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Supplements Fail to Stop Arthritis Pain, Study Says

By [GINA KOLATA](#)

Correction Appended

Two widely used nutritional supplements for [arthritis](#) pain do not effectively soothe patients' aching arthritic knees, a large federal study has found.

The study of the two drugs, glucosamine and chondroitin sulfate, was published today in The New England Journal of Medicine. The study was meant to provide a definitive answer to a question that has baffled doctors and patients alike: do these supplements work?

Americans spent an estimated \$734 million on glucosamine and chondroitin in 2004, according to The [Nutrition](#) Business Journal, making them among the most widely used [dietary supplements](#) in the nation. The two, which are produced by numerous companies, are often sold in combination as a treatment for arthritis.

In the 24-week study, 1,583 patients with osteoarthritis of the knee were randomly assigned to one of five groups. Some patients took glucosamine, some took chondroitin and some took both. Others, serving as comparison subjects, took a placebo or celecoxib, sold as Celebrex, a prescription drug that is approved for osteoarthritis.

No effect was found for glucosamine, chondroitin or a combination of the two. But the study found that the patients who took celecoxib had a statistically significant improvement in their symptoms.

Although the new study found no overall effect for the supplements, the authors and some other medical researchers said that an analysis of a subgroup of patients provided hope — although not definitive evidence — that the supplements taken together might help some people with more severe pain.

"Patients who had more pain did seem to be helped by the combination," said Dr. Daniel O. Clegg, a researcher at the University of Utah School of Medicine who was the lead author of the study.

But Dr. Clegg hastened to add that this observation would have to be confirmed in later studies.

Dr. Marc C. Hochberg, the head of the division of rheumatology and clinical immunology at the University of Maryland, said it was also possible that another type of glucosamine might be effective.

The study used glucosamine hydrochloride because it was the only type that could be manufactured at the time in a sufficiently pure form. In Europe, where glucosamine and chondroitin are sold as drugs, glucosamine comes in the form of glucosamine sulfate, Dr. Hochberg said, and some industry-supported studies have indicated that this form helps.

But others said there was no reason to expect that glucosamine sulfate would be any different from glucosamine hydrochloride. They said they viewed the study's finding that the supplements had no benefit as persuasive.

"It's a null trial," said Dr. David Felson, a rheumatologist at Boston University. "It doesn't work any better than placebo."

Because the supplements are so popular, the results of the trial had been eagerly awaited.

"We've been talking about the importance of this study for the last two or three years," said Dr. John Klippel, president and chief executive of the Arthritis Foundation.

"When people have been asking about glucosamine and chondroitin, we tell them this is the most important study ever done," Dr. Klippel said. "It has a very large number of patients and it is scientifically rigorous."

Previous studies had methodological flaws, and their results were contradictory. A handful of publicly financed trials showed no effect, Dr. Felson and others said. Other studies, financed by supplement makers, "were impressively positive," Dr. Felson said.

Dr. Clegg said the new study, financed by the National Center for Complementary and Alternative Medicine and the National Institute of Arthritis and Musculoskeletal and Skin Diseases, arose after an expert panel in 1998 concluded that "there is a real and urgent public health need to test these agents in a rigorous way."

Glucosamine and chondroitin are substances found naturally in joints, leading some to suggest that they might be helpful for arthritis patients. Glucosamine is a modified sugar that is thought to play a role in the formation and repair of cartilage, and chondroitin is part of a large protein, proteoglycan, that provides elasticity to cartilage.

But, arthritis researchers say, they know of no biological reason why eating those compounds would help people with arthritis.

Dr. Tim McAlindon, chief of rheumatology at Tufts-New England Medical Center in Boston, said that glucosamine traveled to the liver, which then broke it down. Almost no glucosamine that is eaten actually gets into the blood, where it can travel to the joints, Dr. McAlindon said, adding, "The amount that gets beyond the liver is minuscule."

Chondroitin, a large molecule, is digested, Dr. McAlindon said, but it is broken into pieces in the intestines and none of it gets through intact to the joints.

Still, many arthritis patients swear by the supplements, which cost \$30 to \$50 a month, said Dr. Andrew Shao, vice president for scientific and regulatory affairs at the Council for Responsible Nutrition, a trade association for the dietary supplement industry.

Dr. Stephen E. Straus, director of the National Center for Complementary and Alternative Medicine, a sponsor of the new study, said a national survey in 2002 found that about 5.2 million Americans had used one or both supplements in the preceding year. Dr. Straus noted that arthritis joint pain and stiffness were among the leading reasons for seeking alternative medical treatments.

Glucosamine and chondroitin are also marketed for pets — dogs and horses in particular — and veterinarians routinely prescribe them for arthritic animals.

Nancy MacLeod, 65, an administrative assistant who works in Manhattan, said that as far as she was concerned, the supplements worked.

"The difference is like walking on a spike and having padding in your knee," Ms. MacLeod said. "The medical profession says that can't happen, but I'm not in pain and I take no other drugs."

Despite the study's findings, she said, "I'm going to continue doing it."

The study found that in a subgroup, consisting of patients with moderate-to-severe knee pain, 79 percent of those who took the supplements together improved compared with 54 percent of those who took a placebo.

Such findings are viewed by most researchers as fodder for further studies but not as rigorous evidence in themselves, because they can be caused by random fluctuations in data and tend not to be confirmed in subsequent studies.

Some experts, however, said they thought the finding in the subgroup was likely to be real.

"Our take on this study is that it did find that the combination relieved pain in people who have moderate-to-severe pain," said Dr. Klippel of the Arthritis Foundation.

M. Elizabeth Halloran, a biostatistics professor at the Fred Hutchinson [Cancer](#) Research Center and the University of Washington in Seattle, who had no association with the study, also thought there was an effect.

Dr. Halloran said she was swayed not only by the data but also by her sister's experience giving the supplements to her arthritic dog.

"If I had severe pain from osteoarthritis of the knee, based on this study, I would try glucosamine and chondroitin sulfate," Dr. Halloran said.

But Donald Berry, chairman of the department of biostatistics at M. D. Anderson Cancer Center, in Houston, who had no association with the study, said he was completely unconvinced by the subgroup finding.

"This is a spurious subset result if I've ever seen one," Dr. Berry said. "I wouldn't spend a nickel trying to confirm it."

Correction: Feb. 24, 2006

Because of an editing error, an article yesterday about a study of the effectiveness of glucosamine and chondroitin sulfate to ease arthritis pain referred to them incorrectly. They are dietary supplements, not drugs.

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