

# The Placebo Response

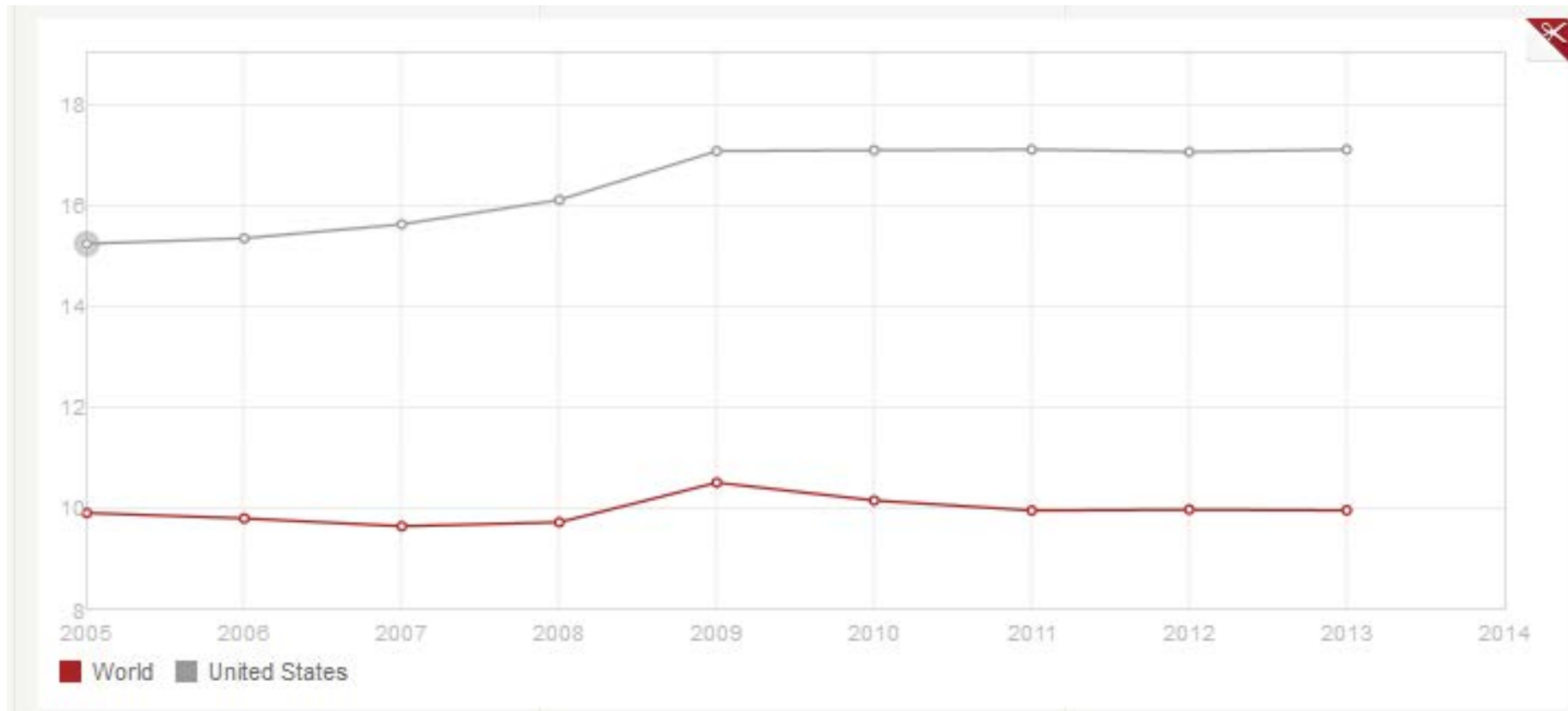
A Literature Review of Its Effects and Ethics

