

NSAIDs and musculoskeletal pain

What this decision aid is for

This decision aid is intended to assist health professionals in consultations with patients in whom various treatment options for osteoarthritis (OA) are being considered. Leaflets for patients explaining osteoarthritis can be found on the CKS website www.cks.library.nhs.uk/home.

Introduction and aims of treatment

OA is long term condition affecting the joints which causes pain and stiffness. No treatment will cure or reverse joint damage. Some people's symptoms improve over time. Most people's symptoms do not get worse very quickly.¹ Treatments can ease the pain and stiffness and help reduce the impact of OA on daily living.¹ Some treatments will work better for some people than others. All treatment choices involve weighing up the possible benefits against the possible harms.

How effective are these treatments for reducing pain?

This decision aid considers the likely benefits, compared with no treatment, of the following:

1. Exercise
2. Muscle strengthening
3. Paracetamol
4. Topical NSAIDs
5. Oral NSAIDs
6. Oral NSAIDs compared with paracetamol

We have put them in increasing order of possible harms (paracetamol is ahead of topical NSAIDs as these can sometimes cause skin reactions).

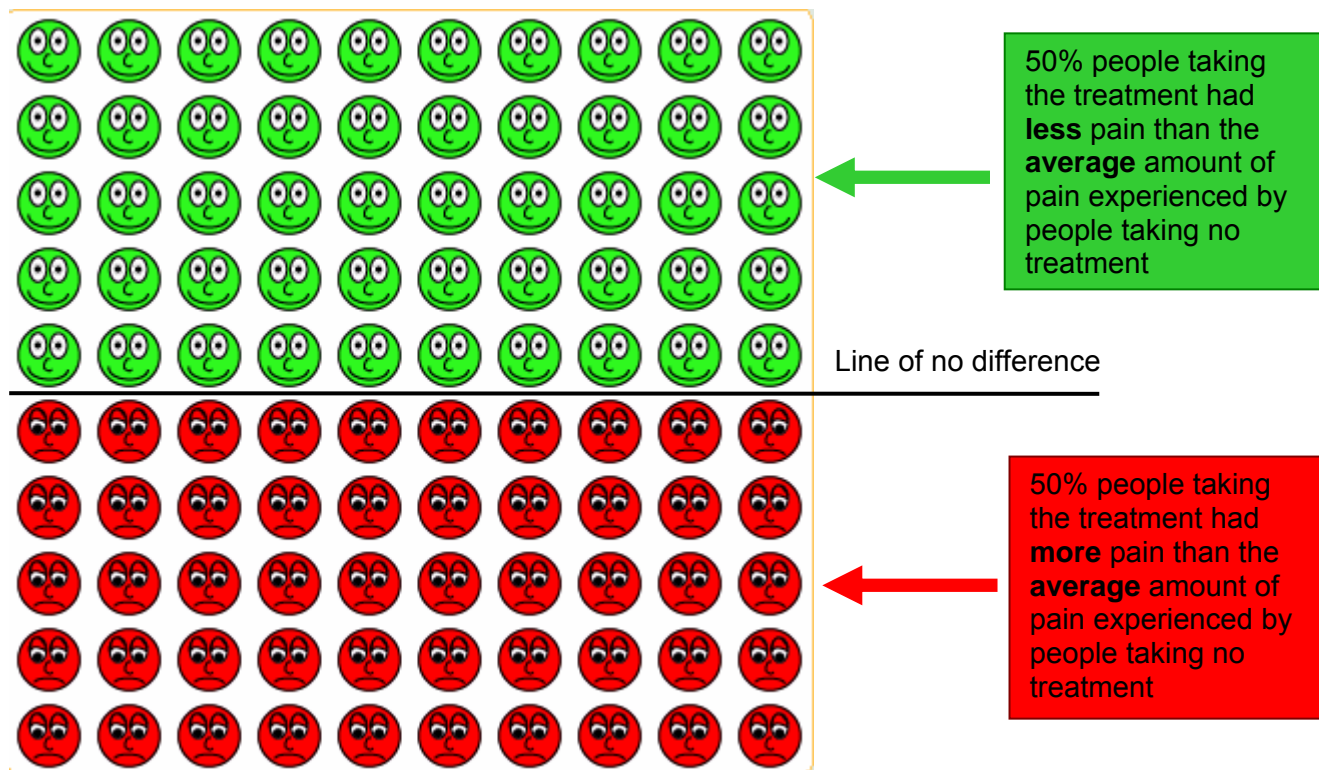
All these treatments seem to help most people a little, but none of them makes a substantial difference for most people.

How the effectiveness of treatments is presented

The Cates plots show how many people who use a treatment are likely to get less pain than the **average** patient who takes no treatment. These are shown as green smiley faces in the diagrams below. Some people's pain does not get better with that treatment and can even be worse than the pain of the **average** patient who takes no treatment. These are shown by the red faces in the pictures below.

