NSAIDs: A risk reduction strategy
Summary

NHS Rotherham

- **Always try non-pharmacological options & simple analgesia first**
  - Paracetamol works for many patients
  - Topical NSAIDs (Non-steroidal anti-inflammatory drugs) may be useful for localised osteoarthritis (OA)
  - Glucosamine sulphate maybe an alternative for knee OA, if it is preferential to avoid NSAIDs (use Valupak®)

- **Avoid NSAIDs in patients:**
  - with CV (cardiovascular) disease or increased risk of CV disease (Including hypertension & diabetes)
  - over 65 years
  - with a history of gastrointestinal (GI) bleed
  - with renal impairment
  - taking aspirin, clopidogrel, SSRIs or anticoagulants
  - taking ACE inhibitors or Sartans

- Use **ibuprofen and naproxen** in preference to other NSAIDs
  - Ibuprofen has lowest GI risk
  - Naproxen has lowest CV risk

- Avoid azapropazone and piroxicam completely and restrict the prescribing of ketoprofen and indometacin

- Use the **lowest effective dose** to control symptoms, and use for **short courses** and not chronically.

- Consider topical NSAIDs (and/or paracetamol) ahead of oral NSAIDs, coxibs or opioids for OA, especially if transient or localised pain (Ibuprofen 5% or 10% gel).

- Consider glucosamine sulphate for knee OA if it is preferential to avoid NSAIDs. Review after 3 months and stop if no improvement. Prescribe Valupak® to ensure quality and cost. Do not use glucosamine hydrochloride.

- If unable to avoid oral NSAIDs in patients with an increased risk of GI bleed then GI protection is recommended (lansoprazole 15mg capsules) i.e. past GI bleed, over 65 years, OA, Rheumatoid Arthritis (RA), over 45 years with back pain, on aspirin/SSRI etc. Enteric Coated, Slow Release and suppositories do not provide any GI protection and are possible a higher risk and are more expensive.

- Coxibs (incl. meloxicam & etodolac) and **diclofenac** are not recommended for routine use because of their risk of adverse CV effects. (Traditional NSAID and PPI are as effective as a coxib alone in reducing GI side effects.) Etoricoxib is contra-indicated in certain patients with hypertension due to its CV risk profile.

If NSAIDs are still required despite a patient having one or more of the above risks factors for an adverse effect, ensure that such patients are informed of these risks, enabling them to make an informed decision whether to continue with their treatment.

For active inflammatory diseases (i.e. RA) ensure a referral to secondary care to consider DMARDs (Disease-modifying anti-rheumatic drugs) as soon as possible, ideally within 3 months of the start of persistent symptoms (> 6 weeks). Do not allow the use of NSAIDs to delay the initiation or optimization of DMARDs and biologicals.

