



ITHACA COLLEGE

Department of Exercise and Sport Sciences

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**HEALTH & SAFETY**  
— S U M M I T —

## The Art & Science of Sports Medicine

### 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**

# OVERALL OBSERVED THERAPEUTIC EFFECT =

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



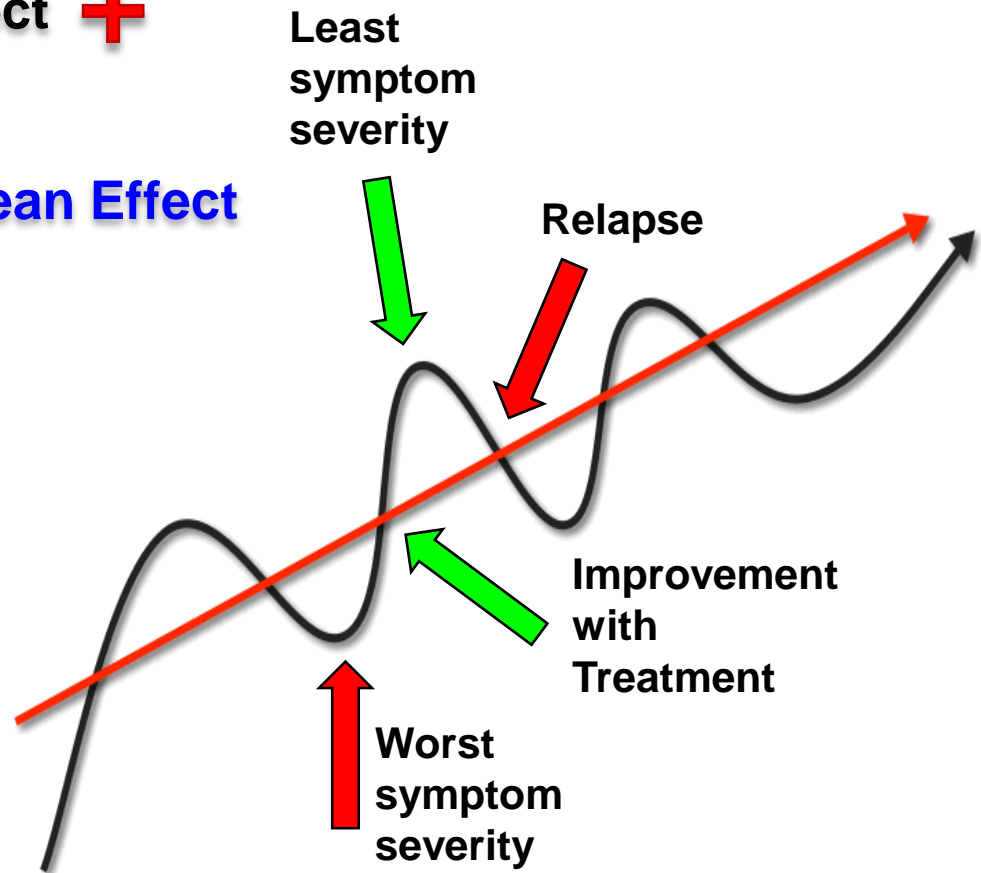
# OVERALL OBSERVED THERAPEUTIC EFFECT =

Inherent Therapeutic Effect +

Natural History Effect +

Regression to the Mean Effect

Extraordinary  
observations are  
almost always followed  
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**Inherent Therapeutic Effect +**

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# 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 +

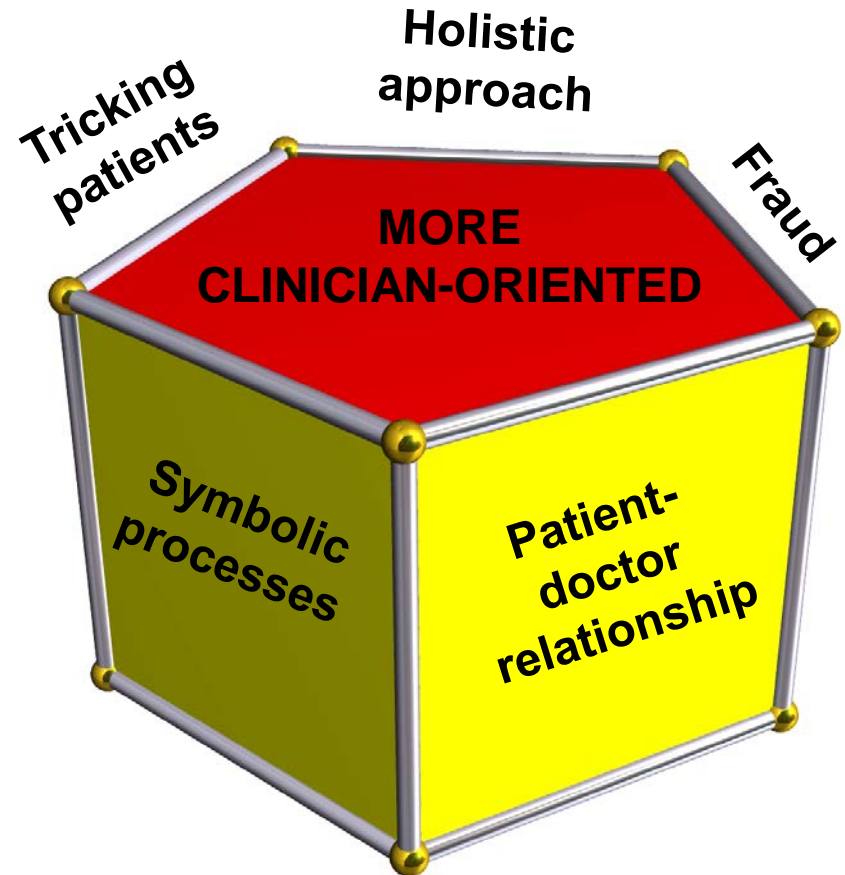
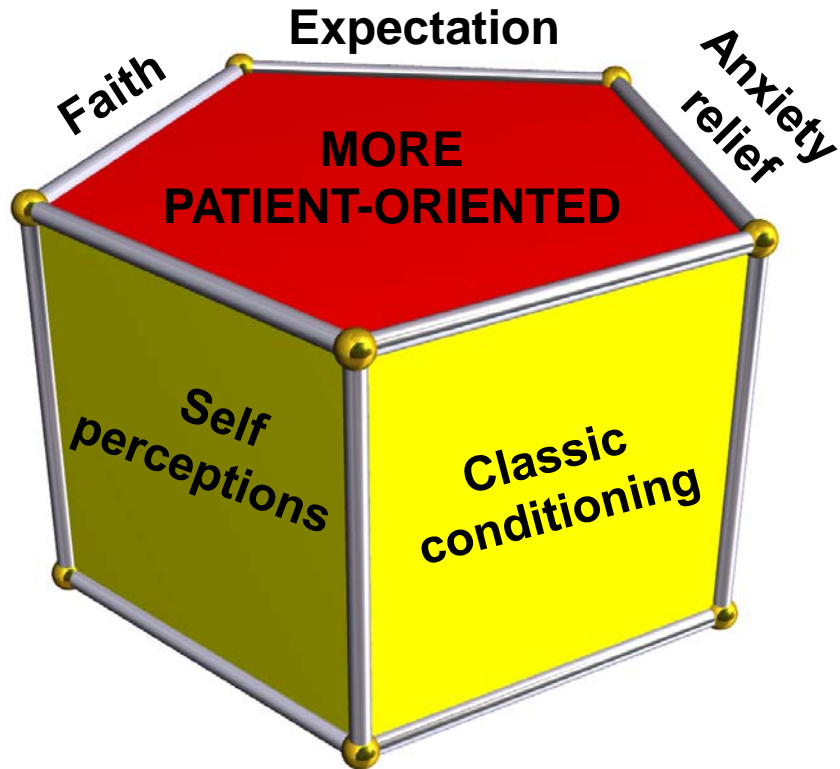
Regression to the Mean Effect +

Hawthorne Effect +

Placebo Effect



What do we (clinicians) think of placebos?