If there was no difference in pain relief in the treatment and no treatment groups, 50% (50 in 100) of the people taking the treatment would rate their pain as better than the **average** amount of pain experienced by people taking no treatment (green faces); 50% of the people taking the treatment would rate their pain as worse than the **average** amount of pain

experienced by people taking no treatment (red faces). This would be shown in a Cates plot like the one below.



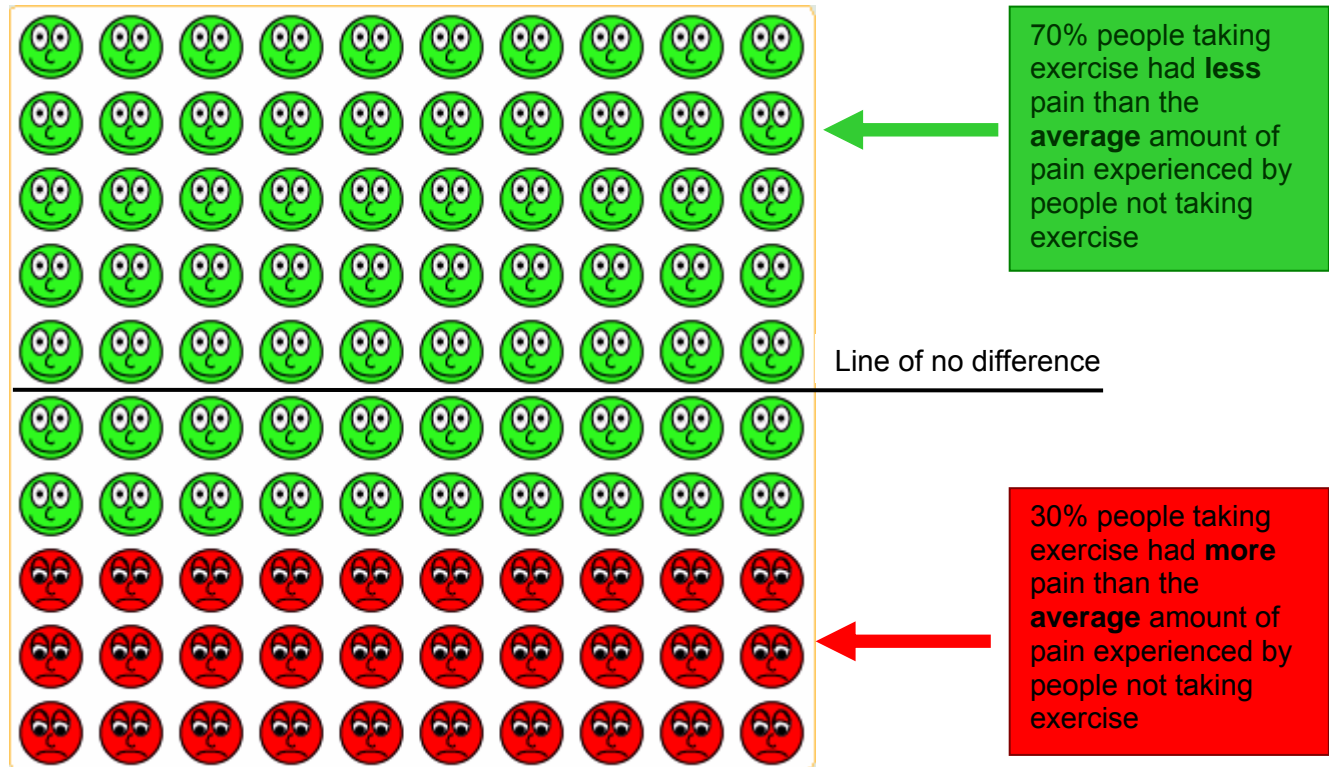
Note, these Cates plots show the **average** response. Half the people in any group (those taking treatment or those taking placebo) will experience more pain than the average of the group, and half the people will experience less pain than group average. People's experience of pain varies, and it is not possible to tell whether a person's pain is more or less than the average level of pain experienced by people in the studies. The difference between pain that is a little more than average and pain that is a little less than average might not be very much. No-one can tell in advance what will happen for an individual person

Source of images

The images have been produced using Dr Chris Cates's software Visual Rx 2.0. More information can be obtained from the website www.nntonline.net

1. Exercise

The studies in a systematic review compared taking exercise (usually walking) with taking no exercise among people with OA of the knee:

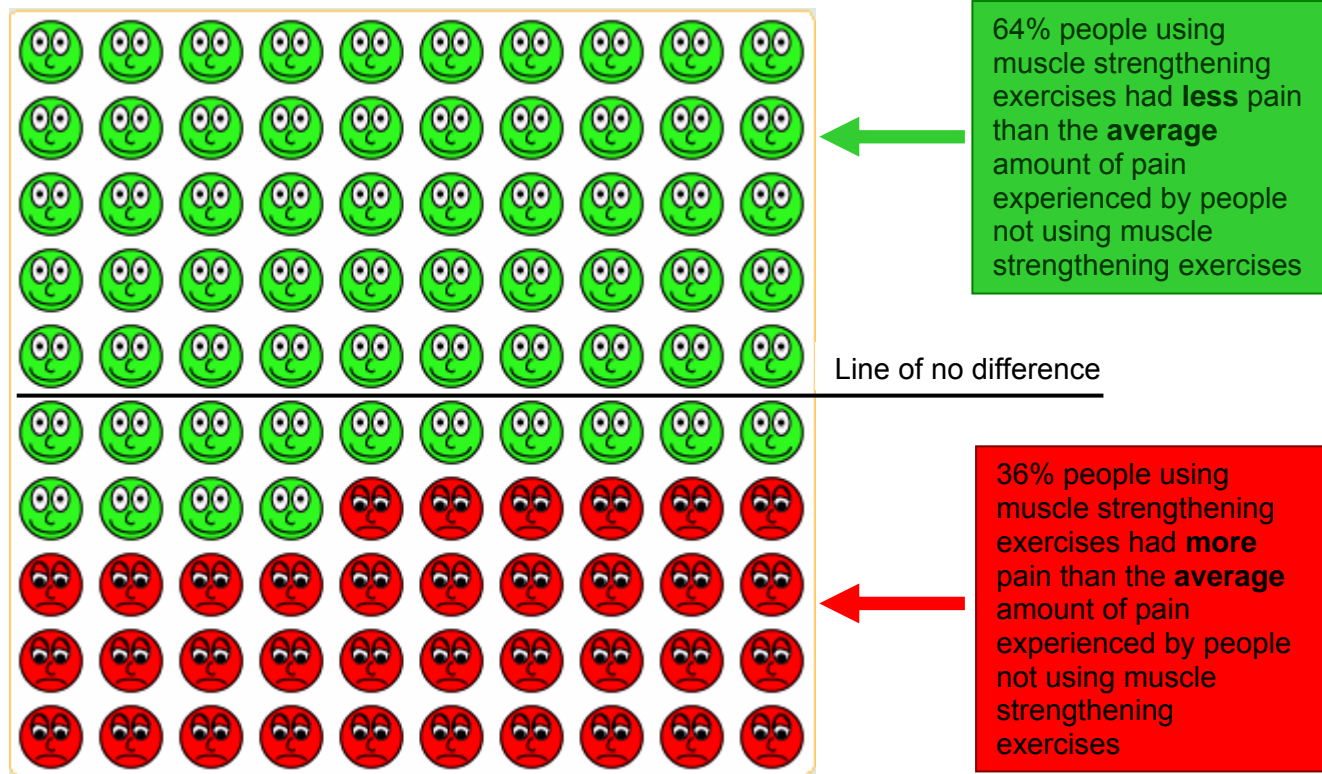


Putting this another way, there is a 70:30 chance of patients having less pain if they take exercise than if they do not

Mean effect size for pain relief = 0.52, 95%CI 0.34 to 0.70²: equivalent percentile approximately 70%³

2. Muscle strengthening

The studies in a systematic review compared the effects of specific exercises to strengthen the quadriceps (the muscles of the thigh) in people with OA of the knee and compared them to no strengthening exercises.

