A network meta-analysis was published in The Lancet May 2016 regarding effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of pain in knee and hip osteoarthritis. For this network meta-analysis, the researchers considered randomized trials comparing any of the following interventions: NSAIDs, paracetamol, or placebo, for the treatment of osteoarthritis pain. They searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the reference lists of relevant articles for trials published between Jan 1, 1980, and Feb 24, 2015, with at least 100 patients per group. The prespecified primary and secondary outcomes were pain and physical function, and were extracted in duplicate for up to seven time points after the start of treatment. The researchers identified 8973 manuscripts from the search, of which 74 randomised trials with a total of 58 556 patients were included in this analysis. Twenty-three nodes concerning seven different NSAIDs or paracetamol with specific daily dose of administration or placebo were considered. All preparations, irrespective of dose, improved point estimates of pain symptoms when compared with placebo. For six interventions (diclofenac 150 mg/day, etoricoxib 30 mg/day, 60 mg/day, and 90 mg/day, and rofecoxib 25 mg/day and 50 mg/day), the probability that the difference to placebo is at or below a prespecified minimum clinically important effect for pain reduction (effect size [ES] −0.37) was at least 95%. Among maximally approved daily doses, diclofenac 150 mg/day (ES −0.57, 95% credibility interval [CI] −0.69 to −0.46) and etoricoxib 60 mg/day (ES −0.58, −0.73 to −0.43) had the highest probability to be the best intervention, both with 100% probability to reach the minimum clinically important difference. Treatment effects increased as drug dose increased, but corresponding tests for a linear dose effect were significant only for celecoxib (P = 0.030), diclofenac (P = 0.031), and naproxen (P = 0.026). They found no evidence that treatment effects varied over the duration of treatment. Model fit was good, and between-trial heterogeneity and inconsistency were low in all analyses. All trials were deemed to have a low risk of bias for blinding of patients. Effect estimates did not change in sensitivity analyses with two additional statistical models and accounting for methodological quality criteria in meta-regression analysis. On the basis of the available data, no role of Paracetamol was found irrespective of dose. The researchers provide sound evidence that diclofenac 150 mg/day is the most effective NSAID available at present, in terms of improving both pain and function. Nevertheless, in view of the safety profile of these drugs, physicians need to consider their results together with all known safety information when selecting the preparation and dose for individual patients.

Non Steroidal Anti Inflammatory Drugs have shown great promise in preventing cancers including colon, esophagus and skin. However, they can increase the risks of heart attacks, ulcers and rare but potentially life-threatening bleeding. A new study suggests there may be ways to reduce these dangerous side effects. Collaborators from the University of Michigan, the National Cancer Institute and the University of Alabama looked at naproxen, which is known to have a lower cardiovascular risk than other NSAIDs. Naproxen, like most NSAIDs and aspirin, does increase the risk for gastric ulcers or bleeding. Here, the researchers used the proton pump inhibitor omeprazole, a commonly used acid inhibitor, in combination with naproxen and tested its effects on cancer prevention in a rat model of bladder cancer. They found that naproxen reduced the incidence of bladder cancer by 75 percent in rats. Omeprazole by itself did not affect the development of cancer but it also did not interfere with the effect of naproxen at preventing tumors. The rats who received naproxen alone or naproxen with omeprazole developed cancer at similarly low rates, while all rats receiving omeprazole alone or no treatment developed bladder cancer. Clinical data in humans has previously shown combining omeprazole plus naproxen reduced gastric toxicity roughly 70 percent. The authors also found that intermittent dosing with naproxen (three weeks on the drugs, followed by three weeks off) was highly effective and likely to reduce gastric toxicity. "Our study shows that naproxen works just as well with a proton pump inhibitor as without. This provides proof of principle that this could be a valuable cancer prevention strategy and one hopes it can advance quickly to a clinical trial for those at high risk of colon, esophageal, squamous cell skin cancer or potentially other cancers," says lead study author Ronald A. Lubet, Ph.D., a scientist with the Chemopreventive Agent Development Research Group at the National Cancer Institute. The current study is published in the American Association for Cancer Research Journal Cancer Prevention Research. "Naproxen is a great candidate for chemoprevention. It comes with a risk of gastrointestinal side effects, but if you can mitigate that with a co-prescription, it's possibly an ideal chemoprevention drug," says study author James Scheiman, M.D., professor of gastroenterology at the University of Michigan Medical School. The combination of naproxen plus a proton pump inhibitor has already been used in people with arthritis. Naproxen and omeprazole are both available over the counter.
Fibromyalgia has Central Nervous System Origins