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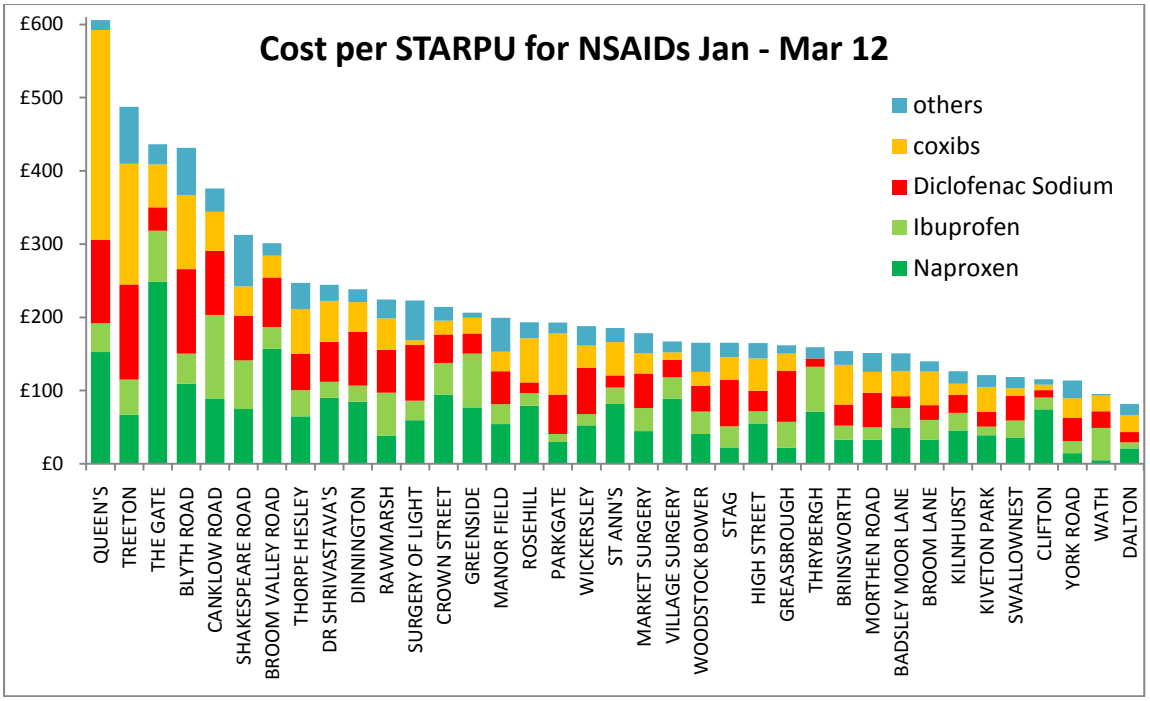
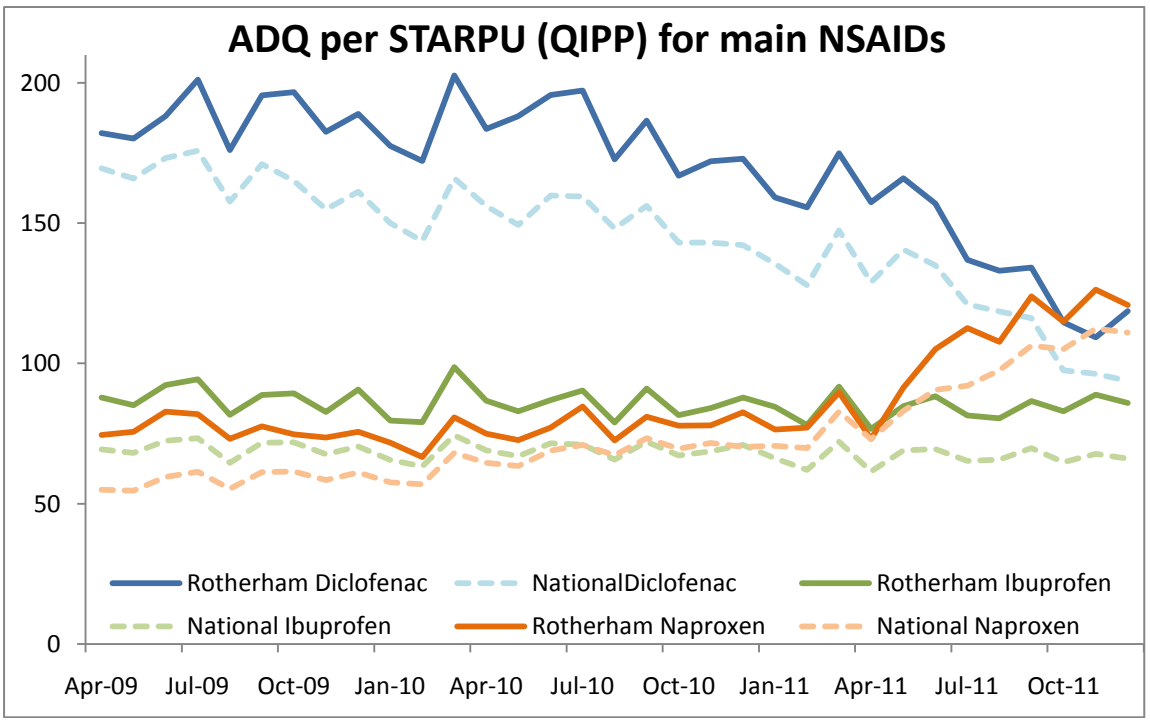
Review: August 2014

NSAIDs: A risk reduction strategy
Current position July 2012

By avoiding using NSAIDs in certain sub-groups of patients, unless absolutely necessary, a prescriber can limit the probability of causing harm. Also, using the lowest effective dose, for the shortest period of time of the most appropriate NSAID, when needed will minimise the risks of the side effects of NSAID. There is nearly a nine fold difference in the cost of prescribing for NSAIDs across practices in NHS Rotherham.



