What is NON-RADIOGRAPHIC Axial Spondyloarthritis (nr-axSpA)?
Non-Radiographic Axial Spondyloarthritis: Introduction

First, What is Non-Radiographic Axial Spondyloarthritis?

Axial – Relating to or situated in the central part of the body, encompassing the full spine and pelvis.

Spondyloarthritis – Inflammatory arthritis involving the spine and peripheral joints.

Non-Radiographic – No definitive damage seen on x-rays of spine, specifically in the sacroiliac (SI) joints.

Nr-axSpA is a form of arthritis belonging to a group of related diseases called spondyloarthritis. Nr-axSpA primarily affects the spine, but other parts of the body can be involved. That is why nr-axSpA is called a systemic disease—meaning it can affect the whole body.

Nr-axSpA is also a chronic disorder. On one hand, that means there is currently no cure for this disease. On the other hand, advancing knowledge and continuing research mean that treatment options are better than ever, and there are many options for helping people with nr-axSpA live full lives.

The Spondylitis Association of America (SAA), with support from UCB, has produced this brochure to provide you with practical information about non-radiographic axial spondyloarthritis (nr-axSpA).

For people with nr-axSpA and those close to them, the disorder and its associated social, functional, and financial consequences present challenges for disease management. That is one big reason why it is so important to take charge of the disease as early as is possible. Experts agree that people with nr-axSpA who learn more about their disease and then use that knowledge to improve their own care ultimately have better outcomes. It is our hope that this pamphlet will make a solid contribution to that effort and provide important tools and valuable knowledge about nr-axSpA.

Information in this brochure cannot replace treatment provided by health care professionals. Every patient is unique, so care plans must fit each individual. If you have questions as you read, please consult with your doctor for more information.

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Signs and Symptoms: How is a Person Affected?

The first symptoms are often described as persistent pain and stiffness in the lower back and buttocks, which come on gradually over the course of a few weeks or months. Sometimes, these symptoms can be severe.

The back pain people with nr-axSpA experience is usually of a type called inflammatory back pain. Key characteristics of inflammatory back pain include pain and stiffness that:
- Start before age 45
- Develop and worsen gradually
- Persist for more than three months
- Ease with physical activity and exercise
- Do not improve with rest
- Get worse with immobility (especially overnight and early morning)

Pain and stiffness in other areas of the body, such as the neck, shoulders, the ribs, hips, knees, and heels, are also common. Inflammation inside the body can sometimes lead to intestinal pain and other problems. Some may experience arthritis in the joints of the arms and legs. Psoriasis (scaly skin rash) may occur in some.

Other Key Symptoms May Include:
- **Iritis / Uveitis** – Inflammation of the eye. Symptoms often occur in one eye at a time, and may include redness, pain, sensitivity to light, and skewed vision. (Note: iritis is a medical emergency and needs immediate attention as untreated eye inflammation may lead to permanent damage and even blindness.)
- **Enthesitis** – Inflammation of the entheses which is where ligaments or tendons attach to the bone. Symptoms include swelling and tenderness. Common areas impacted include the Achilles tendon at the back of the heel, the plantar fascia at the base of the heel, the rib cage, and the spine.
- **Dactylitis** – Inflammation and swelling of an entire finger or toe.

It is important to note that nr-axSpA is a systemic disease, and other organs and body parts may be impacted. Disease course and severity also are likely to vary from person to person.

Non-Radiographic vs. Radiographic Axial Spondyloarthritis (also known as Ankylosing Spondylitis): Differences and Similarities

Non-radiographic axial spondyloarthritis (nr-axSpA) is most closely associated with a highly similar condition called radiographic axial spondyloarthritis (r-axSpA), which is also called ankylosing spondylitis. These two can be thought of as two ends of the spectrum of axial spondyloarthritis.