Fibromyalgia is the second most common rheumatic disorder behind osteoarthritis and, though still widely misunderstood, is now considered to be a lifelong central nervous system disorder, which is responsible for amplified pain that shoots through the body in those who suffer from it. Daniel Clauw, M.D., professor of anesthesiology, University of Michigan, analyzed the neurological basis for fibromyalgia in a plenary session address at the American Pain Society annual scientific meeting. "Fibromyalgia can be thought of both as a discreet disease and also as a final common pathway of pain centralization and chronification. Most people with this condition have lifelong histories of chronic pain throughout their bodies," said Clauw. "The condition can be hard to diagnose if one isn't familiar with classic symptoms because there isn't a single cause and no outward signs." Clauw explained that fibromyalgia pain comes more from the brain and spinal cord than from areas of the body in which someone may experience peripheral pain. The condition is believed to be associated with disturbances in how the brain processes pain and other sensory information. He said physicians should suspect fibromyalgia in patients with multifocal (mostly musculoskeletal) pain that is not fully explained by injury or inflammation. "This does not imply that peripheral nociceptive input does not contribute to pain experienced by fibromyalgia patients, but they do feel more pain than normally would be expected from the degree of peripheral input. Persons with fibromyalgia and other pain states characterized by sensitization will experience pain from what those without the condition would describe as touch," Clauw added. Due to the central nervous system origins of fibromyalgia pain, Clauw advises clinicians to integrate pharmacological treatments, such as gabapentinoids, tricyclics and serotonin reuptake inhibitors, with nonpharmacological approaches like cognitive behavioral therapy, exercise and stress reduction. "Sometimes the magnitude of treatment response for simple and inexpensive non-drug therapies exceeds that for pharmaceuticals," said Clauw. "The greatest benefit is improved function, which should be the main treatment goal for any chronic pain condition. The majority of patients with fibromyalgia can see improvement in their symptoms and lead normal lives with the right medications and extensive use of non-drug therapies."

Pregabalin Significantly Improves Fibromyalgia Pain in Patients Who Also Suffer from Depression

Pregabalin can significantly improve fibromyalgia pain in people who also are being treated for depression, according to research presented at the American College of Rheumatology annual scientific meeting in San Diego. Fibromyalgia is a common health problem that causes widespread pain and tenderness (sensitive to touch). "Depression is common in patients with fibromyalgia," explains Lesley M. Arnold, MD; professor of psychiatry and behavioral neuroscience; University of Cincinnati College of Medicine, Cincinnati, Ohio; and lead investigator in the study. "Many patients present to their doctor for treatment of fibromyalgia pain already taking antidepressants for their depression. This is the first study to evaluate the efficacy and safety of pregabalin for treatment of fibromyalgia pain in patients who are also taking antidepressants for depression." With this in mind, researchers completed a study to determine if pregabalin would affect pain levels in people with fibromyalgia who were also being treated for depression. The study included 197 patients who were, on average, 50 years of age and overwhelmingly white females. To join the study, patients had to meet the 1990 American College of Rheumatology criteria for fibromyalgia (including manual tender point exam), have an average pain level of at least four out of 10 on the numeric rating scale, (0 = no pain and 10 = worst possible pain), have a documented diagnosis of depression and be taking stable dose of an antidepressant medication – either a selective serotonin reuptake inhibitor or a serotonin-norepinephrine reuptake inhibitor. The antidepressant treatment was continued throughout the study. Patients were on study treatment for a total of 14 weeks. There were two six-week treatment periods when patients received either pregabalin or placebo, with a two-week break in between these periods. Each patient was randomly assigned to receive either pregabalin in the first six weeks, then placebo in the last six weeks, or to receive placebo first, then pregabalin. None of the patients knew which treatment they were receiving at any point in the study. Pregabalin was started at a dose of 150mg per day and within three weeks was increased to 300-450mg per day based on patient response; this dose was continued for the rest of the treatment period. During the study, 193 patients received at least one dose of study medication; 181 patients received at least one dose of pregabalin, and 177 received at least one dose of placebo. At the beginning of the study, the average pain score amongst participants was 6.7. The average pain score dropped to 4.84 after treatment with pregabalin and to 5.45 after treatment with placebo. Pregabalin treatment significantly improved patients' pain compared to placebo. "The results of this study demonstrate that pregabalin is safe and effective in reducing fibromyalgia pain in patients who are also taking an antidepressant to treat their depression," says Dr. Arnold.
Recent gut and urinary tract infections may curb the risk of developing rheumatoid arthritis, suggests research published in the *Annals of the Rheumatic Diseases*. One possible explanation could lie in the way in which these infections alter the types of bacteria resident in the gut (microbiome), say the researchers. They set out to look at the impact of different types of infection on the risk of developing rheumatoid arthritis in almost 6500 people. Some 2831 of the entire sample had been newly diagnosed with rheumatoid arthritis between 1996 and 2009. The remaining 3570, who were randomly selected from the population, were healthy, but matched for age, sex, and area of residence with the patients. All participants were asked whether they had had any gut, urinary tract, or genital infections in the preceding two years. They were also asked if they had had prostatitis, or antibiotic treatment for sinusitis, tonsillitis/other throat infection, or pneumonia during this time. The average age of all participants at study entry was 52, and 7 out of 10 of them were women.

