Expectancy & Design Issues in Obesity Research

Me

Counseling Psychology

Crisis Counseling (suicide) connection & altering perceptions/expectations

Personality & Appraisal Psychology

Family Therapist

Clinical Obesity Post-doc (Hopkins)

Hopkins faculty ~15 years (GI & Rheumatology)

Fibromyalgia, CFS

Trained Science Writer

Windsurfing and Working Out

1. What do we want to learn in clinical obesity research? **Effect of diet intervention**
2. What do we really learn in clinical obesity research? **Effect of diet intervention PLUS**
3. What can we do to learn what we really want to learn in clinical obesity research? **Try to design studies to disentangle the PLUS from the effect of the diet intervention**

Map

Power of Expectations

Placebos as Expectancy Primers

Manipulating “Mind Set”

“Mechanisms” of Expectancy Effects

Designing weight loss trials to investigate role of expectancies

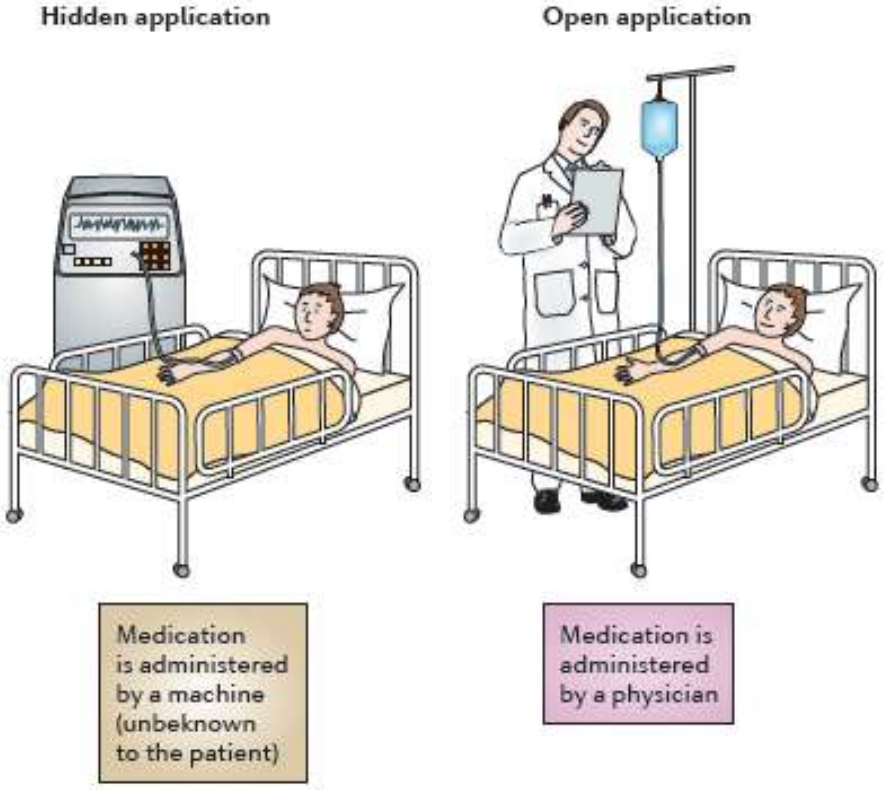

LEANDRO CARVALHO'S
Brazil
BUTT LIFT®
$380.00 VALUE!
FAT-BURNING FOODS

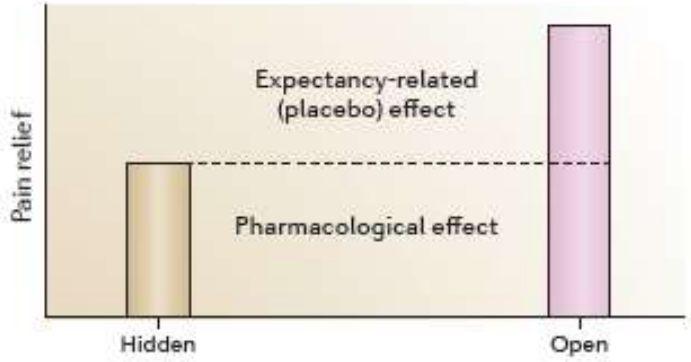

Marie Osmond lost 50 lbs.*
BEFORE


Hey SKINNY!
...YER RIBS ARE SHOWING!
I Can Make YOU a New Man, Too, In Only 15 Minutes a Day!
FREE

