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EXHIBIT 2



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Health Topics

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Handout on Health: Osteoarthritis

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This booklet is for people who have osteoarthritis, their families, and others interested in learning more about the disorder. The booklet describes osteoarthritis and its symptoms and contains information about diagnosis and treatment, as well as current research efforts supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and other components of the National Institutes of Health (NIH). It also discusses pain relief, exercise, and quality of life for people with osteoarthritis. If you have further questions after reading this booklet, you may wish to discuss them with your doctor.

What Is Osteoarthritis?

Osteoarthritis (AH-stee-oh-ar-THREYE-tis) is the most common type of arthritis, especially among older people. Sometimes it is called degenerative joint disease or osteoarthrosis.

Osteoarthritis is a joint disease that mostly affects the cartilage (KAR-til-uj). Cartilage is the slippery tissue that covers the ends of bones in a joint. Healthy cartilage allows bones to glide over one another. It also absorbs energy from the shock of physical movement. In osteoarthritis, the surface layer of cartilage breaks down and wears away. This allows bones under the cartilage to rub together, causing pain, swelling, and loss of motion of the joint. Over time, the joint may lose its normal shape. Also, bone spurs--small growths called osteophytes--may grow on the edges of the joint. Bits of bone or cartilage can break off and float inside the joint space. This causes more pain and damage.

People with osteoarthritis usually have joint pain and limited movement. Unlike some other forms of arthritis, osteoarthritis affects only joints and not internal organs. For example, rheumatoid arthritis--the second most common form of arthritis--affects other parts of the body besides the joints. It begins at a younger age than osteoarthritis, causes swelling and redness in joints, and may make people feel sick, tired, and (uncommonly) feverish.

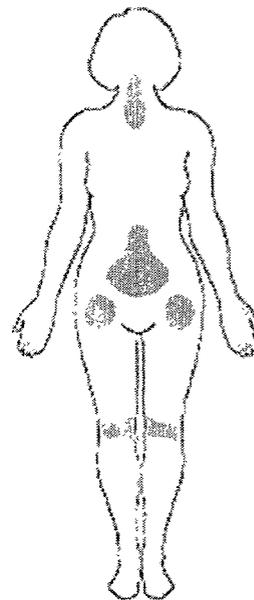
Who Has Osteoarthritis?

Osteoarthritis is one of the most frequent causes of physical disability among adults. More than 20 million people in the United States have the disease. By 2030, 20 percent of Americans--about 70 million people--will have passed their 65th birthday and will be at risk for osteoarthritis. Some younger people get osteoarthritis from joint injuries, but osteoarthritis most often occurs in older people. In fact, more than half of the population age 65 or older would show x-ray evidence of osteoarthritis in at least one joint. Both men and women have the disease. Before age 45, more men than women have osteoarthritis, whereas after age 45, it is more common in women.

How Does Osteoarthritis Affect People?

Osteoarthritis affects each person differently. In some people, it progresses quickly; in others, the symptoms are more serious. Scientists do not know yet what causes the disease, but they suspect a combination of factors, including being overweight, the aging process, joint injury, and stresses on the joints from certain jobs and sports activities.

What Areas Does Osteoarthritis Affect?



Osteoarthritis most often occurs at the ends of the fingers, thumbs, neck, lower back, knees, and hips.

Osteoarthritis hurts people in more than their joints; their finances and lifestyles also are affected.

Financial effects include

- The cost of treatment
- Wages lost because of disability.

Lifestyle effects include

- Depression
- Anxiety
- Feelings of helplessness
- Limitations on daily activities
- Job limitations
- Trouble participating in everyday personal and family joys and responsibilities.

