Advances in analgesia in the older patient

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The average age of the world’s population is increasing rapidly, with those over 80 years of age the fastest growing subsection of older persons. Consequently, a higher proportion of those presenting for surgery in the future will be older, including greater numbers aged over 100 years. Management of postoperative pain in these patients can be complicated by factors such as age and disease-related changes in physiology, and disease-drug and drug–drug interactions. There are also variations in pain perception and ways in which pain should be assessed, including in patients with cognitive impairment. Alterations in pharmacokinetics and pharmacodynamics may influence drugs and techniques used for pain relief. The evidence-base for postoperative pain management in the older population remains limited. However, most commonly used analgesic regimens are suitable for older patients if adapted and titrated appropriately.

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doi:10.1016/j.bpa.2011.06.003
Introduction

The average age of the world’s population is increasing. Changes to date and those predicted to occur by 2050 have been summarised by the United Nations.\(^1\) The proportion of ‘older’ persons (aged 60 years and over; also referred to as elderly\(^2\)) worldwide was 8% in 1950, 11% in 2009, and expected to reach 22% by 2050. In the developed world, over 20% of the population is already in the older group; this is projected to reach nearly a third by 2050. The fastest growing subsection is the ‘oldest-old’ (aged 80 years or more), which comprised one in seven older people and 1.5% of total world population in 2009. This is likely to increase to one in five and 4.5% by 2050, when the number aged over 100 may reach 4.1 million – a ten-fold increase from 2009.

There are likely to be economic and social effects resulting from this rapid ‘grey ing’ of the population. It also means that a much higher proportion of patients presenting for surgery will be older, including greater numbers in the over-80 and over-100 year old age groups.

Management of postoperative pain in older patients may be complicated by a number of factors including a higher risk of age and disease-related changes in physiology and disease-drug and drug–drug interactions. Differences that need to be considered in older persons include possible alterations in perception of pain; ways in which pain is assessed, including in those with cognitive impairment; variations in physiology and potential pharmacokinetic and/or pharmacodynamic consequences in relation to drugs used for pain relief; and the various analgesic techniques that may be employed in the postoperative setting.

The evidence-base for pain management in the older population remains limited, particularly for the oldest-old and frail. In part this is because older patients, especially those with significant medical comorbidities or taking particular medications or with cognitive impairment, are often routinely excluded from studies.\(^3,4\) As the average 70 year old living in the community may have over three medical comorbidities and take seven different medications, there is a need for better evidence specific to this patient group.\(^3\)

This review will look at postoperative analgesia in older and oldest-old patients. However, it is recognised that it may be biological rather than chronological age that has the most effect on any differences. Most study designs do not yet allow for these distinctions and groupings remain based on chronological age.\(^2\)

Effectiveness of acute pain management in older patients

In general, pain is not managed well in older persons.\(^3,5\) Repeated studies have also shown that postoperative pain is poorly controlled in a large proportion of patients of all ages\(^6,7\) and in older patients specifically.\(^8\) Those with dementia are particularly likely to have their pain under-treated.\(^5\) In patients recovering from hip fracture surgery, those with dementia received significantly less opioid than their cognitively intact counterparts of the same age,\(^9–11\) even though the pain experienced by older persons with and without dementia may not differ.\(^12\)

Poor postoperative outcomes are more common in older patients\(^2\) – age greater than 80 years correlates with higher rates of morbidity and mortality after elective and emergency surgery.\(^13–15\) Frailty, measured using validated scales, is more common in the older patient and also increases risk of poor outcomes.\(^16,17\)

Evidence that better pain relief reduces postoperative complication rates remains limited\(^18\) – see later. However, inadequate analgesia can affect general wellbeing. Higher postoperative pain scores have been associated with lower health-related quality of life, prolonged decline in physical and social function, depressed mood, and disrupted sleep patterns.\(^7\) Pain can also adversely affect cognition (see below).

Age-related differences in pain perception

Age-related differences in the neurophysiology of nociception and perception of pain have been reviewed in detail by Gibson and colleagues.\(^19–21\) In general, ageing results in significant structural, functional and neurochemical changes in both the central and peripheral nervous systems. These differences may alter nociceptive processing, including impairment of descending endogenous pain
inhibitory mechanisms, and change the way the older person responds to both brief noxious stimuli and pain from tissue injury.

