

**Weill Cornell
Medicine**

THE HOCUS EFFECT



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Case

- 93yo F hx of GERD, HFrEF (prior ~45%), breast Ca s/p 2005 lumpectomy, 1st degree block p/w bilateral flank pain being admitted for EKG changes called new Afib.
- Hx reveals constipation and straining with BMs
- No chest pain, SOB
- “Trop leak” at 0.09
- After ED mentioned “heart problems” worried about her heart

After 30 minutes of POCUS...

- Communicated results:
 - Poor EF
 - Elderly heart
 - Not much difference from prior echo four months prior

Felt better! Relieved she didn't have an arrhythmia.

Why? Was this a placebo effect?

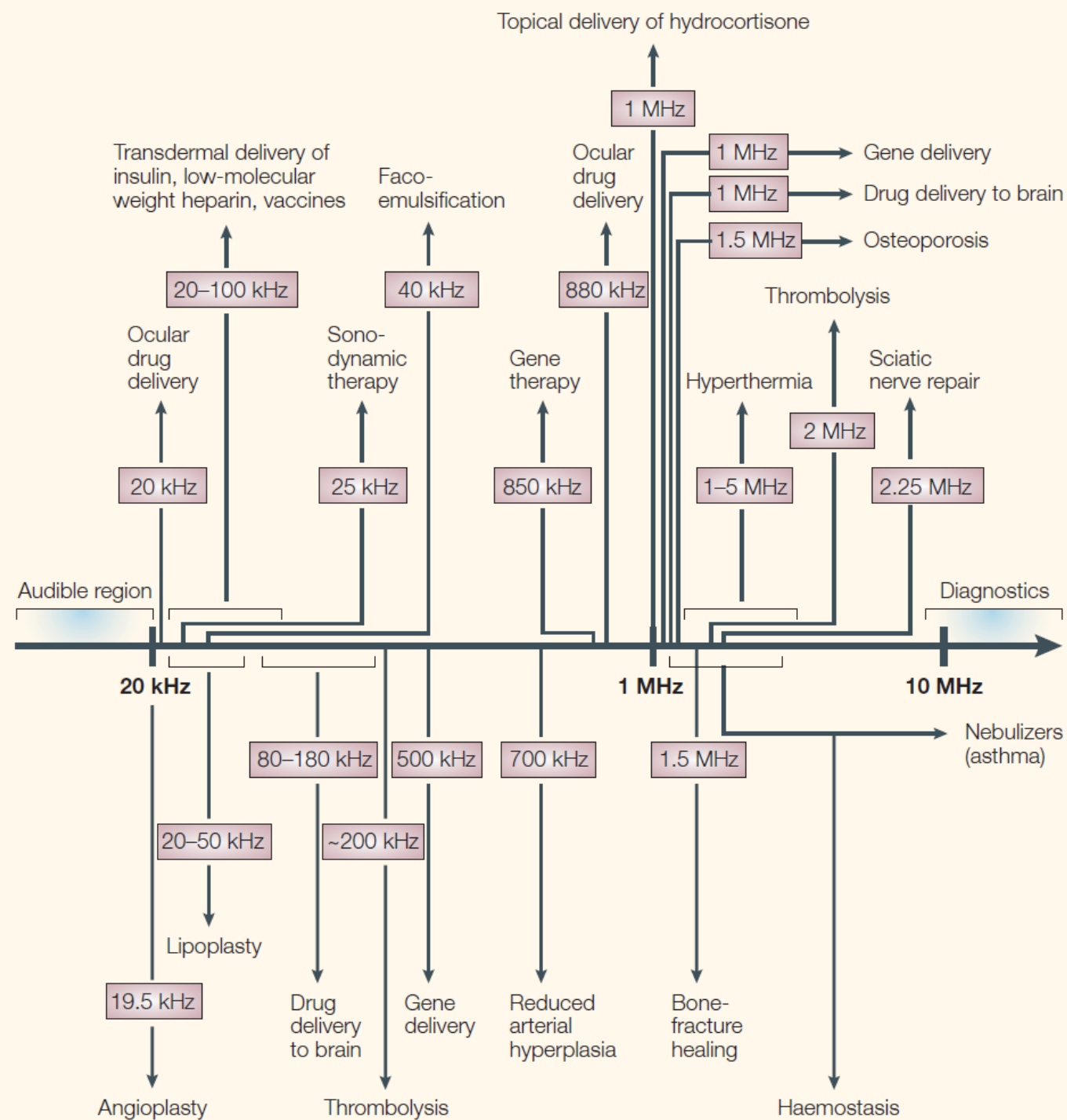
POCUS and Placebos

- Biological effects of US
- Therapeutic US? Placebo controlled studies of US for MSK pain
- POCUS and placebo effects
- Epistemology of Placebos: Learning from Alternative Medicine
- Characteristic and Incidental factors

Ultrasound as Therapy

- Facilitate drug delivery across skin (sonophoresis)
- Promote gene therapy to targeted tissues
- Disrupt blood brain barrier for drug delivery
- Deliver chemo to tumors or thrombolytics to blood clots

What's the Frequency Kenneth?



Mitragotri. 2005. Healing sound: the use of ultrasound in drug delivery and other therapeutic applications *Nature Reviews Drug Discovery*



Could POCUS be more than diagnostic?

- Most biologically therapeutic effects shown *in vitro*
- “The frequently described biophysical effects of ultrasound either do not occur *in vivo* under therapeutic conditions or have not been proven to have a clinical effect under these conditions.”

Baker KG, Robertson VJ, Duck FA. A review of therapeutic ultrasound: biophysical effects. *Phys Ther.* 2001 Jul;81(7):1351–8.

Ultrasound vs Sham Ultrasound

- For numerous MSK complaints, US vs sham US found
 - **Decreased pain**
 - **Better ROM**
 - **Faster return to baseline**
 - **Effects tend to fade quickly over time**
 - **No difference between control and sham groups**