Since the launch of the previous NSAID risk reduction strategies, and the LIS and QP targets in 11/12 the diclofenac use has reduced and naproxen has increased.



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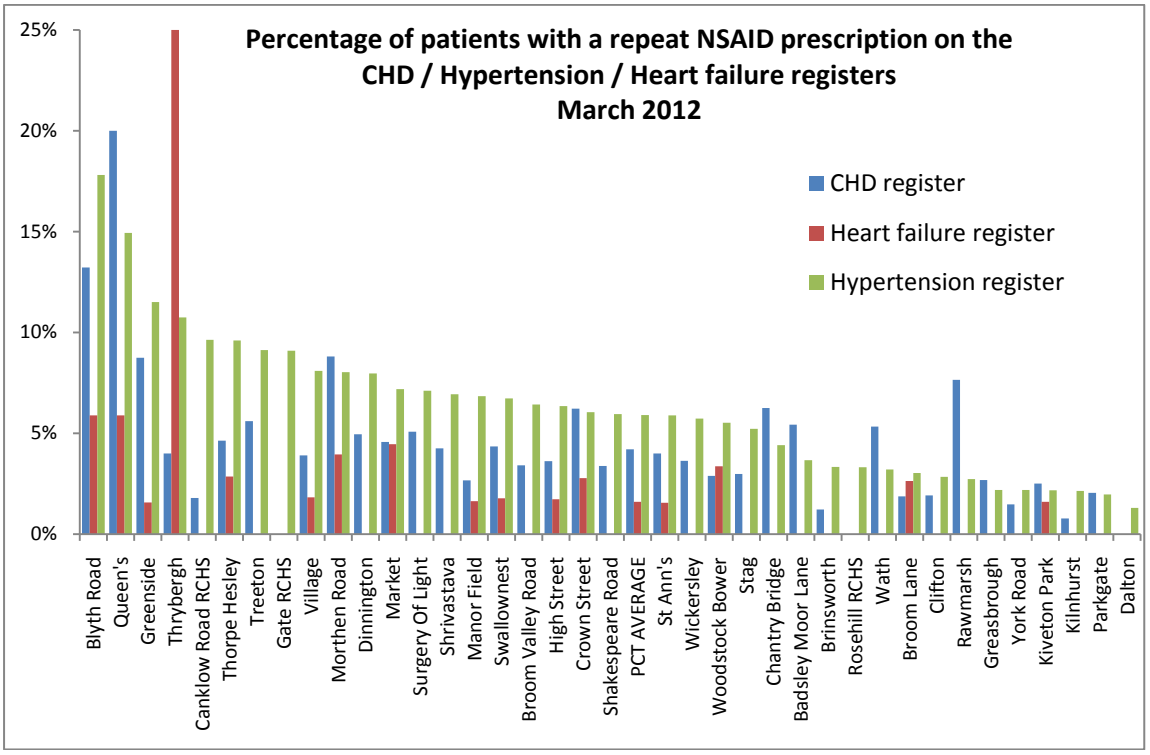
The use of NSAIDs is associated with adverse outcomes in patients with heart failure, and their CV risk requires caution with CHD and hypertension. Therefore for the 12/13 prescribing key performance indicators (Quilt) the percentage of patients on the heart failure / hypertension / CHD registers taking NSAIDs was determined and practices with prescribing above the PCT average have been encourage to review these patients as part of their 10/11 prescribing action plan.



Current patients

This strategy could be used as the basis to undertake medication reviews for patients already prescribed a NSAID. The Medicines Management Team (MMT) would be happy support practiced based work in this area of prescribing. The team have SOPs and patient letters to change people from the higher CV and GI risk NSAIDs over to naproxen (with or without lansoprazole).

NSAIDs: A risk reduction strategy
The Evidence

Evidence for Simple Analgesia
The Bandolier undertook a review (September 04) comparing paracetamol against NSAIDS in the treatment of OA. They concluded that over 6-12 weeks one more patient would discontinue overall, due to lack of efficacy, for every ten patients treated with paracetamol instead of a NSAID. This also means that 9 out of ten patients would continue with paracetamol.[1]

In 2000, there was a survey of 1,799 patients with OA, Rheumatoid Arthritis (RA) and Fibromyalgia. The authors concluded that "If safety and costs are issues, then the recommendation of the American College Rheumatology that paracetamol be tried first seems correct, since 38.2% found paracetamol to be as effective or more effective than NSAIDs.[2]

Indications for topical NSAIDs
The NICE guidance for Osteoarthritis February 2008 states that paracetamol and/or topical NSAIDs should be considered ahead of oral NSAIDs, coxibs or opioids.

