Contextual Effects of Treatments for Patients with Back Pain: Real and Important or *"Just Placebo Effects?"*

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Overview

- Review rationale for use of placebos in drug trials
- Problems using placebo model for non-drug trials
- How to choose control/comparison groups to make trials of non-drug therapies most *clinically useful*
- Observations from 4 RCTs of CIH treatments for chronic back pain: *importance of specific effects of CIH therapies?*
- Summarize and make **PROVOCATIVE** assertions to stimulate discussion

Rationale for "Placebo" Controls in Drug Trials

- Known that patients' beliefs may affect outcomes
- Without evidence a new drug is better an inactive pill and reasonably safe, hard to justify its approval for use
- With drugs able to create identical-looking "placebo" pills to control for all non-specific effects (not possible for other tx)
- Problem: Placebo trials gold standard for RCTs that shaped popular and medical thinking. *Relevance for non-drug trials?*

Challenges Trying to Use Placebo Control Groups for Non-Drug Trials

- Finding valid placebos for non-drug treatments
    - Massage, spinal manipulation, yoga?
    - Mindfulness?
    - *Acupuncture – sham?*
- Credible to patients as real treatment
- Complex interventions: How to control for multiple/synergistic pathways of effectiveness?

Challenges for a non-drug Trialist

- Usually no good placebo for non-drug treatments
- Historically, funders and grant reviewers disliked usual care controls; felt need to rule out "placebo effects"
- Pressured to include placebo-ish/attention controls
- If placebo-ish control is somewhat effective, risk underestimating a treatment's overall effectiveness
- How to interpret results if treatment and "placebo-ish" control arms have similar effects? *(Value of usual care arm).*

Which model best adresses goal of clinical research?

Goal: To discover new and better ways for clinicians to reduce patient suffering, improve QoL, cure when possible, prevention

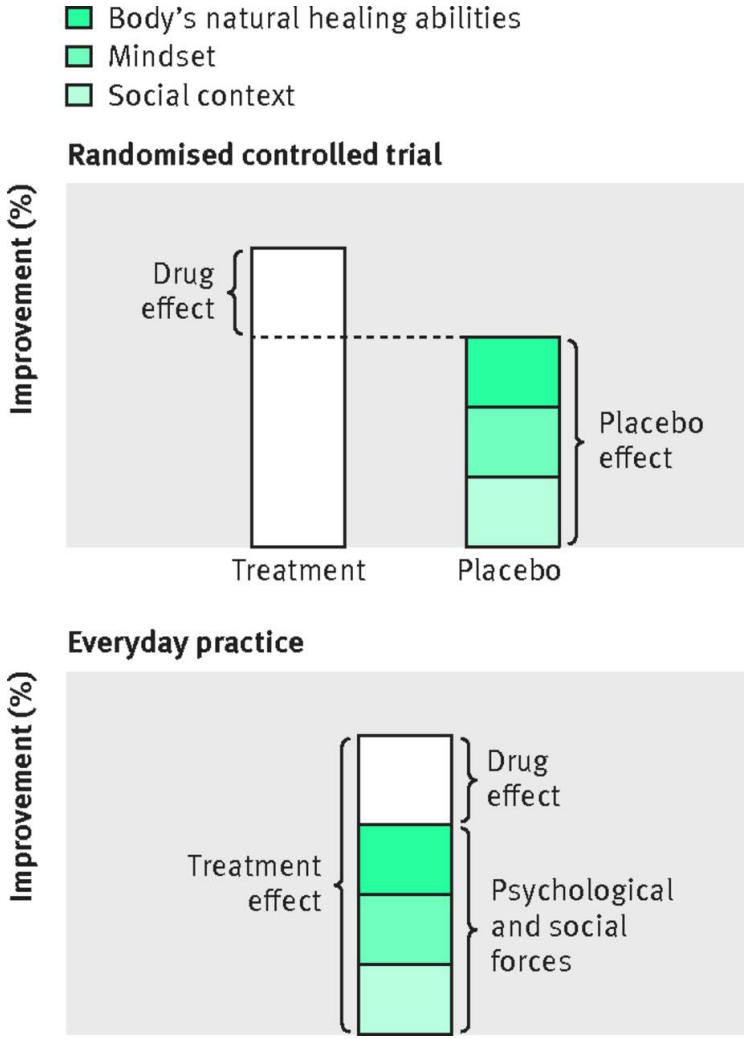
Classic drug model: Total effects > Placebo?