In experimental pain settings using transient non-tissue-damaging noxious stimuli, there appear to be age-related increases in pain thresholds, although results are inconsistent and depend on type of stimulus. The significance of these findings in relation to pain resulting from tissue injury in the clinical setting is not clear. However, it may mean that pain does not function as an 'early warning system' as well as in younger patients and therefore diagnosis and treatment could be delayed. For example, pain may be absent or atypical in nature in up to 50% of older patients with unstable angina and 33% with an acute myocardial infarction (AMI). In patients with an AMI, there was an inverse correlation between higher chest pain scores and lower experimental pain thresholds. The risk of painless AMI increased with older age and was associated with lower pain scores in response to suprathreshold painful stimuli. Older patients with acute intra-abdominal pathology may also report less or no pain compared with their younger counterparts.

Correlations with experimental pain thresholds have not been done for postoperative pain. However, an inverse relationship between increasing age and lower pain intensity (i.e. older patients had lower pain scores) after surgery has been reported.

Using experimental pain stimuli, it has also been shown that changes in temporal summation and prolonged hyperalgesia occur in older persons. That is, ageing may lead to prolonged sensitisation after tissue damage, which could affect recovery from injury as well as increase the risk of chronic neuropathic pain.

Patients with cognitive impairment

The incidence of dementia increases with age. While it is often believed that demented patients experience less pain than cognitively intact individuals, this may not be the case. Patients with early Alzheimer's Disease (AD), for example, had similar experimental pain thresholds and ratings for weak pain stimuli. Functional MRI brain responses to mechanical pressure stimulation also showed no diminution of pain-related activity in patients with AD compared with age-matched controls. Interestingly, 'expectation-induced' analgesia may differ. In AD patients with impaired frontal executive function, the placebo response for analgesia was weakened. This could mean that analgesics are less effective in this patient group and/or that higher doses are required.

A common form of acute cognitive impairment is delirium, but information on whether this can affect pain perception is lacking. Delirium describes acute disturbances of consciousness/mental state developing over a short time, tending to fluctuate throughout the day, and associated with changes in cognition. Postoperative delirium (POD) is more common in older patients – up to 80% depending on type of surgery – and associated with increased morbidity, impaired postoperative rehabilitation and longer hospital stays.

Key factors said to be associated with the development of POD are:

- advancing age
- pre-existing dementia or depression
- disturbances in frontal executive function
- hypoxaemia
- infection
- fluid and electrolyte disturbances
- severe acute pain
- some medications (e.g. opioids, tramadol, benzodiazepines, calcium channel blockers, possibly antihistamines)

Assessment and measurement of pain

Good postoperative pain management in older individuals starts, as with any patient, with a basic pain history, taking into account factors that may affect pain reports or amount of pain experienced,
and appropriate measurement of pain. Assessments should be repeated whenever needed, for example if pain is changing in character or pain relief is inadequate.

In addition to cognitive impairment, other age-related factors may influence reporting of pain, including fear, anxiety, depression, culture and social barriers, implications of the disease and loss of independence. Even though an older patient may not volunteer complaints of pain, pain should be assumed possible if the situation is potentially painful.

Measures of pain

Many studies (performed mainly in the chronic pain setting) have looked at ways to best assess and measure pain in the older patient and compare pain across different adult age groups.

In general, cognitively intact older patients can manage most commonly used unidimensional pain scales. In both experimental and postoperative pain settings, reliability, validity and patient preference are best with numeric rating scales (NRS, a calibrated visual analogue scale [VAS]) and verbal descriptor scales (VDS) using familiar words such as none, slight, mild, moderate and severe, and worst with the VAS. The Faces Pain Scale is also a reliable measure.

In older patients with mild to moderate dementia the VDS is the better measure, although repeated explanation may be needed and adequate time allowed to respond to questions. It may be best to concentrate on reports of present pain; recall of past pain can be less reliable.

In patients with more advanced stages of dementia or with significant POD, use of self-report pain measures should still be attempted. If unsuccessful, observational measures of pain-related behaviours are needed. A number of observer-rated assessment tools are available and evaluations of many have been published. These may be reasonably accurate measures of the presence of pain, but not necessarily pain intensity. Some of these tools, preferably those taking a short time to administer, would be suitable to use in postoperative patients with both advanced dementia or POD.