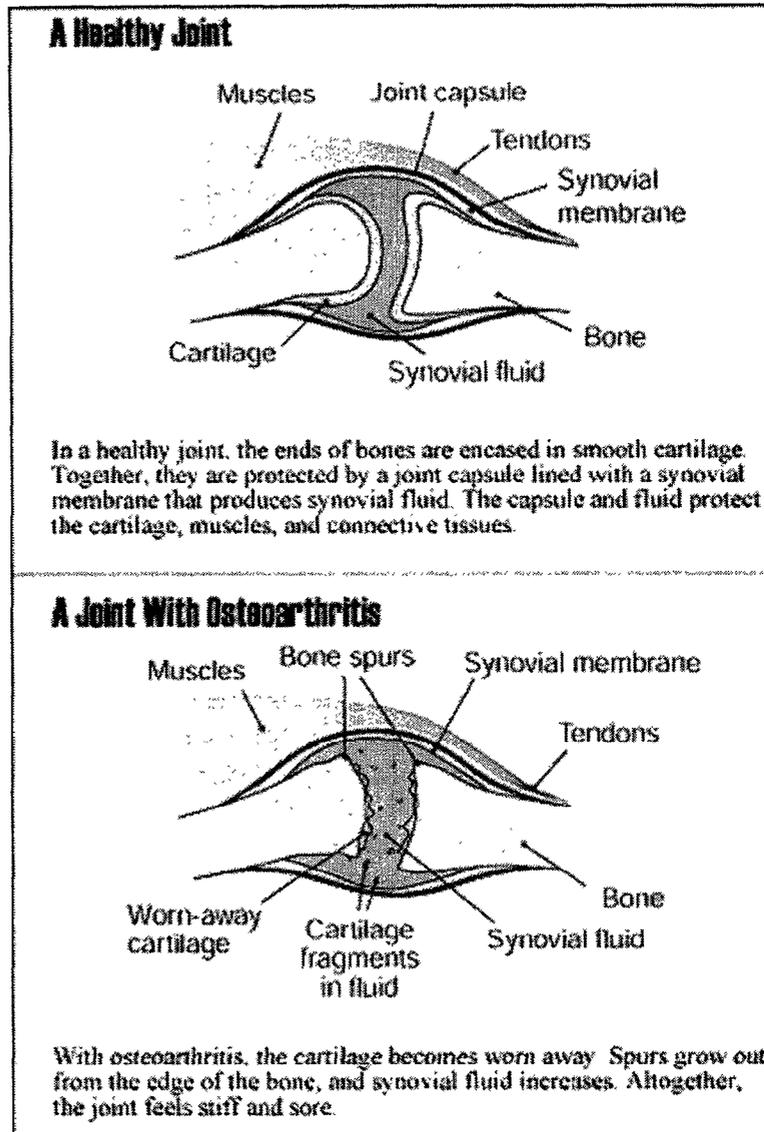
Despite these challenges, most people with osteoarthritis *can* lead active and productive lives. They succeed by using osteoarthritis treatment strategies, such as the following:

- Pain relief medications
- Rest and exercise
- Patient education and support programs
- Learning self-care and having a "good-health attitude."

Osteoarthritis Basics: The Joint and Its Parts

Most joints--the place where two moving bones come together--are designed to allow smooth movement between the bones and to absorb shock from movements like walking or repetitive movements. The joint is made up of:

- **Cartilage:** a hard but slippery coating on the end of each bone. Cartilage, which breaks down and wears away in osteoarthritis, is described in more detail [below](#).
- **Joint capsule:** a tough membrane sac that holds all the bones and other joint parts together.
- **Synovium** (sin-O-vee-um): a thin membrane inside the joint capsule.
- **Synovial fluid:** a fluid that lubricates the joint and keeps the cartilage smooth and healthy.
- **Ligaments, tendons, and muscles:** tissues that keep the bones stable and allow the joint to bend and move. Ligaments are tough, cord-like tissues that connect one bone to another. Tendons are tough, fibrous cords that connect muscles to bones. Muscles are bundles of specialized cells that contract to produce movement when stimulated by nerves.



How Do You Know if You Have Osteoarthritis?

Usually, osteoarthritis comes on slowly. Early in the disease, joints may ache after physical work or exercise. Osteoarthritis can occur in any joint. Most often it occurs at the hands, knees, hips, or spine.

Hands: Osteoarthritis of the fingers is one type of osteoarthritis that seems to have some hereditary characteristics; that is, it runs in families. More women than men have it, and they develop it especially after menopause. In osteoarthritis, small, bony knobs appear on the end joints of the fingers. They are called Heberden's (HEB-err-denz) nodes. Similar knobs, called Bouchard's (boo-SHARDZ) nodes, can appear on the middle joints of the fingers. Fingers can become enlarged and gnarled, and they may ache or be stiff and numb. The base of the thumb joint also is commonly affected by osteoarthritis. Osteoarthritis of the hands can be helped by medications, splints, or heat treatment.

Cartilage: The Key to Healthy Joints

Cartilage is 65 to 80 percent water. Three other components make up the rest of cartilage tissue: collagen, proteoglycans, and chondrocytes.

- **Collagen** (KAHL-uh-jen): a fibrous protein. Collagen is also the building block of skin, tendon, bone, and other connective tissues.
- **Proteoglycans** (PRO-tee-uh-GLY-kanz): a combination of proteins and sugars. Strands of proteoglycans and collagen weave together and form a mesh-like tissue. This allows cartilage to flex and absorb physical shock.
- **Chondrocytes** (KAHN-druh-sytz): cells that are found all through the cartilage. They mainly help cartilage stay healthy and grow. Sometimes, however, they release substances called enzymes that destroy collagen and other proteins. Researchers are trying to learn more about chondrocytes.

Knees: The knees are the body's primary weight-bearing joints. For this reason, they are among the joints most commonly affected by osteoarthritis. They may be stiff, swollen, and painful, making it hard to walk, climb, and get in and out of chairs and bathtubs. If not treated, osteoarthritis in the knees can lead to disability. Medications, weight loss, exercise, and walking aids can reduce pain and disability. In severe cases, knee replacement surgery may be helpful.

Hips: Osteoarthritis in the hip can cause pain, stiffness, and severe disability. People may feel the pain in their hips, or in their groin, inner thigh, buttocks, or knees. Walking aids, such as canes or walkers, can reduce stress on the hip. Osteoarthritis in the hip may limit moving and bending. This can make daily activities such as dressing and foot care a challenge. Walking aids, medication, and exercise can help relieve pain and improve motion. The doctor may recommend hip replacement if the pain is severe and not relieved by other methods.