- Per Cochrane reviews:
 - **OA of hip (No) or knee (maybe small effect, low quality evidence)**
 - **Rotator cuff injuries (No)**
 - **Ankle sprains (No)**
 - **Low back pain (No)**
 - **Carpal tunnel (maybe small effect, low quality evidence)**
 - **Varicose veins (evidence too poor quality to determine)**
 - **Broken bones (evidence too heterogeneous and poor quality to draw conclusions)**

Review	Condition	Conclusions
Robertson 2001	pain and injury	“little evidence” of therapeutic benefit in 10 “acceptable” trials out of 35 candidates; 2 positive trials, 8 negative
Baker 2001	biological effects	“insufficient biophysical evidence” to justify therapeutic use for pain and injury
Buchbinder 2006	tennis elbow	nine studies produced “platinum” level (better than gold!) evidence of “little or no benefit” (for ESWT)
Ho 2007	tennis elbow	conflicting, “unconvincing” evidence of efficacy from a few trials (of ESWT again)
Ho 2007	rotator cuff tendinopathy	limited evidence “supports ... ESWT for chronic calcific rotator cuff tendinitis,” but no non non-calcific
Rutjes 2010	osteoarthritis of knee	a positive update to a previously negative review, which is strange because it’s based on just 5 small, poor quality trials with trivial “positive” results
Shanks 2010	lower limb conditions	inconclusive review of 10 of 15 candidates: “no high quality evidence available”
van den Bekerom 2011	ankle sprains	inconclusive but discouraging review of “five small placebo-controlled trials”; the “potential treatment effects of ultrasound appear to be generally small”
Page 2013	carpal tunnel syndrome	inconclusive but slightly encouraging review of “only poor quality evidence from very limited data” from 11 trials
Ebadi 2014	chronic low back pain	inconclusive and underwhelming review of 7 small trials, none of them good quality
Desmeules 2015	rotator cuff tendinopathy	negative review “does not provide any benefit ... based on low to moderate level evidence” from 11 weak trials



