

A large, 3D-rendered red pill with a white horizontal band across its center. The pill is positioned at the top of the slide and casts a soft shadow on the white background below it.

# The Placebo Effect

A smaller, 3D-rendered blue pill with a white horizontal band across its center. It is positioned at the bottom of the slide and casts a soft shadow on the white background below it.

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# Stuff that's in this talk.

- What is a placebo?
- What is the placebo effect?
- How strong is the placebo effect?
- What affects the placebo effect?
- ~~• What effects affect effects of the placebo effect?~~
- Can placebos have side effects?
- Is it ethical to prescribe placebos?

# What is a placebo?

- A medically inactive treatment intended to deceive the patient.



- From the Latin placēbō (I shall please).

# What is a placebo?

- Can be more than just pills!
  - Injections
  - Sham surgery
  - Fake acupuncture



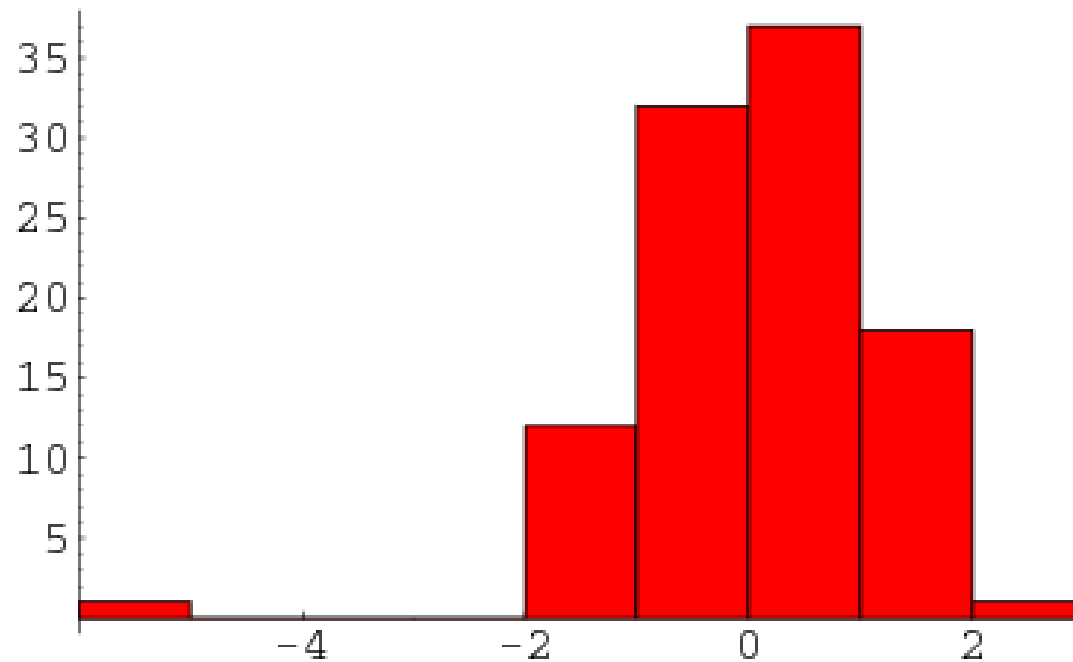
# Placebo Arthroscopic Surgery

## A Controlled Trial of Arthroscopic Surgery for Osteoarthritis of the Knee

J. Bruce Moseley, M.D., Kimberly O'Malley, Ph.D., Nancy J. Petersen, Ph.D., Terri J. Menke, Ph.D., Baruch A. Brody, Ph.D., David H. Kuykendall, Ph.D., John C. Hollingsworth, Dr.P.H., Carol M. Ashton, M.D., M.P.H., and Nelda P. Wray, M.D., M.P.H.  
N Engl J Med 2002; 347:81-88 | July 11, 2002 | DOI: 10.1056/NEJMoa013259

- Patients in the placebo group receive skin incisions and simulated surgery
- All patients reported improvement
- Placebo fared as well as real surgery

# Regression to the Mean?



# “The Powerful Placebo”

- 1955 paper by Henry K. Beecher
- Stressed the importance of randomized placebo-controlled studies
- Noted that ineffective treatments that claimed to be effective performed measurably better than no treatment

# How Powerful is a Placebo?

- Daniel Moerman, 2002 meta-study of gastric ulcers
  - 1692 patients across 31 trials
  - 76% of the 916 treated with drug were healed
  - 48% of the 776 treated with placebo were healed
  - Found large variability of placebo effectiveness between trials



# Placebo side effects?

- Beecher's 1955 paper asserted that placebos could produce negative effects
- Shapiro, Chassan, Morris, and Frick (1974)
  - Claim placebos generate similar side-effects as the drugs they claim to be
- Nocebo: from Latin (I shall harm)
  - Negative effect induced when patient believes a drug won't work

# Are two sugar pills better than one?

- “Placebo effect in the treatment of duodenal ulcer” (de Craen et al., 1999)
  - 2 placebos per day versus 4 placebos per day
  - Showed a relationship between frequency of administration and duodenal ulcer healing
  - Many other factors involved
- Rickets et. Al (1970)
  - ... the dosage of the placebo may be a significant and determining factor in the placebo response, although this is not clearly determined.

# Do you want a red pill or a blue pill?

- Schapira et al. (1970): Study on the Effects of Tablet Colour in the Treatment of Anxiety States
  - Treatment administered with pills in three colours: red, yellow, and green
  - Pills contained oxazepam
  - Anxiety symptoms most improved with green
  - Depressive symptoms responded best to yellow
  - Statistically significant? No.

# Do you want a red pill or a blue pill?

- Blackwell (1972)
- Students given either a pink or blue pill
- Told that one pill was a stimulant and one a sedative
- Both pills were sugar pills
- Blackwell measured alertness and found that the group with the pink pills was more alert than the group with blue pills

# How to Colour Placebos

- Stimulants: red, orange, yellow
- Anti-depressant: blue, green, purple



# Other influencing factors

- Branding increases the placebo effect
- Parenteral or subcutaneous administration is more efficient than oral administration
- A pseudo-acupuncture sham device had a greater effect than a placebo pill in chronic arm pain
- The more complex the procedure including rituals, mysterious powers, high technology and surgery, the larger the effects
- Source: “Placebo and other psychological interactions in headache treatment” (2012)

# Is the placebo powerless?

- Hróbjartsson and Gøtzsche (2004)
  - Systematic review of 114 randomized trials
  - They note that it “is widely believed that placebo interventions induce powerful effects.”
  - They “found no evidence of a generally large effect of placebo interventions. A possible small effect on patient-reported continuous outcomes, especially pain, could not be clearly distinguished from bias.”

# Mechanisms of the placebo effect

- Behavioural adjustments
  - Hotel maid study:  
<http://www.npr.org/templates/story/story.php?storyId=17792517>
- Flawed research methodology
- Expectancy and conditioning



# Ethics of the placebo effect

- Is homeopathy ever helpful?
- The Placebo Paradox
- Honest Placebos:

<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0015591>