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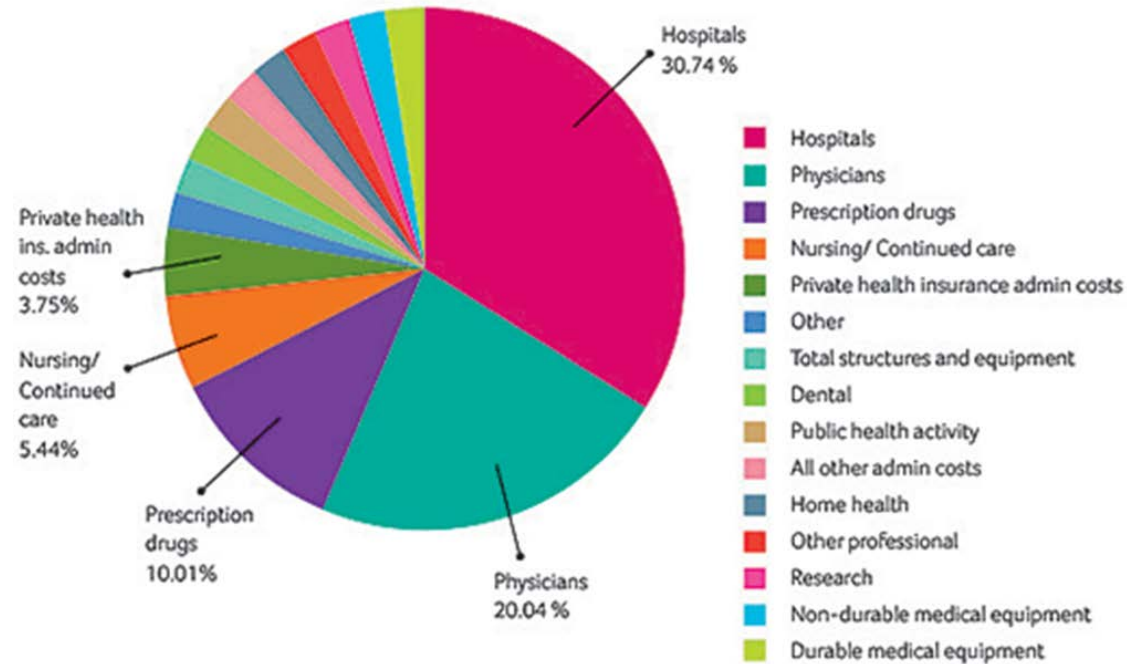
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# Healthcare Expenses as a Portion of GDP



# Healthcare Spending Breakdown

U.S. Health care spending breakdown, 2010



Source: Center for Medicare and Medicaid Services

# Current Placebo Use and Expectations in the U.S. Healthcare System

**Table 2 | Attitudes and behaviours related to prescribing placebos among 679 US general internists and rheumatologists**

Question and categories of response	No (%*)
How likely are you to recommend sugar pill proved to be better than no treatment for fibromyalgia?:	
Very likely	160/654 (24)
Moderately likely	221/654 (34)
Unlikely	205/654 (31)
Definitely not	68/654 (10)
How often do you recommend treatment primarily to enhance patient expectation?:	
Never	129/646 (20)
≤1/month	219/646 (34)
2-3/month	182/646 (28)
≤1/week	116/646 (18)
Is it appropriate to recommend treatment primarily to promote patients' expectations?:	
Obligatory	19/642 (3)
Permissible	380/642 (59)
Permissible only in rare circumstance	197/642 (31)
Never permissible	46/642 (7)

\*Based on actual numbers.

