



ANALYSIS

Making mindset matter

Alia Crum and colleagues argue that acting on the growing evidence about the influence of patient mindset and social context on response to healthcare can improve outcomes

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The current standard for evaluating medications and treatments, the randomised controlled trial, involves identifying the effects of active ingredients by subtracting out effects produced by placebo. This model effectively isolates medical treatment by comparing it against “medically superfluous,” forces of healing, including social context (eg, medical ritual, patient-provider relationship, institutional reputation, branding), mindset of the patient (eg, the patient’s conscious or embodied expectation to heal), and the body’s natural ability to heal itself with time.

The randomised trial is a good and rigorous standard for testing the efficacy of new medications. But what this model obscures is that, in the practice of medicine, the psychological and social elements underlying placebo effects remain an influence in active treatment (⇓). Indeed, medical diagnoses and treatments are never isolated from patient mindsets and social context.

When interacting with patients, physicians communicate scientific evidence within the framework of subjective judgments, expectations of treatment outcomes, and perceived patient preferences. Patients are influenced by their trust in physicians and how their physicians listen to, engage, and inform them. Context or environment, such as the branding, price, and advertising of drugs, or the hospital or doctor’s credentials, also have an influence. Rather than being incidental to treatment, these psychological and social elements play crucial roles in determining clinical outcomes.¹⁻³

From this perspective, the whole meaning of placebo effect changes. It’s no longer a mysterious response to a sugar pill but the scaffolding of psychological and social forces—the support system—on which the total effect of treatment rests. Knowing this, we can move beyond merely asking how a treatment compares with a placebo and begin to ask more useful questions such as what are the components driving placebo responses and what can we, as patients and providers, do to more effectively leverage these components to improve healthcare?

What science says

The placebo response, evoked by people’s mindset (conscious or embodied expectation) that they will heal, can account for clinically significant benefit in an estimated 60-90% of

conditions, including pain, anxiety, depression, Parkinson’s disease, asthma, allergies, hypertension, immune deficiencies, and Alzheimer’s disease and even recovery from surgery.^{1,2} Neurobiological research over the past 30 years has shown that the expectation to heal triggers distinct brain areas associated with anxiety, pain, and reward circuitry, as well as peripheral physiology involved in many biological systems, including the cardiovascular, endocrine, respiratory, nervous, and immune systems.^{1,2} Moreover, this research shows different mindsets evoke distinct, objective correlates that work through a unique cascade of physiological effect to produce the expected outcome. For example, the mindset that pain will be relieved activates endogenous opioid systems in the brain, whereas the mindset that anxiety will be reduced activates corresponding changes in the anterior cingulate and orbitofrontal cortices as well as in sympathetic nervous system activation, resulting in decreasing blood pressure and heart rate.²

Mindsets are also responsible for negative effects or “nocebo” responses, which include heightened pain response after patients are informed that an injection will hurt and increased presence of side effects such as nausea, fatigue, and sexual dysfunction after physician disclosure of possible negative side effects of medication.⁴ An estimated 4-26% of participants randomised to placebo in clinical trials drop out because of nocebo effects.⁵

Research also suggests that the benefits of behavioural treatments are influenced by patients’ mindsets about those behaviours. For example, the physiological effects of nutrients differ depending on individual beliefs about those nutrients.⁶ Likewise, the physical benefits of exercise depend on the degree to which someone perceives a specific physical activity to be “good exercise.”⁷ Studies have shown that believing stress is debilitating for performance or productivity alters cortisol activity and stunts dehydroepiandrosterone response when compared with believing that stress can be enhancing.⁸ And a large cohort study of over 28 000 people found that, after actual levels of stress were controlled for, individuals who believed stress negatively affects health were 43% more likely to die prematurely.⁹

Mindsets do not appear out of nowhere; they are shaped by social context. In medicine these sources include explicit expectations set by the doctor and more subtle social or environmental factors. A review of “open-hidden design” studies found that when medication is administered openly by a physician or healthcare provider who informs a patient they will experience benefit (such as pain relief, reduced blood pressure), it has a significantly greater effect than when it is administered by a hidden machine.¹⁰ These studies show that a doctor’s language matters tremendously,¹¹ but subtle cues like the doctor’s coat and the label, colour, price, and advertising of medication can also make a difference.^{12 13}