**Axial Spondyloarthritis**

| Nr-axSpA: axial spondyloarthritis that is **not radiographic**, meaning that doctors do not see definitive damage on x-rays of the sacroiliac (SI) joints. | R-axSpA: or ankylosing spondylitis: axial spondyloarthritis that is **radiographic**, meaning that doctors are able to see definitive damage on x-rays of the SI joints. |

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Areas of the Body Where Inflammation May Occur

A) Eyes
B) Jaw
C) Neck
D) Shoulders
E) Ribs
F) Rib-Spine Junction
G) Skin (psoriasis)
H) Gastrointestinal Tract
I) Hips
J) Lumbosacral
K) Sacroiliac
L) Wrist
M) Fingers
N) Knee
O) Heel
P) Toes

Iritis/Uveitis is a common symptom.
Is Nr-axSpA Different in Men and Women?

The disease most frequently begins between the ages of 24 and 28 in both men and women. Some recent evidence suggests that a person’s sex can affect the location of initial pain in nr-axSpA. For some women, the neck and peripheral joints are affected first, whereas in men it is much more likely to be the lower back. Women also tend to have more pain overall—especially widespread, fibromyalgia-like pain—than men.

Nr-axSpA diagnosis can be a lengthy and difficult process for both men and women. In general, it takes longer for women to be diagnosed.

Who Gets Nr-AxSpA?

As of this writing, it is estimated that roughly 1.6 million adults in the U.S. have nr-axSpA. Nr-axSpA and related conditions often start in young people, usually under the age of 45. They can also sometimes occur early in life, in juveniles (these cases are called juvenile spondyloarthritis).

Recent studies have found that women are slightly more likely to have nr-axSpA, with demographic reviews showing 55% - 60% of those impacted being women.

The HLA-B27 genetic marker is associated with both forms of axial spondyloarthritis, including nr-axSpA. This association is especially strong in Caucasians: while the marker is found in 7.5% of the general Caucasian population, it is found in up to 70% of Caucasians with nr-axSpA. The gene prevalence varies in other ethnicities.

While testing for the gene can be helpful in making a diagnosis, it is not a diagnostic test. It is simply one possible tool in the search for a diagnosis.
While knowledge and awareness of this condition have grown in recent years, unfortunately, many people still go undiagnosed for years, visit numerous physicians with no answers, and are even misdiagnosed with something else before arriving at the nr-axSpA diagnosis.

Diagnosing nr-axSpA can be difficult, as many of its symptoms can mimic those of other conditions. This, combined with lack of awareness about nr-axSpA, and lack of clear diagnostic tools, contributes to delays in diagnosis, which means delays in accessing effective treatments. That is why a visit to a rheumatologist is important.

If you do not already have a rheumatologist, SAA can help you find one near you at spondylitis.org/Rheumatologist-Directory.

Treating Nr-axSpA

There may be no cure yet, but that doesn’t mean there’s no help. On the contrary, you are part of a vibrant community of experts and people like you—a community that’s driving new innovations in nr-axSpA treatment.

Important recent advances have offered more insight into what triggers the condition, and how best to diagnose and treat it. New medications and interventions are being developed at an increasingly rapid rate, and people living with the disease today are likely to have a substantially higher quality of life than just a decade or two ago. There is reason to hope that new advances in research and treatment will lead to even better outcomes in the near future.

A holistic approach to nr-axSpA, which treats the whole person, includes exercise, wellness practices, stress management, good nutrition, and medications when you and your doctor determine them to be appropriate.
Exercise

Exercise is one of the best tools for controlling nr-axSpA pain. But pain relief isn’t the only reason to exercise. In fact, in no other type of arthritis is the role of exercise more important.

Exercise can counteract some of the impacts of nr-axSpA, helping you maintain more mobility and flexibility, as well as directly increasing strength, endurance, and balance. Medication alone cannot maintain or improve mobility, strength, or function.

But the benefits go beyond physical health, as exercise has been shown to optimize mental health as well. Some of the many benefits of exercise include reducing stress, improving cardiovascular endurance, lowering blood pressure, boosting self-esteem and productivity, increasing HDL or “good” cholesterol, maximizing bone health, managing weight, and possibly even enhancing the body’s response to medications. For individuals with nr-axSpA, there are still more benefits, such as improvement in posture, function, and fatigue, among other things.