The Bandolier website concludes that "Topical NSAIDs provide effective pain relief. This relief seems comparable to that offered by oral NSAIDs. Topical NSAIDs had a combined NNT of 3.1 (2.7 to 3.8) for at least 50% pain relief at two weeks after beginning treatment. Importantly, topical application of NSAIDs is not associated with serious side effects, and therefore provides an effective method of pain relief without the gastrointestinal effects seen with the same drugs taken orally."

The BMJ reported on RCT and preference trial conducted in 26 GP practices in the UK and involved 585 patients.[3] There was no significant differences in the WOMAC global score changes between topical or oral groups in either study (This is a measure of knee pain and disability). There were no differences in major adverse effects in either study. The only significant difference was in secondary outcomes in the RCT: the oral group had more respiratory side-effects (17% v 7%) and the change in serum creatinine was 3.7mmol/l less favourable, and more participants changed treatment because of adverse effects (16% v 1%).

Although manufactures quote that minimal amounts of topical NSAIDs are absorbed systemically, some studies have shown up to 15% absorption. It may therefore be prudent to recommend the same products that have proven to be safe orally as the first line topical agent (i.e. Ibuprofen).

There is the potential for photosensitivity reactions in users of topical ketoprofen, and any such reactions should be reported to the MHRA using a Yellow Card. Topical ketoprofen users should avoid direct sunlight, ultraviolet rays, sunbeds or sunlamps. Ketoprofen should be stopped and medical attention sought if skin reactions develop. Caution should also be exercised for 2 weeks after treatment has been stopped.

Evidence for glucosamine sulphate
NICE guidance doesn't recommend the use of glucosamine sulphate on the NHS due to limited evidence, however they recognize that there is evidence of some benefit: *"… the GDG [Guideline Development Group] felt that it would be beneficial to advise people who wanted to trial over-the-counter glucosamine that the only potential benefits*

identified in early research are purely related to a reduction of pain (to some people, and to only mild or modest degree) with glucosamine sulfate 1500 mg daily. They could also benefit from advice on how to perform their own trial of therapy, that is, to evaluate their pain before starting glucosamine and ensure they review the benefits of glucosamine after three months." [4]

The BMJ[5] in September 2010 reported a meta-analysis of 10 trials including 3803 patients and concluded that when compared with placebo, glucosamine, chondroitin and their combination do not reduce joint pain or have an impact on narrowing of joint space. Glucosamine alone did produce a statically significant reduction of pain intensity of -0.4cm (CI -0.7 to -0.1) compared to placebo using a 10cm visual analogue scale, but it did not cross the boundary of the minimal clinically important difference.

Drugs and Therapeutics Bulletin in 2008[6] report "*the published evidence suggests that oral glucosamine sulphate (1500mg/d) provides modest pain relief in knee osteoarthritis and appears to be relatively safe. In addition, as there are no published trials of Alateris® (Glucosamine hydrochloride), it should not be prescribed on the NHS until such evidence becomes available."*

In Rotherham we are aware that the level of deprivation means that many patients are reluctant to buy over-the-counter medicines. Therefore, a trial of glucosamine sulphate 1500mg once daily may be used for OA of the knee, after trying, or in conjunction with paracetamol. Its use may reduce NSAIDs use, especially in those patients where is it preferential to avoid NSAIDs. It may take several weeks for the full effect to be seen and should be reviewed after 3 months and stopped if no improvement in symptoms.

When prescribed generically the prescription pricing authority will reimburse according to the endorsement on the prescription from the community Pharmacist. The MMT recommends that glucosamine sulphate is prescribed as the brand **Valupak ®** as the 1500mg strength costs only £2.83 for 30 days.