The qualities of the patient-provider relationship, like empathy and understanding, can also produce measurable physiological improvements beyond the effects of actual treatment by boosting patient expectations, lowering anxiety, increasing psychological support, and improving patient mood. For example, physician empathy has been associated with better clinical outcomes for patients with diabetes, including better haemoglobin A_{1c} and LDL cholesterol control¹⁴ and fewer instances of acute metabolic complications.¹⁵ Likewise, a randomised trial in patients with new colds found that positive perceptions of physician caring were associated with decreased severity and duration of symptoms accompanied by corresponding changes in interleukin-8 and neutrophil count.¹⁶ The qualities of the physician-patient relationship can affect health both directly by evoking changes in cardiovascular and immune responses and indirectly by improving adherence and reducing demands for unnecessary medical treatment.^{14 15}

Moving forward

Despite the potential benefits of psychological and social forces in healing, they have received much less attention than drugs and devices. Most physicians are enacting these components on a daily basis, but their awareness of this and effectiveness varies. Physicians receive minimal training in how to harness these forces to their patients’ advantage. Beyond accepting these forces as prevalent and critical components of the clinical encounter, other steps are needed to more effectively understand and harness them. We offer the following recommendations for research, education, and health systems.

Research

The science of health psychology is rapidly improving, sharpening our ability to quantify, understand, and operationalise the clinically relevant effects of subjective experiences of mindsets, connection, and trust. We now need interdisciplinary investigations that manipulate psychosocial elements in the context of existing medical practices. Studies using physiological measures as outcomes will enable us to tackle questions such as how can we inform patients of risks or side effects without causing unnecessary harm? How can we create social contexts, relationships imbued with warmth and competence, for people of all races, genders, ages, and backgrounds? What individual and institutional mindsets can help physicians connect with patients while also prioritising self care and reducing burnout? And how can psychological and social forces help prevent serious oversights, medical errors, diagnostic delay, and unnecessary tests and treatments?^{17 18}

Practice and education

At their best, doctors and patients alike are harnessing the forces behind the placebo effect already. But additional training should be developed to highlight the role of psychological and social

forces in healing and provide the skills and knowledge to help medical students and residents harness their personal strengths to connect with diverse patients; shape patient expectations in the midst of uncertain, or threatening, circumstances; and inform patients about the role of psychological and social forces, enabling them to choose optimal mindsets and shape the social context to their advantage.

Healthcare systems

System reform should align with and promote effective use of psychosocial elements in healthcare. A first step is to rethink and reform standards of randomised trials so that they include natural conditions (no placebo treatment) and conditions in which elements of the social context and mindset are present or absent (high or low placebo conditions), allowing researchers to understand how beliefs, labels, and context can help magnify the effect of the drug and treatment. Additionally, it is time to reconsider best practices for informing patients of side effects to avoid making those side effects more likely.

The right systemic incentives and resources must be provided to ensure that lessons instilled in medical training are implemented and measured to prove their efficacy. This should include providing adequate time and incentives for physicians to harness relationships with patients. Coordinated care models, in which patients have a comprehensive healthcare support team, could help leverage patient mindset and the social context by treating the patient holistically. Advances in medical technology should also be harnessed to free doctors’ time to focus on the social context and relationship of the clinical encounter. When implemented effectively, these technological advancements can lead the physician back to the foundational practice of real medicine, which includes providing the personal touch that can never be replaced by technology alone.¹⁹

No stones left unturned

Tackling the future threats to our health and the increasing complexity of non-communicable diseases will require all the tools at our disposal to improve the health and wellbeing of our population. Alongside advances in drug and surgical treatment, 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. We need to open our own minds to that possibility.

Summary points

Mindsets and the social context affect every medical encounter, for better or for worse

The effects of mindsets and the social context are not magical or mysterious

Sophisticated psychological measures and advanced neurobiological technologies enable them to be measured, categorised, and quantified

Understanding and harnessing psychological and social forces in medicine can help optimise the effects of advancing medical treatments and knowledge