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This might be because the linings of the gut are exposed to a high load of bacterial antigens, which may either initiate or modify inflammation, and so could possibly influence the risk of developing the disease, explain the researchers. In support of their findings, they point out that the infection sites identified in their study are primarily infected with gram negative bacteria, and antibodies used to treat these bacteria have proved effective for treating rheumatoid arthritis.

Scientists have found a marker that can indicate your likelihood of suffering from rheumatoid arthritis (RA) even sixteen years before the condition takes effect. A team from the Kennedy Institute of Rheumatology at Oxford University found that a blood test that looks for antibodies that recognize the protein tenasin-C could reliably show those who will contract the condition. Lead researcher Dr Anja Schwenzer said: 'We knew that tenasin-C is found at high levels in the joints of people with RA. We decided to see if it could be citrullinated and, if so, whether it was a target for the autoantibodies that attack the body in RA. That might also indicate whether it could be used in tests to indicate the disease. 'When we looked at results from more than 2000 patients we found that testing for antibodies that target citrullinated tenasin-C (cTNC) could diagnose RA in around 50% of cases, including some cases not identified by Cyclic Citrullinated Peptide (CCP). It also has a very low rate of false positives -- it is 98% accurate at ruling out RA.' The Kennedy Institute's Professor Kim Midwood said: 'What is particularly exciting is that when we looked at samples taken from people before their arthritis began, we could see these antibodies to cTNC up to 16 years before the disease occurred -- on average the antibodies could be found seven years before the disease appeared. 'When it comes to rheumatoid arthritis, early diagnosis is key with research showing that there is often a narrow 'window of opportunity' following the onset of symptoms for effective treatment. Furthermore, current tests for rheumatoid arthritis are limited in their ability to diagnose disease in different patients. This latest research provides the basis of tests that could improve diagnosis and, importantly, detect disease at a very early stage, with the promise even that people at risk of developing rheumatoid arthritis can be followed before the disease begins. This could have great potential to help patients with rheumatoid arthritis get the right treatment early to keep this painful and debilitating condition under control.' Stephen Simpson, Research Director, for Arthritis Research UK concluded.
Men Also at Risk for Osteoporosis