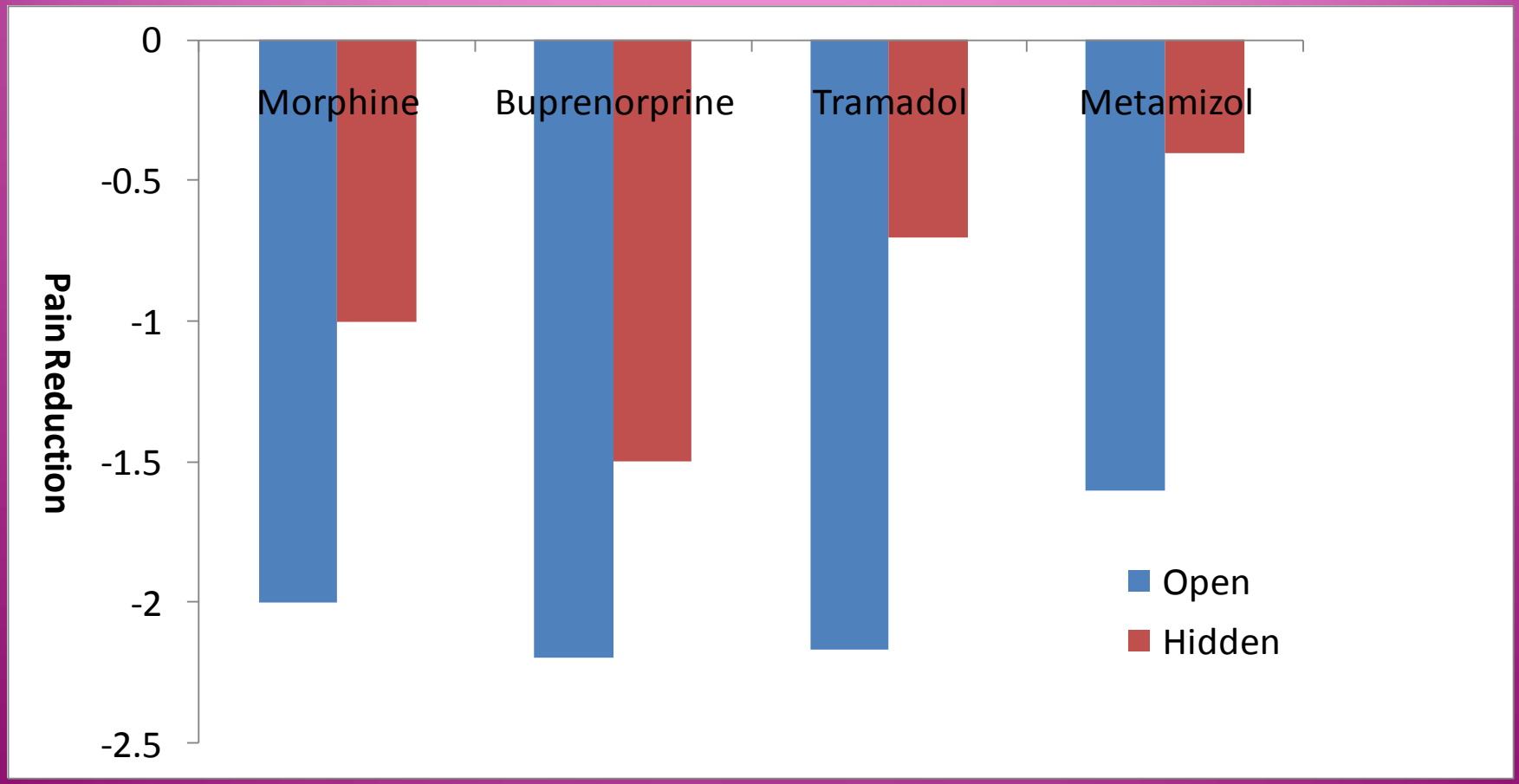

LEG MAGIC™
AS SEEN ON TV

- Expectations





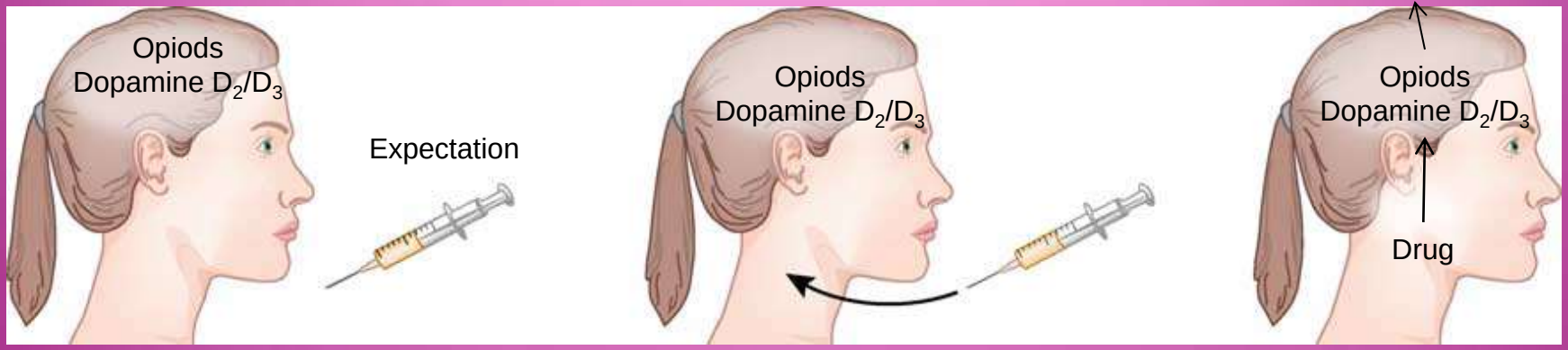
Open and Hidden Administration of Analgesics



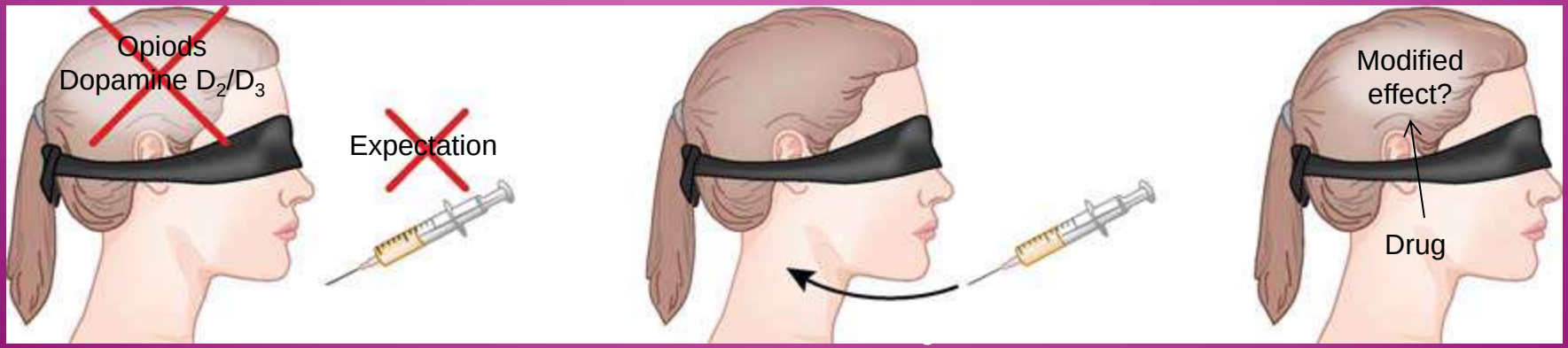
Amanzio et al., 2001

Expectations Can Modify Drug Effects

Possible interaction between drug and expectation effect (open)

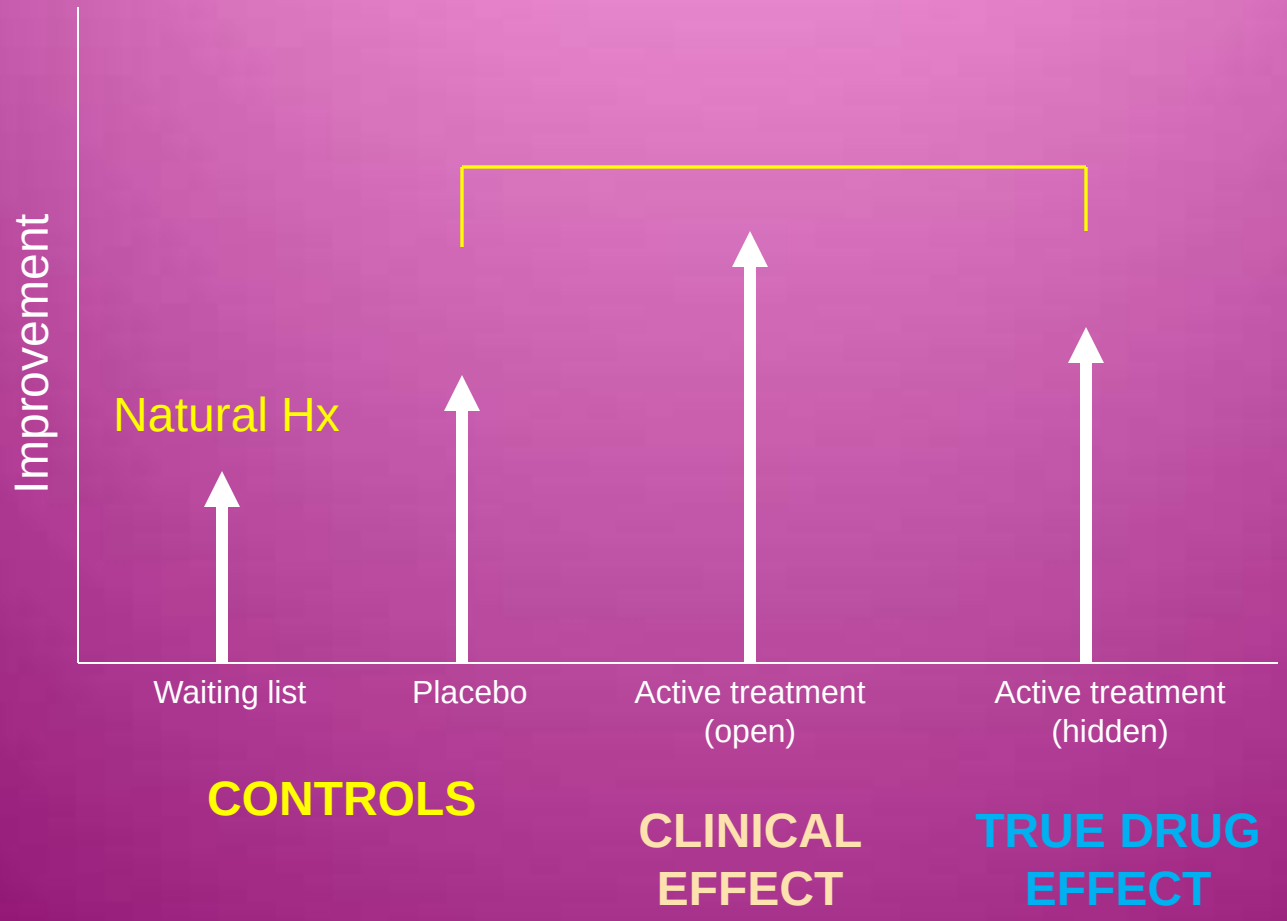


Eliminating expectation effect (hidden)



Benedetti et al., 2011

An effective drug will have a significantly greater effect during hidden administration compared to placebo



What are Expectancies in RCTs?

