# Annals of the Rheumatic Diseases



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## Women with rheumatoid arthritis and those treated with TNF inhibitors may be at increased risk of cervical cancer

Women with rheumatoid arthritis have a higher risk of cervical cancer, and those treated with TNF inhibitors have a further increased risk, though the link is not conclusive.

#### **INTRODUCTION**

Rheumatoid arthritis is a chronic inflammatory disease that affects a person's joints, causing pain and disability. It can also affect internal organs. Rheumatoid arthritis is more common in older people, but there is also a high prevalence in young adults, adolescents and even children, and it affects both men and women. People with rheumatoid arthritis also have an increased risk of getting cancer.

TNF inhibitors belong to a group of medicines called biologic disease modifying antirheumatic drugs, or biologics (sometimes also called bDMARDs), and include adalimumab, etanercept, infliximab, golimumab and certolizumab-pegol. These drugs work by targeting specific molecules that cause inflammation. By doing so, they reduce inflammation in the joints and decrease pain and disease worsening in rheumatoid arthritis.

Cervical dysplasia refers to abnormal changes in the cells on the surface of the cervix – the opening of the uterus (womb) that can be felt inside the vagina. Dysplasia changes are not cancer, but they are considered to be precancerous. Cancer of the cervix (cervical cancer) in women has been linked to the human papilloma virus (HPV). It has been suggested that TNF inhibitors might affect the immune system's ability to deal with viruses. Whether treatment with TNF inhibitors increases the risk of cancers associated with viruses is not known.

#### WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to find out whether there is an increased risk of cervical cancer in women with rheumatoid arthritis, and if this was affected by use of TNF inhibitors. They also hoped to be able to say whether cervical screening had an impact on detecting cervical cancer.

#### WHO WAS STUDIED?

The study looked at Swedish women with rheumatoid arthritis treated with TNF inhibitors (9629 women), or not (34,984 women), during 1999–2012. Women with a previous medical history of cervical cancer were excluded.

#### **HOW WAS THE STUDY CONDUCTED?**

This was a retrospective observational study, which means that the authors used existing databases of patient records to look back and find women for each group. There was no interventional treatment given. They used large national Swedish registers with information on inpatients and outpatients, cancer, comorbidities (other diseases people had), and the treatment and education they received. The women were classified into three groups: people with rheumatoid arthritis that had not been treated with TNF inhibitors, people with rheumatoid arthritis had been treated with TNF inhibitors, and a general population cohort to compare against. The authors then compared how many cases of cervical dysplasia and cervical cancer there were in each group.

#### WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The main findings of the study was that women with rheumatoid arthritis have an increased risk of developing cervical dysplasia, and that women with rheumatoid arthritis treated with TNF inhibitors were also at an increased risk of developing invasive cervical cancer. Lastly, the authors found no major differences in the use of cervical screening between women with rheumatoid arthritis and those in the general population, or between those women with rheumatoid arthritis that were treated with TNF inhibitors and those that were not.

#### ARE THESE FINDINGS NEW?

Yes. This is the first study to show an increased risk of cervical cancer among women with rheumatoid arthritis treated with TNF inhibitors.

#### WHAT ARE THE LIMITATIONS OF THE STUDY?

People selected for treatment with TNF inhibitors are likely to suffer from more severe disease, and are also likely to have tried more different types of medicine. This means it is difficult to separate the effects of worse

disease or previous medicines from the specific effects of TNF inhibitors. There were other limitations in the accuracy of the statistics.

#### WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The authors are currently working on a study of cervical cancer among patients with systemic lupus erythematosus to see if the findings are similar in other inflammatory diseases.

#### WHAT DOES THIS MEAN FOR ME?

If you have rheumatoid arthritis and are treated with TNF inhibitors, your risk of cervical cancer might be moderately increased. However, it is important to remember that even though the relative risk might be increased compared to someone without rheumatoid arthritis, or taking different medicines, the absolute risk is still very low. You can limit your risk by making sure you have been vaccinated against human papilloma virus (HPV) and going for regular smear tests (cervical screening), which can help to identify early cell changes.

If you are taking TNF inhibitors and are concerned about the risks of cancer, you should talk to your doctor. It is important that you do not stop taking your treatment without seeking medical advice.

#### **FURTHER READING**

EULAR recommendations for management. Available at: http://www.eular.org/recommendations\_management.cfm

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