Age-related changes in pharmacokinetics and pharmacodynamics

Ageing is characterised by two concurrent processes: physiological changes that are the natural consequences of advancing years; and an increased likelihood of underlying comorbidities which may affect the handling or effects of medications, or lead to serious drug–drug and disease–drug interactions. These processes make the older patient group a very heterogeneous one, presenting many challenges for the safe and effective provision of postoperative analgesia.

The physiological changes associated with ageing, their pharmacokinetic (PK) and pharmacodynamic (PD) consequences, and possible effects on pain relief or analgesic strategies in older patients are summarised in Table 1 (information taken from multiple references).

Effect on ageing on analgesic and adjuvant drugs

Pharmacokinetics and pharmacodynamic changes in older persons may influence doses required and effects of analgesic drugs. However, the heterogeneity of this group, both in terms of the extent of age-related physiological changes and the presence of comorbidities and concurrent other medications, makes broad generalisations difficult. There is also limited specific evidence about the different analgesic agents and older patients, especially for postoperative pain management.

Paracetamol

Age-related changes in paracetamol PK have been reported. Decreases in clearance and increases in AUC are seen with increasing age, with changes most marked in frail older patients. However, in the absence of significant renal impairment, routine dose reductions appear not to be needed in older persons.
Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) include non-selective inhibitors of the cyclo-oxygenase (COX) enzyme (nsNSAIDs) or COX-2-selective inhibitors (coxibs). Risks and severity of side effects associated with long-term administration are increased in older patients. Concerns relate mainly to cardiovascular system (CVS), renal and gastrointestinal (GI) complications.

NSAIDs have been implicated in a large proportion of all adverse drug reactions requiring hospitalisation in older patients. These patients are more likely to have pre-existing comorbidities (e.g. CVS disease, renal impairment) or be taking concurrent medications that increase the risks.

Evidence supporting an increased incidence of CVS events in patients taking NSAIDs is conflicting. While long-term use of coxibs and some nsNSAIDs increases the likelihood of AMI and stroke overall, these risks may actually be lower in patients of advanced age. Information about the risks of post-operative administration is limited. Short-term use of low-dose NSAIDs to treat acute pain appears not to increase the risk of CVS events.

**Table 1**

<table>
<thead>
<tr>
<th>Physiological variable</th>
<th>Change</th>
<th>Potential PK consequence</th>
<th>Example of possible effects on analgesia/analgesic strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (CO)</td>
<td>↓ or unchanged</td>
<td>↓ CO = ↑ peak plasma concentrations with intravenous (i.v.) bolus dose</td>
<td>↓ initial i.v. bolus dose of CNS depressant drugs (e.g. opioids)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ oral bioavailability</td>
<td>↓ speed of i.v. injection Dose reductions necessary with some drugs; limited/no adjustment needed for most analgesic and adjuvant drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ clearance (CL) = ↑ plasma concentrations for some, not all, high extraction drugs (e.g. morphine, fentanyl)</td>
<td></td>
</tr>
<tr>
<td>Renal clearance</td>
<td>↓ size and functional capacity of kidneys</td>
<td>↓ CL = ↑ plasma concentrations of renally cleared drugs and metabolites</td>
<td>Caution with renally cleared drugs (e.g. gabapentinoids, some NSAIDs) or drugs with renally cleared active metabolites (e.g. morphine, pethidine, dextropropoxyphene)</td>
</tr>
<tr>
<td></td>
<td>↓ in renal blood flow</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ glomerular filtration rate (GFR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body composition</td>
<td>↑ body fat</td>
<td>↑ volume of distribution and half-life of lipophilic drugs</td>
<td>Drug specific – dose based on total body weight (lipophilic drugs) or lean body weight (hydrophilic drugs)</td>
</tr>
<tr>
<td></td>
<td>↓ body water</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ muscle mass (elderly may range from obese to frail)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein binding</td>
<td>↓ albumin</td>
<td>Volume of distribution changes</td>
<td>Possible change in clinical effect related to altered free drug fraction NSAIDs and many LAs and opioids are highly (&gt;90%) protein bound</td>
</tr>
<tr>
<td></td>
<td>↑ alpha-1-acid glycoprotein</td>
<td>↑ hepatic CL of low extraction drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug specific binding changes</td>
<td>Half-life changes Altered cerebral uptake of drug</td>
<td></td>
</tr>
<tr>
<td>Oral and transmucosal absorption</td>
<td>Generally unaffected in the absence of disease</td>
<td></td>
<td>No change in absorption</td>
</tr>
<tr>
<td>Transdermal absorption</td>
<td>↓ for hydrophilic drugs</td>
<td>No change in time to peak concentration for lipophilic drugs</td>
<td>No change required for transdermal fentanyl</td>
</tr>
<tr>
<td></td>
<td>↔ for lipophilic drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramuscular absorption</td>
<td>Muscle perfusion unchanged</td>
<td>No change</td>
<td>Limited evidence. Predict minimal change in absorption</td>
</tr>
<tr>
<td>Subcutaneous (s.c.) absorption</td>
<td>Skin perfusion unchanged at normal temperatures</td>
<td>No change</td>
<td>Limited evidence. Predict minimal change in absorption</td>
</tr>
</tbody>
</table>
to increase the probability of adverse CVS events. The exception is parecoxib and valdecoxib given after cardiac but not non-cardiac surgery (valdecoxib is no longer marketed). Risk of renal complications associated with NSAID administration is higher in older persons. Combination of NSAIDs with diuretics, ACE inhibitors and other nephrotoxic agents increases the incidence of renal failure, as does the presence of pre-existing renal impairment, low serum albumin levels, hypovolaemia and hypotension. Coxibs and nsNSAIDs have similar adverse renal effects. Short-term postoperative use may be reasonable in selected older patients with normal perioperative renal function.