- *Useful for identifying specific effects, new drug approval*

"Pragmatic" model: Total effects > available alternatives (e.g., usual care, treatment B)?

- *Useful for improving care*

Fig 1 The psychological and social forces of healing are typically viewed as in competition with drug effects in placebo controlled trials (top) but in everyday practice they underlie all treatment effects (bottom).



Alia J Crum et al. BMJ 2017;356:bmj.j674

Awareness that healing involves more than just the body is not new

The Anatomy of Melancholy

Robert Burton (1621)

*Cunning men, wizards, and white witches, as they call them, in every village, which, if they be sought unto, will help almost all infirmities of body and mind. . . . **The body's mischiefs…. proceed from the soul: and if the mind be not first satisfied, the body can never be cured.***

Suffering vs. Physical Distress

(EJ Cassel, NEJM, 1982)

"Physicians' failure to understand the nature of suffering can result in medical interventions that (though technically adequate) not only fail to relieve suffering but ***become a source of suffering itself****."*

Important concept of *nocebo effects*

Gordon Waddell – spine surgeon!

(Waddell, Spine, 1987 – Volvo Award Winner!)

It is unlikely that there will ever be a magic cure for all low-back pain, so the physician's role as healer must be accompanied by his or her more ancient role as counselor, helping patients to cope with their problems.

The Healing Encounter
(David Reilly, GP - 2001, Glasgow)

"Our relationship with our patients is the key to self-healing. Medicine is (re)discovering that [we] can sometimes be more powerful than technical factors in creating the outcomes of our care for good or bad--modifying rates of recovery, side effects, complaints and costs"

"Relieving Pain in America"
(IOM, 2011)

"to reduce the impact of pain and the resultant suffering will require a ***transformation*** *in how pain is perceived and judged both by people with pain and by the health care providers who help care for them."*

[and the research community!]

"Making Mindset Matter"
(Crum, BMJ, 2017)

Rather than being incidental to treatment, psychological and social elements play crucial roles in determining clinical outcomes.

"Making Mindset Matter"
(Crum, BMJ, 2017)

Alongside advances in drug and surgical trials, improved understanding of the ability of the social context and patients' mindsets to evoke healing properties in the body can be an extraordinary resource for health and healing.

Summary

- Importance of “contextual” effects for healing well documented
- With advent of “scientific” medicine and rise of double-blind placebo-controlled drug trials, these effects dismissed as “only placebo effects”
- Literature on contextual effects ignored, placebo paradigm still influential
- Has impeded shift to new paradigm better suited for meeting needs of patients……*but some signs of change!*