NSAIDs and Congestive Heart Failure

A case control study from Australia in 2000 studied the link between NSAID use and admission due to heart failure (HF), they gave an odds ratio of 1 to patients that had no history of heart disease and were non-users of NSAIDS (mean age 76). All patients who use NSAIDs are at an increased risk of developing HF and this is considerably increase for those with a history of heart disease.[7]

Heart Disease	NSAID use	Odds ratio (95% CI)
No history	Non User	1
No history	User	1.6 (0.7 to 3.7)
History	Non User	2.5 (1.4 to 4.3)
History	User	26 (6 to 119)

Rodriguez and Diaz in 2003, using data from British GP's, observed that the Relative Risk of HF associated with NSAID use in patients with a prior history of hypertension, diabetes or renal failure was 1.9 (1.3 to 2.8) compared to 1.3 (0.9 to 1.9) in individuals without these conditions.[8]

In 2009, a Danish observational study found that patients who used an NSAID after being diagnosed with HF were at increased risk of death and cardiovascular morbidity. The study followed 107,092 patients who survived their first hospitalisation because of HF, of these 36,354 subsequently claimed at least one prescription for an NSAID or coxib.[9] Risk of death was increased by exposure to most NSAIDs, with the highest risks associated with diclofenac (hazard ratio [HR] for any use, 2.08; 95% CI, 1.95 to

2.21), celecoxib (HR, 1.75; 95% CI, 1.63-1.88), and rofecoxib (HR, 1.70; 95% CI, 1.58 to 1.82). For ibuprofen HR for any use was 1.31 (95% CI, 1.25 to 1.37), and for naproxen 1.22 (95% CI, 1.07 to 1.39); for other NSAIDs as a group, it was 1.28 (95% CI, 1.21 to 1.35). **Use of lower doses of ibuprofen (<1200mg daily) or naproxen (<500mg daily) were not associated with a significantly increased risk.** A similar association was found for hospitalisation due to HF and MI, which occurred in 37.5% and 8.4% respectively. Overall, they recommend that patients with HF should avoid the use of NSAIDs if possible. If an NSAID needs to be used then ibuprofen or naproxen should be used at the lowest dose for the shortest possible time.

NSAIDs and Risk of thromboembolic events

In 2005 the MHRA released two statements on the risk of thrombotic events with NSAIDS. In February they commented that "Selective Cox-2 inhibitors, as a class, may cause an increased risk of thrombotic events compared with placebo and some NSAIDs and the risk may increase with dose and duration of exposure." In the August they commented that "Any cardiovascular risk of non-selective NSAIDs is likely to be small and associated with continuous long-term treatment and higher doses."

A study which researched 9218 cases with a first ever diagnosis of MI against 86,349 controls matched for age, calendar year, sex and practice. They concluded that there was an increased risk of myocardial infarction associated with current use of rofecoxib, diclofenac, and ibuprofen despite adjustments for many potential confounders. An increased risk could not be excluded with other NSAIDS, however, due to lower case numbers no definite conclusions could be made. The numbers need to harm (NNH) for NSAID use in the last 3 months, compared to no use within the last three years[10]

Drug	Age over 65 yrs	Age 25- 65 yrs
Diclofenac	521	1006
Ibuprofen	1005	2444
Rofecoxib	695	1833

A meta-analysis released in 2006 in the BMJ[11] found that selective Coxibs were associated with a highly significant 1.4 fold increase of serious vascular events, largely due to a two-fold increased risk of MI. The absolute excess incidence of vascular events was calculated at **3 to 5 extra people having a vascular event per 1000 patients per year**. The results also indicated that high dose diclofenac and high dose ibuprofen were associated with an increased risk of vascular events but high dose naproxen was not.

Another review of observational studies in 2006 in JAMA[12] confirmed the increased cardiovascular risk with rofecoxib and suggests that celecoxib in commonly used doses does not. It also found that among non-selective NSAIDs, diclofenac had the highest risk of CV events with a summary relative risk of 1.40 (CI 1.16 to 1.70), similar to that of rofecoxib. Naproxen and ibuprofen were not associated with increased risk.

In October 2006, the Commission on Human Medicines gave advice on the latest evidence for cardiovascular thrombotic risks:

- Diclofenac 150mg daily has a thrombotic risk profile similar to that of at least one coxib (etoricoxib) and possibly others
- Naproxen 1000mg daily has a lower thrombotic risk than coxibs and, overall, epidemiological data do not suggest an increased risk of myocardial infarction.
- For ibuprofen at high doses (e.g. 2400mg daily) there may be a small thrombotic risk, but at lower doses (e.g. 1200mg daily or less) epidemiological data do not suggest an increased risk in myocardial infarction.