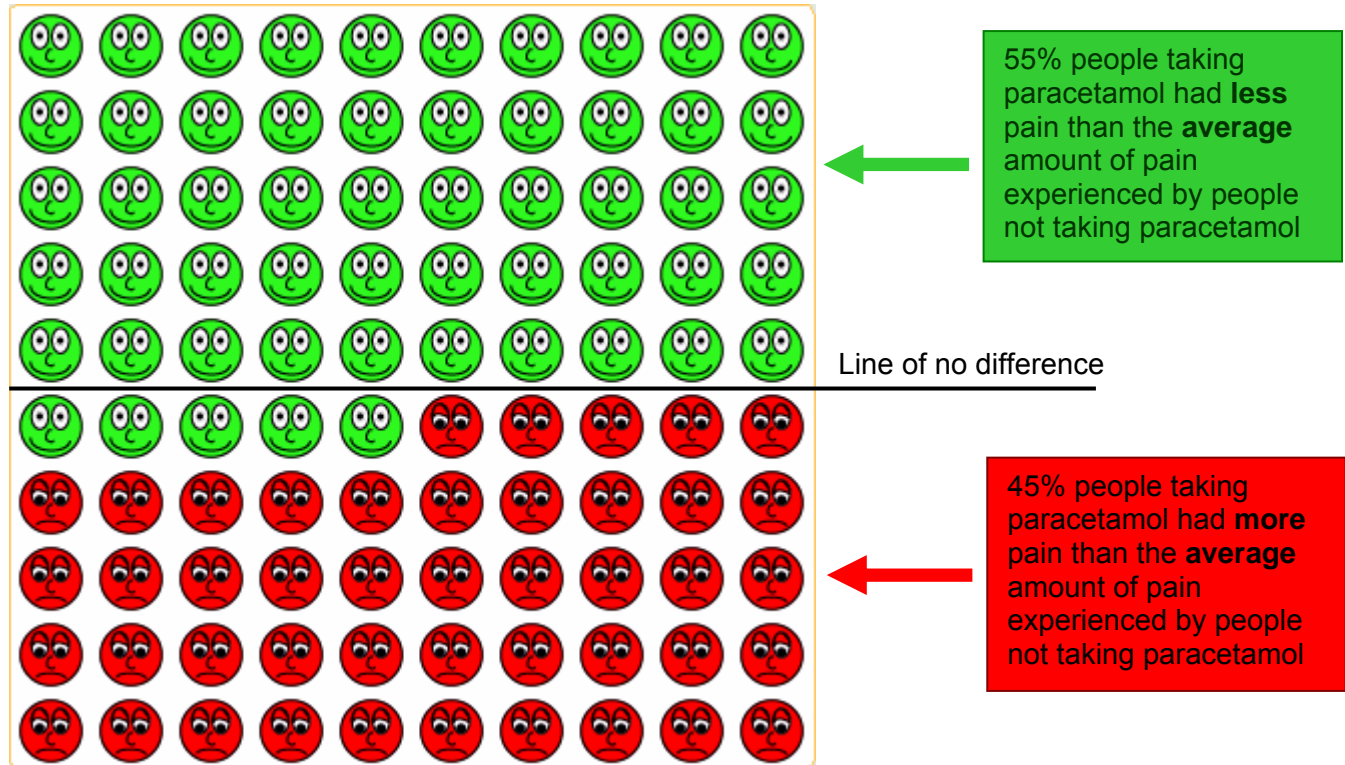


Putting this another way, there is a 64:36 chance of patients having less pain if they do muscle strengthening than if they do not

Mean effect size for pain relief = 0.35, 95%CI 0.23 to 0.42²: equivalent percentile approximately 64%³

3. Paracetamol

The studies in a Cochrane systematic review looked at the effects of paracetamol in people with OA compared with placebo.



Putting this another way, there is a 55:45 chance of patients having less pain if they take paracetamol than if they do not

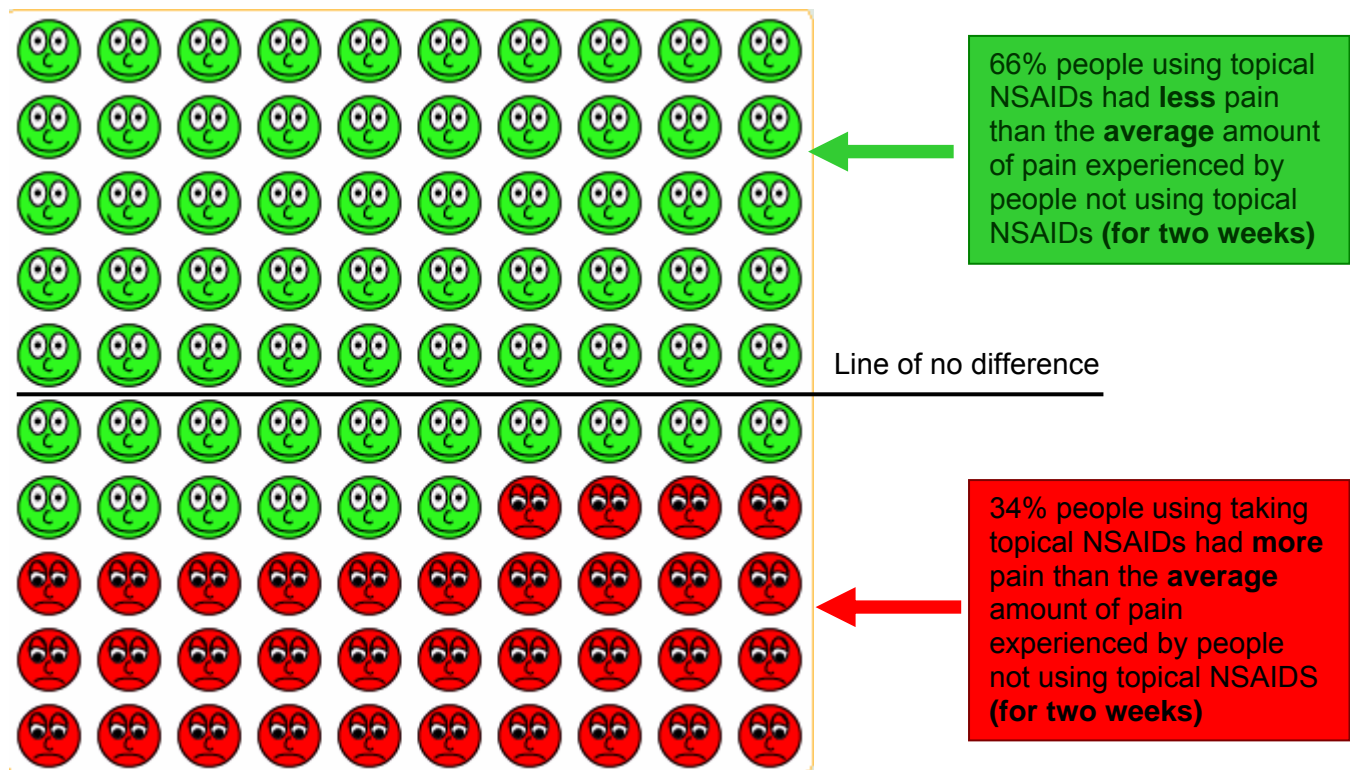
Mean effect size = 0.13, 95%CI 0.04 to 0.22⁴: equivalent percentile approximately 55%³

4. Topical NSAIDs

The studies in a Cochrane systematic review compared topical NSAIDs with placebo in the treatment of OA.

