Millions take antidepressants for chronic pain—but there's little evidence the most commonly prescribed drugs work

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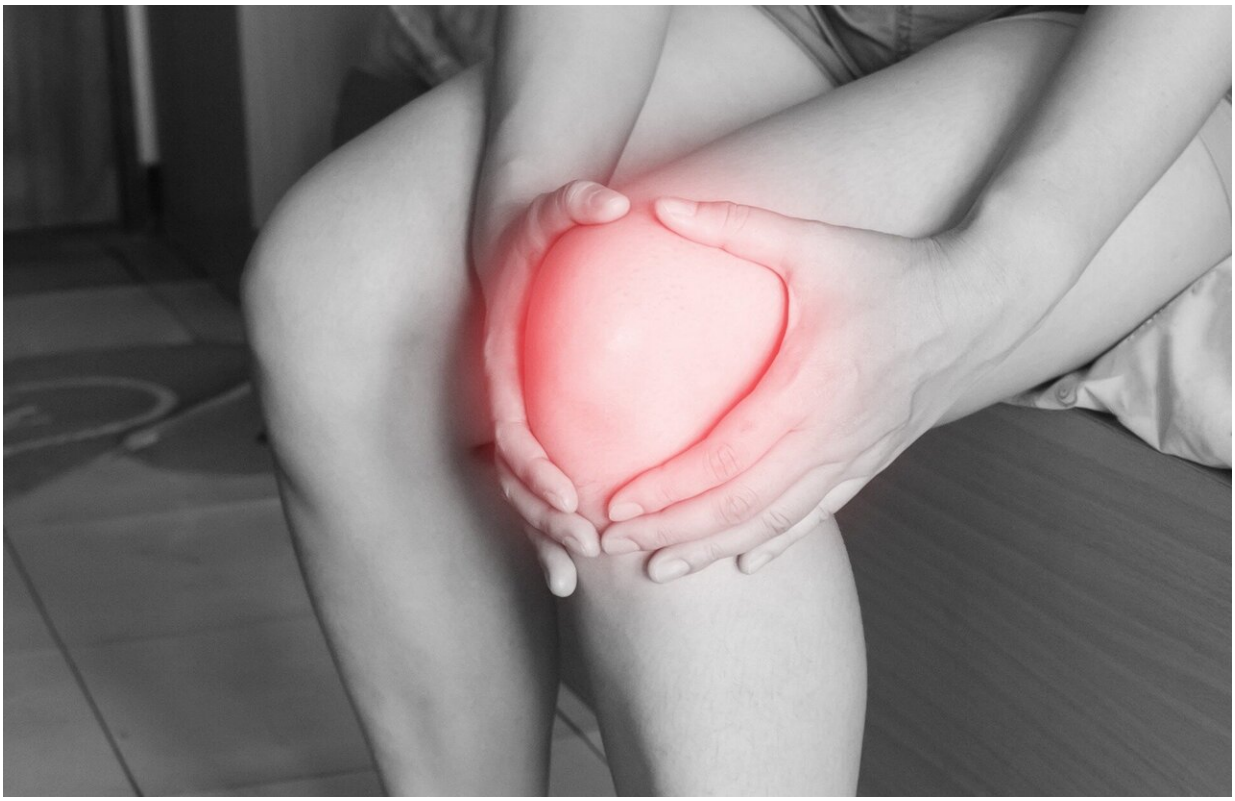

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About 1 in 5 people globally live with chronic pain, and it is a common reason for seeing a doctor, accounting for one in five GP appointments in the UK.

With growing caution around prescribing opioids—given their potential for addiction—many doctors are looking to prescribe other drugs, "off-label," to treat long-term pain. A popular option is antidepressants.

In the UK, doctors can prescribe the following antidepressants for "chronic primary pain" (pain without a known underlying cause): amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine and sertraline. Amitriptyline and duloxetine are also recommended for nerve pain, such as sciatica.

However, our review of studies investigating the effectiveness of antidepressants at treating chronic pain found that there is only evidence for one of these drugs: duloxetine.

We found 178 relevant studies with a total of 28,664 participants. It is the largest-ever review of antidepressants for chronic pain and the first to include all antidepressants for all types of chronic pain.

Forty-three of the studies (11,608 people) investigated duloxetine. We found that it moderately reduces pain and improves mobility. It is the only antidepressant that we are certain has an effect. We also found that a 60mg dose of duloxetine was equally effective in providing pain relief as a 120mg dose.

In comparison, while 43 studies also investigated amitriptyline, the total number of participants was only 3,372, indicating that most of these studies are very small and susceptible to biased results.

The number of studies and participants for the other antidepressants are:

- Citalopram: five studies with 209 participants
- Fluoxetine: 11 studies with 622 participants
- Paroxetine: nine studies with 960 participants
- Sertraline: three studies with 210 participants.

The evidence for amitriptyline, citalopram, fluoxetine, paroxetine and sertraline was very poor, and no conclusions could be drawn about their ability to relieve pain.

This is particularly important as prescribing data shows 15,784,225 prescriptions of amitriptyline in the last year. It is reasonable to assume that a large proportion of these may be for pain relief because amitriptyline is no longer recommended for treating depression.

This suggests that millions of people may be taking an antidepressant to treat pain even though there is no evidence for its usefulness. In comparison, 3,973,129 duloxetine prescriptions were issued during the same period, for a mixture of depression and pain.

In light of our findings, which were published in May 2023, the UK's National Institute for Health and Care Excellence (Nice) recently updated its advice to doctors on how to treat chronic pain.

The updated Nice guidance now suggests 60mg of duloxetine to treat [chronic primary pain] and the same drug and dose to treat nerve pain.

Limited treatment options

GPs often report frustration at the limited options available to them to treat patients experiencing chronic pain. Amitriptyline is cheap to prescribe—only 66p per pack—which may explain the high number of

prescriptions for this drug.

This is an example of how the gap between evidence and clinical practice could harm patients. Although our review was unable to establish the long-term safety of antidepressant use, previous research has highlighted the high rates of side-effects for amitriptyline, including dizziness, nausea, headaches and constipation.

It's important to bear in mind, though, that pain is a very individual experience, and the evidence in our review is based on groups of people. We acknowledge that certain drugs may work for people even when the research evidence is inconclusive or unavailable. If you have any concerns about your pain medication, you should discuss this with your doctor.