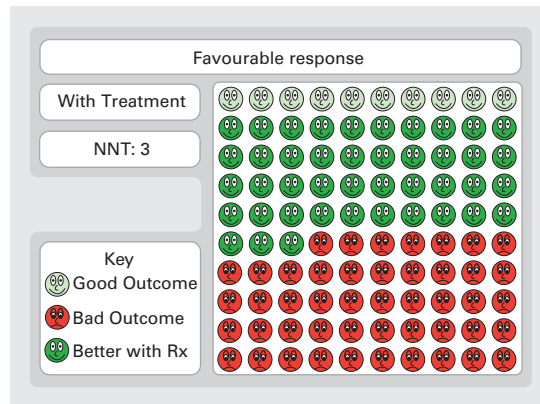


**Table 12.3** Number needed to treat for methotrexate versus placebo (van den Hoogen *et al*,1996)<sup>6</sup>

Outcome	% with placebo	% with methotrexate	Relative risk with methotrexate (95% CI)	Absolute benefit increase (95% CI)	NNT (95% CI)
Favourable response (TSS or VAS improved by 30%+ or CMDC improved by 15%+. If digital ulcers persisted or CMDC decreased 15%+ response was unfavourable despite improvement of TSS or VAS)	1/10 (10%)	8/15 (53%)	5.33 (0.78, 36.33) p = 0.04	43% (5, 67)	3 (2, 20)

Visual Rx Faces 12.1 NNT for MTX versus placebo



# Scleroderma and methotrexate Summaries and decision aid

## How well does methotrexate (MTX) work for treating scleroderma (also known as systemic sclerosis) and how safe is it?

To answer this question, scientists found and analysed 2 high quality studies testing 100 people who had scleroderma. People received either injections or pills of methotrexate or a placebo or sugar pill and were monitored for 6 months or a year. These studies provide the best evidence we have today.

### What is scleroderma and how can methotrexate help?

Scleroderma or systemic sclerosis is a condition where skin, joints, and blood vessels are replaced with thick, hard, fibrous tissue. It is thought that scleroderma is caused by the body's immune system attacking its own tissues. The tissues become inflamed or swollen and produce too much collagen (a tough fibre-like tissue). People with scleroderma will likely have patches of hard skin and pain, swelling and stiffness in their joints and/or damage in their organs, such as the heart, lungs, and kidneys. Disease modifying antirheumatic drugs (DMARDs) can be prescribed to reduce pain and inflammation and to slow the progress of the disease. Methotrexate is a DMARD that may stop scleroderma from getting worse by controlling the immune system.

### How well did methotrexate work?

Two studies showed that more people receiving methotrexate injections had improved skin thickness by 30% and could breathe better by 15% than people receiving a placebo or sugar pill.

When asked, people said that they felt better overall in one study but not in the other study when receiving methotrexate injections.

### What side effects occurred with methotrexate?

Studies of people with scleroderma and studies of people with other diseases have shown that mouth ulcers, nausea, heartburn, rash, and lung problems may occur with methotrexate. Changes in liver enzymes and death may also occur.

### What is the bottom line?

There is "Silver" level evidence that methotrexate decreases skin thickness and symptoms of scleroderma, such as problems breathing.

Stomach and intestinal side effects, and high liver enzyme levels may occur when taking methotrexate. But these side effects may not last long and so many people keep receiving methotrexate.

Based on Pope J, Furst D, Clements P, Ottawa Methods Group. Systemic sclerosis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

## How well does methotrexate (MTX) work for treating scleroderma or systemic sclerosis and how safe is it?

### What is scleroderma and how can methotrexate help?

Scleroderma or systemic sclerosis is a condition where skin, joints, and blood vessels are replaced with thick, hard, fibrous tissue. It is thought that scleroderma is caused by the body's immune system attacking its own tissues. The tissues then become inflamed or swollen and produce too much collagen (a tough fibre-like tissue). There are two types of scleroderma: localised – which affects mainly the skin but can affect the muscles and joints; and generalised – which affects the skin and organs, such as the heart, lungs and kidneys. Localised scleroderma may develop slowly and not cause severe problems, but generalised scleroderma may get worse over time.

Painkillers or analgesics are often prescribed to improve joint pain and swelling. Disease modifying antirheumatic drugs (DMARDs) can be prescribed to reduce pain and inflammation and also to slow the progress of the disease. Methotrexate is a DMARD that may stop scleroderma from getting worse by controlling the immune system. Methotrexate can also cause side effects and therefore it is important to know how well methotrexate works and how safe it is.