Spine: Stiffness and pain in the neck or in the lower back can result from osteoarthritis of the spine. Weakness or numbness of the arms or legs also can result. Some people feel better when they sleep on a firm mattress or sit using back support pillows. Others find it helps to use heat treatments or to follow an exercise program that strengthens the back and abdominal muscles. In severe cases, the doctor may suggest surgery to reduce pain and help restore function.

The Warning Signs of Osteoarthritis

- Steady or intermittent **pain** in a joint
- **Stiffness** in a joint after getting out of bed or sitting for a long time
- **Swelling** or **tenderness** in one or more joints
- A **crunching feeling** or the sound of bone rubbing on bone
- **Hot, red, or tender?** Probably not osteoarthritis. Check with your doctor about other causes, such as rheumatoid arthritis.
- **Pain?** Not always. In fact, only a third of people whose x rays show evidence of osteoarthritis report pain or other

symptoms.

How Do Doctors Diagnose Osteoarthritis?

No single test can diagnose osteoarthritis. Most doctors use a combination of the following methods to diagnose the disease and rule out other conditions:

Clinical history: The doctor begins by asking the patient to describe the symptoms, and when and how the condition started. Good doctor-patient communication is important. The doctor can give a better assessment if the patient gives a good description of pain, stiffness, and joint function, and how they have changed over time. It also is important for the doctor to know how the condition affects the patient's work and daily life. Finally, the doctor also needs to know about other medical conditions and whether the patient is taking any medicines.

Physical examination: The doctor will check the patient's general health, including checking reflexes and muscle strength. Joints bothering the patient will be examined. The doctor will also observe the patient's ability to walk, bend, and carry out activities of daily living.

X rays: Doctors take x rays to see how much joint damage has been done. X rays of the affected joint can show such things as cartilage loss, bone damage, and bone spurs. But there often is a big difference between the severity of osteoarthritis as shown by the x ray and the degree of pain and disability felt by the patient. Also, x rays may not show early osteoarthritis damage, before much cartilage loss has taken place.

Other tests: The doctor may order blood tests to rule out other causes of symptoms. Another common test is called joint aspiration, which involves drawing fluid from the joint for examination.

It usually is not difficult to tell if a patient has osteoarthritis. It is more difficult to tell if the disease is causing the patient's symptoms. Osteoarthritis is so common--especially in older people--that symptoms seemingly caused by the disease actually may be due to other medical conditions. The doctor will try to find out what is causing the symptoms by ruling out other disorders and identifying conditions that may make the symptoms worse. The severity of symptoms in osteoarthritis is influenced greatly by the patient's attitude, anxiety, depression, and daily activity level.

How Is Osteoarthritis Treated?

Most successful treatment programs involve a combination of treatments tailored to the patient's needs, lifestyle, and health. Osteoarthritis treatment has four general goals:

- **Improve joint care** through rest and exercise.
- **Maintain an acceptable body weight.**
- **Control pain** with medicine and other measures.
- **Achieve a healthy lifestyle.**

Treatment Approaches to Osteoarthritis

- Exercise
- Weight control
- Rest and joint care
- Pain relief techniques
- Medicines
- Alternative therapies
- Surgery

Osteoarthritis treatment plans often include ways to manage pain and improve function. Such plans can involve exercise, rest and joint care, pain relief, weight control, medicines, surgery, and nontraditional treatment approaches.

Exercise: Research shows that exercise is one of the best treatments for osteoarthritis. Exercise can improve mood and outlook, decrease pain, increase flexibility, improve the heart and blood flow, maintain weight, and promote general physical fitness. Exercise is also inexpensive and, if done correctly, has few negative side effects. The amount and form of exercise will depend on which joints are involved, how stable the joints are, and whether a joint replacement has already been done. (*See Be a Winner! Practice Self-Care and Keep a "Good-Health Attitude."*)

On the Move: Fighting Osteoarthritis With Exercise

You can use exercises to keep strong and limber, extend your range of movement, and reduce your weight. Some different types of exercise include the following:

Strength exercises: These can be performed with exercise bands, inexpensive devices that add resistance.

Aerobic activities: These keep your lungs and circulation systems in shape.

Range of motion activities: These keep your joints limber.

Agility exercises: These can help you maintain daily living skills.

Neck and back strength exercises: These can help you keep your spine strong and limber.

Ask your doctor or physical therapist what exercises are best for you. Ask for guidelines on exercising when a joint is sore or if swelling is present. Also, check if you should (1) use pain-relieving drugs, such as analgesics or anti-inflammatories (also called NSAIDs), to make exercising easier, or (2) use ice afterwards.

Rest and joint care: Treatment plans include regularly scheduled rest. Patients must learn to recognize the body's signals, and know when to stop or slow down, which prevents pain caused by overexertion. Some patients find that relaxation techniques, stress reduction, and biofeedback help. Some use canes and splints to protect joints and take pressure off them. Splints or braces provide extra support for weakened joints. They also keep the joint in proper position during sleep or activity. Splints should be used only for limited periods because joints and muscles need to be exercised to prevent stiffness and weakness. An occupational therapist or a doctor can help the patient get a properly fitting splint.