Screening women for osteoporosis is now routine, however, when it comes to men, most are never screened and therefore suffer the consequences of the disease. Mary Ruppe, M.D., a Houston Methodist endocrinologist said that, women have a screening safety net. “Between their primary care physician and OB-GYN, women will begin bone density screenings at the appropriate age. Men are less likely to have routine primary care checkups and don’t receive preventative care similar to what is provided for women.” The American College of Physicians recommends that men be assessed yearly for osteoporosis risk factors starting at age 50. The primary risk factor for men is family history, such as women in their family with osteoporosis or parents who suffered a hip fracture. Other factors that can raise a man’s risk of osteoporosis are prescription steroid use, gastrointestinal disease, use of prostate cancer drugs, and alcohol abuse. At age 70, The Endocrine Society recommends that all men begin routine bone density screenings as the risk for osteoporosis increases at this age. Ruppe said the osteoporosis treatment options for men are similar to those available for women. There are several approved medications that alter the cycle of bone formation and loss to help preserve bone strength. She said the key is diagnosing the condition so treatment can begin. “Each year, approximately 80,000 men will suffer a hip fracture, and studies have shown they have a higher mortality rate after a hip fracture than women of the same age. Such data underscores the importance of routine osteoporosis screening for men.” she added.

Early Walking in Toddlers Linked to Stronger Bones

Children who start to walk and jump earlier are more likely to have stronger bones later on in life, research shows. A study, published in the Journal of Bone and Mineral Research, has demonstrated an association between children’s abilities in common movements like jumping, running and walking at 18 months and stronger bones as an adolescent. It is thought that these movements in toddlers place a stress on the bones, causing them to react by becoming wider and thicker, thereby making them stronger than those in children who may not be moving as much. Findings from the study may help to identify who is at a greater risk of osteoporosis and bone fractures in later life. Healthcare scientists from Manchester Metropolitan University and the University of Bristol believe the results could also be partly attributed to children with good early life movement being more physically active as they get older. Researchers analysed data from 2,327 participants from Children of the 90s, a lifelong study of health and wellbeing that has been charting the lives of 14,500 people since they were born in the early 1990s. Movement was assessed at 18 months, and hip and shin bone size, shape and mineral density was measured at 17 years of age, for both males and females, by scanning with X-ray absorptiometry and peripheral computed tomography. The study found the effect was more pronounced in males than in females, suggesting early movement plays less of a role in female bone strength. Another studies from Dr Ireland, published in Bone, showed that babies who started to walk earlier could have up to 40 per cent higher bone mass in their shinbone compared to toddlers who were still crawling at the age of 15 months.

Running may be Better than Cycling for Long-term Bone Health

Exercise that puts greater strain on bones, like running, may improve long-term bone health more effectively than non weight-bearing activities like cycling, conclude the authors of a new study measuring the hormones of mountain ultra-marathon runners. The results of the study are presented at the European Congress of Endocrinology. The researchers measured two vital bone constituents as well as hormones associated with energy regulation. Osteocalcin and P1NP are two proteins associated with bone formation and their levels in blood are an indicator of bone health. Glucagon, leptin and insulin are hormones involved in regulating metabolism and indicate the body’s energy needs. Increasing glucagon levels indicate an energy demand, whilst increasing insulin and leptin levels indicate adequate or excessive energy levels. The researchers measured these three hormones as well as levels of osteocalcin and P1NP in 17 trained runners before and after a 65-km mountain ultramarathon run and compared it to the hormones and bone constituents of twelve adults of the same age who didn’t run the race but did low to moderate physical exercise. Compared to the control group, ultramarathon runners had higher levels of glucagon and lower levels of leptin and insulin when finishing the race. The falling levels of insulin within this group were linked to similarly falling levels of both osteocalcin and P1NP -- suggesting that athletes may be diverting energy from bone formation to power the high-energy demands of their metabolism. However, ultramarathon runners had higher P1NP levels at rest compared to controls, suggesting that they may divert energy from bones during racing but have a net gain in bone health in the long-term. “The everyday man and woman need to exercise moderately to maintain health,” said Dr Giovanni Lombardi, lead author of the study. “However, our findings suggest that those at risk of weaker bones might want to take up running rather than swimming or cycling.” He also said that, osteocalcin communicates with β cells in the pancreas, which regulate the body’s glucose metabolism. “Because running exerts a higher physical load on bone than swimming or cycling, it could be that these forces stimulate bone tissue to signal to the pancreas to help meet its energy needs in the long-term.” he added.