The Placebo Effect

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It is more important to know what sort of person has a disease than what sort of disease a person has.

-Hippocrates
Introduction

The Placebo Effect goes beyond the sugar pill.

Placebos and the Placebo Effect are often mischaracterized, both in clinical practice and also in the available research. The Placebo Effect, including mischaracterizations, genuine biopsychosocial manifestations, and potential role in improving patient outcomes will be presented.

Afterwards, we will be able to…

a) Reconcile the seemingly disparate concepts of “placebo effect” and “healing”.

b) Discuss the characteristics of the placebo effect that can be distinguished from specific biologically-grounded treatment effects.

c) Justify how clinicians can maximize ancillary gains from the placebo effect when treating patients with a biologically-grounded intervention.
OVERALL OBSERVED THERAPEUTIC EFFECT
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Inherent Therapeutic Effect

Beneficial or desirable results of medical treatment... whether EXPECTED, UNEXPECTED, or even, UNINTENDED
OVERALL OBSERVED THERAPEUTIC EFFECT =

Inherent Therapeutic Effect +

Natural History Effect

Spontaneous improvement...
the body does heal itself
OVERALL OBSERVED THERAPEUTIC EFFECT

Inherent Therapeutic Effect

Natural History Effect

Regression to the Mean Effect

Extraordinary observations are almost always followed by more typical ones.
OVERALL OBSERVED THERAPEUTIC EFFECT =

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Extraordinary observations are almost always followed by more typical ones
OVERALL OBSERVED THERAPEUTIC EFFECT =

- Inherent Therapeutic Effect

- Natural History Effect

- Regression to the Mean Effect

- Hawthorne Effect

Patients tend to report better results if they are receiving a particular treatment.
OVERALL OBSERVED THERAPEUTIC EFFECT =

Inherent Therapeutic Effect

Natural History Effect

Regression to the Mean Effect

Hawthorne Effect

Placebo Effect
What do we (clinicians) think of placebos?

Expectation
MORE PATIENT-ORIENTED
Faith
Self perceptions
Classic conditioning
Anxiety relief
Tricking patients
Symbolic processes
Patient-doctor relationship

MORE CLINICIAN-ORIENTED
Holistic approach
Fraud
Common Usage…

Control condition
Sham
Alternative treatment
No treatment

Common Descriptors – in the context of (RCTs)

Nonspecific
Dummy
Inert
Sham
Inactive

Even an “active” treatment, not thought to
“I will please...”
Physician's duty was to "cure occasionally, relieve often, console always."

In Psalms: “Placebo Domino…” I shall please the Lord…

In Canterbury Tales: “Placebo” is the sycophantic brother in The Merchant’s Tale.

PLACEBO: L “I Shall Please”

1300s & earlier

1500s

Physician’s duty was to "cure occasionally, relieve often, console always."

1st use of word "Placebo"

1st clinical demonstration of the Placebo Effect

Late 1700s

“Vis mediciatrix naturae”

Sugar pills
Elixirs
Pharmaceutical syrups

Early 1800s

“Epithet given to please the patient”

Late 1800s

Blinding introduced into pharmaceutical trials
1st modern description of Placebo Effect
“real psychotherapeutic effect...produced”

Early 1900s
Used in both Allopathic and Homeopathic trials

1930s
Use in Clinical Trials as sham treatments

1940s
Still defined as “well-meaning fraud”, “morally useful, but innocuous”

1955
The Powerful Placebo

Roughly 1960-1990s
“Nuisance variable” in clinical research

Past 20 years to current
"Placebo Effect" is being actively studied to clarify mechanisms & context

Clinical trials with ‘No Sig Diff’ between drug & placebo

Terms “Placebo reaction” & “Placebo response” coined

First use of the term “Placebo Effect”

Experimental studies Neurobiological models Imaging
Placebo Effect

Genuine Biopsychosocial Phenomena

Improvements in symptoms, that are attributable to the patient *participating* in a therapeutic encounter

The *effects of rituals, symbols, & clinician interaction* can enhance the effectiveness of pharmaceuticals & other active treatments

Provide relief, rarely cure

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Everything looks great, you can put your shirt back on and I’ll get you a prescription for placebos

Wait…crap…they’re not gonna work now
Placebo Effects are mediated by Endogenous Opioids (internally created chemicals that modulate pain)

Amanzio & Benedetti, J Neurosci, 1999

BUT then also, this can be reversed by administration of naloxone – a chemical that reverses the effects of opioids

Benedetti, Pain, 1996
Genuine Biopsychosocial Phenomena…

**NEUROLOGICAL (Bio)**

*Placebo Effects can reduce activity in the brain (areas most activated by noxious stimulation)*

Genuine Biopsychosocial Phenomena...