Placebo Studies & the Therapeutic Encounter (Kaptchuk), others

Emergence of CIH Trials for Back Pain

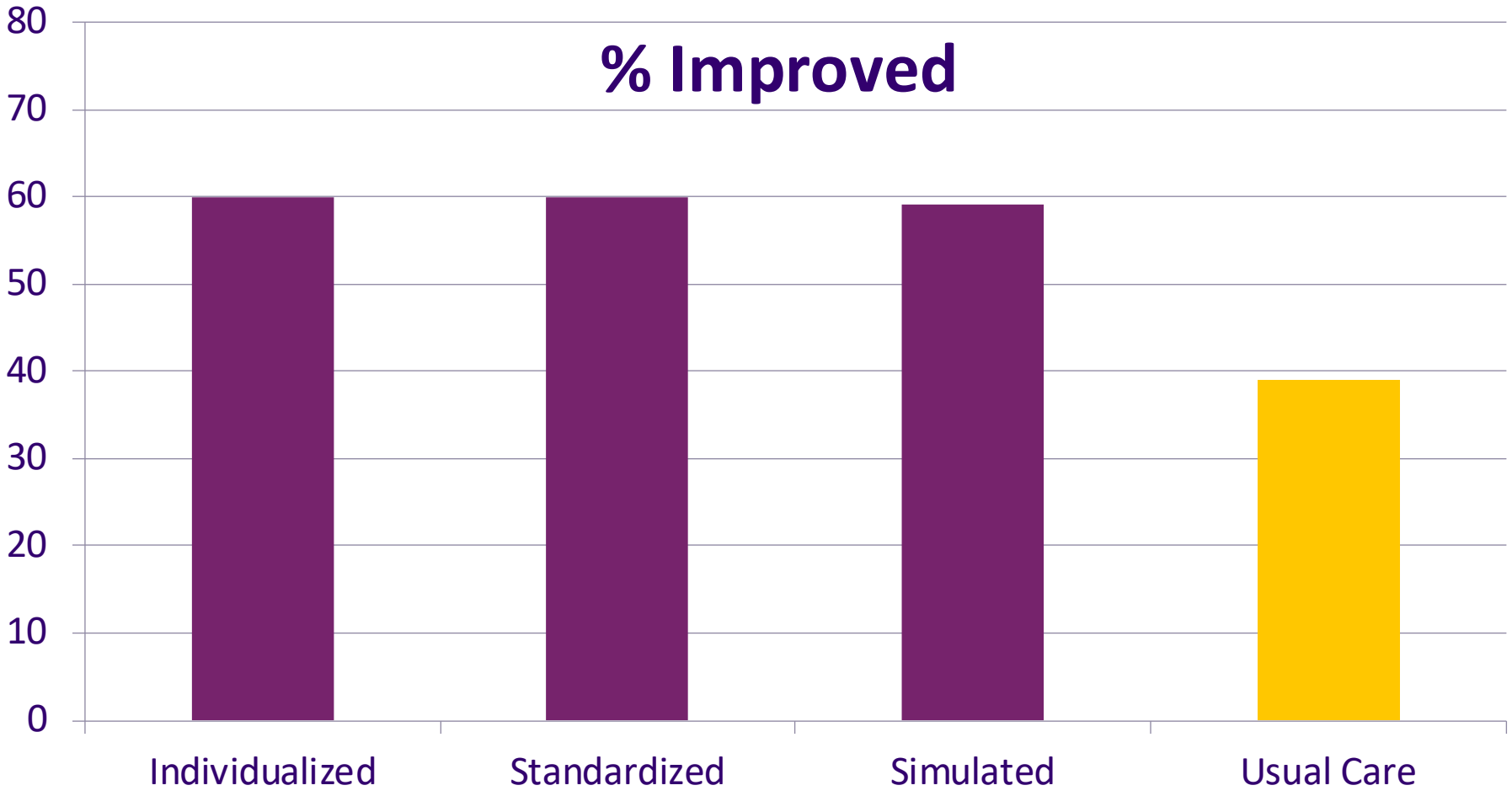
- Many RCTs evaluating CIH treatments for LBP in past 25 yrs.
- Hard to interpret results of trials using placebo-ish or attention controls (e.g., sham acupuncture)
- Trials using “usual care” controls provided clearer answers to pragmatic questions and influenced ACP LBP guidelines
  - Prioritized non-drug over drug treatments!
  - 6 of 13 options for 1st line care for chronic LBP were CIH!

RCTs of CIH Treatments for chronic LBP by Cherkin-Sherman Research Team

- Acupuncture (Cherkin, 2010), Yoga (Sherman, 2011)
- Massage (Cherkin, 2013), Mindfulness-Based Stress Reduction (Cherkin, 2016)

- *Trials used roughly similar study designs, patient populations*
- *All included an active control and usual care (no intervention) control*
- *Outcome: % of patients with clinically meaningful improvement on Roland-Morris Disability Questionnaire after 8 – 26 weeks follow-up*

Acupuncture (8 weeks)