It is important to remember that the benefits seen lasted **only two weeks**: after that time there was **no** difference between the topical NSAIDs and placebo. Also, although the summary of studies was done well, the authors think that some studies may not have been available to them (publication bias): this may have made the benefits seem bigger than they actually are.

For **pain relief after two weeks**, compared with placebo:



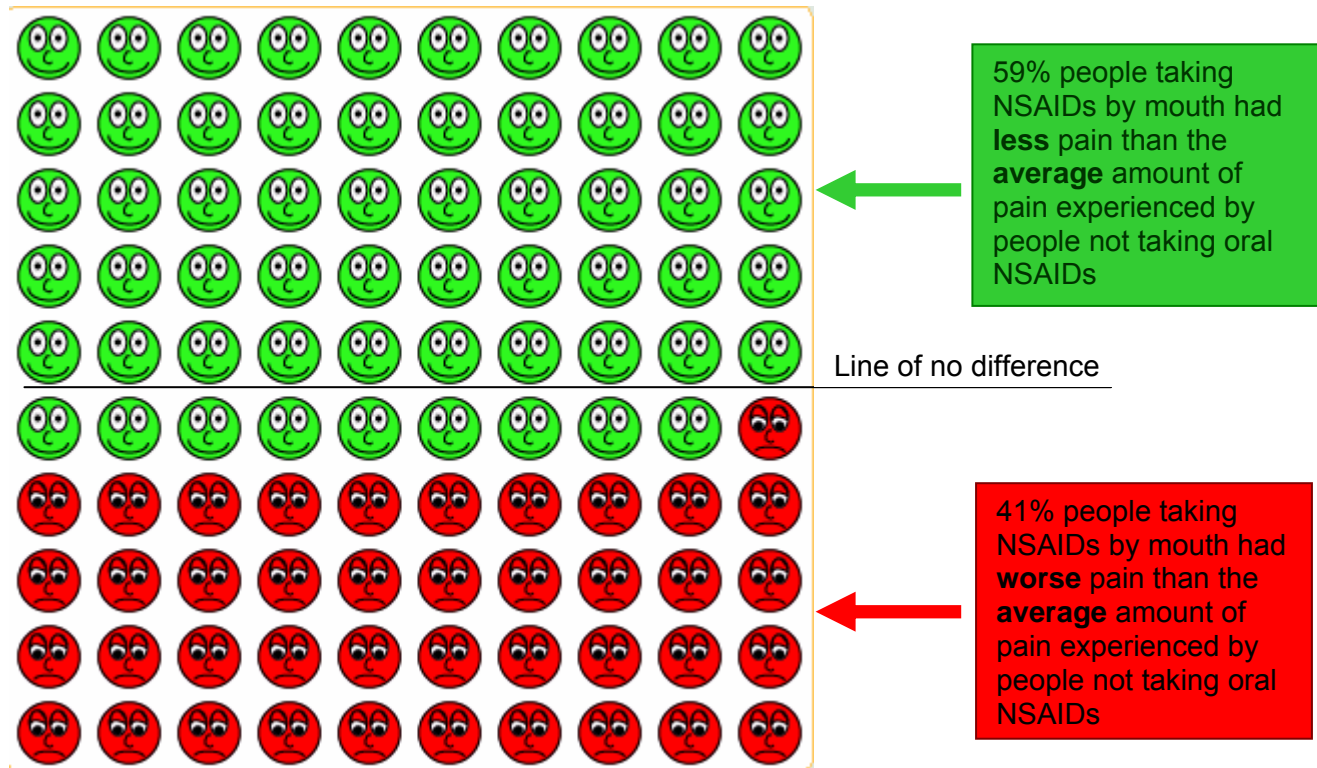
Putting this another way, there is a 66:34 chance of patients having less pain if they use topical NSAIDs than if they do not, **but the benefits only seem to last 2 weeks**

Mean effect size = 0.40, 95%CI 0.15 to 0.65⁵: equivalent percentile approximately 66%³

5. Oral NSAIDs

This meta-analysis of randomised controlled trials looked at oral NSAIDs for the treatment of OA compared with placebo.