## 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  
work on specific symptoms

A close-up photograph of a hand holding a clear, elongated, capsule-shaped pill between the thumb and index finger. The pill is transparent, revealing a lighter, possibly white or yellow, interior. The background is a bright blue sky filled with soft, white, fluffy clouds. The lighting is bright, creating a lens flare effect at the point where the fingers hold the pill.

**“I will  
please...”**

1300s & earlier

PLACEBO: *L.*  
"I Shall Please"

In Psalms: "Placebo Domino..."  
*I shall please the Lord...*

In Canterbury Tales: "Placebo" is  
the sycophantic brother in  
*The Merchant's Tale*

1500s

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

Late 1700s

"*Vis mediatrix naturae*"

1<sup>st</sup> use of word  
"*Placebo*"

1<sup>st</sup> clinical  
demonstration of  
the *Placebo Effect*

Early 1800s

"Epithet given to please the  
patient"

Sugar pills  
Elixirs  
Pharmaceutical  
syrups

Late 1800s

Blinding introduced into  
pharmaceutical trials

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

1<sup>st</sup> modern description of *Placebo Effect*  
"real psychotherapeutic effect...produced"

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

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## 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



*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*



# Genuine Biopsychosocial Phenomena...

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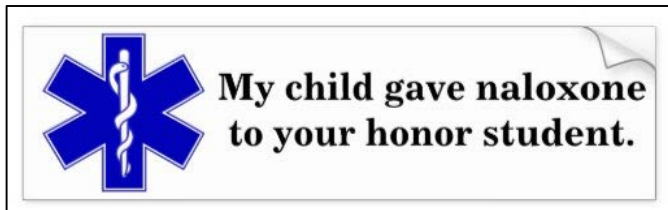
## CHEMICAL (Bio)

Placebo Effects are mediated by Endogenous Opiates  
(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



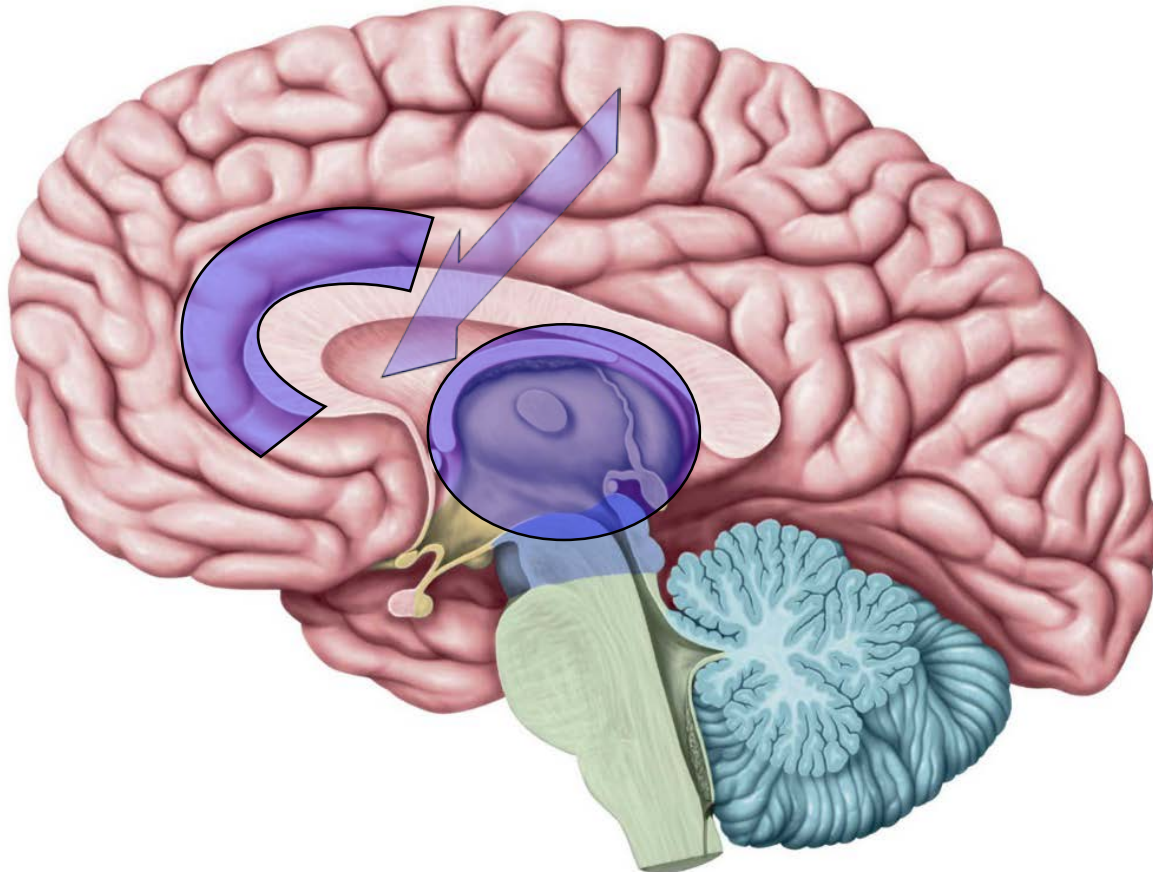
# Genuine Biopsychosocial Phenomena...

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## NEUROLOGICAL (Bio)

Placebos can reduce activity in the brain  
(areas most activated by noxious stimulation)

Wagner & Atlas, *Nat Rev Neurosci*, 2015; Atlas & Wagner, *Handb Exp Pharmacol*, 2014



# Genuine Biopsychosocial Phenomena...

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## PSYCHOLOGICAL (Psycho)

### Expectancy

Kirsch I, *Am Psychol*, 1985



### Classic Conditioning

Siegel S, *The Science of Placebo*, 2002



### Motivation / Desire for Relief

Price et al *Ann Rev Psychol*, 2008

# Genuine Biopsychosocial Phenomena...

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## THERAPEUTIC RELATIONSHIP (Social)

### Rituals & Symbols

#### Clinician-Patient Interaction

Kaptchuk TJ, *Ann Intern Med*, 2002

### Participation in the Therapeutic Encounter

#### Role of Empathy, Listening, Connection, & Engagement

Kaptchuk TJ, *N Eng J Med*, 2015

*“The doctor-patient relationship  
is critical to the placebo effect”  
-Irving Kirsch*



# Genuine Biopsychosocial Phenomena...

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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

Hróbjartson & Gøtzsche, N Engl J Med, 2001

## RE- Meta-analysis in 2010

**Significant placebo effects were seen...Higher effects:**

Hróbjartson & Gøtzsche, Cochrane Database Syst Rev, 2010

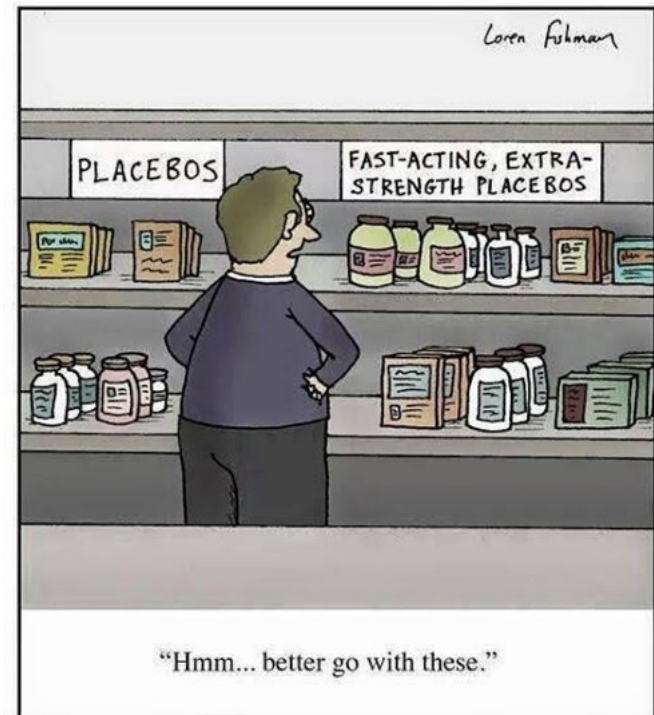
- For pain & nausea
- When physical placebos compared with pill placebos
- When patients are informed about possibility of receiving placebo (in RCT)
- When trials are explicitly designed to study placebo effects

# Placebo Research...

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In the following slides are examples of Results from studies that used placebos for...