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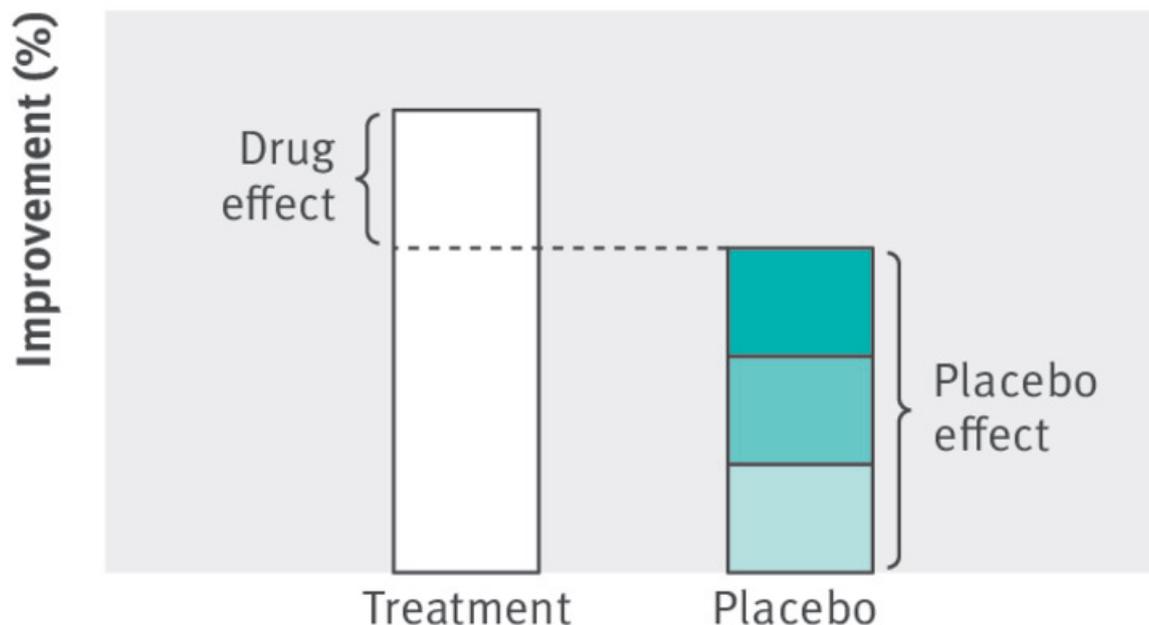
- 1 Price DD, Finniss DG, Benedetti F. A comprehensive review of the placebo effect: recent advances and current thought. *Annu Rev Psychol* 2008;59:565-90. doi:10.1146/annurev.psych.59.113006.09594117550344
- 2 Finniss DG, Kapchuk TJ, Miller F, Benedetti F. Biological, clinical, and ethical advances of placebo effects. *Lancet* 2010;375:686-95. doi:10.1016/S0140-6736(09)61706-220171404
- 3 Espay AJ, Norris MM, Eliassen JC. Placebo effect of medication cost in Parkinson disease: a randomized double-blind study. *Neurology* 2015;84:794-802. doi:10.1212/WNL.000000000000128225632091
- 4 Colloca L, Finniss D. Nocebo effects, patient-clinician communication, and therapeutic outcomes. *JAMA* 2012;307:567-8. doi:10.1001/jama.2012.11522318275
- 5 Amanzio M, Corazzini LL, Vase L, Benedetti F. A systematic review of adverse events in placebo groups of anti-migraine clinical trials. *Pain* 2009;146:261-9. doi:10.1016/j.pain.2009.07.01019781854
- 6 Crum AJ, Corbin WR, Brownell KD, Salovey P. Mind over milkshakes: mindsets, not just nutrients, determine ghrelin response. *Health Psychol* 2011;30:424-9, discussion 430-1. doi:10.1037/a002346721574706
- 7 Crum AJ, Langer EJ. Mind-set matters: exercise and the placebo effect. *Psychol Sci* 2007;18:165-71. doi:10.1111/j.1467-9280.2007.01867.x17425538
- 8 Crum AJ, Salovey P, Achor S. Rethinking stress: the role of mindsets in determining the stress response. *J Pers Soc Psychol* 2013;104:716-33. doi:10.1037/a003120123437923
- 9 Keller A, Litzelman K, Wisk LE. Does the perception that stress affects health matter? The association with health and mortality. *Health Psychol* 2012;31:677-84. doi:10.1037/a002674322201278
- 10 Benedetti F, Maggi G, Lopiano L. Open versus hidden medical treatments: the patient's knowledge about a therapy affects the therapy outcome. *Prev Treat* 2003;6doi:10.1037/1522-3736.6.1.61a.
- 11 Kam-Hansen S, Jakubowski M, Kelley JM. Altered placebo and drug labeling changes the outcome of episodic migraine attacks. *Sci Transl Med* 2014;6:218ra5. doi:10.1126/scitranslmed.300617524401940
- 12 Manios ED, Koroboki EA, Tsigoulis GK. Factors influencing white-coat effect. *Am J Hypertens* 2008;21:153-8. doi:10.1038/ajh.2007.4318174883
- 13 Finkelstein SR, Fishbach A. When healthy food makes you hungry. *J Consum Res* 2010;37:357-67doi:10.1086/652248.
- 14 Hojat M, Louis DZ, Markham FW, Wender R, Rabinowitz C, Gonnella JS. Physicians' empathy and clinical outcomes for diabetic patients. *Acad Med* 2011;86:359-64. doi:10.1097/ACM.0b013e3182086fe121248604
- 15 Del Canale S, Louis DZ, Maio V. The relationship between physician empathy and disease complications: an empirical study of primary care physicians and their diabetic patients in Parma, Italy. *Acad Med* 2012;87:1243-9. doi:10.1097/ACM.0b013e3182628bf22836852
- 16 Rakei DP, Hoefl TJ, Barrett BP, Chewning BA, Craig BM, Niu M. Practitioner empathy and the duration of the common cold. *Fam Med* 2009;41:494-501.19582635
- 17 Verghese A, Brady E, Kapur CC, Horwitz RI. The bedside evaluation: ritual and reason. *Ann Intern Med* 2011;155:550-3. doi:10.7326/0003-4819-155-8-201110180-0001322007047
- 18 Verghese A, Charlton B, Kassirer JP, Ramsey M, Ioannidis JP. Inadequacies of physical examination as a cause of medical errors and adverse events: a collection of vignettes. *Am J Med* 2015;128:1322-4.e3. doi:10.1016/j.amjmed.2015.06.00426144103
- 19 Elder A, Chi J, Ozdalga E, Kugler J, Verghese A. A piece of my mind. The road back to the bedside. *JAMA* 2013;310:799-800. doi:10.1001/jama.2013.22719523982364