Confidence in the occurrence of some future event

Participant Expectancies/Beliefs	Experimenter Expectancies/Beliefs
Treatment will be effective	Treatment will be effective
I am or am not getting the treatment	Results will confirm this
Operates Through (e.g.)	Operates Through (e.g.)
Demand characteristics	Different messages conveyed
Motivation	Interpretation of outcomes
Emotions	Vested interest

Theoretically, blinding distributes expectancies evenly between study groups to minimize bias

Placebos as an Expectancy Primer

A merry heart doeth good [like] a medicine: but a broken spirit drieth the bones.

-Proverbs 17:22

ANNALS OF SCIENCE

THE POWER OF NOTHING

Could studying the placebo effect change the way we think about medicine?

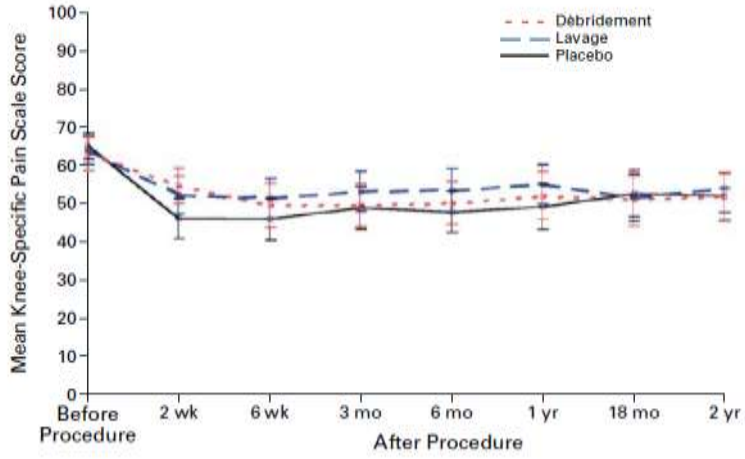
BY MICHAEL SPECTER

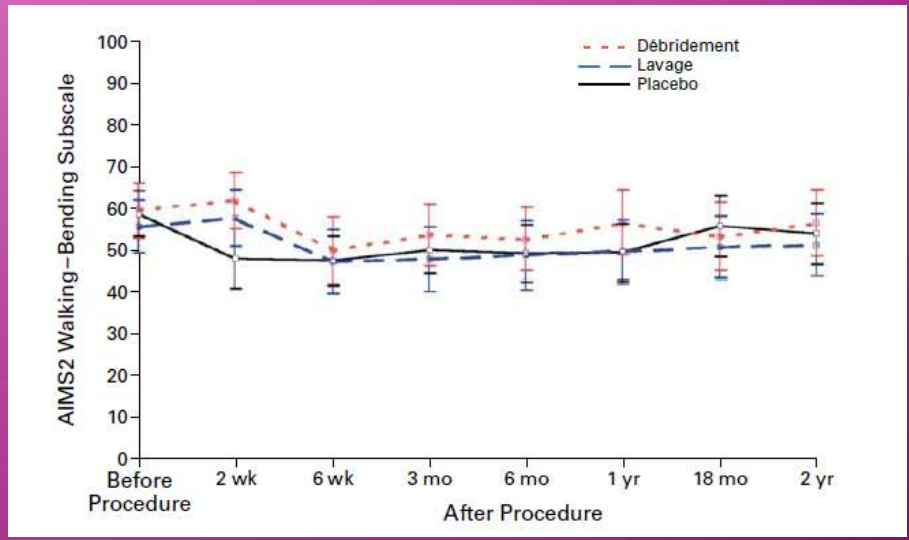
The New England
Journal of Medicine

VOLUME 347 JULY 11, 2002 NUMBER 2

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.





Some Placebo Terms

Placebo Effect = effect following administration of an inert "treatment" (pill, procedure) ["nothing = something"]

Placebo-Related Effect = effect of reassurance, kindness, spending time, empathy etc. [to real or inert treatments]

Placebo Responses = psychobiological phenomenon in response to inert treatments or the placebo-related effects of real treatments [hard to disentangle]

Depression

Anxiety

GI Symptoms

More and more often is better

Better than pills

Beyond Our Expectations

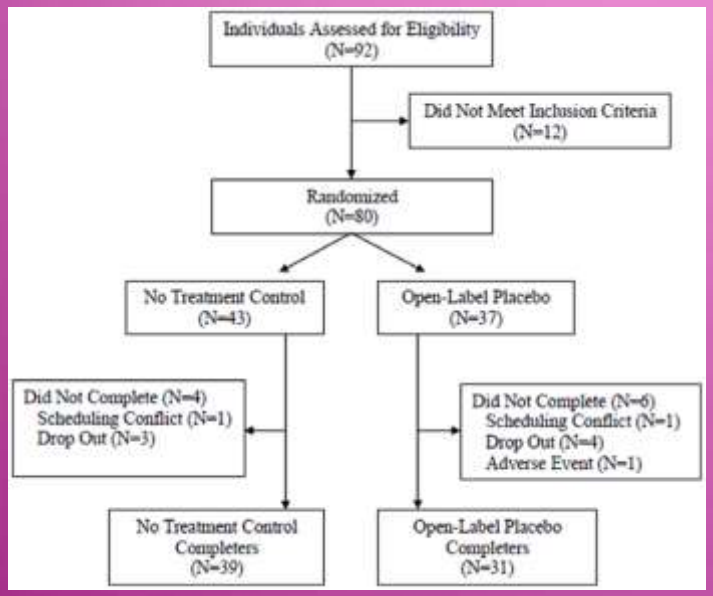
Do placebo effects require deception?

OPEN ACCESS Freely available online

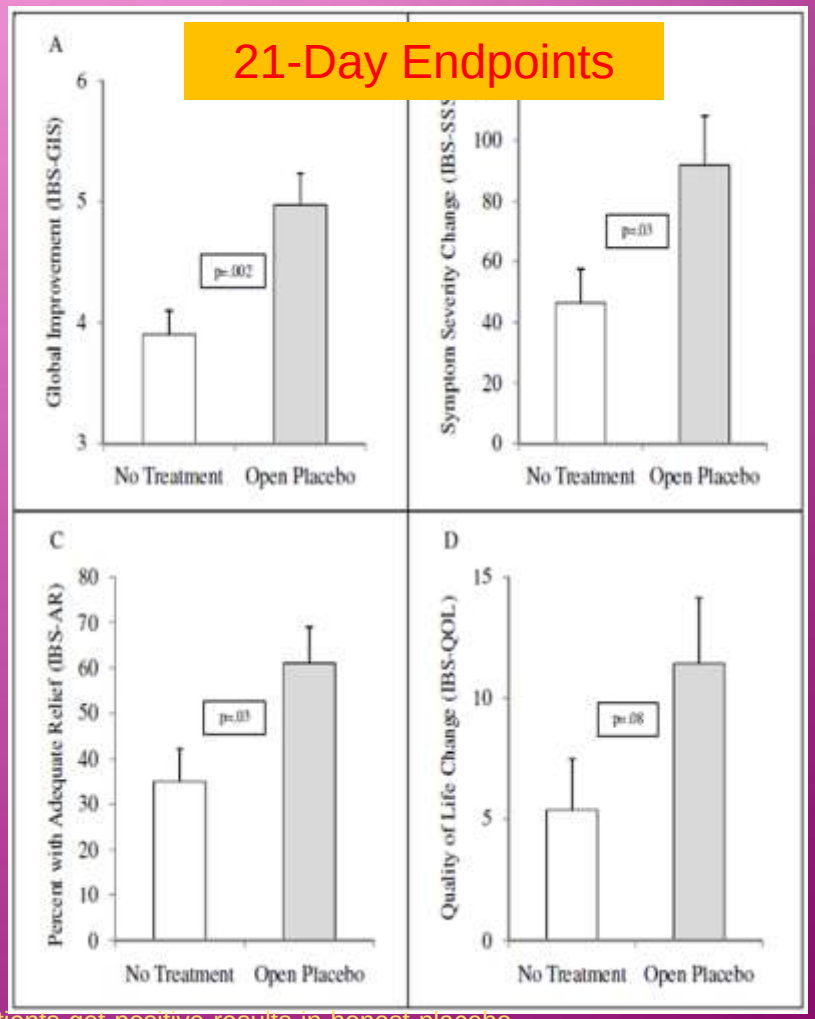
PLoS one

Placebos without Deception: A Randomized Controlled Trial in Irritable Bowel Syndrome

Ted J. Kaptchuk[1,2]*, Elizabeth Friedlander[1], John M. Kelley[3,4], M. Norma Sanchez[1], Efi Kokkotou[1], Joyce P. Singer[2], Magda Kowalczykowski[1], Franklin G. Miller[5], Irving Kirsch[6], Anthony J. Lembo[1]



21-Day Endpoints



"Placebo pills, something like sugar pills, have been shown in rigorous clinical testing to produce significant mind-body self-healing processes."

