Postoperative pain has been poorly managed for decades. Recent surveys from USA and Europe do not show any major improvement. Persistent postoperative pain is common after most surgical procedures, and after thoracotomy and mastectomy, about 50% of patients may experience it. Opioids remain the mainstay of postoperative pain treatment in spite of strong evidence of their drawbacks. Multimodal analgesic techniques are widely used but new evidence is disappointing. Regional anaesthetic techniques are the most effective methods to treat postoperative pain. Current evidence suggests that epidural analgesia can no longer be considered the ‘gold standard’. Perineural techniques are good alternatives for major orthopaedic surgery but remain underused. Infiltrative techniques with or without catheters are useful for almost all types of surgery. Simple surgeon-delivered local anaesthetic techniques such as wound infiltration, preperitoneal/intraperitoneal administration, transversus abdominis plane block and local infiltration analgesia can play a significant role in improvement of postoperative care, and the last of these has changed orthopaedic practice in many institutions. Current postoperative pain management guidelines are generally ‘one size fits all’. It is well known that pain characteristics such as type, location, intensity and duration vary considerably after different surgical procedures. Procedure-specific postoperative pain management recommendations are evidence based, and also take into consideration the role of anaesthetic and surgical techniques, clinical routines and risk–benefit aspects. The role of acute pain services to improve pain management and outcome is well accepted but implementation seems challenging. The need for upgrading the role of surgical ward nurses and collaboration with surgeons to implement enhanced recovery after surgery protocols with regular audits to improve postoperative outcome cannot be overstated.

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Introduction
Pain relief after surgery continues to be a major medical challenge. Poorly managed postoperative pain may delay discharge and recovery, and result in the patient’s inability to participate in rehabilitation programmes, leading to poor outcomes. Recent advances include better understanding of pain mechanisms, physiology and pharmacology, publication of guidelines, establishment of acute pain services (APSs), initiatives such as ‘pain as the fifth vital sign’ and availability of new drugs and devices. However, these advances have not led to any major improvements, and undertreatment of postoperative pain continues as a considerable problem worldwide.¹,²

Prevalence of postoperative pain – still appalling numbers
A leading group of postoperative pain researchers has commented on the current ‘...appalling high rates of significant postoperative pain’.³ A 2011 report from the US National Institutes of Health states that more than 80% of patients suffer postoperative pain, with fewer than 50% receiving adequate pain relief.⁴ US surveys from 1993, 2003 and 2012 have shown that postoperative pain is common and remains undertreated, and that distribution and quality of perceived pain have remained largely unchanged.⁵

A European survey which included 746 hospitals concluded that the management of postoperative pain was suboptimal. Among the problems identified in this 2008 report were absence of pain assessment in 34% of institutions, absence of documentation in 56% of institutions and no written protocols in 75% of institutions.⁶ A similarly disappointing picture emerged from a recent US survey of 301 hospitals (101 teaching hospitals). There were no written protocols in 45% of hospitals, and intravenous patient-controlled analgesia (PCA) was the most common method to treat pain. Interestingly, this was managed by surgeons in 75% of hospitals; nurses were not
allowed to adjust PCA in 38% of hospitals, epidurals in 57% of hospitals and perineural catheters in 79% of hospitals.7

Certain categories of patients are at a greater risk of being undertreated including the pregnant, the paediatric, the elderly, the opioid tolerant and the patient undergoing ambulatory surgery.

**Persistent postoperative pain**

Persistent postoperative pain (PPP) is common, causes disability, lowers quality of life and has economic implications; it is a major cause of chronic pain and therefore an important public health problem.8 Severe PPP affects 2 to 10% of adults undergoing surgery.9 Worldwide, about 235 million patients undergo surgery annually, and this means that millions of patients suffer from the consequences of PPP. The reported incidence of PPP is variable; after some common operations such as thoracotomy, mastectomy, coronary artery bypass and hernia repair, the incidence can be 30 to 50%. After limb amputation, the risk is even higher.10 Over 20 surgical, psychosocial and patient-related genetic and environmental risk factors have been identified. These include preoperative factors such as anxiety, depression, impaired pain modulation, genetic factors, sleep disorders and catastrophising. In the intraoperative and postoperative healing phase, the factors to consider are surgical technique, nerve injury and tissue ischaemia. In the later postoperative period, the important factors are postoperative pain hyperalgesia, chemotherapy or radiotherapy, repeat surgery and a variety of psychosocial factors.1,3,9,10,11 No single factor seems to play a dominant role.

Given the multiplicity of neurotransmitters and pain pathways involved in the transition from acute to chronic pain, it is not surprising that there are no definitive pharmacological interventions to prevent or treat PPP. It would seem logical that a combination of mechanisms needs to be targeted by different approaches to inhibit central sensitisation. Gabapentinoids are considered an interesting class of drugs because of their analgesic effects in neuropathic pain as well as their anxiolytic effects. However, the literature is conflicting. A systematic review of 11 randomised controlled trials (RCTs) showed that gabapentin decreased the incidence of PPP,12 whereas a more recent Cochrane review13 and a meta-analysis14 dispute this. Of the 11 different analgesics evaluated, only intravenous ketamine had a modest effect.13 A meta-analysis showed that the number needed to treat for intravenous ketamine versus placebo was 12. This meta-analysis also reported that reduction of acute pain intensity may not be linked directly to reduced prevalence of development of PPP.15 Intravenous ketamine may be appropriate in patients undergoing painful operations, particularly those who are expected to require large doses of opioids.