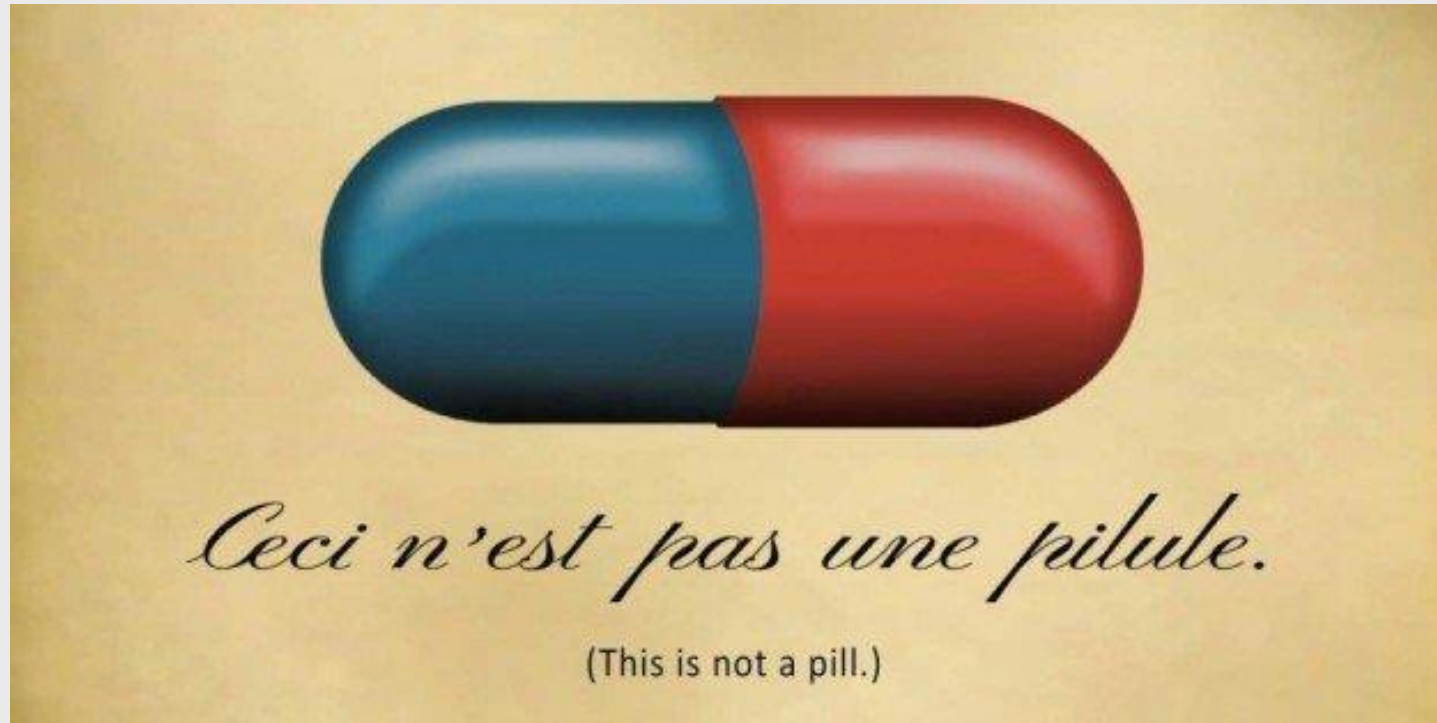
“Musculoskeletal medicine is badly polluted with underpowered studies with untrustworthy ‘promising’ results that are mostly good for the CV’s of the researchers who produce them.”

Ingraham 2018 Does Ultrasound Therapy Work? Pain Science

What about POCUS?