Nondrug pain relief: People with osteoarthritis may find nondrug ways to

relieve pain. Warm towels, hot packs, or a warm bath or shower to apply moist heat to the joint can relieve pain and stiffness. In some cases, cold packs (a bag of ice or frozen vegetables wrapped in a towel can relieve pain or numb the sore area. (Check with a doctor or physical therapist to find out if heat or cold is the best treatment.) Water therapy in a heated pool or whirlpool also may relieve pain and stiffness. For osteoarthritis in the knee, patients may wear insoles or cushioned shoes to redistribute weight and reduce joint stress.

Weight control: Osteoarthritis patients who are overweight or obese need to lose weight. Weight loss can reduce stress on weight-bearing joints and limit further injury. A dietitian can help patients develop healthy eating habits. A healthy diet and regular exercise help reduce weight.

Medicines: Doctors prescribe medicines to eliminate or reduce pain and to improve functioning. Doctors consider a number of factors when choosing medicines for their patients with osteoarthritis. Two important factors are the intensity of the pain and the potential side effects of the medicine. Patients must use medicines carefully and tell their doctors about any changes that occur.

The following types of medicines are commonly used in treating osteoarthritis:

- **Acetaminophen:** Acetaminophen is a pain reliever (for example, Tylenol[®]) that does not reduce swelling. Acetaminophen does not irritate the stomach and is less likely than nonsteroidal anti-inflammatory drugs (NSAIDs) to cause long-term side effects. Research has shown that acetaminophen relieves pain as effectively as NSAIDs for many patients with osteoarthritis. *Warning:* People with liver disease, people who drink alcohol heavily, and those taking blood-thinning medicines or NSAIDs should use acetaminophen with caution.

* Note: Brand names included in this booklet are provided as examples only. Their inclusion does not mean they are endorsed by the National Institutes of Health or any other Government agency. Also, if a certain brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

- **NSAIDs (nonsteroidal anti-inflammatory drugs):** Many NSAIDs are used to treat osteoarthritis. Patients can buy some over the counter (for example, aspirin, Advil, Motrin IB, Aleve, ketoprofen). Others require a prescription. All NSAIDs work similarly: they fight inflammation and relieve pain. However, each NSAID is a different chemical, and each has a slightly different effect on the body.

Side effects: NSAIDs can cause stomach irritation or, less often, they can affect kidney function. The longer a person uses NSAIDs, the more likely he or she is to have side effects, ranging from mild to serious. Many other drugs cannot be taken when a patient is being treated with NSAIDs because NSAIDs alter the way the body uses or eliminates these other drugs. Check with your health care provider or pharmacist before you take NSAIDs in addition to another medication. Also, NSAIDs sometimes are associated with serious gastrointestinal problems, including ulcers, bleeding, and perforation of the stomach or intestine. People over age 65 and those with any history of ulcers or gastrointestinal bleeding should

use NSAIDs with caution.

COX-2 inhibitors: Several new NSAIDs--valdecoxib (Bextra), celecoxib (Celebrex), and rofecoxib (Vioxx)--from a class of drugs known as COX-2 inhibitors are now being used to treat osteoarthritis. These medicines reduce inflammation similarly to traditional NSAIDs, but they cause fewer gastrointestinal side effects. However, these medications occasionally are associated with harmful reactions ranging from mild to severe. (See [Current Research](#).)

- **Other medications:** Doctors may prescribe several other medicines for osteoarthritis, including the following:

Topical pain-relieving creams, rubs, and sprays (for example, capsaicin cream), which are applied directly to the skin.

Mild narcotic painkillers, which--although very effective--may be addictive and are not commonly used.

Corticosteroids, powerful anti-inflammatory hormones made naturally in the body or manmade for use as medicine. Corticosteroids may be injected into the affected joints to temporarily relieve pain. This is a short-term measure, generally not recommended for more than two or three treatments per year. Oral corticosteroids should not be used to treat osteoarthritis.

Hyaluronic acid, a medicine for joint injection, used to treat osteoarthritis of the knee. This substance is a normal component of the joint, involved in joint lubrication and nutrition.

Questions To Ask Your Doctor or Pharmacist About Medicines

- How often should I take this medicine?
- Should I take this medicine with food or between meals?
- What side effects can I expect?
- Should I take this medicine with the other prescription medicines I take?
- Should I take this medicine with the over-the-counter medicines I take?

Most medicines used to treat osteoarthritis have side effects, so it is important for people to learn about the medicines they take. Even nonprescription drugs should be checked. Several groups of patients are at high risk for side effects from NSAIDs, such as people with a history of peptic ulcers or digestive tract bleeding, people taking oral corticosteroids or anticoagulants (blood thinners), smokers, and people who consume alcohol. Some patients may be able to help reduce side effects by taking some medicines with food. Others should avoid stomach irritants such as alcohol, tobacco, and caffeine. Some patients try to protect their stomachs by taking other medicines that coat the stomach or block stomach acids. These measures help, but they are not always completely effective.