- IBS
- Asthma
- Knee OA
- Migraines



# IBS

(Kaptchuk et al, *BMJ*, 2008)

% Improvement

G.I.S.

Reported

“Adequate Relief”

No  
Treatment



3%

## 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

Placebo



37%

Placebo +  
Support



62%



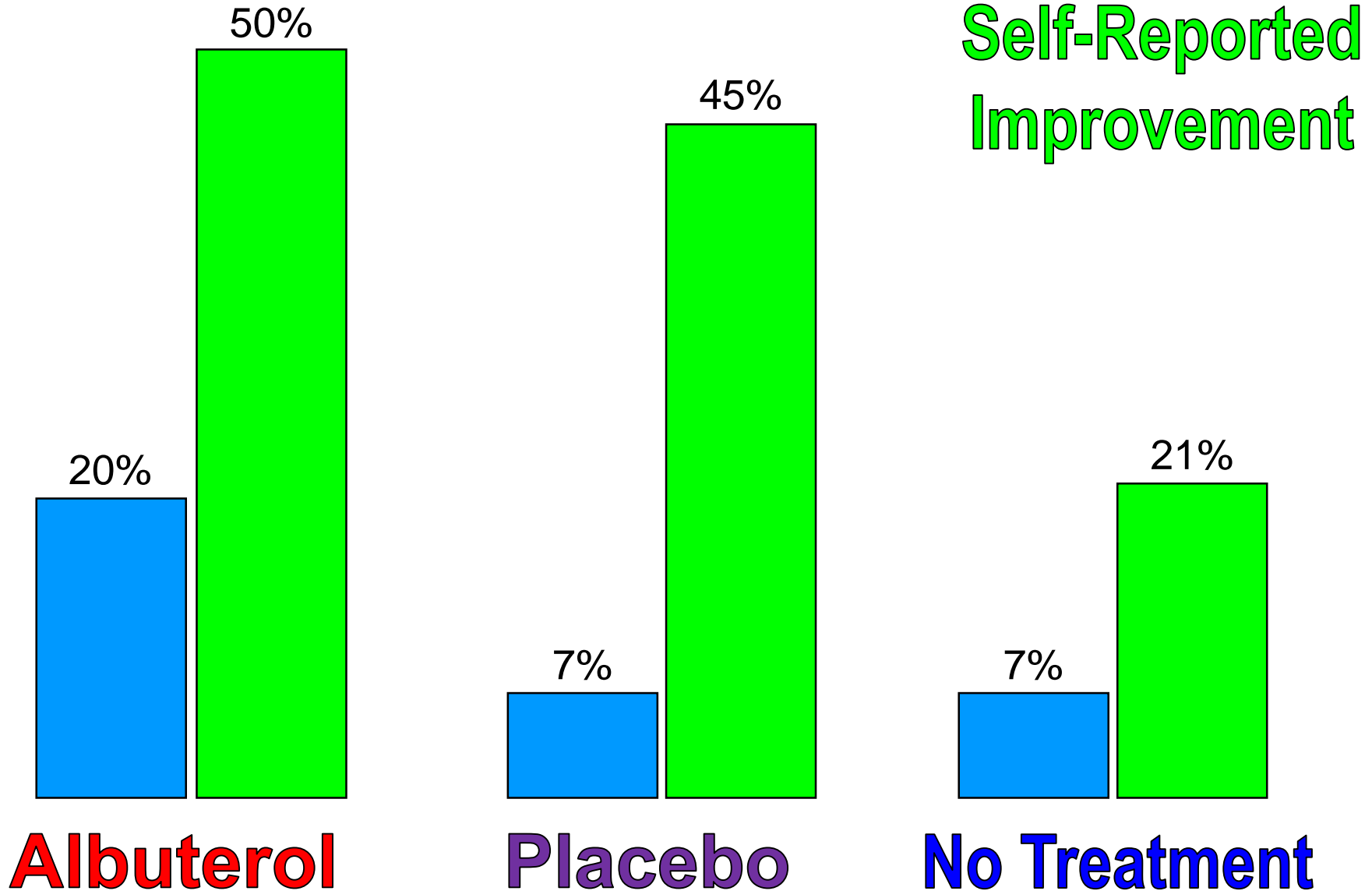
# ASTHMA

(Wechler et al, N Engl J Med, 2011)

% Improvement

FEV<sub>1</sub>

Self-Reported  
Improvement



# KNEE OA & HA or SALINE INJECTION

(Zhang et al, *Ann Rheum Dis*, 2008)