Took 2 placebo pills twice a day

http://www.wcvb.com/health/Patients-get-positive-results-in-honest-placebo-study/-/9848730/12986658/-/11h1v6bz/-/index.html

Kaptchuk TJ et al. (2010)

Letter to the Editor

Psychotherapy and Psychosomatics

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DOI: 10.1159/000337053

Open-Label Placebo for Major Depressive Disorder: A Pilot Randomized Controlled Trial

John M. Kelley[a–c], Ted J. Kaptchuk[b], Cristina Cusin[c], Samuel Lipkin[c], Maurizio Fava[c]

[a]Psychology Department, Endicott College, Beverly, Mass., [b]Program in Placebo Studies, Beth Israel Deaconess Medical Center and Harvard Medical School, and [c]Depression Clinical and Research Program, Massachusetts General Hospital and Harvard Medical School, Boston, Mass., USA

tients who are more compliant have better outcomes, and therefore the placebos should be taken faithfully, and (d) positive expectations increase placebo effects, but it is OK to have doubts. Although the rationale was scripted, treating psychiatrists were encouraged to deliver the rationale in a natural and supportive manner that allowed for questions and answers. All participants provided written informed consent. Patients were paid USD 20 for each completed assessment, and all patients were offered 3 months of free psychiatric treatment after the trial.

Our principal goal was to examine the feasibility of conducting trials of open-label placebo for MDD. Recruitment for this study was the fastest of the ten most recently conducted MDD studies in the Depression Clinic at Massachusetts General Hospital. The mean number of patients screened per month was 4.13 as

Table 1. Improvement in depressive symptoms after treatment with open-label placebo

a Symptom improvement by treatment group at 2 weeks

Measure	Waitlist (n = 9)	Open-label (n = 11)	Difference	95% CI	d	p
HAM-D-17	−0.67 ± 4.00	1.64 ± 4.52	2.30	−1.76 to 6.36	0.54	0.26
QIDS	−0.22 ± 2.44	2.27 ± 3.88	2.50	−0.64 to 5.63	0.77	0.13
SDQ	1.38 ± 10.77	3.70 ± 18.98	2.33	−13.68 to 18.33	0.15	0.75

b Pre-post symptom levels and improvement after 4 weeks of placebo treatment

Measure	Pre (n = 20)	Post (n = 20)	Difference	95% CI	d	p
HAM-D-17	18.00 ± 4.94	14.75 ± 6.61	3.25	0.44 to 6.06	0.56	0.03
QIDS	14.85 ± 2.68	12.10 ± 4.34	2.75	0.95 to 4.55	0.76	0.005
SDQ	146.94 ± 19.71	137.06 ± 27.50	9.89	2.08 to 17.70	0.41	0.02

Effect size larger than is typically seen in anti-depressant drug trials

The Placebo Orientation Meeting

Placebo Effect/Expectancy Building: Explain power of the placebo effect and how placebo treatment can lead to substantial relief whether placebo is concealed or unconcealed.

Rationale = build expectancies.

Conditioning: Explain how the body can respond automatically to placebo pills like Pavlov's dogs that salivated when they heard a bell. Can produce physiological response independent of conscious belief. Examples of conditioning placebo responses and in pain conditions.

Rationale = reassure that response to placebo can produce changes in physiology.

Realistic Attitude Toward Belief/Disbelief: Explain that positive expectations can be helpful but are not necessary. Beliefs may wax and wane during the trial.

Rationale = belief and disbelief are both compatible with placebo response and comfort with either is important.

Emphasize Importance of Adherence: Explain that studies show that people who take placebo pills faithfully do much better. Commitment to performing the ritual of treatment may be more important than anything else.

Rationale= adherence is vital and supports the conditioning aspect of placebo.

“Impure” Placebos

Intermission

I am available for personal training

Double-Blind, Placebo-Controlled Clinical Trials as Gold Standard

Isolate and estimate the direct effects of a drug on blood pressure

- "Tight" inclusion/exclusion criteria
- Drug vs. Placebo (indistinguishable)
- Randomize to drug or placebo
- Blind to allocation
- Present identical information (e.g., effects, side effects)
- Identical quantity and quality of staff contact
- Careful monitoring of adherence
- Precise and standardized BP measurements
- Assess belief about treatment allocation

Try to control, not eliminate, expectancies/bias

Applications to Weight and Eating

PSYCHOLOGICAL SCIENCE

Research Article

Mind-Set Matters

Exercise and the Placebo Effect

Alia J. Crum and Ellen J. Langer

Harvard University

ABSTRACT—*In a study testing whether the relationship between exercise and health is moderated by one's mind-set, 84 female room attendants working in seven different hotels were measured on physiological health variables affected by exercise. Those in the informed condition were told that the work they do (cleaning hotel rooms) is good exercise and satisfies the Surgeon General's recommendations for an active lifestyle. Examples of how their work was exercise were provided. Subjects in the control group were not given this information. Although actual behavior did not change, 4 weeks after the intervention, the informed group perceived themselves to be getting significantly more exercise than before. As a result, compared with the control group, they showed a decrease in weight, blood pressure, body fat, waist-to-hip ratio, and body mass index. These results support the hypothesis that exercise affects health in part or in whole via the placebo effect.*

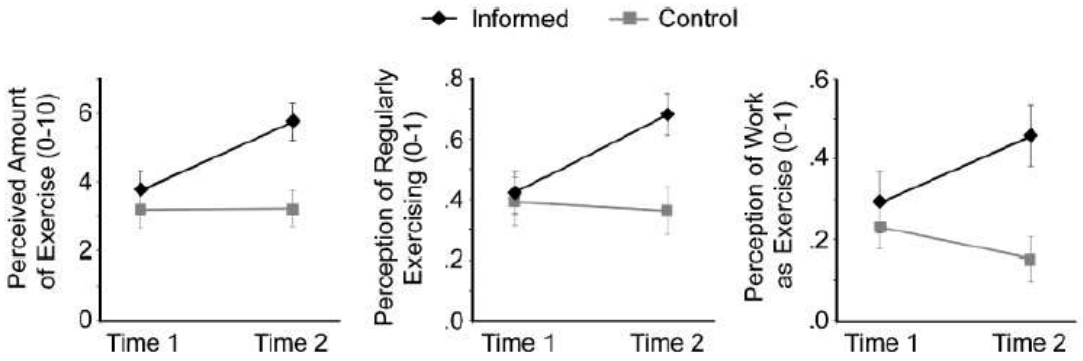


Fig. 1. Changes in self-reported exercise as a function of time and group. Bars denote standard errors of the means.