Surgery: For many people, surgery helps relieve the pain and disability of

osteoarthritis. Surgery may be performed to

- Remove loose pieces of bone and cartilage from the joint if they are causing mechanical symptoms of buckling or locking
- Resurface (smooth out) bones
- Reposition bones
- Replace joints.

Surgeons may replace affected joints with artificial joints called prostheses. These joints can be made from metal alloys, high-density plastic, and ceramic material. They can be joined to bone surfaces by special cements. Artificial joints can last 10 to 15 years or longer. About 10 percent of artificial joints may need revision. Surgeons choose the design and components of prostheses according to their patient's weight, sex, age, activity level, and other medical conditions.

The decision to use surgery depends on several things. Both the surgeon and the patient consider the patient's level of disability, the intensity of pain, the interference with the patient's lifestyle, the patient's age, and occupation. Currently, more than 80 percent of osteoarthritis surgery cases involve replacing the hip or knee joint. After surgery and rehabilitation, the patient usually feels less pain and swelling, and can move more easily.

Nontraditional Approaches: Among the alternative therapies used to treat osteoarthritis are the following:

- **Acupuncture:** Some people have found pain relief using acupuncture (the use of fine needles inserted at specific points on the skin). Preliminary research shows that acupuncture may be a useful component in an osteoarthritis treatment plan for some patients. (See [Current Research](#).)
- **Folk remedies:** Some patients seek alternative therapies for their pain and disability. Some of these alternative therapies have included wearing copper bracelets, drinking herbal teas, and taking mud baths. While these practices are not harmful, some can be expensive. They also cause delays in seeking medical treatment. To date, no scientific research shows these approaches to be helpful in treating osteoarthritis.
- **Nutritional supplements:** Nutrients such as glucosamine and chondroitin sulfate have been reported to improve the symptoms of people with osteoarthritis, as have certain vitamins. Additional studies are being carried out to further evaluate these claims. (See [Current Research](#).)

Health Professionals Who Treat Osteoarthritis

Many types of health professionals care for people with osteoarthritis:

- **Primary care physicians.** Doctors who treat patients before they are referred to other specialists in the health care system.
- **Rheumatologists.** Medical doctors who specialize in treating arthritis and related conditions that affect joints, muscles, and bones.

- **Orthopaedists.** Doctors who specialize in treatment of and surgery for bone and joint diseases.
- **Physical therapists.** Health professionals who work with patients to improve joint function.
- **Occupational therapists.** Health professionals who teach ways to protect joints, minimize pain, and conserve energy.
- **Dietitians.** Health professionals who teach ways to use a good diet to improve health and maintain a healthy weight.
- **Nurse educators.** Nurses who specialize in helping patients understand their overall condition and implement their treatment plans.
- **Physiatrists (rehabilitation specialists).** Doctors who help patients make the most of their physical potential.
- **Licensed acupuncture therapists.** Health professionals who reduce pain and improve physical functioning by inserting fine needles into the skin at various points on the body.
- **Psychologists.** Health professionals who help patients cope with difficulties in the home and workplace resulting from their medical conditions.
- **Social workers.** Professionals who assist patients with social challenges caused by disability, unemployment, financial hardships, home health care, and other needs resulting from their medical conditions.

Be a Winner! Practice Self-Care and Keep a "Good-Health Attitude"

People with osteoarthritis can enjoy good health despite having the disease. How? By learning self-care skills and developing a "good-health attitude."

Self-care is central to successfully managing the pain and disability of osteoarthritis. People have a much better chance of having a rewarding lifestyle when they educate themselves about the disease and take part in their own care. Working actively with a team of health care providers enables people with the disease to minimize pain, share in decisionmaking about treatment, and feel a sense of control over their lives. Research shows that people with osteoarthritis who take part in their own care report less pain and make fewer doctor visits. They also enjoy a better quality of life.

Self-Management Programs Do Help

People with osteoarthritis find that self-management programs help them

- Understand the disease
- Reduce pain while remaining active
- Cope physically, emotionally, and mentally
- Have greater control over the disease
- Build confidence in their ability to live an active, independent life.

Self-Help and Education Programs: Three kinds of programs help people learn about osteoarthritis, learn self-care, and improve their good-

health attitude. These programs include

- Patient education programs
- Arthritis self-management programs
- Arthritis support groups.

These programs teach people about osteoarthritis, its treatments, exercise and relaxation, patient and health care provider communication, and problem solving. Research has shown that these programs have clear and long-lasting benefits.