Looking at **pain** and compared to placebo:



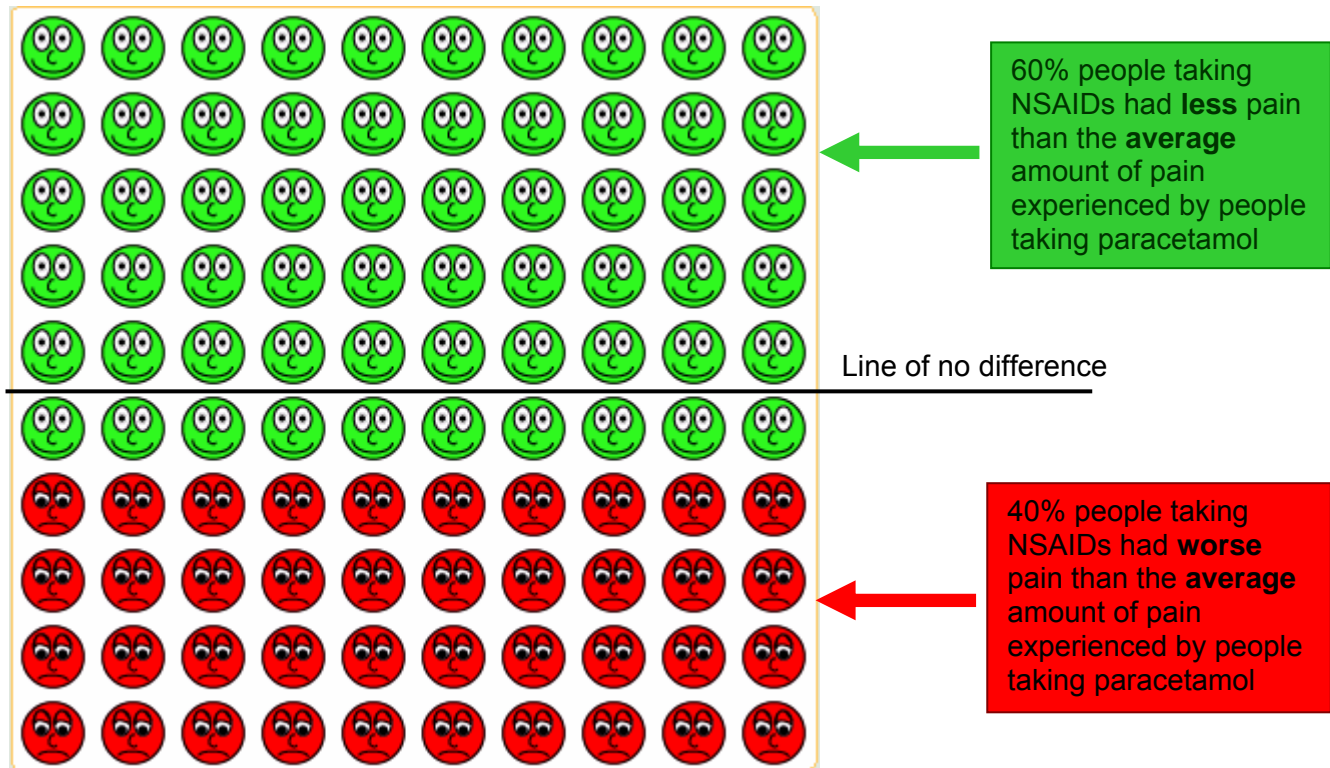
Putting this another way, there is a 59:41 chance of patients having less pain if they take oral NSAIDs than if they do not.

Mean effect size =0.23, 95%CI 0.16 to 0.31⁶: equivalent percentile approximately 59%³

6. Oral NSAIDs compared with paracetamol

A well-conducted meta-analysis of 10 randomised controlled trials looked at oral NSAIDs for the treatment of OA compared with paracetamol

Looking at **overall pain** and compared to paracetamol:



Putting this another way, there is a 60:40 chance of patients having less pain if they take oral NSAIDs than if they take paracetamol

Mean effect size =0.25, 95%CI 0.17 to 0.33⁴: equivalent percentile approximately 60%³

Harms

Gastrointestinal (GI) risks^{7,8}

Dyspepsia

- All oral NSAIDs can cause dyspepsia.
- Dyspepsia is common, even in people who do not take NSAIDs.
- Patients taking oral NSAIDs are more likely to develop dyspepsia than those patients who take paracetamol or use topical NSAIDs.
- There are many other causes of dyspepsia, so we cannot give numbers to help patients decide.

Serious GI side effects

- All oral NSAIDs are associated with serious GI side effects, e.g. perforation, ulcer, bleeding.
- People who do not take NSAIDs can also develop stomach ulcers.
- Patients taking oral NSAIDs are more likely to develop serious GI side effects than those patients who take paracetamol or use topical NSAIDs.
- People are at high risk of serious NSAID-induced GI adverse events if they have one or more of the following risk factors:
 - Age 65 years or older.
 - History of GI ulcer, GI bleeding, or gastroduodenal perforation.
 - Concomitant use of medications that are known to increase the likelihood of upper GI adverse events (e.g. anticoagulants, aspirin [even low-dose], and corticosteroids).
 - Serious comorbidity, such as cardiovascular disease, hepatic or renal impairment (including dehydration), diabetes, or hypertension.
 - Requirement for prolonged NSAID use.
 - Use of the maximum recommended dose of an NSAID.
- Additional risk factors for NSAID-induced GI adverse events have also been identified, including:
 - The NSAID used.
 - The presence of *Helicobacter pylori* infection.
 - Excessive alcohol use.
 - Heavy smoking.