- No placebo-controlled trials
 - Hospital Medicine or ED POCUS
 - Cardiology Echo
- But relevant evidence suggestive
 - Increased patient satisfaction with ED POCUS (Howard et al. 2014)
 - Maximize pt confidence in ED MDs (Claret et al. 2016)
- Why so understudied?

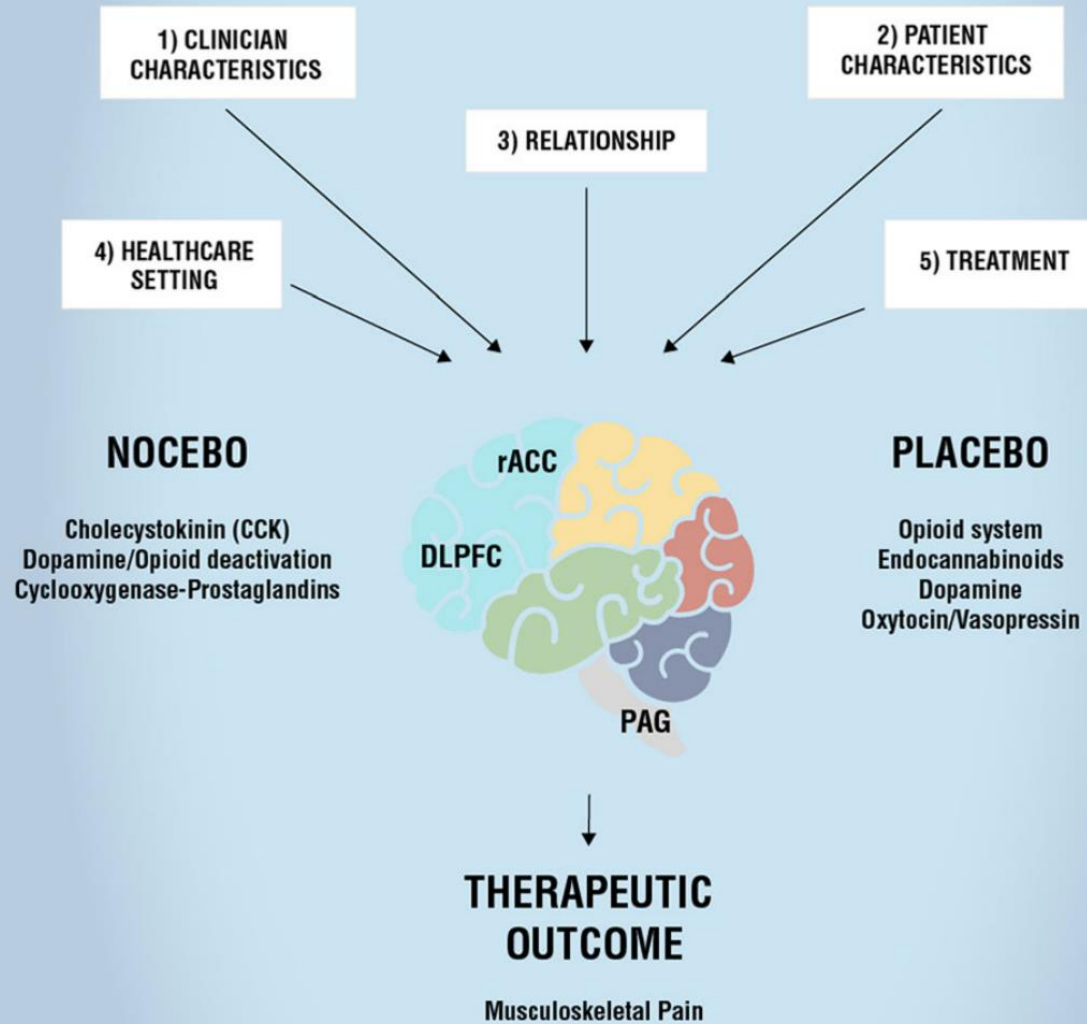
The Placebo effect of Ultrasound



Lessons from Alternative Medicine

- For numerous MSK complaints, US vs sham US found
 - **Decreased pain**
 - **Better ROM**
 - **Faster return to baseline**
 - **Effects tend to fade quickly over time**
 - **No difference between control and sham groups**
- Many studies of alternative treatments with similar results
- Why do control and treatment both show positive effects?