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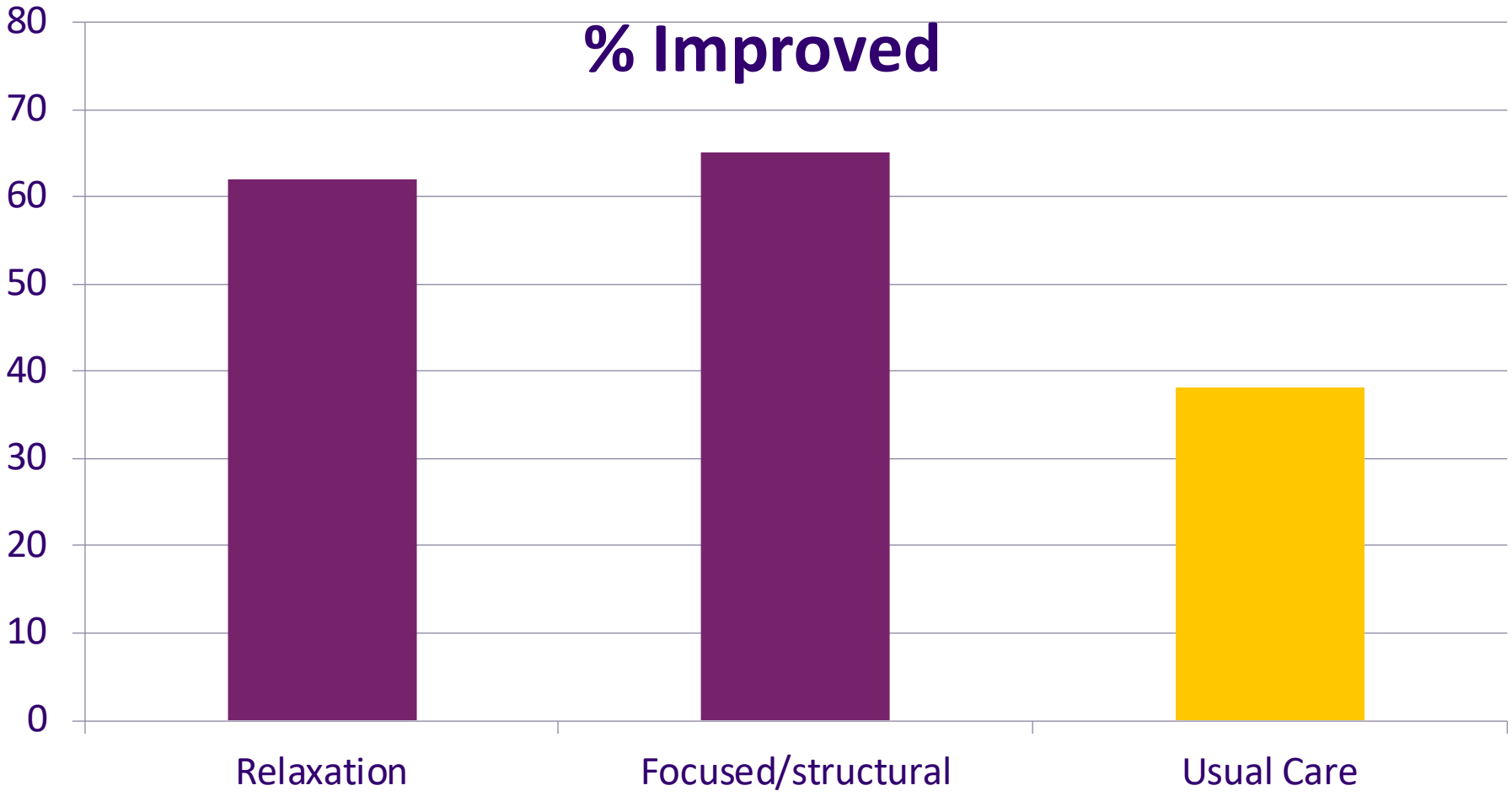
Massage (10 weeks)