Older patients are also more prone to NSAID-related GI ulcers and bleeding, the incidence increasing with advancing age. Overall, risks are greater with long-term use of nsNSAIDs compared with coxibs. Risks are also higher when drugs showing a high degree of inhibition of both COX isozymes (indomethacin, piroxicam, ketorolac, ketoprofen, naproxen) are given, or if longer half-life or slow-release drugs or high doses are used. Acute GI ulceration and bleeding may also follow short-term use of nsNSAIDs. The risk is increased with higher doses, use for longer than five days, prior history of GI ulceration and older age.

NSAIDs can also interfere with the actions of some drugs commonly used in older patients – for example, warfarin, diuretics and ACE inhibitors; concurrent use of ibuprofen (and possibly naproxen) may interfere with cardioprotective effects of low-dose aspirin.

**Opioids and tramadol**

All opioids used for the treatment of acute pain can be used in older patients, although some may be preferable to others in certain situations. Limited information specific to this patient group is available. Age is known to be a better clinical predictor of postoperative opioid requirement than patient weight, with an inverse relationship between average dose and age. However, large inter-individual variations in opioid requirements even in older patients mean that doses must still be titrated for each patient in order to achieve good analgesia without significant adverse effects, and minimise the CNS and functional consequences of inadequate analgesia.

There are some age-associated differences in the PK of different opioids in older patients, however, these variations are not usually large enough to account for the two- to four-fold decrease in the amount of opioid needed to get the same degree of pain relief. Changes in PD have a significant clinical effect: the ageing brain appears to be more sensitive to opioids. Initial use of lower doses in older patients is suggested, but these should be increased, in the absence of side effects, if analgesia is inadequate.

Reduced ventilatory responses to hypoxia and hypercapnia in older persons may increase the risk of ventilatory failure during high demand states (e.g. pneumonia, heart failure). Combined with reduced respiratory reserves, this could make them more susceptible to opioid-induced ventilatory depression. The risk has been reported to be higher in older patients. However, as with other patients, significant ventilatory depression can generally be avoided if appropriate monitoring and responses are in place.

There is little work comparing opioid-related cognitive changes in younger and older patients. After just a single dose of oral oxycodone (10 mg), there was no difference in cognitive impairment between the two groups. However, management of postoperative pain commonly requires multiple opioid doses. In older patients, fentanyl may cause less postoperative cognitive dysfunction and confusion than morphine; pethidine and tramadol increased the risk compared with morphine and other opioids.

Advancing age is associated with a steady decline in GFR (see Table 1) and the risk of adverse effects may be increased when opioids that have renally cleared active metabolites are used. This applies to all of the commonly used opioids except fentanyl and buprenorphine.

Hepatic function also decreases with age. However conjugation, the main form of metabolism of opioids such as morphine and hydromorphone, is relatively well preserved.