VOL 55, NO 8 / AUGUST 2006

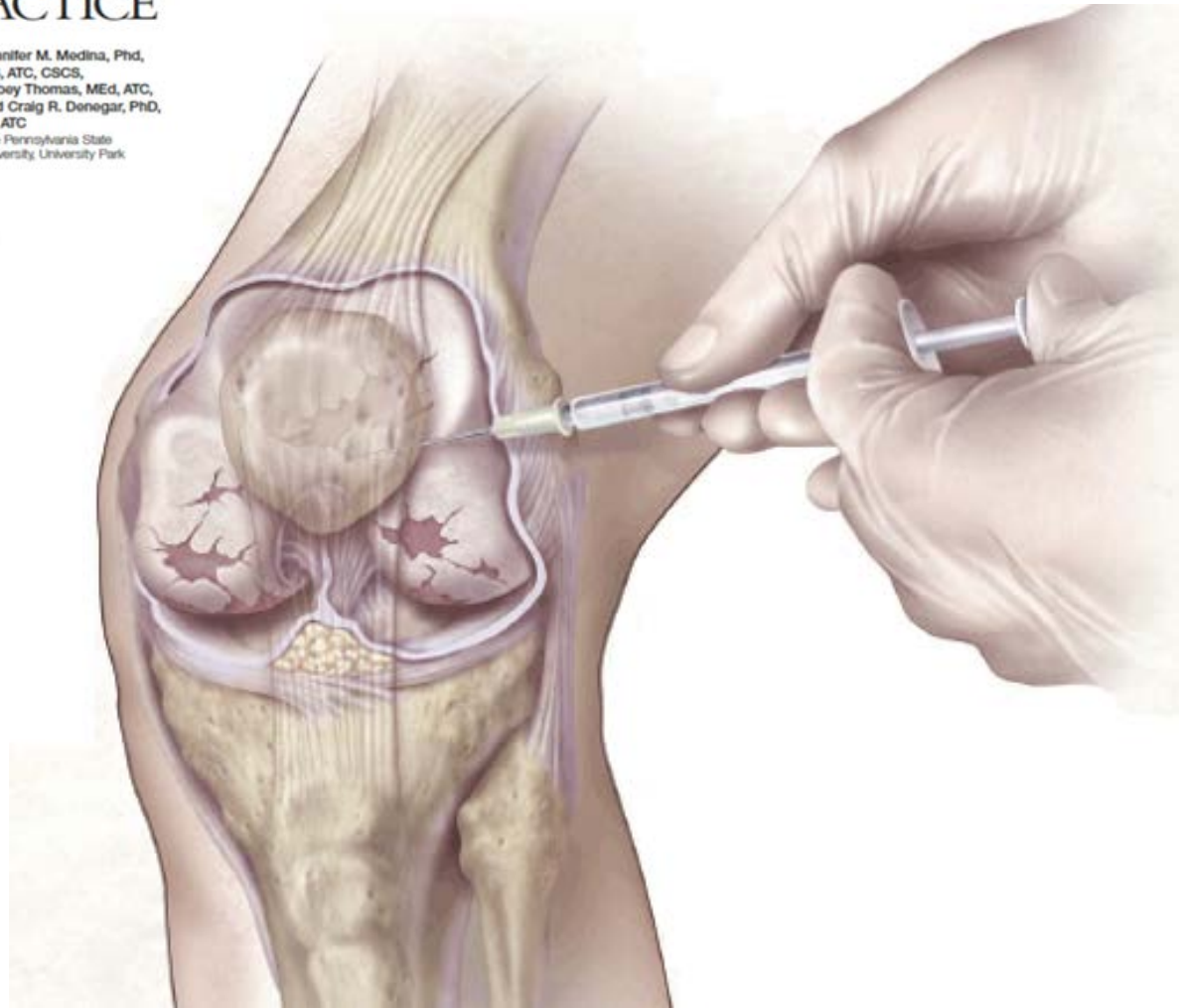
THE JOURNAL OF  
FAMILY  
PRACTICE

## Knee osteoarthritis: Should your patient opt for hyaluronic acid injection?

A meta-analysis of hyaluronic acid's effects  
on pain, stiffness, and disability

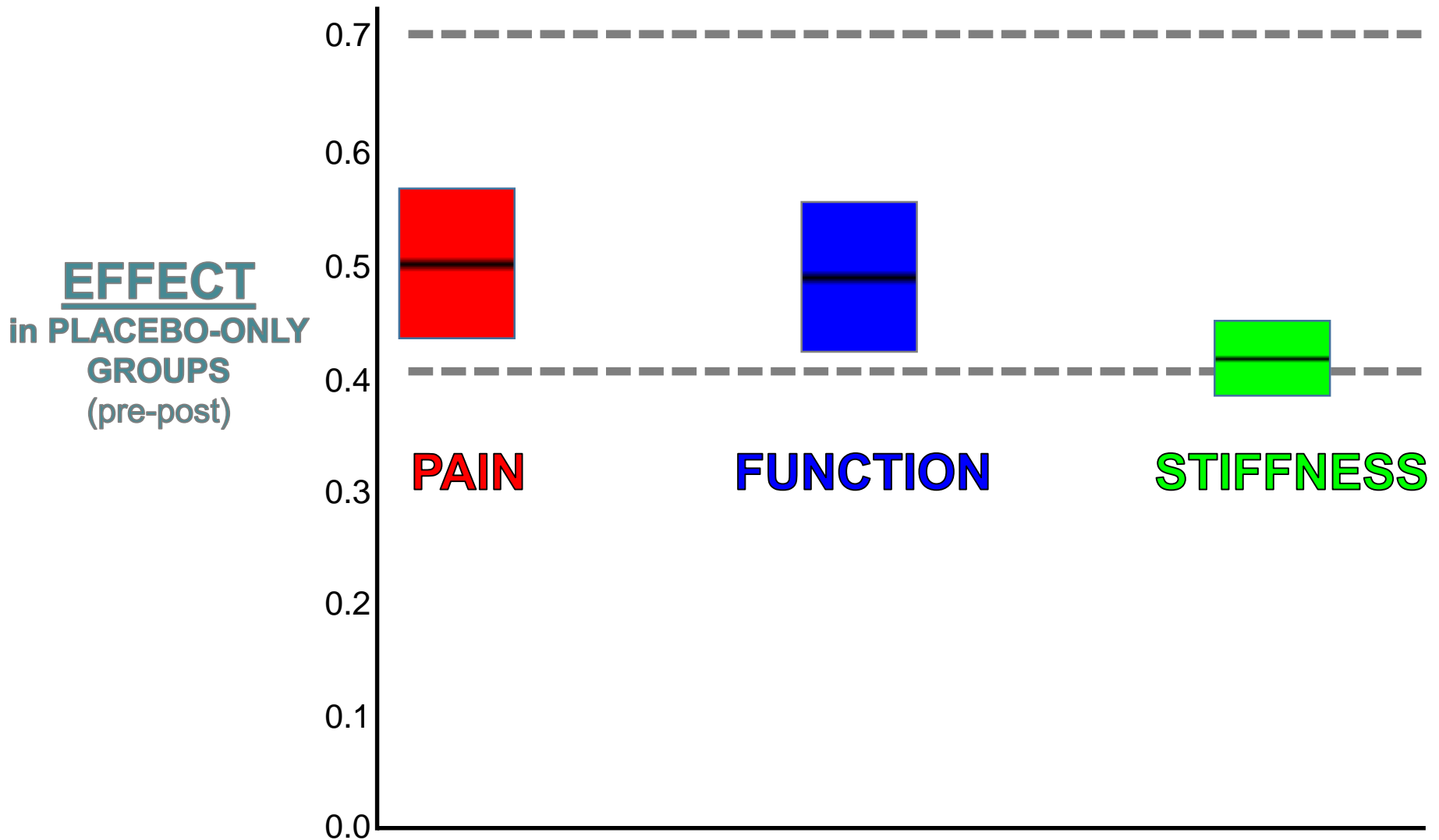
Jennifer M. Medina, PhD,  
MS, ATC, CSCS,  
Abbey Thomas, MEd, ATC,  
and Craig R. Denegar, PhD,  
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The Pennsylvania State  
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Media



