IAN MACKEY

To treat pain, study people in all their complexity

Clinical research needs to investigate not simply drugs, but the psychology of why and how individuals experience pain, says **Beth Darnall**.

Last month, the US National Institutes of Health (NIH) formally launched a multi-agency effort to combat the country's opioid-addiction crisis. Funds for research into controlling opioid misuse and treating pain will nearly double in 2018, to US$1.1 billion.

The forces behind this epidemic extend beyond overprescription: most of the tens of thousands of deaths caused by opioid overdose in the United States each year result from illicit use. Still, an inadequate understanding about how to treat pain has certainly contributed. We need to characterize patients better, and we need more studies that incorporate non-drug treatments alongside any form of medication.

Consider this crucial question: what is the first treatment you should give a person for chronic pain, or even many acute injuries? Most clinicians now agree that the answer should not be opioids. Fewer recognize that the question is not which pill to use instead, but what system of interventions — including medication — and monitoring to implement.

Too often, pain is treated as a purely biomedical problem. It is a biopsychosocial condition. Psychological treatment can be combined with medication to equip people with the tools to better control their pain experience. Psychological therapies can also lower risks such as addiction, because the emphasis is on engaging patients in managing their daily actions to help themselves to feel better in the long run, rather than relying solely on passive medications. Yet a common clinical practice is to recommend such psychosocial strategies for pain only after all medications have failed.

It is hard for clinicians to learn which treatments to use, because our research system shuns the very patients we need to understand. Pain-research trials often exclude adults who have depression, anxiety and other disorders, those who take other prescription medications and those over the age of 70, who tend to have multiple co-morbities.

To treat pain better, we should attend to these complex patients, rather than exclude them. One effort to do so is the Collaborative Health Outcomes Information Registry, or CHOIR (http://choir.stanford.edu), which my colleagues developed with NIH support. The platform collects data on the patients we personally see in our pain clinic every day: their age and sex; how they are sleeping; how pain affects their daily routine; their mobility, strength and endurance; how they engage with friends and family; which other medications they take; what other diagnoses they have. It also tracks treatments and responses over time. Clinicians can easily follow their own patients' progress, and the system can be programmed to recommend tailored treatments or patient education.

Researchers can look for patterns among groups of patients. For example, several studies suggest that most people taking opioids long-term do not benefit from them (see go.nature.com/2vylvkp). However, almost all clinicians who treat chronic pain observe that some people do quite well on opioids. We need to be able to predict who those individuals are. Otherwise, we are either going to exclude people from a treatment that benefits them or expose them to a risky medication.

We know, for instance, that people who worry more about pain, or who report feeling helpless in the face of it, are at risk of prolonged pain and opioid use after surgery (M. M. Wertli *et al. Spine* **39**, 263–273; 2014). My colleagues and I are currently assessing whether an online education app can help patients to manage their worries, decrease pain and limit opioid use after surgery.

More such pragmatic clinical trials are needed. So are accessible tools, such as CHOIR, to implement these trials. We are currently building a CHOIR network across the United States, Canada and Israel to integrate data and answer questions about which of several commonly used pain treatments works best, and in which individuals. Ideally, we will then use the results of these trials to inform clinicians continuously about the most safe and effective treatment to prescribe for their patients.

And we need to study how placebo effects could enhance pain treatment, by deliberately integrating them into clinical trials. I am not talking about sugar pills, but about a strategy called placebo optimization. Simple pain-science education, cognitive regulation and relaxation skills can help empower patients to reduce pain processing in the brain, gain better control over their symptoms and garner more benefit from medical treatments.

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Patients can actually be primed for relief. For instance, placebo optimization could involve emphasizing to patients that we have evidence suggesting that various treatment plans — such as gently tapering opioid dosing — can be done without increased pain. Clinicians also need strategies for detecting and minimizing 'nocebo' effects: in this case, negative expectations and fears about pain that can undermine the effectiveness of medical treatment.

We need to incorporate psychology and complexities into clinical trials and medical care. More funding for treating opioid addiction and misuse is welcome. But essential, too, are funds for investigating pain as a condition in itself.

In 2016, the Institute of Medicine estimated that up to one-third of the US population lives with ongoing pain. Chronic pain, the main cause of disability, is more prevalent than diabetes or heart disease. It costs the US economy up to $630 billion every year in health care and lost productivity, and lowers the quality of too many lives. Although precise numbers are hard to come by, NIH spending breakdowns show that the agency committed just over $500 million in 2017 to broad pain research. Finding better ways of treating pain is surely worth a greater investment. ∎

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