**Choice of opioid**

Morphine and hydromorphone both have renally excreted active metabolites. Morphine 6-glucuronide (M6G) is a potent mu-opioid receptor agonist. Accumulation in older patients with
Reduced renal function can increase the risk of respiratory depression.\textsuperscript{55} Hydromorphone may be a better choice in older patients because it has no 6-glucuronide metabolite.\textsuperscript{55} However, the 3-glucuronide metabolites of both hydromorphone and morphine have CNS excitatory properties and may contribute to the risk of confusion.\textsuperscript{55}

As well as hydromorphone, oxycodone, fentanyl and buprenorphine appear to be safe choices for use in older patients.\textsuperscript{55} Oxycodone is metabolised primarily to renally excreted active metabolites, noroxycodone and oxymorphone, but these have clinically negligible effects.\textsuperscript{32} Fentanyl has no active metabolites and buprenorphine is metabolised to buprenorphine-3-glucuronide (inactive) and nor-buprenorphine, which has 40 times less analgesic effect than the parent drug.\textsuperscript{32}

Methadone is not recommended as first-line use in older patients because of its highly variable and unpredictable PK.\textsuperscript{53} Avoidance of pethidine in older patients is also suggested.\textsuperscript{34} Norpethidine, the major metabolite, is renally cleared, neuroexcitatory, and associated with a greater risk of delirium and cognitive impairment compared with other opioids.\textsuperscript{53}

Tramadol is an atypical centrally acting analgesic with combined opioid agonist and serotonin and noradrenaline reuptake inhibitor effects.\textsuperscript{34} Its active metabolite, 0-desmethyltramadol, is renally excreted and a more potent mu-opioid receptor agonist than the parent drug.\textsuperscript{34} Lower daily doses in older patients is suggested.\textsuperscript{32} Tramadol causes less respiratory depression and constipation than opioids, which could be of benefit.\textsuperscript{34} However, its use is associated with an increased risk of POD.\textsuperscript{36}

Other analgesic and adjuvant drugs

Changes may be needed to dose regimens of some other analgesic and adjuvant drugs used for postoperative pain management in older patients. The PK and PD effects of age and the changes needed, if any, are summarised in Table 2.

### Analgesic techniques in the older patient

#### Patient-controlled analgesia

Patient-controlled analgesia (PCA) is an effective and safe method of pain relief in older patients (even those in their ninth decade) with reasonably intact cognition and, as with other patients, leads to better analgesia than intermittent opioid injections.\textsuperscript{34} In comparisons of PCA use in younger and older patients, there were no differences in pain relief, satisfaction or concerns about risks of complications or addiction,\textsuperscript{56} and similar patterns of PCA use, with no differences in dose/demand ratios or met/unmet demands.\textsuperscript{57} Patients with POD may use PCA effectively, but higher opioid requirements and less effective analgesia have been reported.\textsuperscript{58}

#### Epidural analgesia

In general adult populations, epidural analgesia is superior to parenteral opioids for postoperative analgesia.\textsuperscript{32} This was also true in patients aged 70 years and over after major abdominal surgery, where pain relief, bowel activity and mental status (but not risk of POD) were better with patient-controlled epidural analgesia than i.v. PCA.\textsuperscript{59} Epidural infusions also improved pain relief but not rehabilitation after hip fracture surgery\textsuperscript{60} and led to less pain but not opioid-related adverse effects following hip arthroplasty.\textsuperscript{61}

Despite better pain relief, there is limited and conflicting evidence regarding the effect of epidural analgesia on postoperative complication rate.\textsuperscript{18} While no specific comparisons of younger and older patients exist, there is some evidence of benefit from studies involving patients having types of surgery likely to be more common in older age groups. In patients undergoing thoracic or abdominal surgery, epidural analgesia significantly reduced the risk of postoperative pneumonia and MI compared with parenteral opioid analgesia.\textsuperscript{62} In contrast, however, in high-risk patients undergoing major abdominal surgery, postoperative morbidity was not reduced.\textsuperscript{63} Epidural infusions have also been shown to reduce postoperative complications after abdominal aortic surgery,\textsuperscript{64} and supraventricular arrhythmias and pulmonary complications but not MI or stroke after cardiac surgery.\textsuperscript{65}
Older patients are more sensitive to the effects of epidurally-administered local anaesthetics (LA). Using same volumes of LA, the concentration required to produce effective motor blockade decreased as patient age increased. Epidural spread of LA is also influenced by increasing age, with the same volume/same concentration of LA resulting in higher sensory block levels and more intense motor blockade. Bradycardia and hypotension are more common in older patients with epidural analgesia. It therefore seems prudent to reduce epidural infusion rates in older patients.