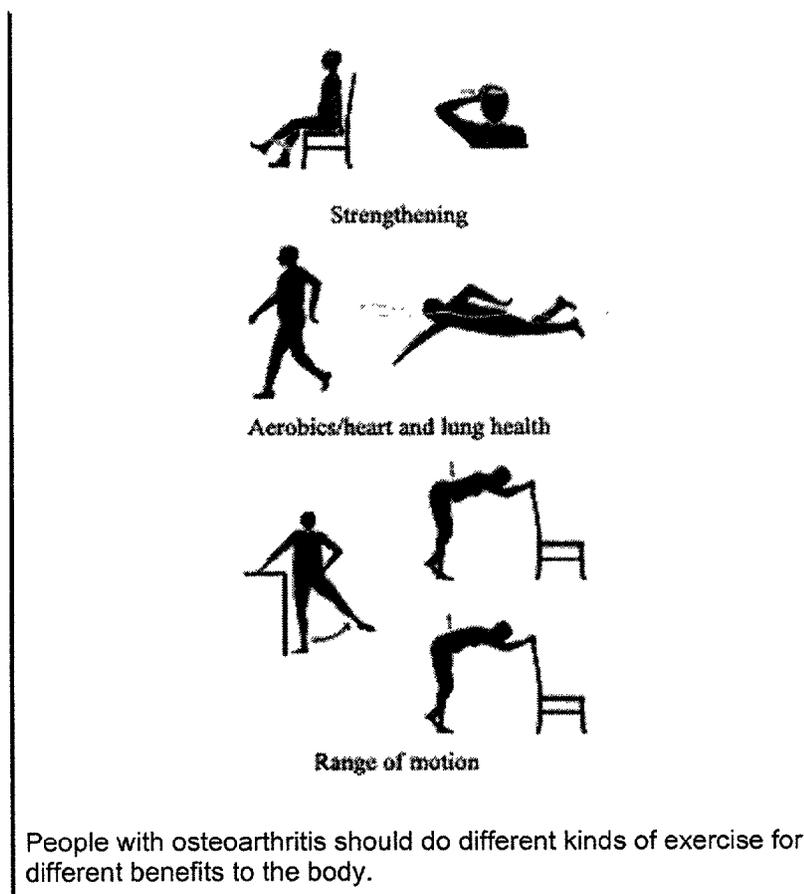
Exercise: Regular physical activity plays a key role in self-care and wellness. Two types of exercise are important in osteoarthritis management. The first type, therapeutic exercises, keep joints working as well as possible. The other type, aerobic conditioning exercises, improve strength and fitness, and control weight. Patients should be realistic when they start exercising. They should learn how to exercise correctly, because exercising incorrectly can cause problems.

Most people with osteoarthritis exercise best when their pain is least severe. Start with an adequate warmup and begin exercising slowly. Resting frequently ensures a good workout. It also reduces the risk of injury. A physical therapist can evaluate how a patient's muscles are working. This information helps the therapist develop a safe, personalized exercise program to increase strength and flexibility.

Many people enjoy sports or other activities in their exercise program. Good activities include swimming and aquatic exercise, walking, running, biking, cross-country skiing, and using exercise machines and exercise videotapes.

People with osteoarthritis should check with their doctor or physical therapist before starting an exercise program. Health care providers will suggest what exercises are best for you, how to warm up safely, and when to avoid exercising a joint affected by arthritis. Pain medications and applying ice after exercising may make exercising easier.

Exercises for Osteoarthritis



Body, Mind, Spirit: Making the most of good health requires careful attention to the body, mind, and spirit. People with osteoarthritis must plan and develop daily routines that maximize their quality of life and minimize disability. They also need to evaluate these routines periodically to make sure they are working well.

Good health also requires a positive attitude. People must decide to make the most of things when faced with the challenges of osteoarthritis. This attitude--a good-health mindset--doesn't just happen. It takes work, every day. And with the right attitude, you will achieve it.

Enjoy a "Good-Health Attitude"

- Focus on your abilities instead of disabilities.
- Focus on your strengths instead of weaknesses.
- Break down activities into small tasks that you can manage.
- Incorporate fitness and nutrition into daily routines.
- Develop methods to minimize and manage stress.
- Balance rest with activity.
- Develop a support system of family, friends, and health professionals.

Current Research

The leading role in osteoarthritis research is played by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS),

within the National Institutes of Health (NIH). The NIAMS funds many researchers across the United States to study osteoarthritis. It has established a Specialized Center of Research devoted to osteoarthritis. Also, many researchers study arthritis at NIAMS Multipurpose Arthritis and Musculoskeletal Diseases Centers and Multidisciplinary Clinical Research Centers. These centers conduct basic, laboratory, and clinical research aimed at understanding the causes, treatment options, and prevention of arthritis and musculoskeletal diseases. Center researchers also study epidemiology, health services, and professional, patient, and public education. The NIAMS also supports multidisciplinary clinical research centers that expand clinical studies for diseases like osteoarthritis.

For years, scientists thought that osteoarthritis was simply a disease of "wear and tear" that occurred in joints as people got older. In the last decade, however, research has shown that there is more to the disorder than aging alone. The production, maintenance, and breakdown of cartilage, as well as bone changes in osteoarthritis, are now seen as a series or cascade of events. Many researchers are trying to discover where in that cascade of events things go wrong. By understanding what goes wrong, they hope to find new ways to prevent or treat osteoarthritis. Some key areas of research are described below.