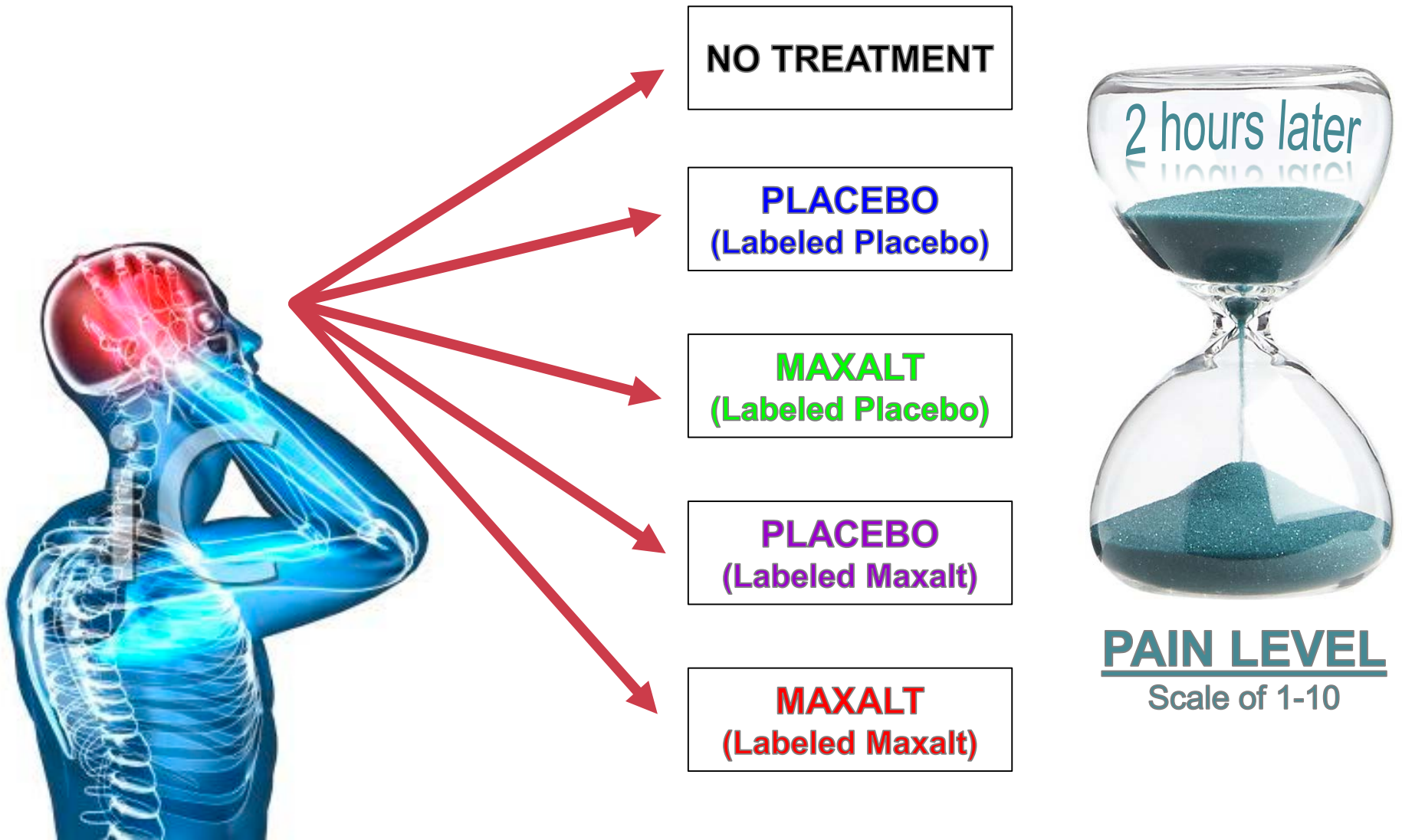
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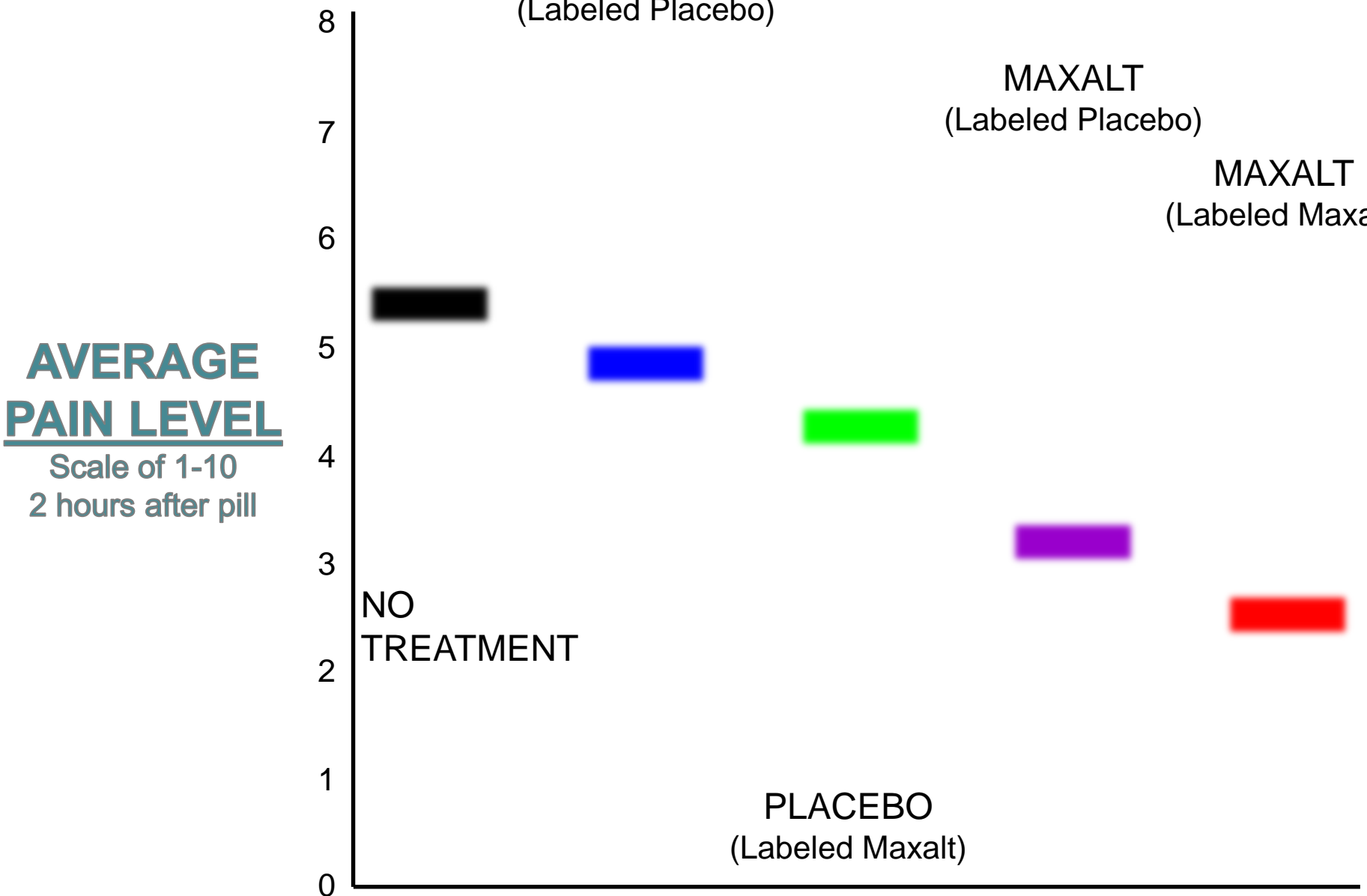
# MIGRAINES

(Kam-Hansen et al, Sci Transl Med, 2014)



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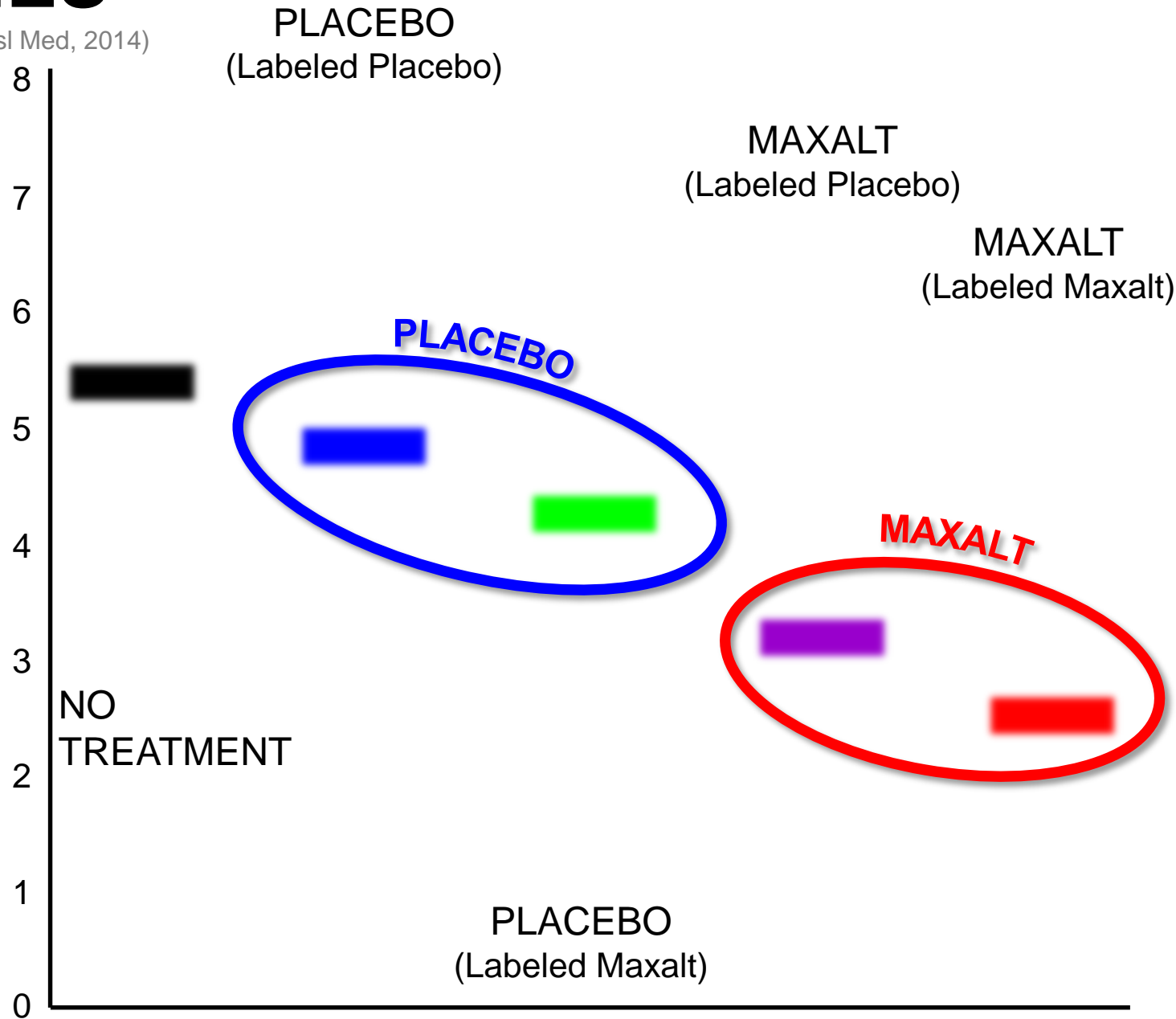