Intrathecal analgesia

Intrathecal morphine has been used successfully in older and oldest-old patients for a variety of major surgical procedures. Studies using a variety of morphine doses (50–4000 µg [mcg]) have shown that it provides better pain relief after major surgery than other opioid analgesia, although the risk of ventilatory depression is higher. Concern about the risk of ventilatory depression has led to suggestions that patients over the age of 70 years be monitored in intensive care settings. However, risks may be related to the amount given, rather than the use of the drug itself. Several trials in older patient groups have shown no increase in risk at doses up to 200 mcg. Doses of 100 mcg were reported to provide the optimal balance between analgesia and side effects. However subsequent work has shown good results with doses as low as 50 mcg. Older patients given up to 200 mcg may be safely nursed by trained staff, following well designed protocols, in a general ward environment, when under the supervision of an experienced Acute Pain Service.

Other regional analgesia

Regional blockade in older patients may be as effective as epidural analgesia but lead to fewer adverse effects. After total knee arthroplasty in older patients, those given continuous femoral and sciatic nerve blocks had more intense motor blockade in the operated limb, but a lower incidence of side effects. Although it has not been shown that regional anaesthesia leads to a lower incidence of POD and cognitive impairment compared with general anaesthesia, after fractured neck of femur fixation, patients using patient-controlled femoral nerve analgesia had a lower incidence of POD compared with those given systemic analgesia only. Continuous lumbar plexus blockade after total hip arthroplasty, a common operation in older patients, led to better analgesia than opioids for 48 h postoperatively.
Duration of sensory and motor block was increased in older patients compared with younger ones following combined sciatic/lumbar plexus block,\(^7\) a finding that has been replicated for brachial plexus\(^7\) and sciatic nerve\(^8\) blocks.

Unlike epidural analgesia, the spread of local anaesthetic in the paravertebral space did not differ with patient age.\(^8\)

**Summary**

Despite a limited evidence-base relating to postoperative pain management in the older population, most analgesic regimens used in younger patients are suitable if adapted appropriately. If this is done, effective analgesia without an increased incidence of adverse effects is possible for most patients. However, management in cognitively impaired patients remains challenging, largely due to difficulties with assessment, making individual titration of pain relief problematic.

### Practice points

In older persons:

- Age-related physiological changes are progressive; it is difficult to separate out effects on drugs used for postoperative pain relief and effects of disease states.
- Undertreatment of acute pain remains common, especially in patients with significant cognitive impairment.
- The pattern of pain and pain intensity in acute conditions may be altered or diminished, which may delay appropriate diagnosis and treatment.
- Of the unidimensional self-report measures of pain used in the clinical setting, verbal descriptor and numerical rating scales are preferred.
- Most drugs and techniques used for acute pain management can be used in older patients. However, especially in view of the higher incidence of comorbidities and concurrent use of other drugs, each must be carefully adjusted to suit each patient.
- Requirement for both opioids and local anaesthetics decrease with ageing; reductions in the doses of some other drugs are also suggested.
- Of the non-opioid analgesics, paracetamol is the preferred option; NSAIDs should be used with caution and for a short duration only if prescribed.

### Research agenda

- Information about changes in pain perception, assessment of pain and pain management in the older population is improving.\(^2\) However, further studies of postoperative pain management are needed – particularly in oldest-old and frail patients and those with cognitive impairment.
- For most drugs used in acute pain treatments, there is reasonable knowledge about age-related changes in PK. Of greater importance, in many instances, would be better information about PD changes and ageing as well as the effects of various disease states and cognitive function.
- The may be a benefit to new approaches to the study of the PK, PD, efficacy and safety of analgesic drug in young and old patients. Finding two cohorts matched for all but ‘age’ is difficult. Much information can been extracted from heterogeneous populations by collecting ‘sparse’ data and constructing population based PK-PD models that can assist with dose individualisation and optimal therapy for every patient, not just the ‘average patient in a clinical trial’.\(^8\)


44. Cusack BJ. Pharmacokinetics in older persons.

45. Liukas A, Kuusniemi K, Aantaa R et al. Pharmacokinetics of intravenous paracetamol in elderly patients.


47. Barkin RL, Beckerman M, Blum SL et al. Should nonsteroidal anti-inflammatory use in younger and older surgical patients?