Animal Models: Animals help researchers understand how diseases work and why they occur. Animal models help researchers learn many things about osteoarthritis, such as what happens to cartilage, how treatment strategies might work, and what might prevent the disease. Animal models also help scientists study osteoarthritis in very early stages before it causes detectable joint damage.

Diagnostic Tools: Some scientists want to find ways to detect osteoarthritis at earlier stages so that they can treat it earlier. They seek specific abnormalities in the blood, joint fluid, or urine of people with the disease. Other scientists use new technologies to analyze the differences between the cartilage from different joints. For example, many people have osteoarthritis in the knees or hips, but few have it in the ankles. Can ankle cartilage be different? Does it age differently? Answering these questions will help us understand the disease better.

Genetics Studies: Researchers suspect that inheritance plays a role in 25 to 30 percent of osteoarthritis cases. Researchers have found that genetics may play a role in approximately 40 to 65 percent of hand and knee osteoarthritis cases. They suspect inheritance might play a role in other types of osteoarthritis, as well. Scientists have identified a mutation (a gene defect) affecting collagen, an important part of cartilage, in patients with an inherited kind of osteoarthritis that starts at an early age. The mutation weakens collagen protein, which may break or tear more easily under stress. Scientists are looking for other gene mutations in osteoarthritis. Recently, researchers found that the daughters of women who have knee osteoarthritis have a significant increase in cartilage breakdown, thus making them more susceptible to disease. In the future, a test to determine who carries the genetic defect (or defects) could help people reduce their risk for osteoarthritis with lifestyle adjustments.

Tissue Engineering: This technology involves removing cells from a healthy part of the body and placing them in an area of diseased or damaged tissue in order to improve certain body functions. Currently, it is used to treat small traumatic injuries or defects in cartilage, and, if successful, could eventually help treat osteoarthritis. Researchers at the

NIAMS are exploring three types of tissue engineering. The two most common methods being studied today include cartilage cell replacement and stem cell transplantation. The third method is gene therapy.

- **Cartilage cell replacement:** In this procedure, researchers remove cartilage cells from the patient's own joint and then clone or grow new cells using tissue culture and other laboratory techniques. They then inject the newly grown cells into the patient's joint. Patients with cartilage cell replacement have fewer symptoms of osteoarthritis. Actual cartilage repair is limited, however.
- **Stem cell transplantation:** Stem cells are primitive cells that can transform into other kinds of cells, such as muscle or bone cells. They usually are taken from bone marrow. In the future, researchers hope to insert stem cells into cartilage, where the cells will make new cartilage. If successful, this process could be used to repair damaged cartilage and avoid the need for surgical joint replacements with metal or plastics.
- **Gene therapy:** Scientists are working to genetically engineer cells that would inhibit the body chemicals, called enzymes, that may help break down cartilage and cause joint damage. In gene therapy, cells are removed from the body, genetically changed, and then injected back into the affected joint. They live in the joint and protect it from damaging enzymes.

Comprehensive Treatment Strategies: Effective treatment for osteoarthritis takes more than medicine or surgery. Getting help from a variety of care professionals often can improve patient treatment and self-care. (See [Health Professionals Who Treat Osteoarthritis](#).) Research shows that adding patient education and social support is a low-cost, effective way to decrease pain and reduce the amount of medicine used.

Exercise plays a key part in comprehensive treatment. Researchers are studying exercise in greater detail and finding out just how to use it in treating or preventing osteoarthritis. For example, several scientists have studied knee osteoarthritis and exercise. Their results included the following:

- Strengthening the thigh muscle (quadriceps) can relieve symptoms of knee osteoarthritis and prevent more damage.
- Walking can result in better functioning, and the more you walk, the farther you will be able to walk.
- People with knee osteoarthritis who were active in an exercise program feel less pain. They also function better.

Research has shown that losing extra weight can help people who already have osteoarthritis. Moreover, overweight or obese people who do not have osteoarthritis may reduce their risk of developing the disease by losing weight.

Using NSAIDs: Many people who have osteoarthritis have persistent pain despite taking simple pain relievers such as acetaminophen. Some of these patients take NSAIDs instead. Health care providers are concerned about long-term NSAID use because it can lead to an upset stomach, heartburn, nausea, and more dangerous side effects, such as ulcers.

Scientists are working to design and test new, safer NSAIDs. One

example currently available is a class of selective NSAIDs called COX-2 inhibitors. Traditional NSAIDs prevent inflammation by blocking two related enzymes in the body called COX-1 and COX-2. The gastrointestinal side effects associated with traditional NSAIDs seems to be associated mainly with blocking the COX-1 enzyme, which helps protect the stomach lining. The new selective COX-2 inhibitors, however, primarily block the COX-2 enzyme, which helps control inflammation in the body. As a result, COX-2 inhibitors reduce pain and inflammation but are less likely than traditional NSAIDs to cause gastrointestinal ulcers and bleeding. However, research shows that some COX-2 inhibitors may not protect against heart disease as well as traditional NSAIDs, so check with your doctor if you have concerns.