Believing that you have a physically active job produces improvement on hard outcomes

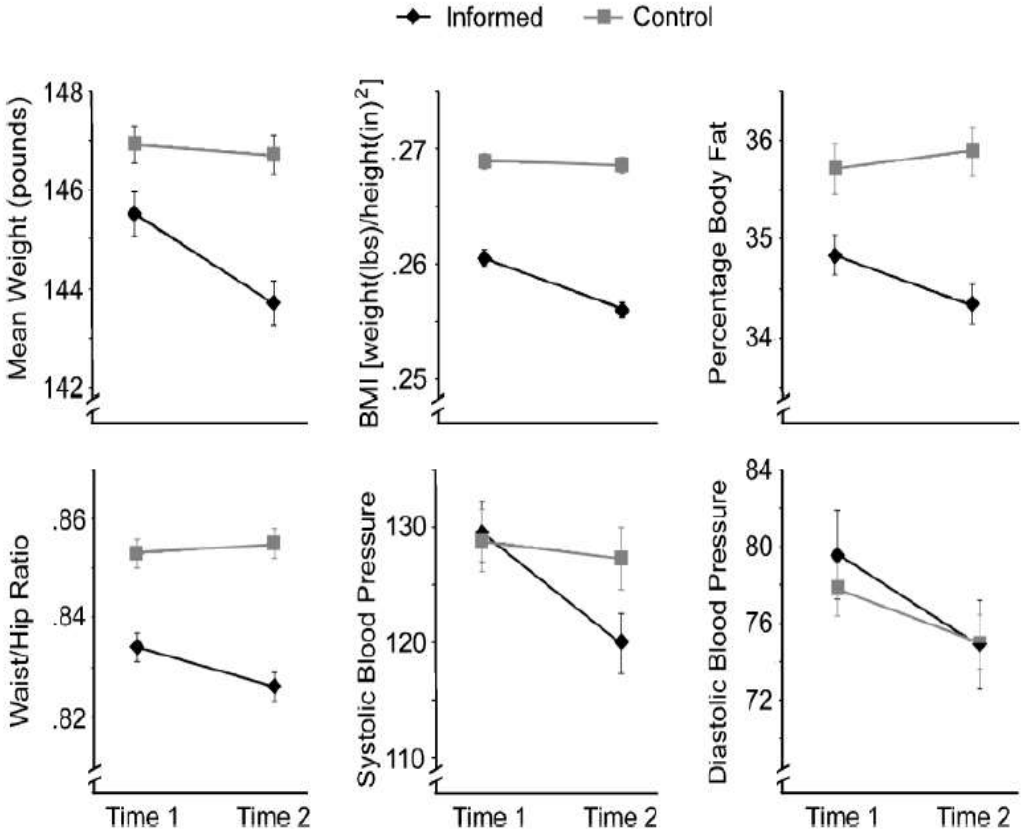


Fig. 2. Changes in physiological dependent variables as a function of time and group. Bars denote standard errors of the means. BMI = body mass index.

Health Psychology
2011, Vol. 30, No. 4, 424–429

0278-6133/11/$12.00 DOI: 10.1037/a0023467

BRIEF REPORT

Mind Over Milkshakes: Mindsets, Not Just Nutrients, Determine Ghrelin Response

Alia J. Crum
Yale University

William R. Corbin
Arizona State University

Kelly D. Brownell and Peter Salovey
Yale University

Objective: To test whether physiological satiation as measured by the gut peptide ghrelin may vary depending on the mindset in which one approaches consumption of food. ***Methods:*** On 2 separate occasions, participants (n = 46) consumed a 380-calorie milkshake under the pretense that it was either a 620-calorie "indulgent" shake or a 140-calorie "sensible" shake. Ghrelin was measured via intravenous blood samples at 3 time points: baseline (20 min), anticipatory (60 min), and postconsumption (90 min). During the first interval (between 20 and 60 min) participants were asked to view and rate the (misleading) label of the shake. During the second interval (between 60 and 90 min) participants were asked to drink and rate the milkshake. ***Results:*** The mindset of indulgence produced a dramatically steeper decline in ghrelin after consuming the shake, whereas the mindset of sensibility produced a relatively flat ghrelin response. Participants' satiety was consistent with what they believed they were consuming rather than the actual nutritional value of what they consumed. ***Conclusions:*** The effect of food consumption on ghrelin may be psychologically mediated, and mindset meaningfully affects physiological responses to food.

Consume a 380-calorie shake but **are told that it is either:** (1) a 620-calorie "indulgent" shake or (2) a 140-calorie "sensible" shake

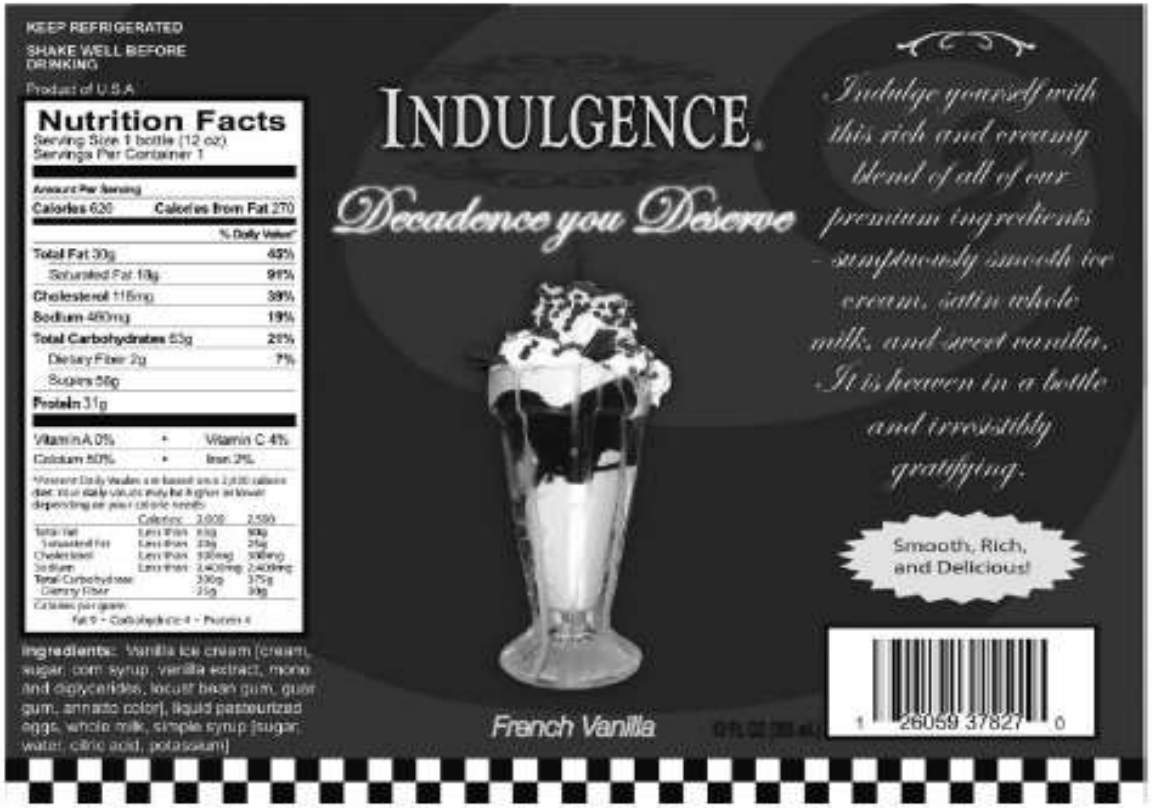


Figure 1. Indulgent shake label.