It is often difficult to exercise or participate in physical activity if pain persists due to active inflammation. It’s important to work with your doctor to find ways to control pain, inflammation, and stiffness so that you can maintain an exercise program. A good treatment plan must include exercise and physical activity. Physical therapists can help you craft an individualized stretching, cardio, and strengthening program to fit your unique needs.

There are 4 main types of exercises recommended:

- Range-of-Motion or Stretching
- Aerobic or Cardiovascular
- Strengthening
- Balance

An ideal exercise program will incorporate each of the types of exercise noted above.

SAA has developed a number of exercise resources for those with nr-axSpA and related diseases, including a video of workouts and routines designed specifically for those with spondyloarthritis. SAA offers a wealth of other information and resources, including a free, downloadable PDF demonstrating helpful stretches and strengthening moves.

Visit spondylitis.org/Exercise-Posture for more information and to download the poster.
Diet and Nutrition

Many specialized diets have gained popularity among people with arthritis. To date, there have been small studies suggesting that for some people, an anti-inflammatory diet may play a role in managing arthritis symptoms. There is some evidence that certain foods tend to cause more inflammation in the body, while other foods can help reduce it.

Experts agree on certain guidelines to good nutrition, such as:

- Eat a variety of healthy foods rich in antioxidants, such as colorful vegetables and fruits
- Eat foods rich in omega 3 fatty acids, such as salmon, flax seeds, and certain nuts
- Use fat (especially saturated fat found in animal products), sugar, and salt in moderation
- Minimize processed foods, fried foods, and other products high in artificial ingredients
- Drink 8 to 10 glasses of water per day

If you think that you are affected—either negatively or positively—by certain foods, try keeping a food diary for a while to keep track of results. However, nr-axSpA symptoms can come and go without an apparent explanation, and this can make it difficult to track such patterns over a short period of time. A longer tracking period would provide better information. Registered dieticians are helpful in this area and can work to fine-tune ideal nutrition for your particular needs; ask your rheumatologist for a referral.

More information on the role of diet in nr-axSpA and related conditions is available at spondylitis.org/Diet-Nutrition.

Medications

For many people with nr-axSpA, nonsteroidal anti-inflammatory drugs (NSAIDs) are a strong first line of defense. This is because they help reduce inflammation and pain.

However, if you are taking NSAIDs and symptoms are still interfering with your quality of life, your doctor may suggest trying a biologic medication, such as a TNF inhibitor or IL-17 inhibitor. These drugs can be remarkably effective in treating moderate to severe nr-axSpA, and may even have an impact on the course of the disease. Not everyone with nr-axSpA needs them or will benefit from them. Other medications at times used in nr-axSpA include methotrexate and sulfasalazine, though these medications are only effective in treating arthritis of the hands, feet, and extremities; they do not help the back.

New drugs regularly reach the market for nr-axSpA and related diseases. For an up-to-date listing of medications used to treat these conditions, please visit spondylitis.org/medications.

SAA has also developed an overview of the 2019 Axial Spondyloarthritis Treatment Recommendations, which discusses detailed treatment recommendations in clear and simple terms for patients and families. You will find that resource at spondylitis.org/treatment-information.

Be sure to discuss the risks and benefits of your treatment options with your doctor so you can together develop the most appropriate management plan for you.
Managing the Emotional Impact, and Finding Support

Living with a chronic illness like nr-axSpA can, at times, be difficult. That is why it is important to be gentle with and easy on yourself. Seeking support is a crucial part of this process. Research tells us that people with nr-axSpA who have a solid support system do better than those who do not.

SAA can help you get in touch with others who have nr-axSpA, and find peer support. Find local support groups, online message boards, personal stories from others, an active online community, and more at spondylitis.org/Community.

If you find yourself struggling with the mental and emotional impacts of this disease, it can be helpful to consult with a psychologist or other mental health professional who specializes in working with people who have a chronic illness. The more positive support you can bring into your life, the easier it will be to keep nr-axSpA from imposing limitations.

Complications and Risks

Many complications are associated with nr-axSpA. It is important to be aware of and discuss these with your doctor. Always contact your doctor if you notice any new symptom in any part of your body.

