Editorials
The dangers of NSAIDs:
look both ways

“... deaths from NSAIDs remain very high: more deaths than from road traffic accidents and twice as many deaths as from asthma or cervical cancer.”

Preventable adverse drug reactions (ADRs) are responsible for 10% of hospital admissions in older people at a cost of around £800 million annually. Non-steroidal anti-inflammatory drugs (NSAIDs) are responsible for 30% of hospital admissions in older people at a cost of around £800 million annually. The dangers of NSAIDs:

HARMs OF NSAIDS
From the first day of use, all NSAIDs increase the risk of gastrointestinal (GI) bleeding, myocardial infarction, and stroke. NSAIDs reduce prostaglandin synthesis, with differences in the extent of inhibition of the enzymes COX-1 and COX-2. All NSAIDs increase both bleeding and cardiovascular disease (CVD) risk but selective COX-2 inhibitors are more likely to cause cardiovascular events, whereas less selective NSAIDs are more likely to cause GI bleeds. The risk of bleeding and of cardiovascular events is considerably higher in older people, of whom many take medicines known to interact with NSAIDs.

NSAIDs affect the cardiovascular, GI, renal, and respiratory systems. NSAIDs reduce the antiplatelet effect of aspirin and have a thrombogenic effect on platelet function. NSAIDs increase systolic blood pressure by 5 mmHg and increase fluid retention. In patients taking coxibs, diclofenac, and higher-dose ibuprofen, these effects cause an excess risk of 7–9 non-fatal and 2 fatal cardiovascular events per 1000 patients per year. All NSAIDs double the risk of hospitalisation due to heart failure.

NSAIDs use in patients aged >65 years more than doubles the risk of acute kidney injury in the next 30 days.

NSAIDs can precipitate bronchospasm and 5–10% of adult patients with asthma will have an acute deterioration in symptoms after taking NSAIDs. NSAIDs are also associated with a rise in HbA1c in type 2 diabetes.

Comorbidity and polypharmacy increase with age, as does the incidence of chronic musculoskeletal conditions such as osteoarthritis, for which NSAIDs are often prescribed. NSAIDs increase the risk of hospitalisation in older people, and multiple comorbidities and polypharmacy compound the risk of CVD and bleeding events.

Bleeding is the better-known consequence with all types of NSAID use. Non-selective NSAIDs increase the risk of a GI bleed 4-fold, whereas COX-2 inhibitors increase this risk 3-fold. Co-prescription of NSAIDs with corticosteroids increases bleeding risk 12-fold, spironolactone 11-fold, and selective serotonin reuptake inhibitors (SSRIs) 7-fold. GI bleeds while taking NSAIDs are more likely to be fatal, with a mortality of 21%, whereas in patients not taking NSAIDs it is 7%.

Older people have a higher baseline risk of cardiovascular events, GI bleeds, and impaired renal function, all of which are further increased by NSAIDs. NSAID prescribing is common in this older population, with 9% of patients aged >70 years receiving a prescription for >3 months. Self-medicating is also extensive and 30% of a general population sample in the Netherlands reported NSAID use within the preceding 4 weeks.

The National Institute for Health and Care Excellence (NICE) defines high-risk patients as: aged >65 years; interacting medications (including 20% of patients >75 years); patients with diabetes, hypertension, cardiovascular disease, renal or liver impairment; patients with a history of peptic ulcer or GI bleeding; and those taking long term NSAIDs or maximum doses.

WHAT SHOULD A GP DO INSTEAD?

What should a GP do for common musculoskeletal and osteoarthritis pains? The simplest and most effective way to reduce risk from NSAIDs is to avoid their use in older people and prescribe an alternative whenever possible. NICE recommends paracetamol or a topical NSAID as first line for pain relief in older patients or the use of opioid analgesics. Where an NSAID cannot be avoided, naproxen together with a proton pump inhibitor (PPI) is the least worst option. However, even with a PPI, patients will remain at increased risk of cardiovascular and renal harm from NSAIDs including naproxen.

Evidence for superiority of NSAIDs over paracetamol as analgesia for patients with osteoarthritis is poor, with small trial numbers and poor design. Many patients report neither of these drugs provide adequate pain relief. NICE recommends paracetamol at the lowest effective doses as the treatment of choice for osteoarthritis in older people, stepping up to a weak opioid if needed. NSAIDs may be slightly more effective than placebo for the treatment of low back pain but at the cost of significantly more side effects. Paracetamol has not
Systematic quality improvement initiatives are long overdue.

IT systems using ‘trigger tools’ are capable of systematically identifying patients at older ages at high risk of bleeding and CVD to allow clinical review. Systematic quality improvement initiatives are long overdue. These should engage local stakeholders, disseminate guidance and education, provide IT support, and develop identifiable peer audit including financial incentives. They need to include patients, community pharmacists, and dentists, and align improvement programmes across primary and secondary care. The use of NSAIDs is long overdue for system-wide attention.

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