

Painkillers don't work as well for women. Here's why.

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Pain is one of the oldest complaints in medical history, and for millennia, treatments have been administered with a one-size-fits-all approach. It wasn't until recently that experts officially acknowledged one radical truth: Women experience pain differently than men, and by default, they don't respond to treatments as well.

Research shows that girls, women, and people assigned female at birth feel more severe pain than men, and are more likely to experience chronic conditions such as migraine, irritable bowel syndrome, fibromyalgia, and osteoarthritis. Yet, doctors are more likely to dismiss or ignore them, which leads to delays in treatment that exacerbate their pain.

At the same time, several studies show that over-the-counter and prescription painkillers like ibuprofen, steroids, and opioids aren't as effective in women compared to men. And the truth is, experts *still* don't understand why, says Elizabeth Losin, a neuroscientist who studies sex

differences in pain response and perception.

Before 1993, researchers were not required to include women in clinical research funded by the National Institutes of Health, the largest public funder of clinical trials in the U.S. This was based on the notion that women's menstrual cycles would skew test results and the fear of harming a potential pregnancy. Instead, researchers assumed that if a drug was safe and effective in men, it would be in women too.

But that couldn't be further from the truth. "The bottom line is that we don't know as much about women's biology and how it relates to pain as we could and should," says Losin, a Bennett Pierce Associate Professor in Caring and Compassion in Adulthood and Aging at Penn State University.

Still, scientists are developing some theories about why women experience pain differently and how that limits their treatment options.

Why pain medications aren't as effective for women

Most theories on why some pain medications fall short in women involve sex hormones, says Kiran Patel, an anesthesiologist and pain management physician with Northwell Health in New York City.

Estrogen, which women produce more of than men, slows stomach emptying, increases body-fat ratio, and reduces the amount of certain drug-binding proteins in blood plasma—all of which research shows affects how medications are distributed and broken down in the body.

Women's immune systems are also more active compared to men's partly because of their sex hormones. As a result, women have greater inflammatory responses that could explain why they use prescribed painkillers more often and need higher doses that they take for longer periods than men.

Two types of anti-inflammatory drugs called glucocorticosteroids and NSAIDs, for example, appear to offer men more pain relief than women, according to research.

Studies have also found sex-related differences in response to opioids, says Amy Baxter, a former pediatric emergency physician and pain researcher who founded Pain Care Labs.

Some have suggested that women have fewer mu-opioid receptors, the main protein that binds to opioids and regulates pain. This implies that women could "need more opioids to get the same bang for their buck to overload their pain," Baxter says. But the jury is still out on this theory because evidence is conflicting—some studies have found no difference in doses for women using opioids and still others have suggested they require lower doses.

Why women have more side effects from pain meds

Because women have historically been excluded from clinical trials, many available drugs have unknown side effects and safety risks for this half of the population.

A 2020 [study](#) found major sex differences in how the body breaks down 86 different drugs, including morphine and prednisone. Women metabolized nearly all of them more slowly than men, which led to higher concentrations of the drugs in their blood and more adverse side effects, including nausea, headaches, seizures, and hallucinations.

Side effects from certain drugs are sometimes so severe that women refuse to take higher doses, Patel says, or quit their medication altogether.

In serious cases, drugs have been discontinued to protect women from further harm. Between 1997 and 2001, the Food and Drug Administration [withdrew 10 prescription drugs](#) from the U.S. market—eight of which were pulled because they posed greater health risks for women, according to a 2001 [report](#) by the U.S. Government Accountability Office.

The drug Posicor, for example, which was approved to treat angina and high blood pressure, was found to slow or stop the heart rate of healthy people, particularly older women. Two antihistamines sold under the brand names Seldane and Hismanal were removed because they increased the risk of a potentially fatal heart arrhythmia in women.

Patel says the data reflects what she sees in her clinic and underscores the need to dose men and women differently to avoid unnecessary side effects.

The consequences of untreated pain

Women who can't get the pain relief they need may suffer lifelong consequences. For one, their injury or condition is more likely to worsen, extending their recovery time and boosting the odds they develop complications from procedures, Patel says. Meanwhile, daily tasks like work, laundry, or tending to children become extremely difficult to impossible to accomplish.

It doesn't help that women "have more responsibilities that are non-negotiable," Baxter says. For instance, [a 2019 Gallup poll](#) found that women in heterosexual relationships were more likely to cook, clean, do laundry, wash dishes, grocery shop, and care for children on a daily basis. "If you're a male in pain, it's a lot easier in society to [relax]. But the female existence means there's no way to opt out...and that could contribute to our pain perception."

"And so for women, being disabled is a bigger issue," Baxter adds.

Over time, acute pain can morph into the chronic kind, Patel says. For some people, this might look like anxiety or depression; for others, it could be substance abuse in a last-ditch effort to self-medicate.

And when addictive opioids are involved, the stakes are higher, Baxter says.

“Because women have some degree of reward deficiency, they’re more prone to addiction and opioid overdose,” Baxter says. “So when women start misusing opioids, the amount they use increases faster, and they have more cravings.”

Women are also thought to have lower tolerance to opioids because of differences in body mass and metabolism. So they can overdose and develop a dependence on smaller amounts of the drug.

The data are sobering. Although more men die from prescription opioid overdoses than women per year, deaths among women have increased 642 percent since 1999 compared with 439 percent among men, according to the NIH.

The future of pain relief for women?

Experts say much more work is needed to improve transparency within clinical trials so that women can have safe and effective pain relief options.

But there has been some improvement. For example, researchers are trying to identify biomarkers that could quantify women’s pain and speed the development of new treatments.

In the meantime, self-advocacy is key for women dealing with pain, Losin says.

“When we interact with our medical system, we have to really advocate for ourselves because it doesn’t necessarily happen on its own,” she says. “Not that it should be our responsibility, but the more research you can do ahead of time to participate more actively in your care, the better off you’ll be.”