CONTEXTUAL FACTORS (CFs)



The paradox of sham therapy and placebo effect in osteopathy

A systematic review

Francesco Cerritelli, MSc^{a,b,c,*}, Marco Verzella, PT^{a,d}, Luca Cicchitti, DO^{a,d}, Giandomenico D'Alessandro, DO^{a,d}, Nicola Vanacore, PhD^e

Journal of Evaluation in Clinical Practice ISSN1365-2753

PERSONAL VIEW

Problematic placebos in physical therapy trials

Matthew Maddocks MCSP PhD,¹ Roger Kerry FMACP MCSP MSc,² Andrew Turner PhD³ and Jeremy Howick PhD⁴

Deconstructing the Placebo Effect and Finding the Meaning Response

Daniel E. Moerman, PhD, and Wayne B. Jonas, MD

Ann Intern Med. 2002;136:471-476.

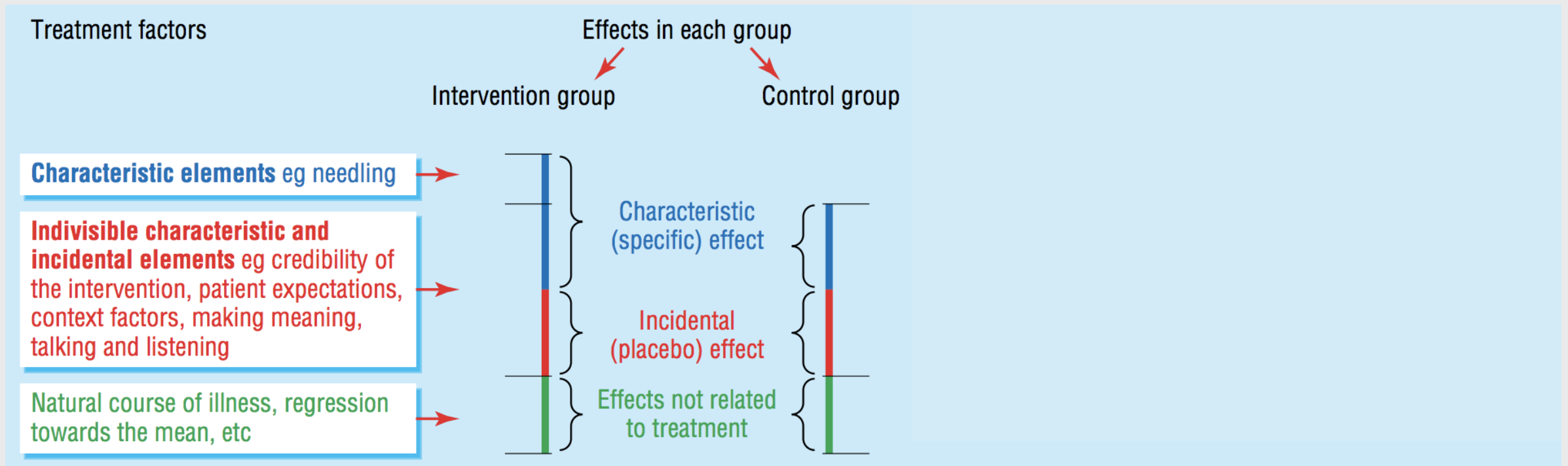
Rethinking Placebo and Nocebo

- Meaning Response (Moerman 2002)
- Positive/negative care effect (Blease 2011)
- Contextual healing (Miller & Kaptchuk 2008)



Characteristic & Incidental Treatment Factors

- Characteristic effect: Theoretically derived therapeutic action or strategy believed to be causally responsible for outcome
- Assumptions of placebo controlled trials
 - **Incidental factors are generic, unlinked to particular environment**
 - **Characteristic effects & incidental effects independent and additive (vs intertwined and synergistic)**



