The primary care–specialty income gap has largely been corrected, at an estimated cost of $4 billion.[5]

I appreciate the enthusiasm of Dr Maa and colleagues for the surgical hospitalist, particularly in emergency and trauma care. However, I do not believe this is the answer to the shortage of general surgeons, who not only do emergency and trauma care but often perform endoscopy and other general surgical operations in critical access hospitals.

Philosophically, I have difficulty with medical or surgical hospitalists. My objection to the medical hospitalist system is that patients may perceive that they are being abandoned by their primary care physician at a time of their most dire need—when they are sufficiently ill to require hospitalization. I would hope that this sense of abandonment is not present in a surgical hospitalist system. When we train "physicians who operate," we try to instill judgment about the need for surgery. But if operation is required, the operator must be thoroughly competent. I believe that such decisions are more informed when the physician/surgeon is familiar with the patient. The surgical hospitalist system may aid trauma and emergency care in urban centers but will not solve the access problem in small rural hospitals.

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RESEARCH LETTER

Commercial Features of Placebo and Therapeutic Efficacy

To the Editor: It is possible that the therapeutic efficacy of medications is affected by commercial features such as lower prices. Because such features influence patients' expectations,[1] they may play an unrecognized therapeutic role by influencing the efficacy of medical therapies, especially in conditions associated with strong placebo responses.[2,3] To investigate this possibility, we studied the effect of price on analgesic response to placebo pills.

Methods. In 2006 we recruited 82 healthy paid volunteers in Boston, Massachusetts, using an online advertisement. Each participant was informed by brochure about a (purported) new opioid analgesic approved by the Food and Drug Administration; it was described as similar to codeine with faster onset time, but it was actually a placebo pill. After randomization, half of the participants were informed that the drug had a regular price of $2.50 per pill and half that the price had been discounted to $0.10 per pill (no reason for the discount was mentioned). All participants received identical placebo pills and were paid $30. Participants were blinded to the study purpose, and researchers were blinded to group assignment. The study was approved by the Massachusetts Institute of Technology institutional review board, and all participants provided written informed consent and were debriefed after the study.

The protocol followed an established approach for studying pain.[4] Electrical shocks to the wrist were calibrated to each participant's pain tolerance. After calibration, participants received the test shocks, rating the pain on a computerized visual analog scale anchored by the labels "no pain at all" and "the worst pain imaginable." Participants received all possible shocks in 2.5-V increments between 0 V and their calibrated tolerance. Stimulation at each intensity level was carried out twice for each participant (before and after taking the pill), and the change in reaction to the stimulation was assessed. Visual analog scale ratings were converted to a 100-point scale, the postpill score for each voltage was subtracted from the prepill score, and the mean of these differences was calculated for each participant.

The percentage of participants experiencing a mean score reduction vs increase was compared between the 2 groups using a 2-tailed χ^2 test. Because stronger pain may be associated with stronger placebo responses,[5] we also compared results for the 50% most painful shocks for each participant. In addition, mean differences at each voltage between the 2 groups were compared overall with a sign test and individually with *F* tests. A *P* value of .05 was considered statistically significant. Analyses were performed using SPSS version 15 (SPSS Inc, Chicago, Illinois).

Results. Patient characteristics are shown in the TABLE. In the regular-price group, 85.4% (95% confidence interval [CI], 74.6%-96.2%) of the participants experienced a mean pain reduction after taking the pill, vs 61.0% (95% CI, 46.1%-75.9%) in the low-price (discounted) group ($P = .02$). Similar results

occurred when analyzing only the 50% most painful shocks for each participant (80.5% [95% CI, 68.3%-92.6%] vs 56.1% [95% CI, 40.9%-71.3%], respectively; $P = .03$).