Increased Risk of Osteoporosis

Nr-axSpA is an inflammatory disease with the major site of inflammation being in the bone next to the joint (doctors call this an osteitis). Very often, MRIs from nr-axSpA patients show minimal inflammation in the joint but striking inflammation in the bone next to the joint. In addition, what is essentially unique for nr-axSpA and related diseases is that this inflammation in the bone is also typically seen where ligaments and tendons attach to the bone (enthesitis). If this local inflammation in the vertebrae is not controlled, it will ultimately result in fragile bones.

There is also a second way people with nr-axSpA can develop fragile bones. Systemic inflammation causes the release of certain chemicals into the blood that activate cells in bone that can dissolve bone mineral. These cells are called osteoclasts, and secrete acid, which dissolves bone very efficiently.

As a result, people with nr-axSpA suffer from a double whammy when it comes to bone health. They have inflammation locally within the bone of the spine, but also release molecules into the blood that cause activation of osteoclasts. This is one reason why those with nr-axSpA and related conditions are at much higher risk of spine fractures.

For women with nr-axSpA, menopause is an especially precarious period, as the rapid decrease in sex hormone production also results in the activation of osteoclasts.

Is there anything that can be done about this?

Yes—a great deal, in fact. First, everyone should make sure that they stay active, not only to preserve strength and flexibility, but also to preserve bone mineral. The cells that make bone mineral—osteoblasts—love weight-bearing exercise. But they can only do their work properly if they are supplied with the proper nutrients. This means plenty of vitamin D and calcium each day.

Doctors prefer calcium that is sourced through nutrition, and the recommended amount depends on your age, bone health, and risk factors for osteoporosis. A good rule of thumb is that one good helping of a dairy product—yogurt, cheese, a tall glass of skim milk—or one tablet of extra-strength Tums, provides 300mg of elemental calcium. Other calcium rich foods include collard greens, and fortified cereals. If you are thinking of buying a specialized calcium supplement or something similar, compare labels to make sure you’re getting the most benefit for your money. In particular, read the label and make sure you know how much elemental calcium is in the product, because this is what really counts, and not the total grams of each tablet (which is what is often on the front label).
Doctors also recommend approximately 800 units of vitamin D per day, though this should be discussed with your rheumatologist. Vitamin D is found in foods such as salmon, swordfish, cod liver oil, and fortified foods and beverages. Exposure to sunlight is another source. Numerous vitamin D supplements are also available.

Several medications are also effective for the treatment of osteoporosis. These include agents belonging to a class of drugs called bisphosphonates. They have been demonstrated effective in most forms of osteoporosis and are equally beneficial to men and women. Biologic medications have also been shown to increase bone density, likely by suppressing bone inflammation.

**Fatigue and Pain**

Fatigue is a common complaint in nr-axSpA, and one that doesn’t often receive the attention it deserves. Fatigue can negatively impact one’s work, family or social life, ability to focus, and even emotional state.

Uncontrolled inflammation is the factor most closely associated with fatigue in nr-axSpA, studies have shown. If inflammation is extensive, then the body must use energy to deal with it, producing feelings of profound, chronic tiredness. The release of certain cell messengers (cytokines) during the inflammatory process also can produce the sensation of fatigue, as well as mild to moderate anemia in some cases, which itself can further exacerbate fatigue. When inflammation is well controlled and the disease is properly managed, fatigue often lessens and energy returns.

Uncontrolled pain and stiffness can make it difficult to sleep. Besides causing fatigue, sleep deprivation can increase pain, creating a feedback loop of pain causing sleeplessness, which then causes more pain, and so on.

Depression also causes fatigue directly by lowering energy levels, as well as indirectly by interfering with sleep. Depression lowers serotonin, a hormone that helps regulate the internal clock that controls sleeping and waking. As such, depression and insomnia can reinforce each other if not properly treated. Those with chronic pain are more likely to suffer from depression. There is also a feedback loop between pain and depression, with each one making the other worse.

For all of these reasons, effective pain management is crucial. Though many people with nr-axSpA respond well to medications alongside exercise and physical therapy, others experience more severe pain even with appropriate treatment. In these cases, it is important to work with your medical team to find appropriate solutions and design a comprehensive plan to treat the pain. Speaking with your rheumatologist about pain and fatigue is the first step.