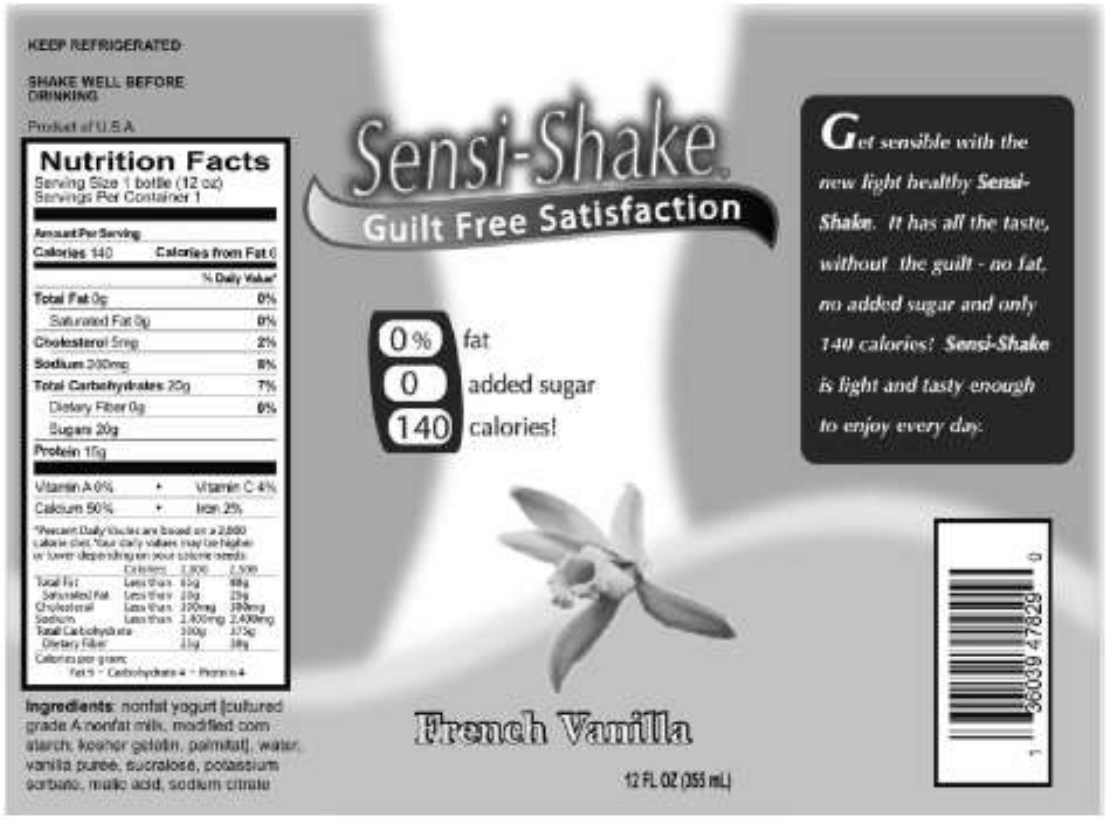


Figure 2. Sensible shake label.

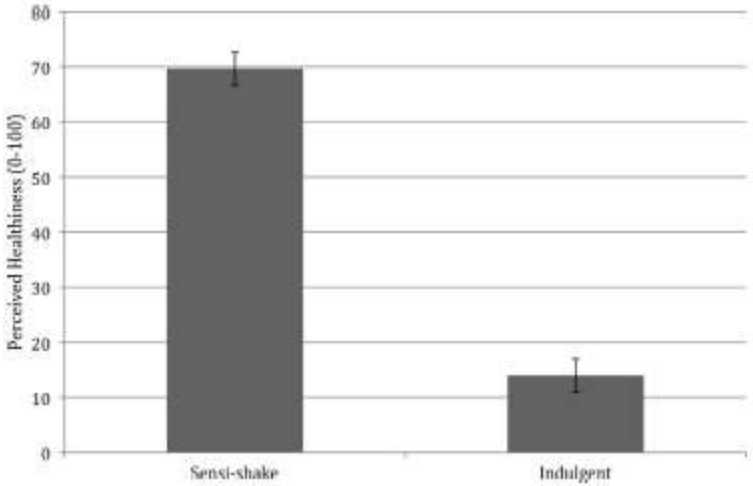
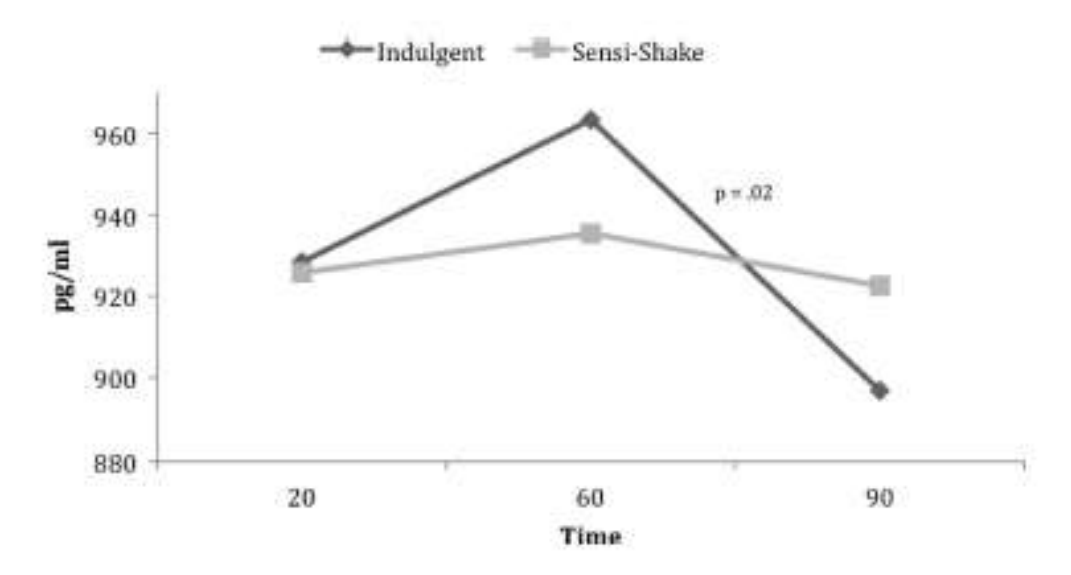


Figure 3. Differences in perceived healthiness as a function of shake label. Error bars reflect standard errors of the mean.

Effects independent of dietary restraint

Ghrelin



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Research report

Taking weight-loss supplements may elicit liberation from dietary control. A laboratory experiment ☆

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Liberating effect
Weight-loss supplements
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ABSTRACT

Given that changes in diet and exercise habits are difficult to initiate and maintain, the use of weight-loss supplements has become an appealing alternative approach to weight management for many individuals. The current research examined whether the use of weight-loss supplements induced overly optimistic assessments of progress toward weight reduction, leading to psychological abdication of dietary regulation. Participants were randomly assigned to take either an identified placebo or a purported weight-loss supplement (actually the same placebo). Each participant reported perceived progress toward weight reduction following the manipulation. Consumption of snacks in a taste test and choice of sugary drinks were recorded. The results showed that participants receiving a purported supplement ate more in a taste task and preferred larger quantities of sugar in their reward drinks than did controls. Mediation analysis supported that the perception of progress toward weight reduction contributed to the liberating effect. Using weight-loss supplements may increase perceived progress toward weight reduction but decrease dietary self-regulation. These thought-provoking findings can serve as a basis for educating the public about the myth that they are free to feel liberated from the need to regulate their eating when using weight-loss supplements.

Those who were told that they were taking a weight loss supplement reported greater progress toward their weight loss goals YET ate more in a taste task and consumed more sugary drinks compared to those told they were taking a placebo

Table 1
Participant demographics and descriptive statistics for the measures.

Community sample	Weight-loss supplement		Control	
	n	%	*n*	%
Gender				
Female	20	50.0	20	50.0
Male	17	50.0	17	50.0
Age				
18–24	5	13.5	5	13.5
25–40	24	64.9	25	67.6
41+	8	21.6	7	18.9
Dietary supplement users	18	51.3	17	46.1
Overweight (BMI > 25)	13	35.1	13	35.1
		M (*SD*)		*M* (*SD*)
Time since last meal (h)		1.60 (0.51)		1.73 (0.58)
Number of daily supplements taken		0.62 (0.67)		0.65 (0.68)
BMI		23.84 (3.93)		23.81 (3.73)
Perceived goal progress (1–7)		4.65 (1.99)		3.48 (1.04)
Amount of nougat consumed (g)		47.30 (13.67)		36.62 (11.06)
Proportion of sugar-free beverages chosen		0.11 (0.31)		0.38 (0.49)
Amount of sugar chosen for the drink (0–4)		2.30 (1.31)		1.23 (1.27)

Note: Total sample size for both groups was $n = 37$. Units of the dependent measure are presented in parentheses.