Less evidence is available for other NSAIDs, but they may be associated with a small risk of thrombotic events, especially with long duration of treatment and high doses.

A UK Health Technology Assessment suggested that celecoxib was associated with a higher risk of MI compared to non-selected NSAIDs (1.77). Other studies have demonstrated a higher risk of cardiovascular events with diclofenac (1.40) and indometacin (1.30) but not with ibuprofen, naproxen or piroxicam. Another UK study found an increased risk of MI associated with diclofenac (1.55) and ibuprofen (1.24) but not with naproxen.[13]

Therefore in Rotherham each year there is an estimated **TEN** premature or avoidable CV events due to diclofenac usage and a further TWO from coxib usage. This is higher than the **SEVEN** GI haemorrhages each year estimated from the usage of **ALL** NSAIDs in Rotherham.

NSAIDs and Renal Toxicity

A study from Tennessee USA in 2004 studied cases of first admission to hospital with acute renal failure (Pl Cr ≥ 180 micro mol/L)

- NSAID use was higher (18%) in cases than in controls (11%)
- For current NSAID users the ODDS ratio was 1.6 (95% CI 1.3 to 1.9)
- Those who had stopped using NSAIDs within the past 30 days had no increased risk of renal failure[14]

This study confirms that the risk of a patient having a GI event or renal event associated with NSAID use significantly increases with the age of the patient.

Hospital Admission for an acute GI event or acute renal failure due to NSAID use[15]

Age	GI event	Renal Event
	RR (95% CI)	RR (95% CI)
30-39	0.65 (0.57 to 075)	0.61 (0.35 to 1.07)
40-49	0.84 (0.75 to 0.94)	0.57 (0.35 to 0.94)
50-59	1	1
60-69	1.09 (0.99 to 1.2)	2.31 (1.68 to 3.18)
70-79	1.20 (1.09 to 1.32)	4.70 (3.49 t 6.33)
≥ 80	1.61 (1.46 to 1.78)	8.79 (6.55 to 11.8)

In 2007, Gooch et. al. determined the chronic use of all NSAIDs (including coxibs) causes a deterioration in GFR. A total of 10,184 patients (mean age 76 years, 57% female) were followed for a median of 2.75 years to explore the association between NSAID use and GFR.[16] High dose NSAID users experienced a 26% increase risk for the primary outcome of decrease in eGFR of >15ml/min/1.732. A linear association between cumulative NSAID dose and change in mean GFR was seen. No risk differential was identified between the selective (coxibs) and standard NSAID users.

The authors concluded that high cumulative NSAID exposure is associated with an increase risk for rapid CKD progression in the setting of a community-based elderly population. For older patients with CKD, these results suggest that both standard NSAIDs and coxibs should be used cautiously and chronic exposure should be avoided.

NSAIDs and GI effects

There is an established relationship between age and NSAID related upper gastro-intestinal bleed (UGIB) or death, with the risks increasingly markedly in patients over 75 years of age.

Risk of NSAID- related GI bleeding or death by age[17]

Age range (years)	Number taking NSAIDS	Number with GI bleed	Chance of GI bleed due to NSAID in one year	Chance of dying from a GI bleed due to a NSAID in one year
16-45	2100	1	1 in 2100	1 in 12353
45-64	3200	5	1 in 646	1 in 3800
65-74	2280	4	1 in 570	1 in 3353
75	1540	14	1 in 110	1 in 647

Rodriguez and Diaz in 2000 compared the risk of an UGIB compared to non-users. Although the confidence intervals are wide the study showed a greater risk of an upper GI bleed with piroxicam, indomethacin and ketoprofen compared to the other NSAIDS. The high risk associated with azapropazone is well established and its indications have been subject to CSM restrictions for a number of years[18].

In June 2010, Rodriguez *et. al.* undertook a systematic review of studies published between 2000 and 2008 and evaluated the risks of an UGIB and NSAID use[19]. The relative risk (RR) of an UGIB was 4.5 times greater for a traditional NSAID and 1.88 for coxibs. NSAIDs with long half life's and slow-release formulations were associated with a greater risk of UGIB.