**Fertility, Pregnancy, and Postpartum**

**Fertility and Medications**

Nr-axSpA does not impair fertility in women or in men. Among drugs used to treat the condition, however, it is recognized that sulfasalazine can impair the maturation of sperm cells and therefore impair fertility in men. After stopping the medication, fertility should return to normal in 2 or 3 months.

Azoospermia (the condition of having few or no sperm cells) occurs only rarely during therapy with methotrexate and is reversible after stopping the medication.

Neither of these drugs impair fertility in women, though it’s important to note that methotrexate should not be taken by women during pregnancy, as it has caused birth defects and death in unborn babies. Anyone trying to conceive is advised not to take methotrexate. Finally, some women experience problems with ovulation and implantation when taking NSAIDs and are advised to avoid these drugs throughout pregnancy.

For more information about medication safety in pregnancy, please visit spondylitis.org/women and mothertobaby.org.
Pregnancy and Delivery

Nr-axSpA has no known harmful effects on pregnancy or the baby.

Studies suggest that in contrast to rheumatoid arthritis, pregnancy does not improve disease symptoms in nr-axSpA and related diseases. In general, there is no consistent pattern to disease activity during pregnancy, though it may increase in activity starting at around week 20. It may be that pregnant women stop taking their medications when they find out they are pregnant and therefore disease activity increases. It may also be that the physical impact of pregnancy contributes to disease activity. Women who need to take a biologic medication before pregnancy are more likely to have flares during pregnancy if they stop their biologic. When disease activity increases during pregnancy, patients are more likely to have problems with gestational diabetes, preeclampsia, infection, preterm labor, preterm deliveries, and babies that are small for their gestational age.

During pregnancy, a sudden swelling has occasionally been documented in the knee or ankle joints. In some patients, pain at the site where ligaments and tendons attach to bone and a feeling of tightness in the chest wall have been reported; uveitis can also be more active during this period.

Women with nr-axSpA frequently have active disease at some stage of pregnancy. Many people find it helpful to, when possible, discuss these issues with relevant health professionals before becoming pregnant. Experts recommend working closely with your doctor to determine the best course of treatment while pregnant.

Disease activity increases in many women up to 12 weeks after delivery, but it is unclear how much of this relates to the stress or lifestyle changes associated with new parenthood. As a rule, disease activity returns to a pre-pregnancy pattern during the year following delivery.

Looking to the Future

It is important to emphasize that most people with nr-axSpA do well and are generally satisfied with their care. If your symptoms are not being treated or you are unhappy with your treatment, it is important that you speak with your physician. Don’t downplay how you really feel, and explore ways to change your care. The future looks promising for people with nr-axSpA. We have learned much about the causes of the disease, and new treatments have been introduced that appear to not only reduce the symptoms, but may even slow down progression. It is important to remember that people with a chronic illness have considerable power to help themselves. SAA is here to offer support, information, and helpful resources. Reach out today! We look forward to hearing from you.
The Spondylitis Association of America was the first, and remains the largest, resource in the U.S. for people affected by spondyloarthritis. For more than 35 years, SAA has dedicated all of its resources to funding medical research, education, advocacy, and supportive programs and services that directly benefit the spondylitis community.

By joining SAA you gain access to tools that will improve your own quality of life while also making a difference for the millions affected throughout the nation. Join today and receive:

- **“Spondylitis Plus,”** our information-packed, advertising-free quarterly news magazine
- SAA’s Patient-to-Patient Recommended Rheumatologist Directory
- Access to exclusive Members-Only content on spondylitis.org
- A complimentary copy of our guidebook, **“Your Guide to Living with Ankylosing Spondylitis”**
- Discounts on SAA educational and awareness products, such as books, DVDs, and exclusive, limited-edition SAA logo items
- The satisfaction of knowing that you are part of an extraordinary community of patients, friends, family, and healthcare professionals dedicated to finding the cure!

There are over 100 types of arthritis. At SAA, we focus on one – yours. So that no one has to face spondylitis alone.

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