\*Based on actual numbers of respondents. All 679 respondents answered most questions. Percentages reflect 352 responses of 637 respondents who deemed the question relevant. The 285 respondents who marked "irrelevant—I do not prescribe placebo treatments" were not included in these percentages. 44.74%

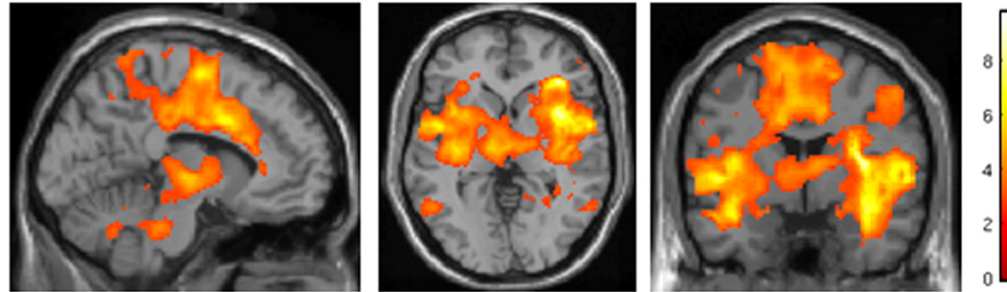
# What Sort of Placebos are Generally Prescribed?

**Table 3** | Treatments used as placebo in past year and how they are described to patients among 679 US general internists and rheumatologists

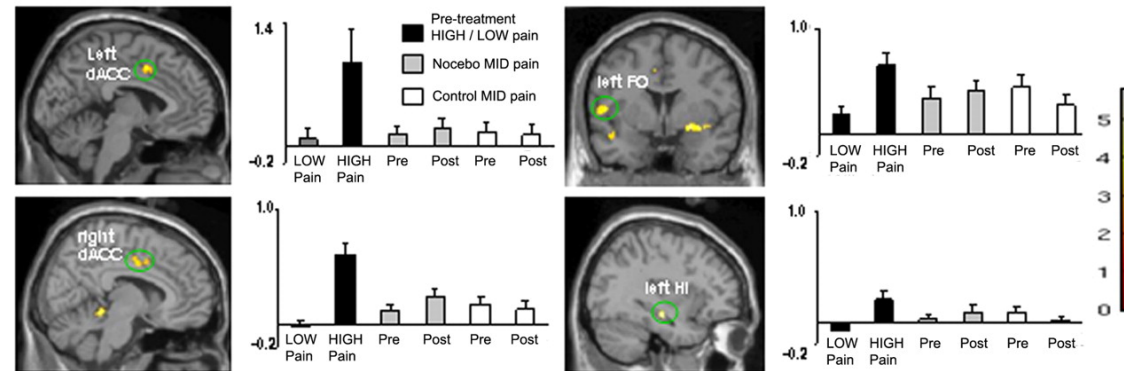
Question and response items	No (%*)
Recommended as "placebo treatment" in past year:	
At least one of any type	370/679 (55)
Over counter analgesics	267/648 (41)
Vitamins	243/648 (38)
Sedatives	86/652 (13)
Antibiotics	85/644 (13)
Saline	18/623 (3)
Sugar pills	12/642 (2)
How placebo treatments are typically described to patients:	
Not used	285/637 (45)
Medicine	62/352 (18)
Placebo	18/352 (5)
Medicine with no known effects for your condition	31/352 (9)
Medicine not typically used for your condition but might benefit you	241/352 (68)

A, fMRI signal changes invoked by all RP pretreatment high pain stimuli minus all pretreatment low pain stimuli applied on both placebo and control sites.

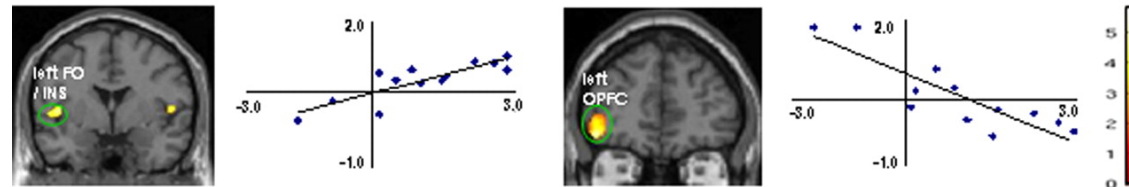
A. Activations during encoding of pain sensation