Clinical Obesity Research

Clinical obesity researchers, to the extent possible, try to use strict RCT methodology

-Randomization to diet interventions

-Precise outcomes measurement

Blinding is typically not possible because participants are given instructions and are prescribed a specific set of behaviors that reveal the particular diet condition that they have been randomized to **(no placebo-control diet condition)**

Study participants are typically not given identical information because the diets require different information, prescriptions, and required actions

This creates a set of uncontrolled confounds, such as:

-Information & Beliefs

-Competence, credibility, authority

-Expectancies

-Differential contact time

-Different levels of required action (e.g., self-monitoring)

that MAY make it difficult to isolate and estimate diet effects

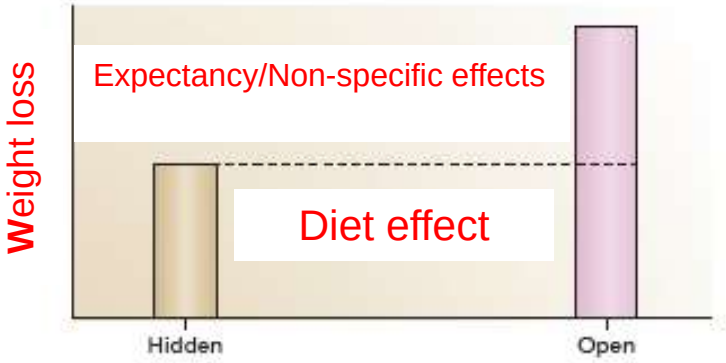
Hidden application

Opaque Feeding Tube

Diet

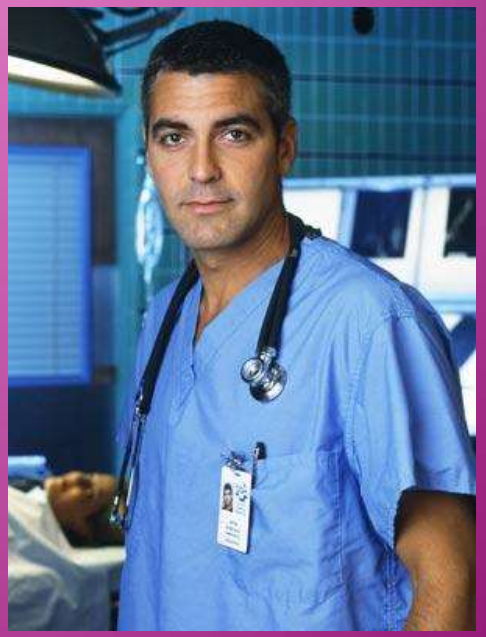
is administered by a machine (unbeknown to the patient)

Diet prescription administered by dietitian



Interventionists: Differential enthusiasm, reassurance, encouragement, interpersonal skills

Some people are natural born healers!



Potential Mechanisms for Participant Expectancies

Research Context

Patient & Staff Factors

Information & Diet Prescription

Attention/Therapeutic Relationship

Psychosocial Factors

Expectation for improvement

Persuasive rationale for diet

Adherence/monitoring

Desire to lose weight

Clinical environment

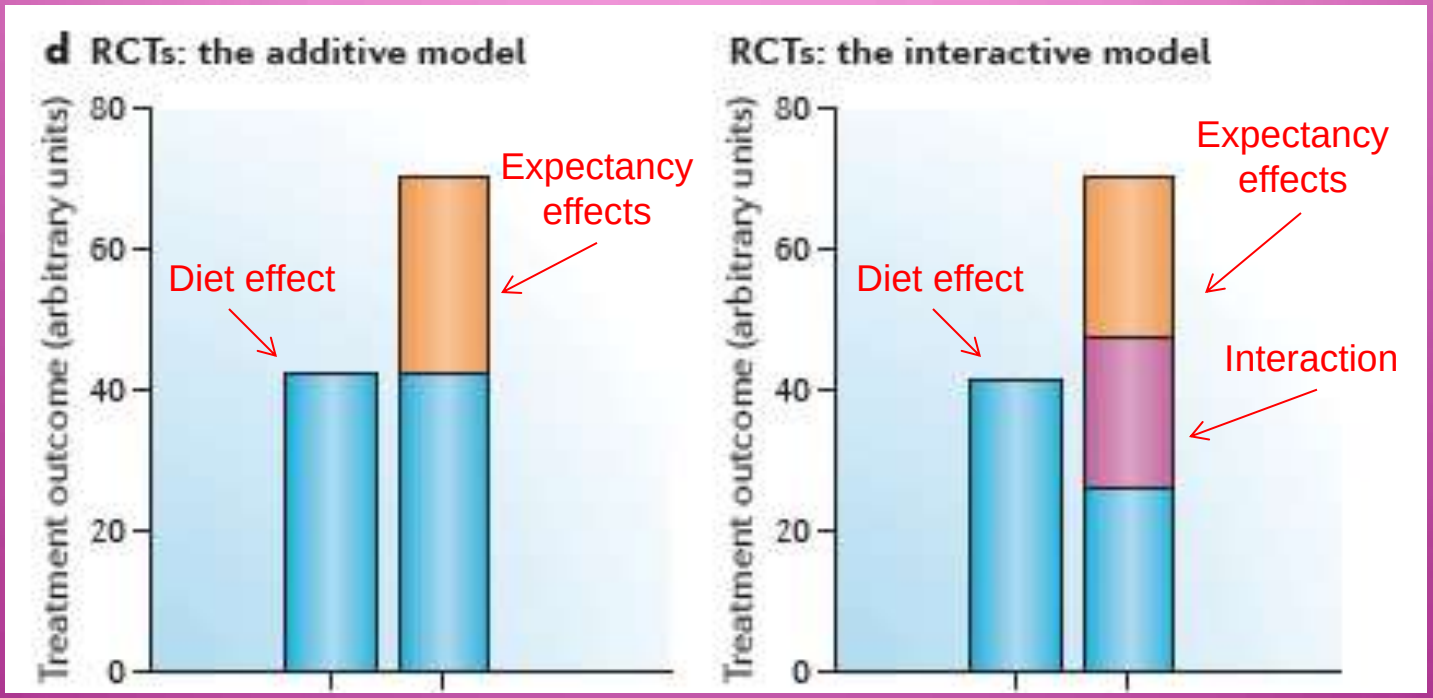
"Skill" of interventionist

Therapeutic Response

Subjective Outcomes [e.g., energy, quality of life, wellness]

Objective Outcomes [e.g., weight, cholesterol]

Effects are not only the result of an intervention but also the effects embedded within the research context



Diet effect is inflated by expectancy/non-specific effects

Diet effect interacts with expectancy/non-specific effects such that expectancies play a differential role in one of the diets tested

“Package of Care” Argument

Real interest is in the effects of the whole treatment experience (including expectancies and other non-specific effects) and NOT in the individual components

Prevalent in CAM world

Camouflages ineffective procedures or components [never fly in a drug trial!]

