Two of the world's most widely used painkillers—ibuprofen and acetaminophen (paracetamol)—may be worsening one of the greatest threats to global health: antibiotic resistance.

A new study from the University of South Australia, published in *npj Antimicrobials and Resistance*, found that the everyday drugs not only relieve pain and fever but can also accelerate bacterial resistance to antibiotics.

Researchers discovered that when ibuprofen and acetaminophen were taken alongside ciprofloxacin, a broad-spectrum antibiotic, *Escherichia coli* bacteria developed more genetic mutations than with the antibiotic alone. The mutations helped the bacteria grow faster and resist not only ciprofloxacin but also several other classes of antibiotics.

Even more concerning, the effect was amplified when the two painkillers were used together.

"This shows the problem of antibiotic resistance is even more complex than we thought," said lead researcher Associate Professor Rietie Venter. "We found that both ibuprofen and acetaminophen activate bacterial defense systems, helping microbes pump out antibiotics before they can work."

The findings have serious implications for older adults in residential care, where multiple medications are often prescribed. Painkillers, sleep aids, blood pressure and diabetes drugs are commonly given alongside antibiotics, creating an environment where gut bacteria can adapt and become resistant.

Antibiotic resistance already kills an estimated 1.27 million people worldwide each year, according to the World Health Organization, which has called it one of the greatest threats to human health. Overuse and misuse of antibiotics have long fueled the problem, but this study suggests non-antibiotic drugs may also play a role.

The team also examined other medications often used in aged care, including diclofenac, furosemide, metformin, atorvastatin, tramadol, temazepam, and pseudoephedrine. While the most striking effects were linked to ibuprofen and acetaminophen, the findings suggest other common drugs could influence how bacteria respond to antibiotics.

The researchers caution that patients should not stop taking painkillers, but they urge doctors to be more mindful of how medications are combined, particularly in vulnerable groups.

“Antibiotics have saved millions of lives, but if bacteria keep finding ways to resist them, we could return to a time when simple infections were deadly,” Venter said.

The study calls for further investigation into how widely used medications interact with antibiotics, underscoring the need for safer prescribing practices in the fight against resistance.