Relative Risk (RR) of NSAID Non-users = 1

NSAID	Rodriguez and Diaz 2000	Rodrigeuz 2010
	RR (95% CI)*	**RR (95% CI)**
Celecoxib	n/a	1.42 (0.85 – 2.37)
Ibuprofen	1.9 (1.6 - 2.20)	2.69 (2.17 – 3.33)
Diclofenac	3.3 (2.8 - 3.9)	3.98 (3.36 – 4.72)
Meloxicam	n/a	4.15 (2.59 – 6.64)
Naproxen	4.0 (3.5 - 4.6)	5.63 (3.83 – 8.28)
Ketoprofen	**4.6 (3.3 - 6.4)**	**5.57 (3.94 – 7.87)**
Indometacin	**4.6 (3.8 - 5.5)**	**5.40 (4.16 – 7.00)**
Piroxicam	**6.3 (5.5 - 7.2)**	**9.94 (5.99–16.50)**
Azapropazone	**27.5 (12 - 62.9)**	**n/a**

*Only NSAIDS where more than 2 studies had been published were included.

These studies confirms the CSM findings (1994 & 2000)

	NSAID	Comment
High Risk	**Azapropazone**	Highest risk use only as a second line agent for rheumatoid arthritis, ankylosing spondylitis and acute gout
Intermediate Risk	**Piroxicam**, Indometacin, Ketoprofen, Diclofenac, Naproxen	Piroxicam may be associated with a higher risk than other NSAIDS in this group
Low Risk	Ibuprofen	Lowest risk

Piroxicam and GI toxicty

In July 2007 the European Medicines Agency (EMEA) issued new advice on the use of piroxicam. This advice relates to all systemic forms of the drug and concluded that piroxicam should no longer be used for treatment of short-term painful and inflammatory conditions, and that it should not be the first choice NSAID treatment for the symptomatic relief of OA, RA and ankylosing spondylitis. This was due to the risk of serious GI and skin reactions compared to other NSAIDs.

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Review: August 2014

The GI bleed risk of differing formulations

Many patients take NSAIDs as Slow-Release (SR), Enteric-Coated (EC) and even as suppositories in the hope that this reduces the indigestion and the risk of gastrointestinal (GI) problems and bleeds. However, the effects of NSAIDs on the mucosal prostaglandins of the GI track are systemic, and using other formulations may by-pass first pass metabolism and/or prolong the systemic levels and effects.

A Danish population based cohort study of over 150,000 NSAID users in 2002[20], showed that upper GI bleeds were more prevalent when MR preparations and suppositories were used, and that an EC provided no protection. These results may be confounded by the use of the presumed low-risk formulations in patients with previous GI problems.

	Observed/ expected	95% CI
Tablets	3.25	2.9 - 3.7
Slow-release tablets	4.23	3.2 - 5.5
Enteric-coated tablets	3.58	2.2 - 5.5
Suppositories	8.47	4.4 - 14.8

Cox-II Selective inhibitors (coxibs) and GI toxicity

Coxibs have not shown consistent gastrointestinal benefit when compared against standard NSAIDs, especially if used with a proton pump inhibitor (PPI), and have a do have risk of unwanted cardiovascular effects. Celecoxib was compared with diclofenac plus omeprazole in a prospective randomized controlled trial of 287 people who had a negative test for *Helicobacter pylori* and had healed ulcers that had bled. The probability of recurrent bleeding did not differ significantly between the two groups at 6 months, being 4.9% and 6.4% respectively.[21]

A double-blind RCT for the assessment of upper gastrointestinal safety of etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison was reported in the Lancet in 2007[22]. The results were based on 3 pooled studies of which upper GI events were **not** primary endpoints therefore there is uncertainty on significance of results. But the result showed

- An NNT 243 for patients with any clinical GI event: HR 0.69 ARR 0.41
- An NNT 256 for patients with uncomplicated GI event:
- HR 0.57 ARR 0.39
- For patients with complicated GI event the results were not significant
- The addition of GI protective therapy and/or aspirin did not appear to alter the difference in event rate per sub-group, but this sub-group analysis is not powered and p-values are not quoted so significance is questioned.

The benefits of etoricoxib are small; to prevent **one** complicated GI event would need to treat **256** patients with etoricoxib rather than diclofenac over 18 months. This uncomplicated GI event may or may not be clinically significant.