Trying to Estimate the Effects of Expectancies in Diet Comparison Study

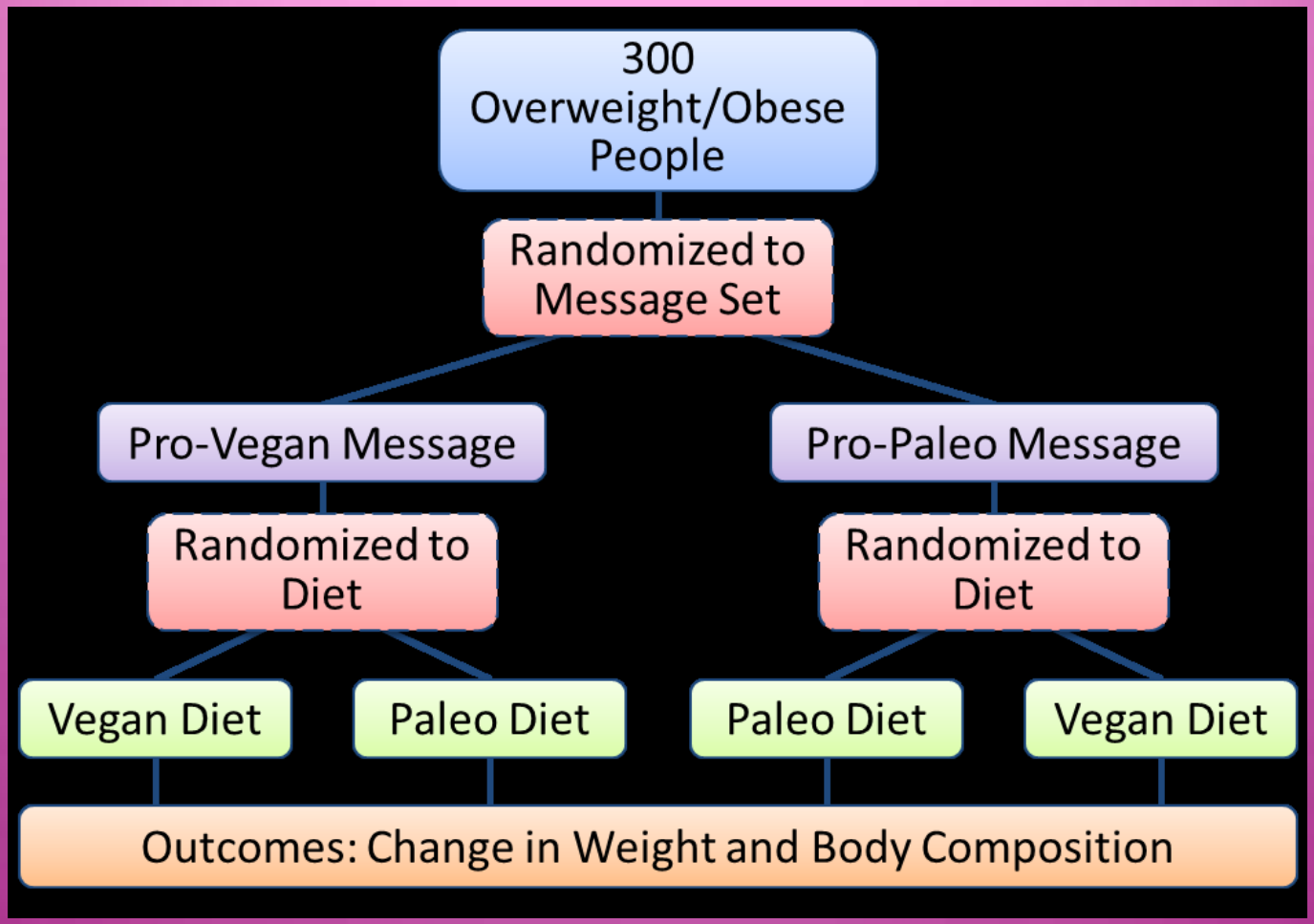


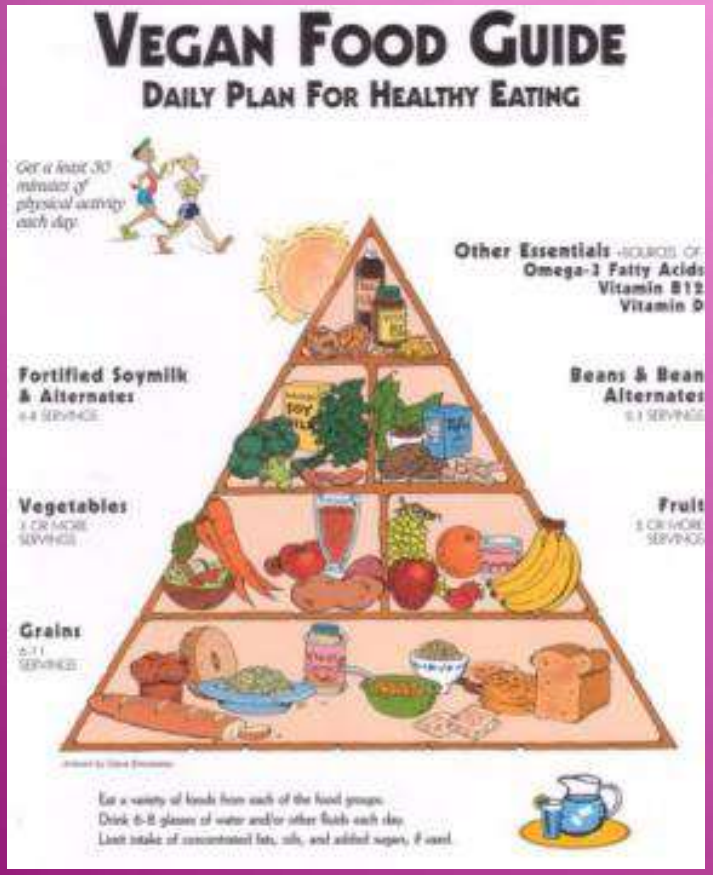
Table 1: 2 x 2 Factorial Design Combining Two Types of Messages and Two Diets

Message Set Assignment	Diet Assignment	
	Vegan (VD)	Paleo (PD)
Pro-Vegan Message (PV)	PV-VD	PV-PD
Pro-Paleo Message (PP)	PP-VD	PP-PD

"Message Sets"

- **Pro-Vegan Message (PV):** told that the purpose of the study is to compare the effects of the vegan diet (VD) to a comparator diet, and that it is expected that the VD will produce greater weight loss compared to the other diet, but the study needs to be conducted to confirm that the VD is, in fact, the superior diet.
- **Pro-Paleo Message (PP):** told that the purpose of the study is to compare the effects of the paleo diet (PD) to a comparator diet, and that it is expected that the PD will produce greater weight loss compared to the other diet, but research needs to be conducted to confirm that the PD is superior

Diets


VEGAN FOOD GUIDE
DAILY PLAN FOR HEALTHY EATING
Get a least 30 minutes of physical activity each day.
Other Essentials
Omega-3 Fatty Acids
Vitamin B12
Vitamin D
Fortified Soymilk & Alternates
Beans & Bean Alternates
Vegetables
Fruit
Grains
Eat a variety of foods from each of the food groups.
Drink 6-8 glasses of water and/or other fluids each day.


NUTS & BERRIES
FRUITS
VEGETABLES
MEATS
PALEO APPROVED FOOD PYRAMID

What about Staff Expectancies?

J. Psychiat. Res. Vol. 2, pp. 61–72. Pergamon Press Ltd. Printed in Great Britain

A LONGITUDINAL STUDY OF THE EFFECTS OF EXPERIMENTER BIAS ON THE OPERANT LEARNING OF LABORATORY RATS*

ROBERT ROSENTHAL and REED LAWSON

Dept. of Social Relations, Harvard University, Cambridge, Ma
and
Dept. of Psychology, Ohio State University, Columbus, Ohi

(*Received* 20 *August* 1963)
(*Revised* 4 *December* 1963)

	Bright	Dull	t	p <0·10 (two-tailed)
I. Satisfaction with Experiment	9·1	6·6	4·40	0·001
II. Ratings of *Ss*				
1. Aggressive (new scale)	3·3	1·2	<1	
2. Healthy (new scale)	6·5	6·1	<1	
3. Friendly (new scale)	2·5	5·5	1·32	
4. Bright	5·0	−2·6	2·64	0·03
5. Clean	5·9	6·1	<1	*
6. Tame	2·6	4·3	<1	*
7. Pleasant	5·2	3·7	1·07	
8. Like	4·1	2·2	1·28	

On the basis of questionnaire data obtained in this and in an earlier study, it appeared that *Es* believing their *Ss* to have been bred for brightness were more satisfied with their participation in the experiments, liked their *Ss* more, watched them more intently and found them to be more pleasant. They tended also to be more enthusiastic, friendly, encouraging, pleasant and interested in their rat's performance, but were less talkative and less loud when working with their *S*. But perhaps the crucial difference was that these *Es* may have handled their *Ss* more; a difference which could, on the basis of other research,[9] account for their superior learning.

Evaluating Expectancy Effects in Weight Loss Measurement

Confederates reveal study condition (Treatment vs. control) to outcomes assessor

Does it influence/bias recording of weight?

What we know

Favorable responses arise directly from treatment as well as from the social processes (e.g., words, beliefs, expectations etc) embedded within the delivery of the treatment

Interventionists can differentially activate non-specific effects through reassurance, encouragement, and talent as a healer

So, in Clinical Obesity Research…

Expectancy and non-specific effects may be potential confounds

The absence of blinding increases susceptibility to these confounds

If these confounds make more than a trivial difference, then the results of may not offer valid estimates of the effects of diet interventions

To be continued….