Paterson & Dieppe. 2005. Characteristic and incidental (placebo) effects in complex interventions such as acupuncture. *BMJ*. 330(7501): 1202–1205



Characteristic & Incidental Treatment Factors of US

- Environment:
 - ED vs wards
 - Equipment – the bigger the better
 - Props – gel, heat
- Rituals – Physician demonstration of mastery/competence
- MD time at bedside – “the laying of hands”
- Images (Unlike sham US in MSK pain studies)
- Conditioning
- Patient expectations
- Reassurance/Communication (Unlike sham US in MSK pain studies)

- Variations in culture & language - concordance

Equipment

- “The evidence for the existence of an enhanced placebo effect for devices and procedures is intriguing but by no means conclusive.”
Kaptchuk et al. 2000. Clinical Epi 53(8)
- Evidence derived from most trials prior to informed consent regulations
- ECSW therapy for plantar fasciitis



“Shockwave therapy equipment is generally bigger & more badass.”

Ingraham 2018 Does Ultrasound Therapy Work? Pain Science

Rituals, Time at Bedside

- “Context, ritual, setting, and tone of voice of the examiner induce psychobiological events that produce measurable change in levels of neurotransmitters”

Verghese et al. 2011. The Bedside Evaluation: Ritual and Reason. *Annals Internal Med*

Finniss et al. 2010. Biological, clinical, and ethical advances of placebo effects. *Lancet*.

- Socioemotional factors most important aspect of MD communication

Di Blasi et al. 2001 Influence of context effects on health outcomes: a systematic review. *Lancet*.