# MIGRAINES

(Kam-Hansen et al, Sci Transl Med, 2014)

## AVERAGE PAIN LEVEL

Scale of 1-10  
2 hours after pill



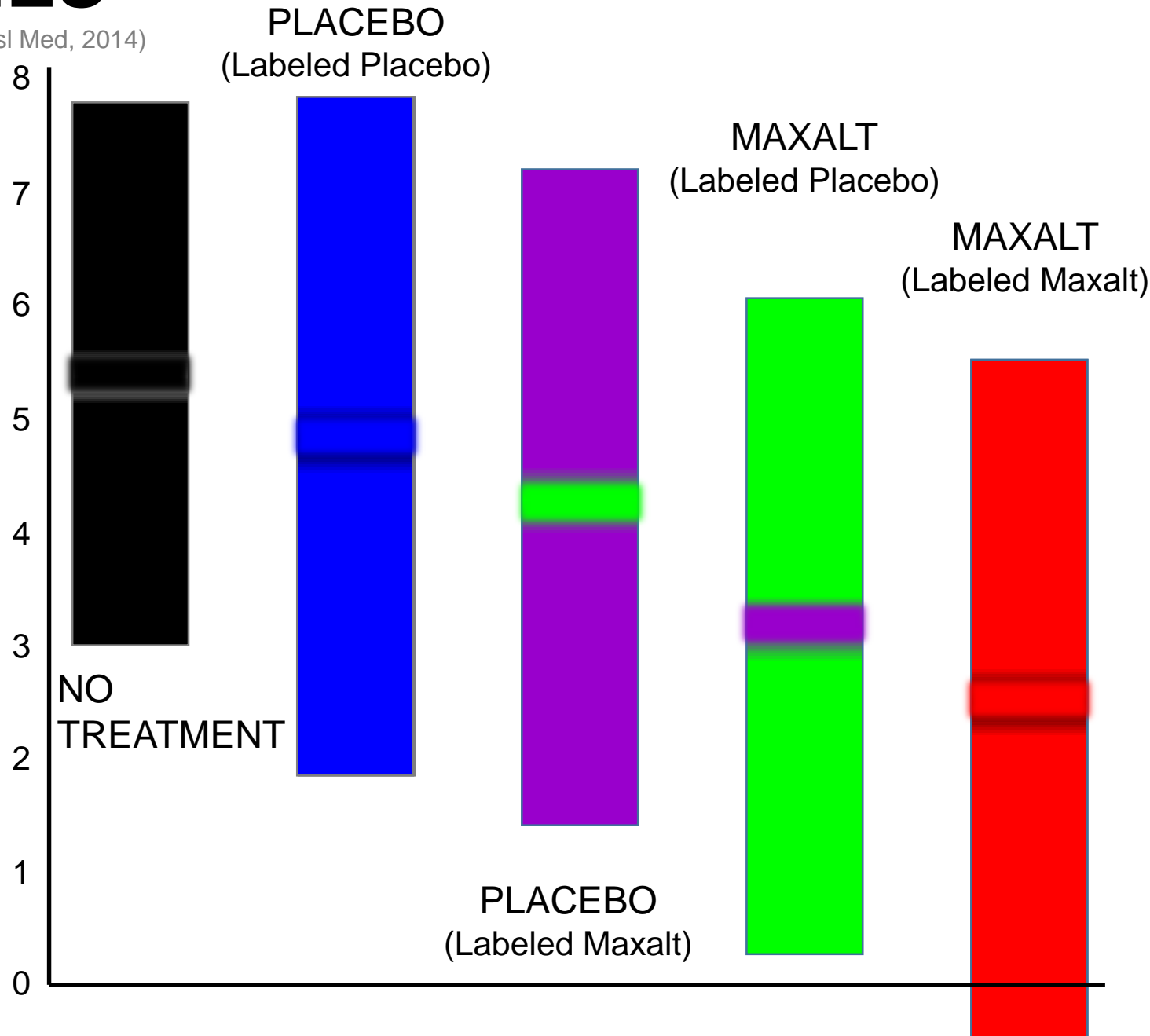
# MIGRAINES

(Kam-Hansen et al, Sci Transl Med, 2014)