### How did the scientists find the information and analyse it?

The scientists searched for studies that examined the treatment of scleroderma. Not all studies found were of a high quality and so only those studies that met high standards were selected.

Studies were randomised controlled trials where a group of patients received methotrexate and were compared to patients who received a placebo or a sugar pill.

### Which high quality studies were examined in this summary?

Two high quality studies were examined. A total of 100 patients with scleroderma received either an injection of methotrexate or a placebo and were followed for about 6 to 12 months.

One study tested 29 patients for 24 weeks: 17 patients received a weekly injection of 15 mg of methotrexate and 12 received a placebo injection.

One study tested 71 patients for 1 year: 35 patients received methotrexate pills weekly and 36 received a placebo.

Improvement was measured by testing skin thickness or whether the skin could be pinched into a fold, general wellbeing, presence of ulcers or sores on the skin, and breathing.

### How well did methotrexate work?

One study showed that more patients receiving methotrexate injection had improved skin thickness by 30%, could breathe better by 15%, and felt better overall by 30%, compared to patients receiving a placebo:

- 10 out of 100 patients had improved with a placebo
- 53 out of 100 patients had improved with methotrexate.

The other study showed that more patients receiving methotrexate pills had improved skin thickness and breathing compared to patients receiving a placebo:

- 24 out of 100 more patients benefited from receiving methotrexate than a placebo (sugar pill).

But in this study, improvement in overall wellbeing as measured by the patients themselves and as measured by their doctor was the same when receiving methotrexate or a placebo.

### What side effects occurred with methotrexate?

Studies of people with scleroderma and studies of people with other diseases have shown that mouth ulcers, nausea, heartburn, rash, and lung problems may occur. Changes in liver enzymes and death may occur when receiving methotrexate:

- 65 out of 100 patients had abnormal liver enzyme levels or other side effects with methotrexate
- 17 out of 100 patients had the same side effects as above while receiving a placebo.

### What is the bottom line?

There is “Silver” level evidence that methotrexate decreases skin thickness and symptoms of scleroderma, such as problems with breathing.

Stomach and intestinal side effects, and high liver enzyme levels may occur when taking methotrexate. But these side effects may not last long and so many people keep receiving methotrexate.

Based on Pope J, Furst D, Clements P, Ottawa Methods Group. Systemic sclerosis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

## Information about scleroderma and treatment

### What is scleroderma?

Scleroderma or systemic sclerosis is a condition where skin, joints, and blood vessels are replaced with thick, hard, fibrous tissue. It is thought that scleroderma is caused by the body's immune system attacking its own tissues. People with scleroderma will likely have patches of hard skin and have pain, swelling, and stiffness in their joints.

There are two types of scleroderma: localised – which affects mainly the skin but can affect the muscles and joints; and generalised – which affects the skin and organs, such as the heart, lungs, and kidneys. Localised scleroderma may develop slowly and not cause severe problems. But generalised scleroderma may get worse over time. If scleroderma is not treated, it may result in:

- ulcers or sores on toes and/or fingers
- trouble swallowing
- heartburn
- problems breathing well
- problems digesting food
- problems with your heart and kidneys
- surgery

### What can I do on my own to manage my disease?

✓ moisturise skin ✓ exercise ✓ protect skin and joints ✓ rest and relax ✓ avoid smoking

### What treatments are used for scleroderma?

Five kinds of treatment may be used alone or together. The common (generic) names of treatment are shown below.

1. *Pain medicines and non-steroidal anti-inflammatory drugs (NSAIDs)*
  - Acetaminophen
  - Acetylsalicylic acid
  - Celecoxib
  - Diclofenac
  - Ibuprofen
  - Indomethacin
  - Nabumetone
  - Naproxen
  - Piroxicam
  - Rofecoxib
  - Sulindac
2. *Disease modifying antirheumatic drugs (DMARDs)*
  - Methotrexate
  - Cyclophosphamide
  - 5-Fluorouracil
3. *Corticosteroids*
  - Dexamethasone
4. *Prostacyclins*
  - Epoprostanol
  - Treprostinil
5. *Miscellaneous therapies*
  - Stem cell transplantation
  - Bovine type I collagen
  - Bosentan
  - Angiotensin-converting enzyme inhibitors (ACE inhibitors)

### What about other treatments I have heard about?

There is not enough evidence about the effects of some treatments. Other treatments do not work. For example:

- Acetylsalicylic acid
- Alpha interferon
- Anti-TGF beta
- Anti-oxidants
- Chlorambucil
- Cyclofenil
- Dipyridamole
- Gamma interferon
- Ketotifen
- N-acetylcysteine
- Penicillamine
- Potassium aminobenzoate (POTABA)
- Relaxin

### What are my choices? How can I decide?

Treatment for your disease will depend on your condition. You need to know the good points (pros) and the bad points (cons) about each treatment before you can decide.