- Some NSAIDs (coxibs and ibuprofen 1200 mg daily or less) are less likely to cause GI side effects than others. But the coxibs are more likely than some other NSAIDs to cause myocardial infarction (MI) and stroke (see below). They are contra-indicated in patients with established cardiovascular disease.
- Use of a proton pump inhibitor (PPI) with any NSAID reduces the risk of GI side effects.
- Because many factors affect the chances of developing stomach ulcers, we cannot give numbers to help patients decide.

Cardiovascular risk⁷

- Coxibs, as a class, are associated with a lower GI risk than other NSAIDs, but they are more likely to cause MI and stroke. Diclofenac also seems to be associated with a similar excess CV risk to that of coxibs.
- The chance of an NSAID causing an MI or stroke is low but it is greater if the patient:
 - Has CV disease, peripheral vascular disease, cerebrovascular disease or moderate/severe heart failure.
 - Has type 2 diabetes.
 - Has other risk factors for CV disease.
 - Is older, particularly ≥ 65 years (even in the absence of CV risk factors).
 - Is a smoker.
 - Is male.
- Ibuprofen (at less than 1200mg daily) and naproxen at 1000mg daily do not appear to increase the risk of MI or stroke.
- Cardio-renal effects of NSAIDs (oedema, hypertension, heart failure) may be important contributors to long term CV risk. NSAIDs may differ in their cardio-renal effects – etoricoxib in particular may be associated with a poor cardio-renal profile.
- Because many factors affect the chances of developing an MI or stroke, we cannot give numbers to help patients decide.

Weighing it all up⁷

In helping patients decide what to do about their OA pain, there are at least three things that need to be weighed up:

- How bad their pain is, how it affects their life and how much relief they get, or are likely to get, from the treatment(s) they use.
- What they think about the risks of GI side effects, especially the risk of serious GI events. The size of this risk will be affected by their individual circumstances (see previous section).

- What they think about the risks of MI and stroke. The size of this risk will be affected by their individual circumstances (see previous section). The cardio-renal effects of NSAIDs may also be important (see previous section).

Note:





- All treatments seem to help most people’s symptoms a little, but none of them makes a substantial difference for most people.
- No-one can tell in advance what will happen for an individual person.
- It is always best to use the lowest dose of NSAID that patients can manage, and take the NSAID for the shortest time they can manage, to control the symptoms of their OA.

Thinking about switching from NSAIDs with a greater risk of causing MI and stroke⁷




If the patient is currently taking an NSAID which has a greater risk of causing MI and stroke (e.g. a coxib or diclofenac), they may want to consider changing this to another medicine. It is important patients come to the decision that is right for them.

We have summarised the possible consequences below:

If they switch to paracetamol:

- They will probably have the same risk of MI or stroke as if they were not taking paracetamol or any NSAID 
- They will probably have the same GI risk as if they were not taking paracetamol or any NSAID 
- They might find they have more pain than when they were taking the NSAID, although about 40% of people find paracetamol better or as good at controlling pain as an NSAID^{9,10}  

If they switch to ibuprofen 1200 mg a day or less

- They will probably have the same risk of MI or stroke as if they were not taking ibuprofen or any other NSAID 
- They will probably have a lower GI risk than if they were taking diclofenac and most other NSAIDs, but a greater risk than if they were not taking any NSAID (including ibuprofen) at all (although this risk can be reduced by taking a PPI)  

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- They might find they have more pain than when they were taking the other NSAID, but the pain control might be just as good



If they switch to naproxen 1000 mg a day^a

- They will probably have the same risk of MI or stroke as if they were not taking naproxen or any other NSAID
- They will probably have slightly greater risk of GI problems than if they were taking diclofenac or some other NSAIDs (although this risk can be reduced by taking a PPI)
- They might find they have more pain than when they were taking the other NSAID, but the pain control might be just as good