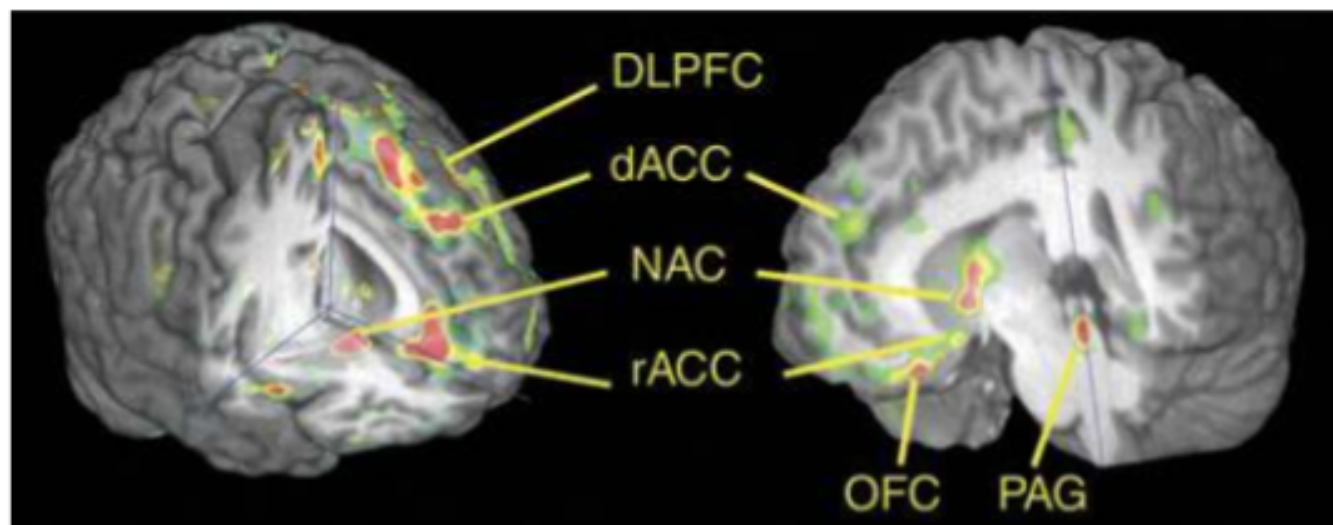
B. Representative regions involved in nocebo hyperalgesia