Drugs to Prevent Joint Damage: No treatment actually prevents osteoarthritis or reverses or blocks the disease process once it begins. Present treatments just relieve the symptoms. Researchers are looking for drugs that would prevent, slow down, or reverse joint damage. One experimental antibiotic drug, doxycycline, may stop certain enzymes from damaging cartilage. The drug has shown some promise in clinical studies, but more studies are needed. Researchers also are studying growth factors and other natural chemical messengers. These potential medicines may be able to stimulate cartilage growth or repair.

Acupuncture: During an acupuncture treatment, a licensed acupuncture therapist inserts very fine needles into the skin at various points on the body. Scientists think the needles stimulate the release of natural, pain-relieving chemicals produced by the brain or the nervous system. Researchers are studying acupuncture treatment of patients who have knee osteoarthritis. Early findings suggest that traditional Chinese acupuncture is effective for some patients as an additional therapy for osteoarthritis, reducing pain and improving function.

Nutritional Supplements: Nutritional supplements are often reported as helpful in treating osteoarthritis. Such reports should be viewed with caution, however, since very few studies have carefully evaluated the role of nutritional supplements in osteoarthritis.

- **Glucosamine and chondroitin sulfate:** Both of these nutrients are found in small quantities in food and are components of normal cartilage. Scientific studies on these two nutritional supplements have not yet shown that they affect the disease. They may relieve symptoms and reduce joint damage in some patients, however. The National Center for Complementary and Alternative Medicine at the NIH is supporting a clinical trial to test whether glucosamine, chondroitin sulfate, or the two nutrients in combination reduce pain and improve function. Patients using this therapy should do so only under the supervision of their doctor, as part of an overall treatment program with exercise, relaxation, and pain relief.
- **Vitamins D, C, E, and beta carotene:** The progression of osteoarthritis may be slower in people who take higher levels of vitamin D, C, E, or beta carotene. More studies are needed to confirm these reports.

Hyaluronic Acid: Injecting this substance into the knee joint provides long-term pain relief for some people with osteoarthritis. Hyaluronic acid is a natural component of cartilage and joint fluid. It lubricates and absorbs shock in the joint. The Food and Drug Administration (FDA) approved this therapy for patients with osteoarthritis of the knee who do not get relief from exercise, physical therapy, or simple analgesics. Researchers are

presently studying the benefits of using hyaluronic acid to treat osteoarthritis.

Estrogen: In studies of older women, scientists found a lower risk of osteoarthritis in women who had used oral estrogens for hormone replacement therapy. The researchers suspect having low levels of estrogen could increase the risk of developing osteoarthritis. Additional studies are needed to answer this question.

Hope for the Future

Research is opening up new avenues of treatment for people with osteoarthritis. A balanced, comprehensive approach is still the key to staying active and healthy with the disease. People with osteoarthritis should combine exercise, relaxation education, social support, and medicines in their treatment strategies. Meanwhile, as scientists unravel the complexities of the disease, new treatments and prevention methods should appear. They will improve the quality of life for people with osteoarthritis and their families.

Additional Resources

National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institutes of Health
1 AMS Circle
Bethesda, MD 20892-3675
(301) 495-4484 or (877) 22-NIAMS (free of charge)
TTY: (301) 565-2966
Fax: (301) 718-6366
niamsinfo@mail.nih.gov
www.niams.nih.gov

NIAMS provides information about various forms of arthritis and rheumatic diseases. It distributes patient and professional education materials and also refers people to other sources of information.

American College of Rheumatology
1800 Century Place, Suite 250
Atlanta, GA 30345
(404) 633-3777
Fax: (404) 633-1870
www.rheumatology.org

This association provides referrals to rheumatologists and physical and occupational therapists who have experience working with people who have osteoarthritis. The organization also provides educational materials and guidelines.

American Academy of Orthopaedic Surgeons
P.O. Box 2058
Des Plaines, IL 60017
(800) 824-BONE (2663) (free of charge)
www.aaos.org

The academy provides education and practice management services for orthopaedic surgeons and allied health professionals. It also serves as an advocate for improved patient care and informs the public about the

science of orthopaedics. The orthopaedist's scope of practice includes disorders of the body's bones, joints, ligaments, muscles, and tendons. For a single copy of an AAOS brochure, send a self-addressed stamped envelope to the address above or visit the AAOS Web site.

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Arthritis Foundation
1330 West Peachtree Street
Atlanta, GA 30309
Call your local chapter (listed in the telephone directory),
or (800) 283-7800 (free of charge)
www.arthritis.org

The foundation is a major voluntary organization devoted to supporting research on arthritis and other rheumatic diseases. The foundation publishes a free pamphlet on osteoarthritis and a magazine for members on arthritis and related conditions. It also provides up-to-date information on treatments, nutrition, alternative therapies, and self-management strategies. Chapters nationwide offer exercise programs, classes, support groups, physician referral services, and free literature.

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About NIAMS and Its Clearinghouse:

The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health (NIH), is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides

health information and information sources. Additional information can be found on the NIAMS Web site at www.niams.nih.gov.

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