**AVERAGE  
PAIN LEVEL**

Scale of 1-10  
2 hours after pill

...with  
Standard  
Deviations





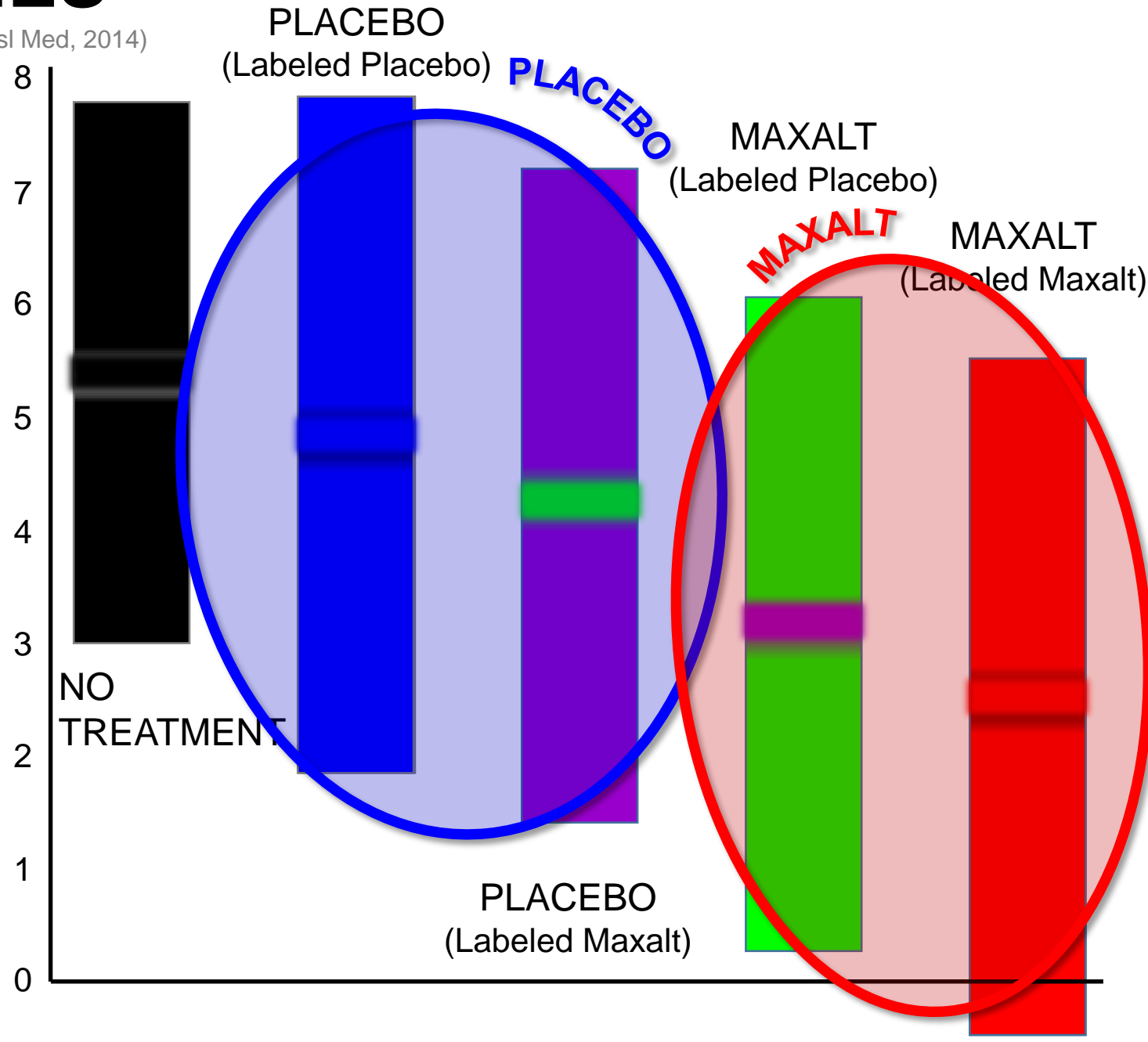
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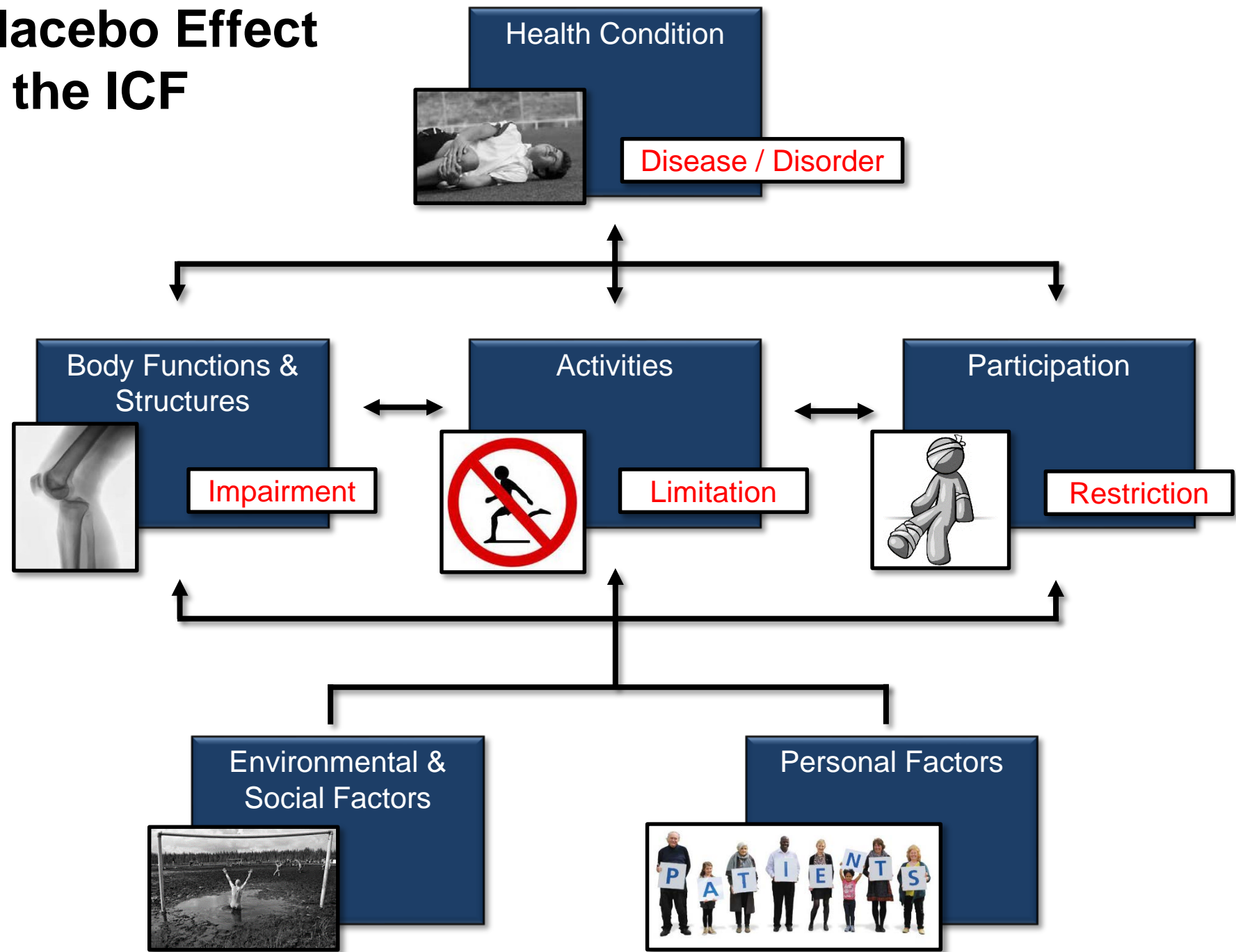
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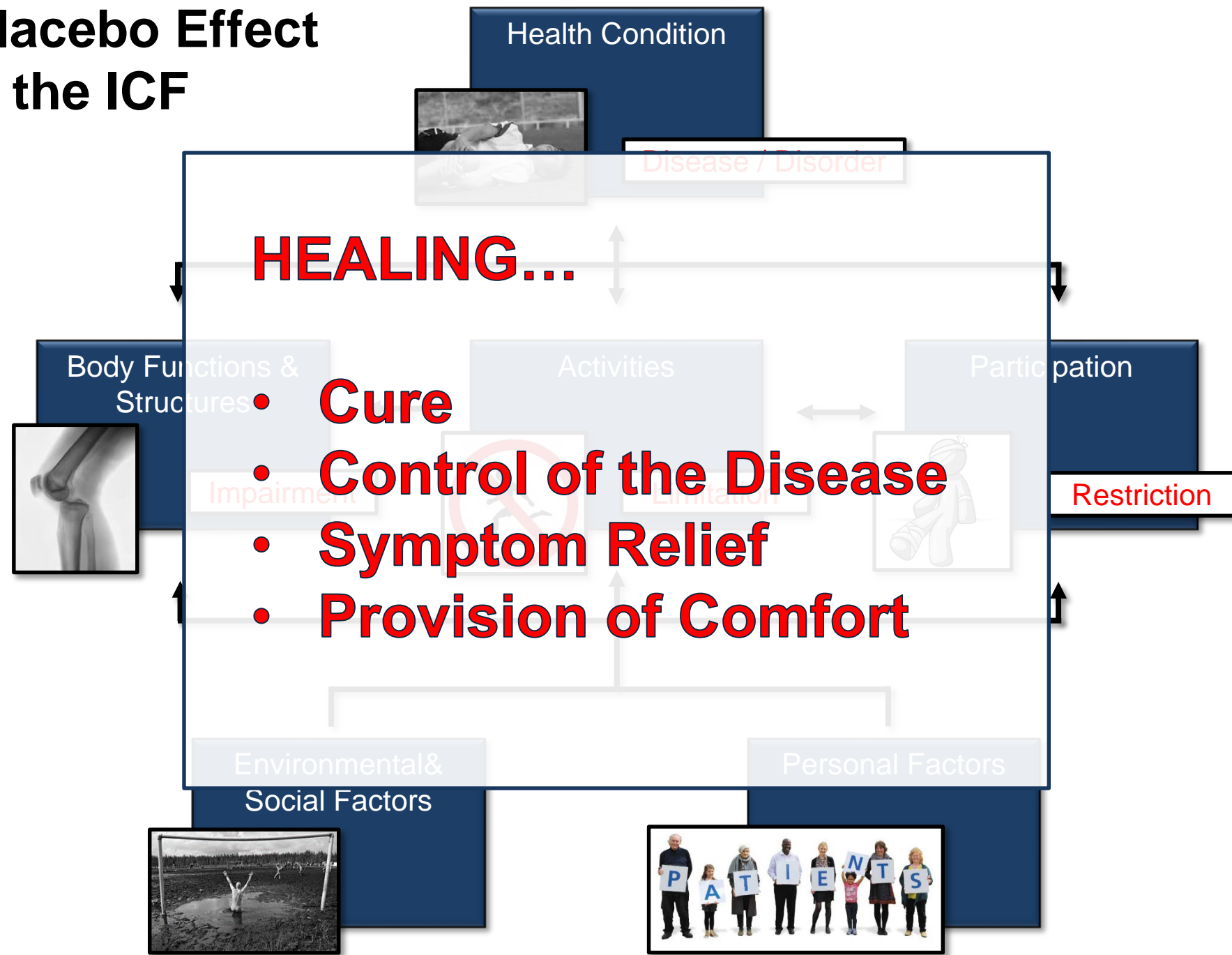