C. Representative regions correlated with nocebo hyperalgesia

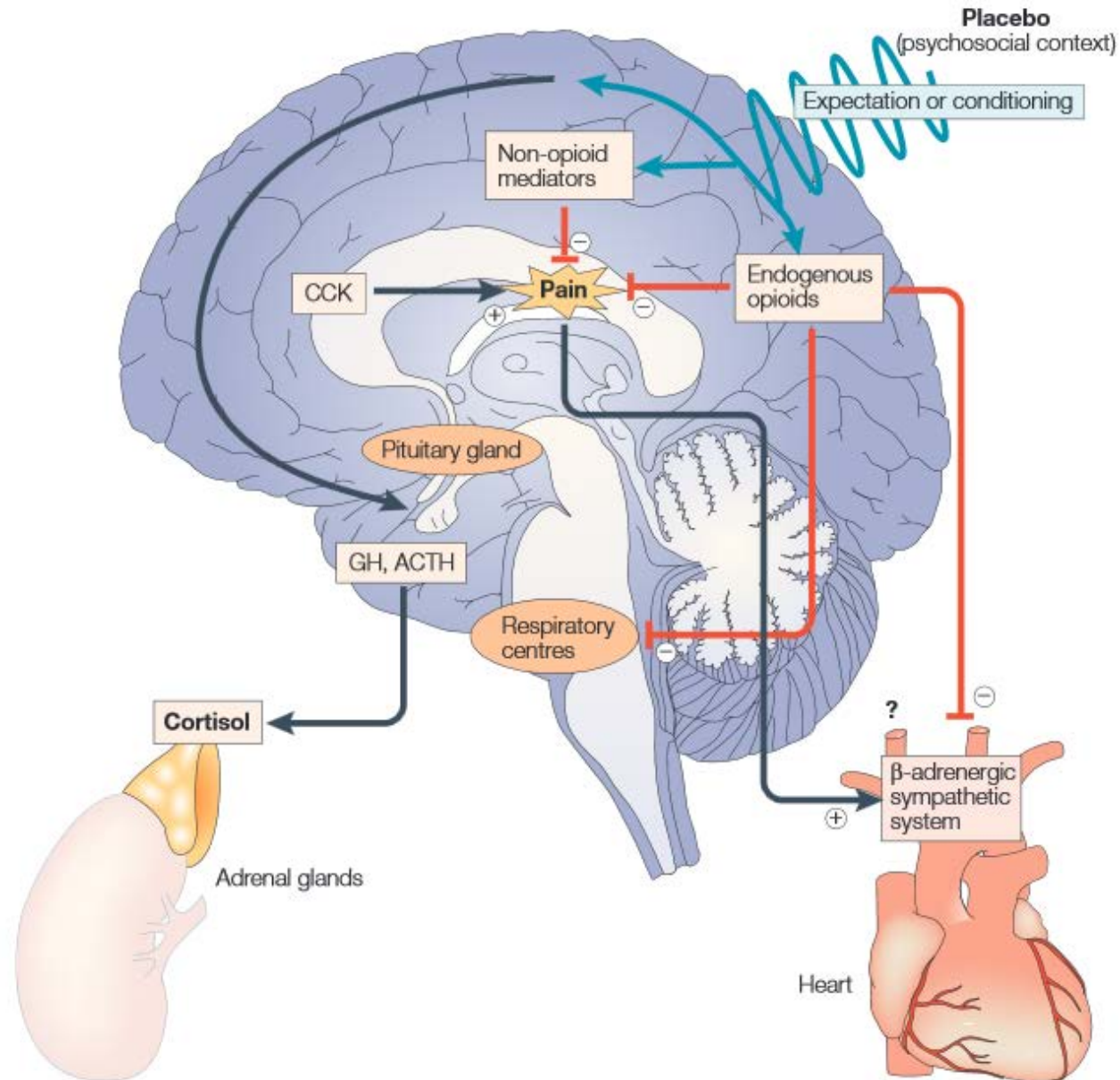


Jian Kong et al. J. Neurosci. 2008;28:13354-13362



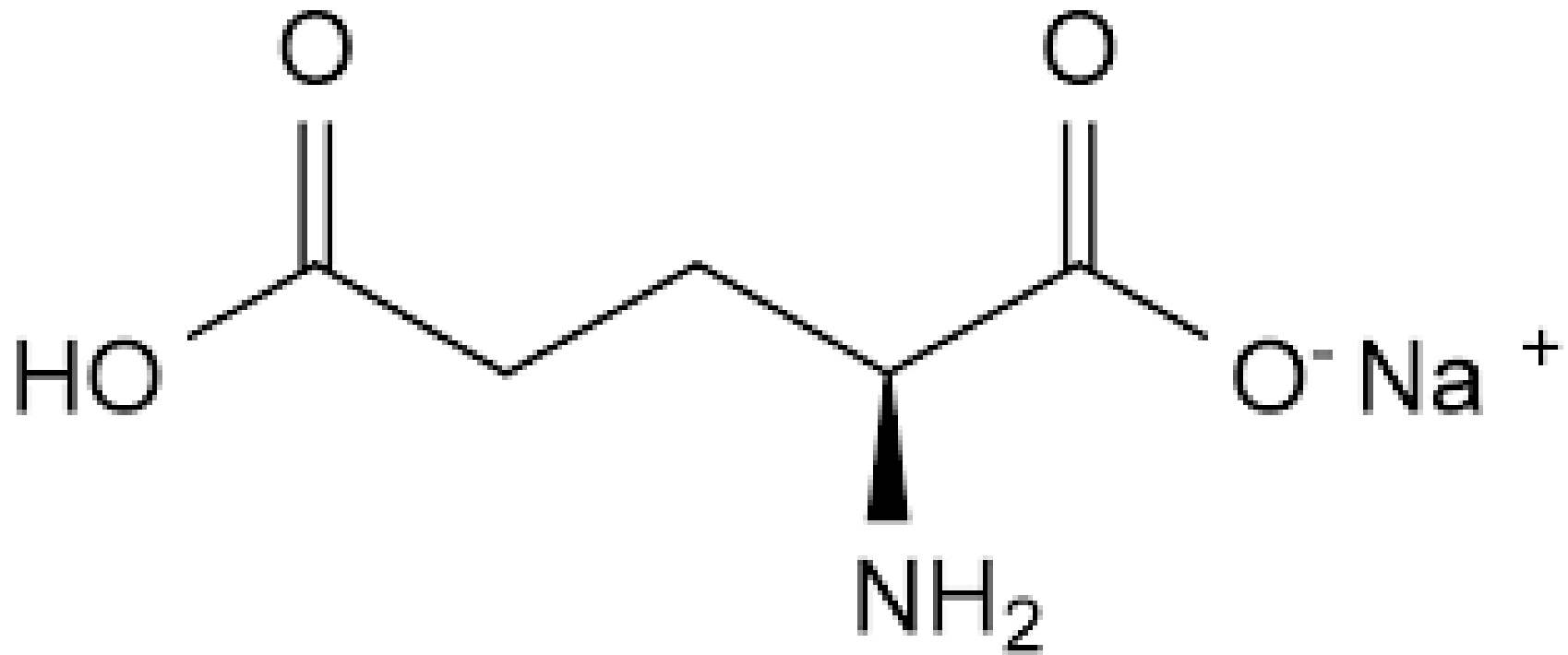
**Figure 1.** Placebo-induced activation of regional  $\mu$ -opioid receptor mediated neurotransmission. Some of the areas in which significant activation of  $\mu$ -opioid neurotransmission during sustained pain were observed after the introduction of a placebo with expectation of analgesia in two different experimental designs. On the left (Zubieta et al. 2005) there was evidence of dorsolateral prefrontal cortex activation, related to individual expectations of analgesia. On the right (Scott et al. 2008), prefrontal activation was localized in the orbitofrontal cortex, and correlated with nucleus accumbens endogenous opioid and dopamine release. DLPFC = dorsolateral prefrontal cortex, OFC = orbitofrontal cortex, rACC = rostral anterior cingulate (BA 25), dACC = dorsal area of the rostral anterior cingulate (BA 24), NAC = nucleus accumbens, PAG = periaqueductal gray.

# Hormonal Pathways





# Monosodium Glutamate



# The Healing Ritual

- Any set of social cues or actions that helps induce a placebo response.
- May be overly-theatrical or complex
- May be a simple social or environmental cue



# Placebo Response in “Alternative” Medicines is Socially Related

- Voodoo in Haitian Populations in NYC
- Prevalence of Faith Healings in more rural communities
- Socioeconomic status is not necessarily an indicator of CAMs, but it determines more of what sort of CAM a patient pursues



# Complications to the Placebo Effect

- Hawthorne Effect



- Pygmalion Effect



# Prevalence of Patients Pursuing the Placebo Effect

- Yearly Prevalence of CAMs is uncertain
- Only 5% of CAMs show any improvement over a pure placebo (Frass, et al., 2012)
- Go for the healing ritual, stay for the placebo response (Cumes, 2013)



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