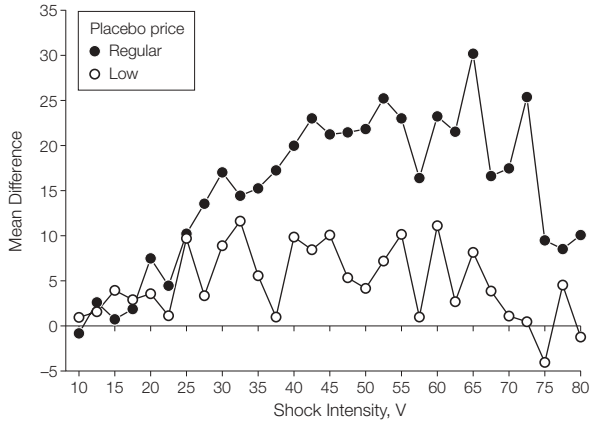
Considering all voltages tested, pain reduction was greater for the regular-price pill ($P < .001$). In addition, for 26 of 29 intensities (from 10 to 80 V), mean pain reduction was greater for the regular-price pill (FIGURE).

Table. Comparison of Participants Assigned to Regular-Price Placebo vs Low-Price (Discounted) Placebo

	Regular Price (n = 41)	Low Price (n = 41)	*P* Value
Women, No. (%)	27 (65.9)	24 (58.5)	.50
Age, mean (SD), y	30.9 (12.4)	30.0 (11.4)	.74
Calibrated maximum tolerance, mean (SD), V	51.8 (18.7)	54.9 (23.3)	.50
Shocks received, No. (SD)	18.2 (7.2)	18.6 (9.1)	.80
Change in pain scores[a]			
All shocks, No. (%) [95% CI]			
Pain reduction	35 (85.4) [74.6-96.2]	25 (61.0) [46.1-75.9]	.02[b]
Pain increase	6 (14.6) [3.8-25.5]	16 (39.0) [24.1-54.0]	
Highest-intensity shocks only, No. (%) [95% CI][c]			
Pain reduction	33 (80.5) [68.3-92.6]	23 (56.1) [40.9-71.3]	.03[b]
Pain increase	8 (19.5) [7.4-31.6]	18 (43.9) [28.7-59.1]	

Abbreviation: CI, confidence interval.
[a] Comparison of participants experiencing a mean reduction in pain after vs before the placebo pill was administered (visual analog scale point reduction between 0.01 and 48.4) and those experiencing a mean increase in pain (visual analog scale point increase between 0 and 29.2).
[b] Two-tailed χ^2 test.
[c] Highest 50% of shocks by intensity.

Figure. Pain Ratings by Voltage Intensity



No.															
Regular price	41	41	41	40	37	31	27	23	21	20	18	14	12	9	8
Low price	41	41	41	40	38	31	29	27	24	19	17	11	7	5	4

Mean difference in pain ratings, after vs before placebo, by voltage intensity. Higher value indicates greater pain reduction. The table depicts the intensity of the shocks and the number of observations in the regular-price and low-price conditions. *P* value is less than .05 for the shock intensities 27.5 V through 30.0 V, 35.0 V through 75.0 V, and 80.0 V.

Comment. These results are consistent with described phenomena of commercial variables affecting quality expectations[1] and expectations influencing therapeutic efficacy.[4] Placebo responses to commercial features have many potential clinical implications. For example, they may help explain the popularity of high-cost medical therapies (eg, cyclooxygenase 2 inhibitors) over inexpensive, widely available alternatives (eg, over-the-counter nonsteroidal anti-inflammatory drugs) and why patients switching from branded medications may report that their generic equivalents are less effective. Studies of real-world effectiveness may be more generalizable if they reflect how medications are sold in addition to how they are formulated. Furthermore, clinicians may be able to harness quality cues in beneficial ways,[6] for example, by de-emphasizing potentially deleterious commercial factors (eg, low-priced, generic).

These findings need to be replicated in broader populations and clinical settings to better understand how communicating quality cues with patient populations can maximize treatment benefits and patient satisfaction.

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