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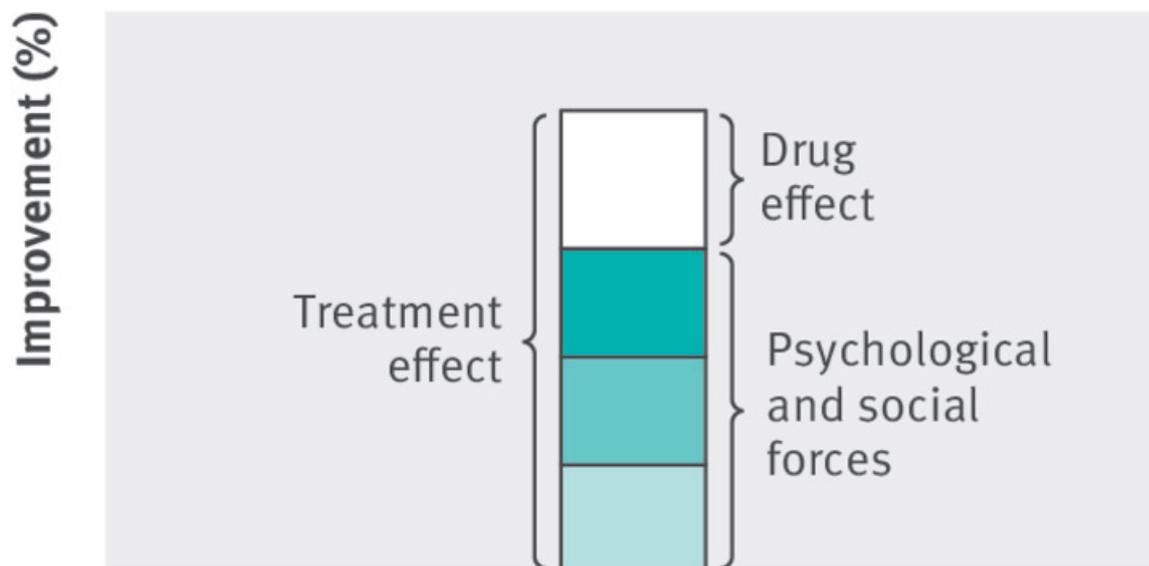
Figure

- Body’s natural healing abilities
- Mindset
- Social context

Randomised controlled trial



Everyday practice



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). Relative percentages of placebo response and drug responses vary across drugs and conditions

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