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## The void in opioid research

The National Institutes of Health's plans to tackle the opioid epidemic in the United States can treat only the symptoms, not the cause.

Alls for urgent action on the opioid crisis in the United States have been coming thick and fast. So, too, have the possible solutions: Congress is currently considering 57 opioid-related bills. This comes after President Donald Trump declared the crisis a public-health emergency last year. No one would dispute that. In 2016, more than 53,000 people in the United States died from an opioid overdose — more than double the figure in 2010 — and the increasing use, misuse and abuse of heroin, fentanyl and other opiates, including prescription drugs, shows no signs of slowing.

Action is needed — but what? The problem is that nobody can agree on possible solutions. Indeed, some of the proposals passing before Congress this week have conflicting intentions on matters such as how best to implement addiction treatment. Only rigorous research and evidence can steer this debate and identify the most effective ways to intervene. Yet, so far, a series of White House commissions has done little but talk.

Congress did, at least, start to put real money towards the issue this year — a total of US\$4.6 billion, including an extra \$500 million for research at the US National Institutes of Health (NIH). And this month, NIH director Francis Collins and colleagues laid out their plans to spend this latter windfall (F. S. Collins *et al. J. Am. Med. Assoc.* http://doi.org/cq38; 2018).

The agency's initiative is called Helping to End Addiction Longterm (HEAL) and divides its research strategy into two prongs: improving treatments for addiction and overdose, and improving pain management. The plan could have great value, but unfortunately it includes some questionable priorities.

On the positive side, the NIH plans to spend nearly 20% of HEAL funding on an initiative to test public-health interventions — such as better screening for addiction — through partnerships with emergency departments, justice systems and other sectors. It will spend \$10 million on developing and improving therapies for babies who are born addicted to opioids, and about \$29 million on expanding and improving its network of clinical trials for various therapies. A little under half of the money will be carried forward to the next financial year, to be used for praiseworthy programmes including prevention research, precision medicine for pain and addiction, and non-pharmacological and integrated models of pain management.

All good. Yet a great deal of the money will go towards drug development — and that's a less essential investment. The NIH would be better served by determining how best to deploy existing treatments, instead of spending years on expensive efforts to develop new ones. Current overdose-reversal drugs, such as naloxone, work extremely well, although access in an overdose situation remains a problem. Non-addictive painkillers such as paracetamol and ibuprofen can, in certain combinations, be as effective as opioids for some kinds of pain, but there is great need for improved scientific understanding, particularly of chronic pain.

Meanwhile, some ethicists have criticized the NIH's agenda as overly friendly to the pharmaceutical industry. Many critics argue that the

industry had a major role in starting the epidemic in the first place, by promoting drugs such as OxyContin (oxycodone) as non-addictive. To its credit, the NIH has stepped back from its initial plan for HEAL, which involved a direct partnership with industry, combining public and private money to fund drug development. In 2017, the agency held a series of closed-door meetings with the Food and Drug Administration and dozens of pharmaceutical companies, including representatives from opioid manufacturers Purdue Pharma of Stamford, Connecticut, and Janssen, headquartered in Beerse, Belgium. Both companies are facing multiple lawsuits from US states for deceptive marketing and hiding reports of adverse events. (In an interview with *Nature* last month, Collins said that he had invited industry repre-

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sentatives because "we may as well hear what the various companies had to offer in terms of ways to address this public-health crisis".)

The NIH reversed course this April, on the advice of an ethics committee that recommended the agency refrain from taking cash from industry partners. That advice came

soon after revelations that NIH-funded researchers and employees convening a study on whether alcohol could improve health had courted funding from the alcohol industry — a practice forbidden by NIH policy. On 15 June, the agency announced that it had terminated the study.

The NIH's revised plan for HEAL will fund opioid research exclusively with federal money, and will involve industry partners only in setting up a clinical-trial network for drug testing and a system for sharing biomarkers. The agency will not partner with companies involved in litigation related to the opioid crisis. However, any industry relationship still has potential for a conflict of interest or undue influence. Transparency over those relationships — and continued federal funding — will be key to avoiding that. Pharmaceutical companies, meanwhile, should do their part by participating fully in HEAL research and by sharing data openly.

Even at their best, the NIH's findings will be able only to alleviate the symptoms of the opioid epidemic — helping people who are already addicted. What they cannot do is tackle its roots, which are a complex tangle of social and political issues including economic disparities, lack of access to comprehensive health care and mental-health services, outdated policies banning evidence-based initiatives such as local safe-injection facilities, a proliferation of deadly synthetic drugs and poor prescribing practices by physicians.

Curing the opioid epidemic requires funding, new public-health initiatives and enforcement of policies that address these problems. Drug overdose is now the leading cause of death for under-50s in the United States. With just 4% of the world's population, the country accounts for around 27% of all global overdose deaths. No matter how many new drugs are developed, only evidence-based policy — and the political will to enforce it — can begin to prevent this modern tragedy from spiralling further out of control.