## Scleroderma (systemic sclerosis) decision aid

### Should I take methotrexate?

This guide can help you make decisions about a treatment your doctor is asking you to consider. It will help you to:

1. Clarify what you need to decide.
2. Consider the pros and cons of different choices.
3. Decide what role you want to have in choosing your treatment.
4. Identify what you need to help you make the decision.
5. Plan the next steps.
6. Share your thinking with your doctor.

#### Step 1: Clarify the decision

##### What is the decision?

Should I take methotrexate to decrease pain and slow the progress of scleroderma/systemic sclerosis?

Methotrexate can be taken as a pill daily or as an injection received weekly.

##### When does this decision have to be made? Check one

within days       within weeks       within months

##### How far along are you with this decision? Check one

- I have not thought about it yet
- I am considering the choices
- I am close to making a choice
- I have already made a choice

## Step 2: Consider the pros and cons of different choices

### What does the research show?

Methotrexate is classified as: **Likely beneficial**

There is “Silver” level evidence from 2 studies of 100 people with scleroderma testing methotrexate. The studies lasted up to 1 year. These studies found pros and cons that are listed in the chart below.

### What do I think of the pros and cons of methotrexate?

1. Review the common pros and cons that are shown below.
2. Add any other pros and cons that are important to you.
3. Show how important each pro and con is to you by circling from one (\*) star if it is a little important to you, to up to five (\*\*\*\*\*) stars if it is very important to you.

PROS AND CONS METHOTREXATE TREATMENT	
PROS (number of people affected)	How important is this to you?
<b>Decreases skin thickness</b> in 53 out of 100 people with methotrexate in 10 out of 100 without methotrexate	* * * * *
<b>Makes breathing easier</b> in 53 out of 100 people with methotrexate in 10 out of 100 without methotrexate	* * * * *
<b>May improve overall well-being</b> in 53 out of 100 people with methotrexate in 10 out of 100 without methotrexate	* * * * *
<b>Other pros:</b>	* * * * *
CONS (number of people affected)	How important is this to you?
<b>Side effects: mouth ulcers, nausea, heartburn, rash, lung problems</b> in 65 out of 100 people with methotrexate in 17 out of 100 people without methotrexate	* * * * *
<b>Long term side effects are rare but include liver damage</b>	* * * * *
<b>Monthly clinic visits and blood tests are needed</b>	* * * * *
<b>Personal cost of medicine</b>	* * * * *
<b>Other cons:</b>	* * * * *

### What do you think of taking methotrexate? Check one

- Willing to consider this treatment  
 Pros are more important to me than the Cons
- Unsure
- Not willing to consider this treatment  
 Cons are more important to me than the Pros

### Step 3: Choose the role you want to have in choosing your treatment

Check  one.

- I prefer to decide on my own after listening to the opinions of others
- I prefer to share the decision with: \_\_\_\_\_
- I prefer someone else to decide for me, namely: \_\_\_\_\_

### Step 4: Identify what you need to help you make the decision

<b>What I know</b>	Do you know enough about your condition to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know which options are available to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the good points (pros) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the bad points (cons) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>What's important</b>	Are you clear about which <b>pros</b> are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you clear about which <b>cons</b> are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>How others help</b>	Do you have enough support from others to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you choosing without pressure from others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you have enough advice to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>How sure I feel</b>	Are you clear about the best choice for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you feel sure about what to choose?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure

*If you answered No or Unsure to many of these questions, you should talk to your doctor.*

### Step 5: Plan the next steps

#### What do you need to do before you make this decision?

For example – talk to your doctor, read more about this treatment or other treatments for scleroderma.

### Step 6: Share the information on this form with your doctor

It will help your doctor understand what you think about this treatment.

*Decisional Conflict Scale* © A O'Connor 1993, Revised 1999.

Format based on the Ottawa Personal Decision Guide © 2000, A O'Connor, D Stacey, University of Ottawa, Ottawa Health Research Institute.