Reassurance

The impact of communicating normal results: Lessons from cardiac catheterization

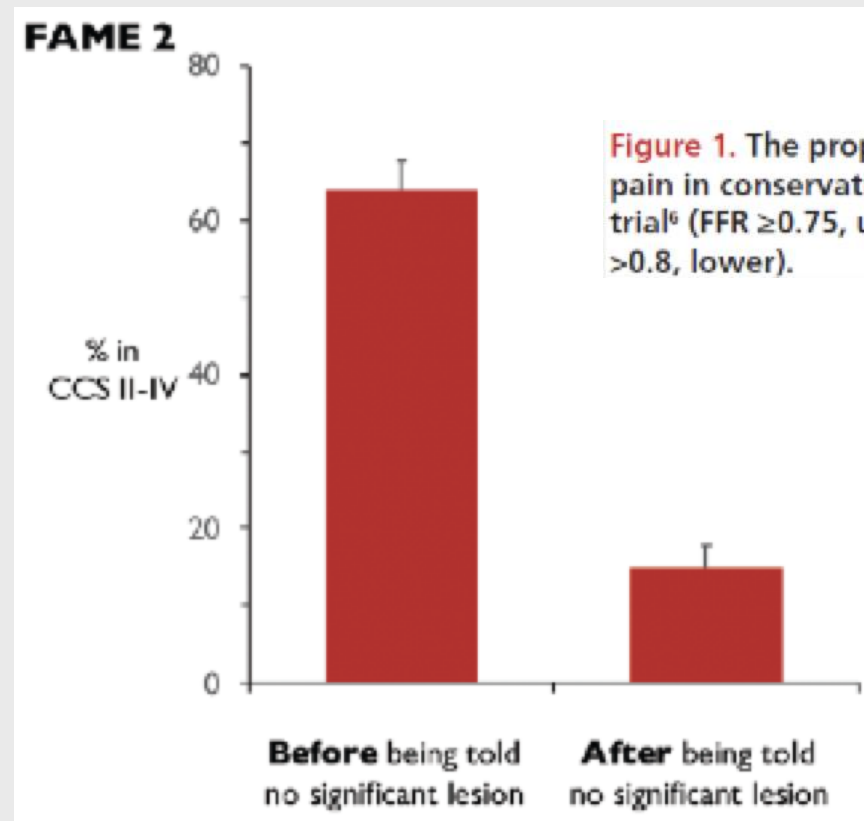
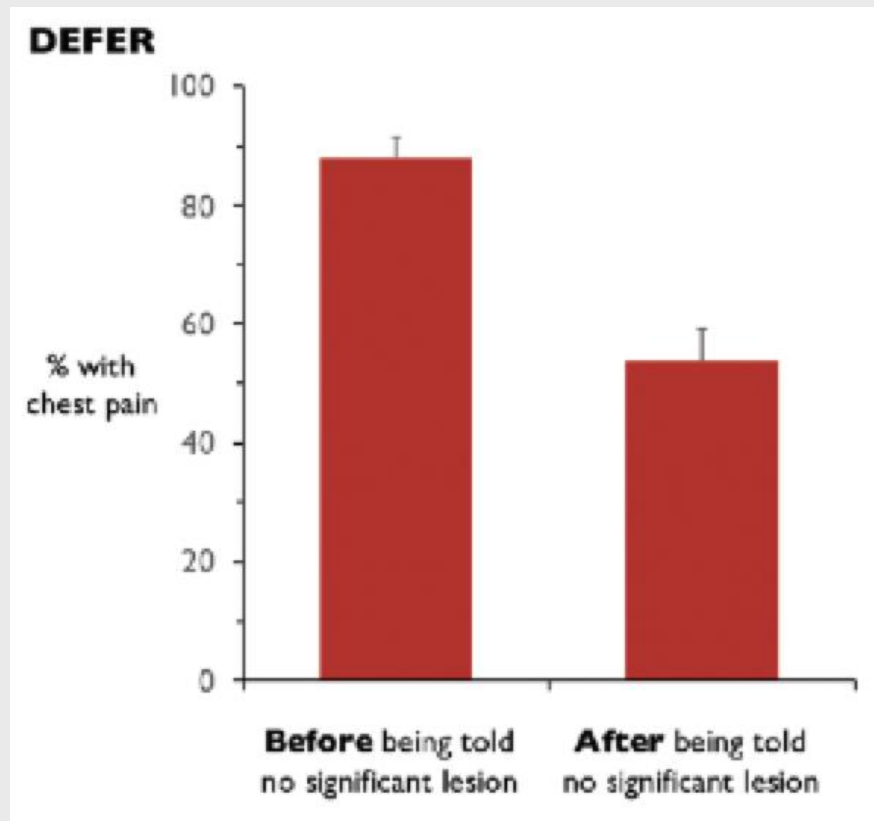


Figure 1. The proportion of patients experiencing chest pain in conservatively managed groups of the DEFER trial⁶ (FFR ≥ 0.75 , upper) and the FAME 2⁷ registry (FFR > 0.8 , lower).

Rajkumar et al. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004665.

Case

- POCUS performed in the context of:
- Linguistic concordance
- Improved bed arrangement in ED
- Reassured by other positive results (no actual Afib, flat troponins)

Conclusions

- Ultrasound has placebo effects in MSK studies
- No studies of placebo effects of POCUS for hospitalists/ED
- Placebo studies are difficult in contextually rich environments
- Clinical POCUS has numerous incidental effects inextricable from US that make empirical placebo analysis challenging
- POCUS practitioners should be aware of potential for placebo effects and remain conscious of what may modulate them
 - **Environment**
 - **Bedside manner**
 - **Rituals**
 - **Equipment**
 - **Reassurance/communication**

A4



PLAX



Echo

Eccentric LVH

Severely reduced LVEF

Left atrial dilatation.

Dilated aortic root.

Mild aortic regurgitation.

Mild to moderate mitral regurgitation.

No pulmonary hypertension.

LV systolic function appears further reduced compared to prior; slightly greater mitral regurgitation and less tricuspid regurgitation.