# Placebo Effect & the ICF



# Placebo Effect & the ICF



# Placebo Effect & EBP

Strength of

Recommend

**“Though placebos  
may provide relief,  
they rarely cure”**

Kaptchuk TJ, N Eng J Med, 2015

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

Examples: Pain, RTP, Nausea

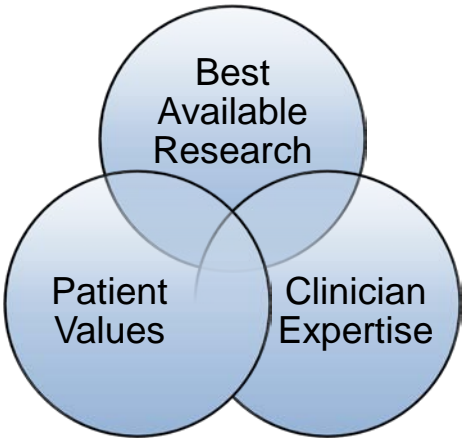
ent-oriented evidence

patient-oriented evidence

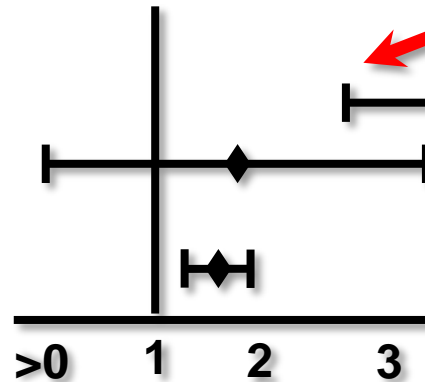
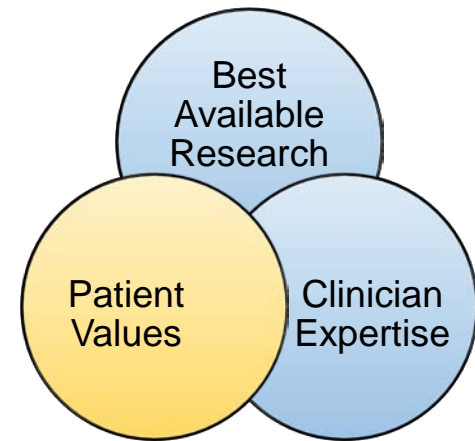
disease-oriented evidence

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

Examples: BP, ROM, strength



# Placebo Effect & EBP



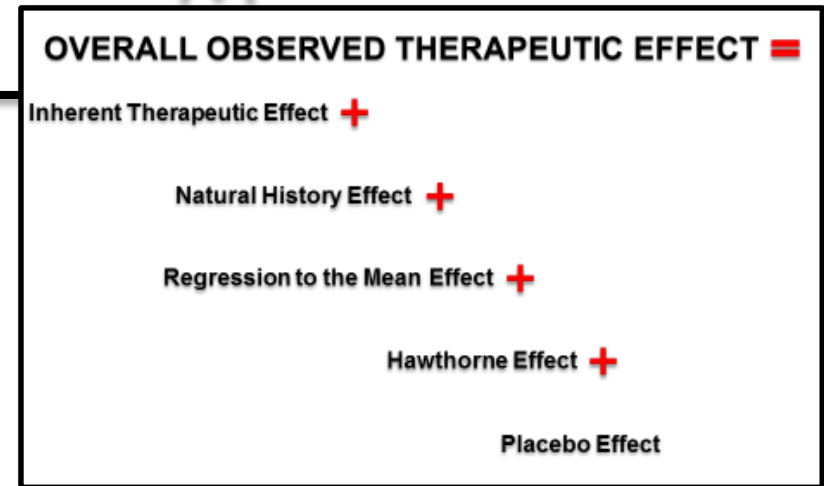
What does it mean when my results fall here?

## 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*?



Compliance  
Fidelity  
Adherence

"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."

-Leslie A, *Am J Med*, 1954



# OVERALL OBSERVED THERAPEUTIC EFFECT =

Inherent Therapeutic Effect +

- Traditional Western, Allopathic Medicine

Natural History Effect +

- Complementary & Alternative Medicine

Regression to the Mean Effect +

- Placebos

*Holistic vs Reductionist*

Hawthorne Effect +

*Systems approach*

Placebo Effect

All 3 of these are likely contributors to BOTH the Placebo Effect and the Inherent Therapeutic Effect

# Summary

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In clinical research & practice, **placebos & the placebo effect should not be treated as a nuisance variable**

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:

## Biological

Chemical

Neurological

## Psychological

Expectation of success

Classic conditioning

Motivation / Desire for relief

## Social

Clinician-Patient

Relationship

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Relationship

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.



## Summary

The Placebo Effect goes beyond the sugar pill.

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

**Patient's Perspective + Clinician's Prediction**

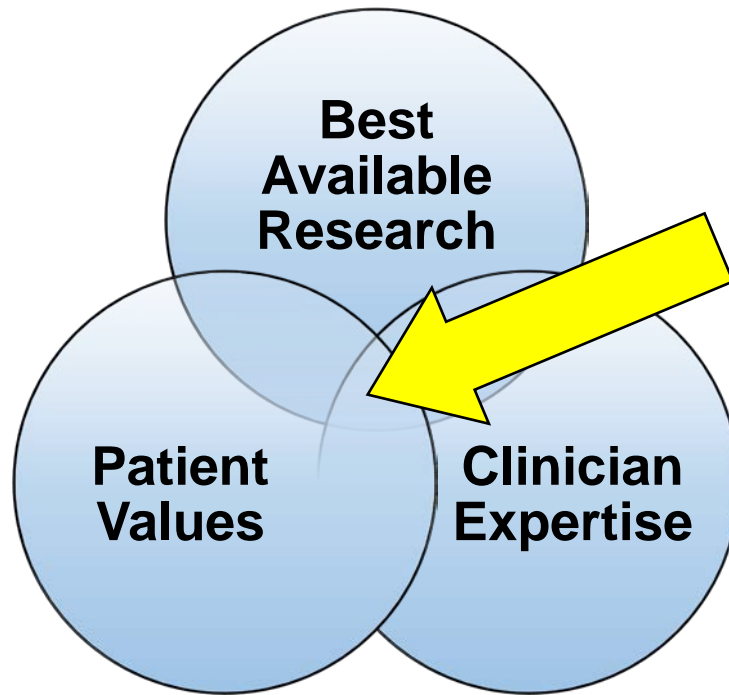
**= *REALITY***



## Summary

# Patient's Perspective + Clinician's Prediction

**= REALITY**



**CLINICAL  
DECISION - MAKING**

*An Evidence-Based Approach*

**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

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# ITHACA COLLEGE

Department of Exercise and Sport Sciences

*“Commitment to Excellence”*