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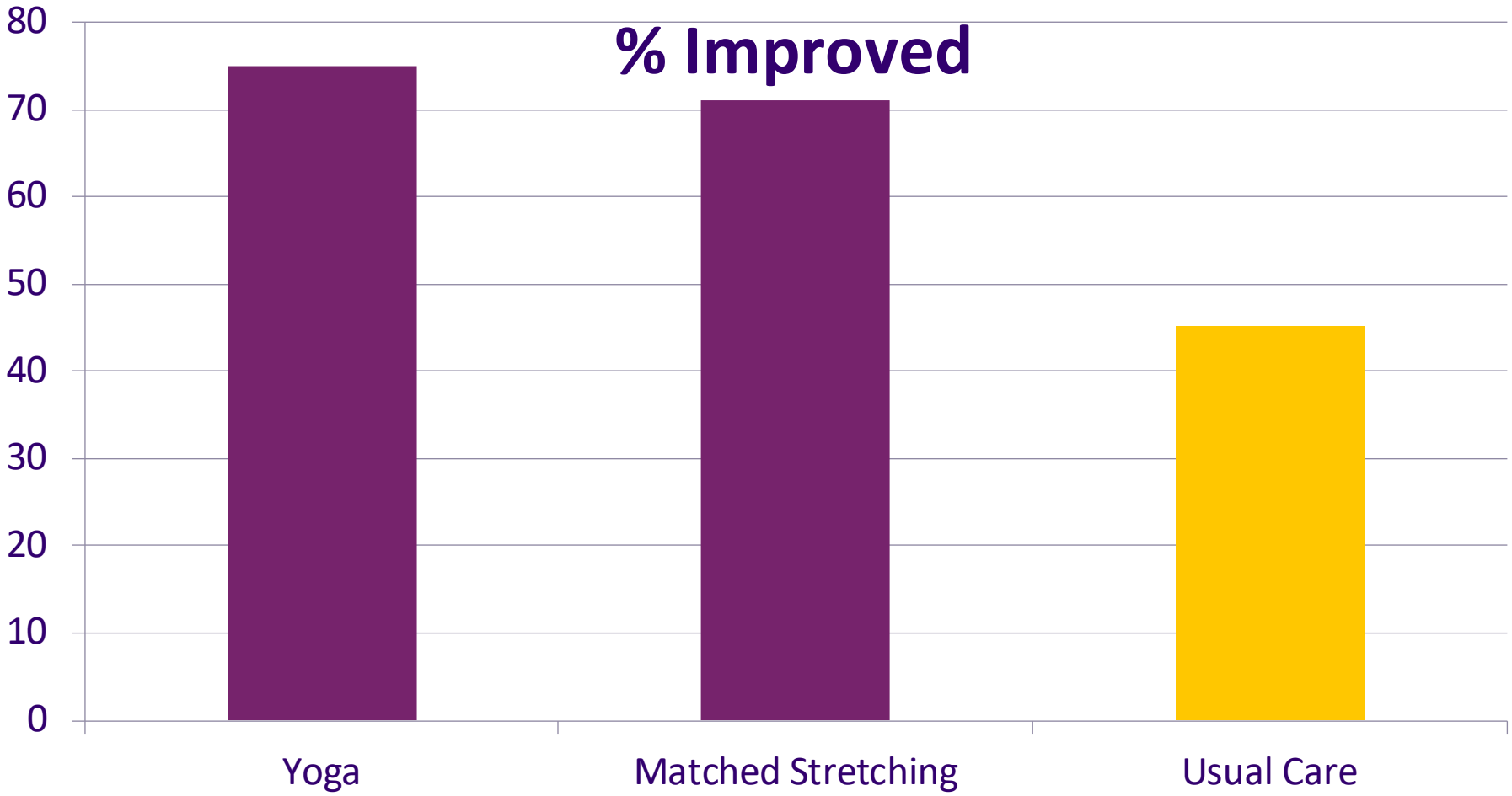
Yoga (12 weeks)