**PSYCHOLOGICAL**
(Psycho)

**Expectancy**

**Classic conditioning**

**Motivation / Desire for relief**
Genuine Biopsychosocial Phenomena…

THERAPEUTIC RELATIONSHIP  
(Social)

**Rituals & Symbols**  
Clinician-Patient Interaction  

**Participation in the Therapeutic Encounter**  
Role of Empathy, Listening, Connection, & Engagement  

“The doctor-patient relationship is critical to the placebo effect”  
-Irving Kirsch
IBS
(Kaptchuk et al, BMJ, 2008)

% Improvement
G.I.S.
Reported
“Adequate Relief”

Additive Effect
Increased perception of improvement when (placebo) treatments are personalized to fit the patient’s needs
(Webb et al, J Consult Clin Psychol, 2013)

No Treatment
3%

Placebo

Placebo + Support
37%
62%
Genuine Biopsychosocial Phenomena…

**Interaction** of these (and many other) BIOPSYCHOSOCIAL FACTORS that influence the placebo effect

Coste & Montel, Rheumatol, 2016

**Meta-analysis in 2001**
130 RCTs (of placebo vs. no treatment)
**No significant effects for placebo…**, not a powerful clinical effect


**RE- Meta-analysis in 2010**
**Significant placebo effects were seen**…**Higher effects:**

Hróbjartson & Gøtzsche, Cochrane Database Syst Rev, 2010

- For pain & nausea
- When physical placebos compared with pill placebos
- When patients are informed about possibility of receiving placebo (in RCT)
- When trials are explicitly designed to study placebo effects
ASTHMA

50%

20%

Aalbuterol

45%

7%

Placebo

21%

7%

No Treatment

% Improvement

FEV₁
Self-Reported Improvement
KNEE OA & HA Injection

(Zhang et al, Ann Rheum Dis, 2008)
KNEE OA & HA Injection
(Zhang et al, Ann Rheum Dis, 2008)
MIGRAINES
(Kam-Hansen et al, Sci Transl Med, 2014)
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PLACEBO
(Labeled Placebo)

MAXALT
(Labeled Placebo)

MAXALT
(Labeled Maxalt)

NO TREATMENT

PLACEBO
(Labeled Maxalt)

AVERAGE PAIN LEVEL
Scale of 1-10
2 hours after pill
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...with Standard Deviations
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AVERAGE PAIN LEVEL
Scale of 1-10
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...with Standard Deviations
Placebo Effect & the ICF

- Health Condition
  - Disease / Disorder
- Body Functions & Structures
  - Impairment
- Activities
  - Limitation
- Participation
  - Restriction
- Environmental Factors
- Personal & Social Factors
Placebo Effect & the ICF

HEALING...

- Cure
- Control of the Disease
- Symptom Relief
- Provision of Comfort

Body Functions & Structures

Activities

Participation

Disease / Disorder

Restriction

Environmental Factors

Personal & Social Factors

Placebo Effect & the ICF
**Placebo Effect & EBP**

“Though placebos may provide relief, they rarely cure”


**Strength of Recommendation Taxonomy**

- **A** Consistent & good-quality patient-oriented evidence
- **B** Inconsistent or limited-quality patient-oriented evidence
- **C** Consensus, usual practice, opinion, disease-oriented evidence

Intermediate, physiologic, or surrogate end points that *may or may not reflect improvements in patient outcomes*

Examples: BP, ROM, strength

Morbidity, mortality, *symptom improvement*, cost reduction & *quality of life*

Examples: Pain, RTP, Nausea

**Best Available Research**

**Clinician Expertise**

**Patient Values**
PATIENT VALUES

Often described as “What the Patient wants…” This is OK, but may be a limited view

The Clinician has to consider:

- What is the patient willing to do?
- What is the patient willing to do properly?
- What is the patient willing to continue to do?

Placebo Effect
& EBP

Adherence
Fidelity
Compliance
"It is important to distinguish the very respectable, conscious use of placebos. The effects of placebos in RCTs has been shown to be very large. Their use in the correct place is to be encouraged. What is inefficient is the use of relatively expensive drugs as placebos."

-Archie Cochrane 1972

"Because medicine has been so concerned with its scientific growth, too little attention has been paid to advancing the art of medicine, to which therapy with placebos belongs, and consequently knowledge of the use of placebos has not progressed significantly."

OVERALL OBSERVED THERAPEUTIC EFFECT

Inherent Therapeutic Effect

Natural History Effect

Regression to the Mean Effect

Hawthorne Effect

Placebo Effect

• Traditional Western, Allopathic Medicine

• Complementary & Alternative Medicine

• Placebos

Holistic vs Reductionist Systems approach

All 3 of these are likely contributors to BOTH the Placebo Effect and the Inherent Therapeutic Effect
Placebos can improve symptoms, which can be characterized as *healing* from a patient-centered perspective.
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The *research evidence associated with placebos is limited*, and at this point, the conclusion reached is that *placebos may have a place within traditional, allopathic treatment protocols*.
**Summary**

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In clinical research & practice, placebos & the placebo effect *should not* be treated as a nuisance variable.
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Current research indicates that there are different mechanisms by which the placebo effect is facilitated. These mechanisms can be broken down into 3 categories to include:

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Although placebos have often been used in clinical trials, they are typically compared to an ACTIVE TREATMENT condition only, leading to some gray area about what is a placebo effect and what is just variation in treatment results.
Summary

The Placebo Effect goes beyond the sugar pill.
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It is a real effect, centered on an applied (research evidence - supported or - unsupported) intervention, and should not be disregarded. In the broader context of a biopsychosocial approach to medicine, the placebo effect does “treat”, i.e., symptom relief does indicate improvement in health.

Summary
Treatment is an ever-shifting paradigm, continual re-examination & re-weighting of what “should” happen & what “could” happen is necessary.
In clinical practice, where a majority of patient visits are for conditions that cannot be explained on a pathophysiological basis, and for which no specific treatment is available, it is essential that physicians understand the concepts and principles of placebos & placebo effects and, when appropriate, use them correctly.

-Carruthers et al, 2000
Commitment to Excellence