References

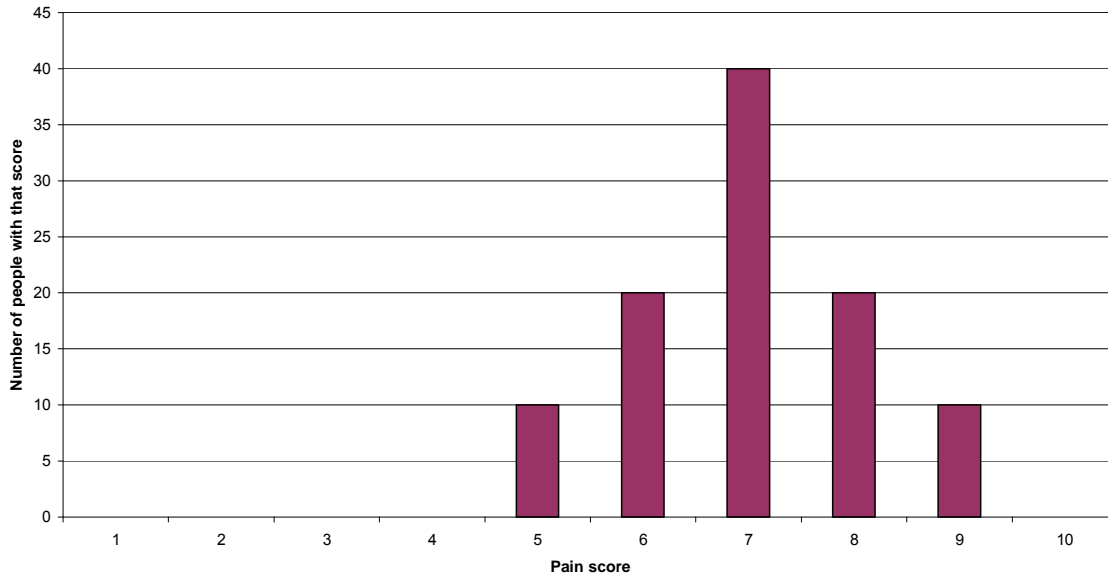
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^a There is less evidence for the balance of risks with lower doses of diclofenac and naproxen

Appendix – more about effect sizes¹¹

Imagine a group of 100 people with OA. We could ask them to score how bad their pain was out of 10 (1 means no pain, 10 means the worst pain imaginable). Different people would rate their pain differently because they experience different amounts of pain. If we asked them to do this while they took no treatment, we might find the results looked like this if we plotted them on a graph:

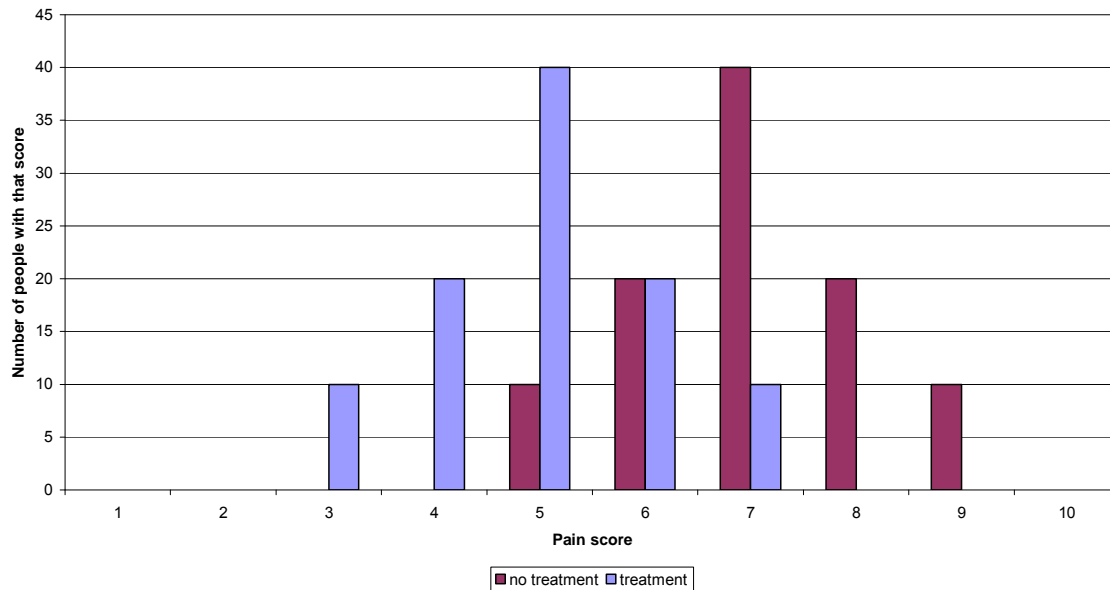
Pain scores with no treatment



The taller the column, the more people said their pain was that bad (for example, 20 people said their pain was 6 out of 10). The **average** pain score was 7 out of 10. But equal numbers of people scored their pain as worse than that (8 or 9 out of 10) or better than that (5 or 6 out of 10)

Suppose we ask 100 similar people to take a treatment, and after a period of time, asked them to rate their pain on the same scale. We might see the results shown on the following page.

Pain scores with treatment compared to no treatment



We can see that the **average** pain score with treatment was lower (better): it was 5 out of 10 compared to 7 out of 10. But again, equal numbers of people scored their pain as worse or better than that. Importantly, some people's pain **with** treatment was the same as some people's pain **without** treatment, and some people's pain may have decreased from, say, 7 out of 10 to 6 out of 10, which they might or might not have thought was important to them

Nevertheless, we can see that 90 people out of 100 who were taking the treatment said their pain was better than the **average** score in the people not taking treatment.

Effect size is a way of expressing the difference between treatments and the amount to which the results from the two groups overlap.