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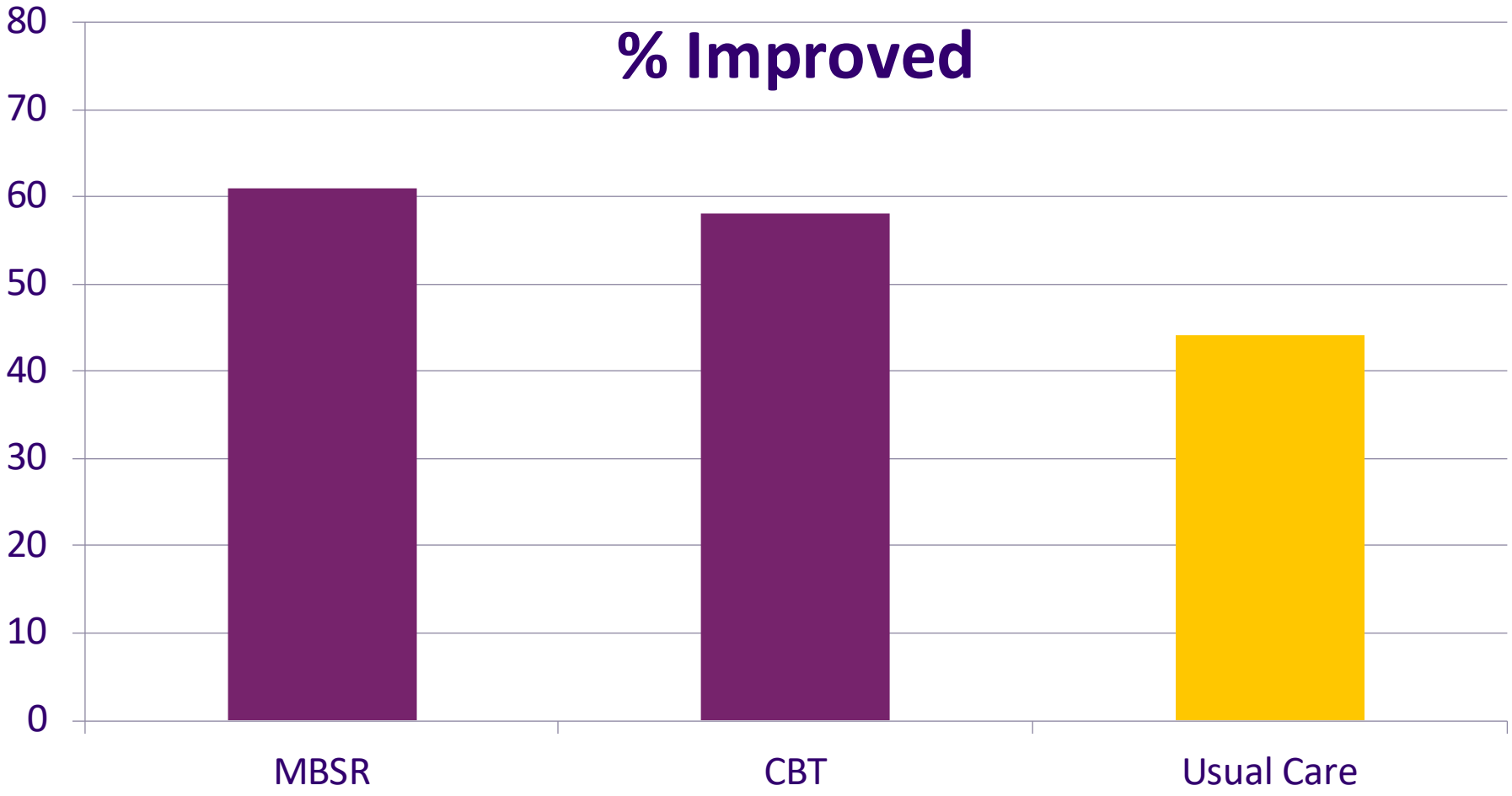
Mindfulness-Based Stress Reduction
(26 weeks)



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Observations

In the 4 trials

- Effects of active treatments similar both within (e.g., MBSR and CBT) and across (e.g. acupuncture, yoga) trials (60%-70%)
- Effect of usual care groups similar across trials (40%)
- *Active treatments equally effective, better than usual care*
- *Does mix of specific and non-specific effects vary across treatments? Possible "specific" effects less important than we think in CIH treatments, mostly non-specific?*

Intriguing Questions

- *Are the context effects of providing patients a credible treatment in a caring, compassionate and engaged manner more important than the specific effects of the treatment?*
- *Could patient outcomes be improved if clinicians maximized these context effects of their care*?

Is Paradigm Shifting?

- After 70 years with drug model gold standard, still resistance to viewing context effects as legitimate and worthy of study
- Emerging research shows context effects play important role in healing, maybe more potent than specific effects
- Is this the beginning of a paradigm shift that could radically change clinical practice?
- Are we ready for a *National Institute of Healing Science*?

PROVOCATIVE ASSERTION #1

Because the effects on patient outcomes of the ***context*** *in which care is provided for LBP may be greater than the* ***specific*** *effects of treatments,* ***substantially*** *improving care for LBP will require paying more attention to optimizing the context effects of care.*

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PROVOCATIVE ASSERTION #2

Because changes necessary to improve context of care for LBP are essentially same changes necessary to improve care in general (e.g., listening, compassion, addressing patient's unique needs), trying to improve care specifically for LBP would be inefficient and possibly futile (LBP ~3% of PCPs' patients). Instead, efforts should focus on transforming care in general, including optimization of context effects of care.

"Let the healing begin!"