Additional risks with SSRIs

The link between SSRIs and UGIBs is firmly established, and a meta-analysis in 2007 reviewed a number of studies involving 153,000 patients. They quantified the increase in UGIB risk with NSAIDs as:

- In patients over 50 years with no UGIB risk factors the NNH per year is 411 for SSRIs alone, and 106 with concomitant NSAIDs[23]

Additional risks with aspirin, clopidogrel and warfarin

An observational study in 2007 looked at the risk of bleeding for individuals taking warfarin, clopidogrel, aspirin, NSAIDs and coxibs and various combinations, (4028 cases) compared against controls and adjusted for potential confounders[24]. There was a similar increased risk of GI bleeding with both standard NSAIDs and coxibs. Also, when in combination with clopidogrel or warfarin the risk was greater than that observed with each drug alone and there was no significant difference between the standard NSAID and coxibs.

Drug or combination	Rate Ratio*	CI
NSAID	1.78	(1.61 – 1.97)
Coxibs	1.64	(1.31 - 2.06)
Clopidogrel & NSAID	2.90	(1.58 – 5.35)
Clopidogrel & Coxibs	2.60	(1.09 – 6.23)
Warfarin & NSAID	4.79	(2.79 – 8.21)
Warfarin & Coxibs	4.62	(1.48 – 14.43)

*adjusted for potential confounders and compared to none of the study

Use of Gastro-protective agents

Proton-Pump Inhibitors (PPIs) are generally considered to be the preferred choice for gastro-protection; they are effective and well tolerated. PPIs reduce the risk of endoscopic gastric ulcers by 63% and the risk of duodenal ulcers by 81%.[25]

NICE guidance recommend a PPI should be co-prescribed with an NSAID (including coxibs) for anyone with OA or RA, and anyone 45 years of age or older with chronic low back pain, choosing the PPI with the lowest acquisition cost. They also suggest a PPI should be considered for anyone receiving an NSAID who is at high risk of GI side-effects, including those over 65years or using them long term.

Choice of NSAID

Systemic reviews found no important difference in efficacy between different NSAIDs for the symptoms of musculoskeletal disorders[26]. Two Cochrane systematic reviews found that celecoxib and rofecoxib were no more effective for clinical outcomes than non-selective NSAIDs in people with RA or OA.[27,28] Therefore, due to no difference in efficacy, apart from individual experience, the choice of NSAIDs is decided purely on the safety profiles:

- **Ibuprofen** is recommended as the first line agents if GI risk factors (i.e. past GI bleed, over 65, on aspirin/clopidogrel etc).
- **Naproxen** is recommended as the first line agents if CVS risk factors. (i.e. previous CVS disease, hypertension, heart failure, diabetes etc)
- Avoid **azapropazone** and **piroxicam.** They are definitely associated with a greater incidence of GI bleeding than the other NSAIDS.
- **Ketoprofen** and **indometacin** are possibly more GI toxic than other NSAIDs.
- The place for Coxibs is minimal and should be avoided in any patients with CVS disease.

Rheumatoid Arthritis and other inflammatory conditions

NICE guidance for Rheumatoid arthritis issued in February 2009, now places a higher importance for the use of Disease-modifying anti-rheumatic drugs (DMARDs) and

biologicals to modify the disease process to slow or stop radiological progression which is closely correlated with progressive functional impairment.[29]

Key priorities for implementation are:

- Patients with suspected persistent synovitis of undetermined cause should be referred for specialist opinion.
- People with newly diagnosed active RA should be offered a combination of DMARDs (incl. methotrexate) as first line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms.

Symptom control:

- Offer analgesics (e.g. paracetamol, codeine or compound analgesia) to people with RA whose pain control is not adequate to potentially reduce their need for long term treatment with NSAIDs or coxibs
- Oral NSAIDs or coxibs should be used at the lowest effective dose for the shortest period of time **(i.e. DO NOT use as a permanent solution to symptom control – but for flares and while waiting for DMARD and biological modification)**
- If NSAIDs or coxibs are not providing satisfactory symptom control, review the DMARDs or biological drug regimen

Other evidence

There is much more evidence available to support the points viewed in this strategy. Websites such as Clinical Knowledge Summaries, the NHS National Library for Health and NPCi can provide a useful resource for the latest information.

- http://cks.library.nhs.uk/
- http://www.library.nhs.uk/Default.aspx
- http://www.npci.org.uk/

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Review: August 2014