"Let the healing begin!"

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Thank you for your interest!

PROVOKED?

I welcome your thoughts and questions!

Interesting Article on Placebos

"Why placebo pills work even when you know they're a placebo"

Darwin A Guevarra, PhD (UCSF Postdoc)

Kari A Leibowitz, PhD

Google: Aeon, placebo pills, 2022

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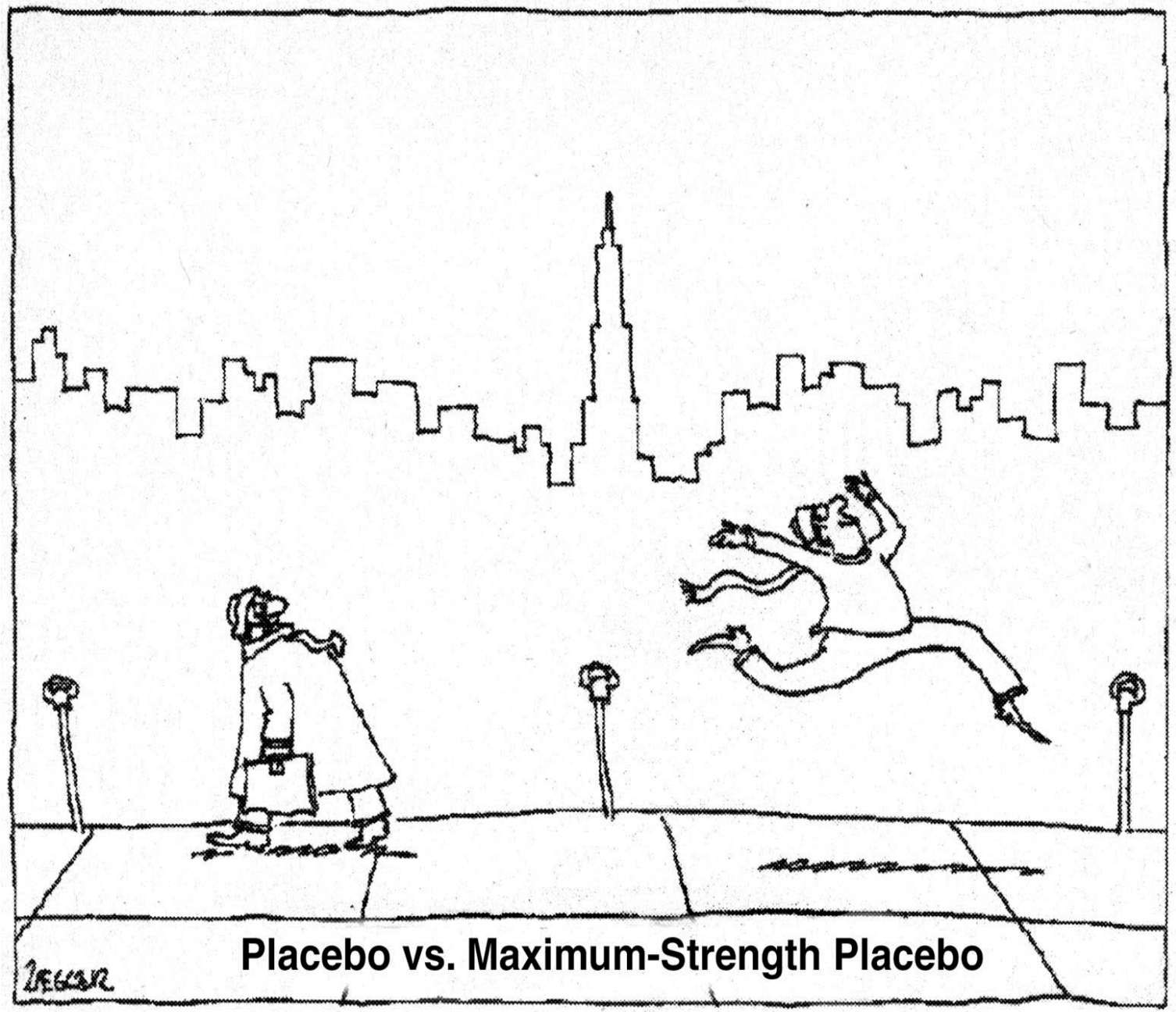

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