Surgeons can play an important role in reducing PPP by using minimally invasive and nerve-sparing techniques such as sentinel node biopsy for mastectomy, thereby avoiding axillary dissection and intercostal nerve damage. Thoracoscopic techniques spare intercostal nerves and avoid the use of rib retractors. Intracostal sutures (versus pericostal sutures) have been shown to be associated with lower pain scores up to 3 months after thoracotomy.16

At present, one of the most promising strategies to reduce PPP seems to be the use of regional techniques. A recent Cochrane review of 23 RCTs showed that epidural anaesthesia and paravertebral block, may prevent PPP after thoracotomy and breast cancer surgery in about one out of every four to five patients treated. The data consistently favoured regional anaesthesia, and three studies favoured wound infiltration for hernia repair, iliac crest harvesting and vasectomy.17

In conclusion, more than 20 years after the first reports of development of a chronic pain state lasting months or years after surgery,1 there is no definitive evidence for the role of any intervention to prevent or treat this complex entity. Intravenous ketamine may have a modest role. Regional anaesthesia techniques show some promise, and should be used more frequently because they also reduce the need for opioids. An APS may have a role in identifying at-risk patients and in follow-up after they are discharged home.8 Given the very high prevalence, it is time to include the risk of PPP in preoperative information routines, particularly for patients at high risk.

**Pharmacological management – no major breakthroughs**

**Opioid therapy**

In spite of the growing awareness of the value of multimodal pain management plans, opioid monotherapy remains the foundation of postsurgical pain therapy. A recent retrospective review based on more than 300 000 patients across 380 US hospitals showed that about 95% of surgical patients were treated with opioids.18 Opioids are widely used because they are highly effective for relieving moderate-to-severe postoperative pain, do not have a ceiling effect and are available in a wide variety of formulations. There is also a long tradition of decades of opioid use, familiarity with the technique and accumulated experience. However, opioids have many dose-limiting side-effects that range from bothersome to life-threatening, including nausea, vomiting, constipation, oversedation, somnolence and respiratory depression.1,18 Elderly or sleep apnoeic patients, the obese and smokers are all at increased risk of oversedation and respiratory depression. Patients may self-limit their opioid use to reduce opioid side-effects, but this can lead to inadequate analgesia. Opioid-related adverse events have been associated with an increase in overall cost, length of stay and even decreased survival during in-hospital resuscitation.19 However, these developments
have not resulted in reduced use of opioids. Indeed, the use of opioids has increased in recent years, both for inpatients\(^1\) and outpatients.\(^2\)

The introduction of new analgesic drugs has been incredibly slow and hardly any new drugs have come to the market in the last 50 years.\(^3\) Postoperative pain management is still based on the use of traditional opioids, paracetamol, NSAIDs and local anaesthetics. The main innovations have been in the use of older drugs in new delivery systems and routes of administration such as transdermal (fentanyl, buprenorphine), intranasal (fentanyl, sufentanil, diamorphine, ketamine), oral transmucosal (fentanyl) and sublingual (buprenorphine, sufentanil). The other innovations have been in the development of extended-release local anaesthetics and epidural morphine (now withdrawn from the market). A transdermal system using iontophoresis to allow rapid transfer of fentanyl to the circulation allowed the patient to self-administer 40 \(\mu\)g of fentanyl with a 10-min lockout time. This transdermal PCA system was shown to provide comparable analgesia to that seen with intravenous morphine PCA.\(^2\)\(^4\) This ‘needle-free PCA system’ was approved by the US and European regulatory agencies but was voluntarily withdrawn because of technical problems. The impressive device is undergoing further development and might re-emerge.

**Multimodal analgesia – much rhetoric, disappointing evidence**

The concurrent use of more than one class of analgesic drug or technique to target different mechanisms of analgesia has been advocated to improve analgesia through additive or synergistic effects while reducing opioid-induced side-effects.\(^1\)\(^2\)\(^4\) In general, the main aim is to reduce or eliminate the use of strong opioids which are recognised to have many disadvantages and unacceptable side-effects. A large number of nonopioids are available including paracetamol, NSAIDs, local anaesthetics, gabapentinoids, ketamine and glucocorticoids. Although the concept of multimodal analgesia is widely accepted, the literature on the possible harmful effects of combining analgesics is poorly studied. There is also surprisingly little evidence to show that using an arsenal of different analgesics is better than more simple regimens.\(^2\)\(^5\) Meta-analyses have shown beneficial analgesic effects when opioids are combined with nonopioid drugs such as paracetamol, NSAIDs, \(\alpha_2\)-delta modulators (gabapentin, pregabalin), \(\alpha_2\)-agonists (clonidine, dexmedetomidine), ketamine and magnesium. However, with the exception of a combination of paracetamol and NSAIDs, there is no meta-analysis of combinations of different nonopioids. There is hardly any literature on a combination of three or more analgesics, which is a common clinical practice.\(^2\)\(^6\) In general, research into multimodal analgesia has not shown a consistent level of success because of a large number of variables in available studies. These include a variety of analgesics or analgesic modalities and different doses and drug combinations, making it difficult to draw relevant conclusions.

A recent review of systematic reviews and meta-analyses showed that the 24-h morphine-sparing effects of nonopioids as monotherapy are rather modest.\(^27\) A systematic review of adverse effects of nonopioids found that paracetamol was associated with trivial adverse effects but the use of NSAIDs was associated with anastomotic leakage. Gabapentinoids, especially pregabalin, were associated with an increased risk of sedation, dizziness and visual disturbances.\(^14\)\(^27\)\(^28\) There is also increasing concern regarding substance misuse and abuse of gabapentin\(^29\) and pregabalin.\(^30\)

The concept of multimodal analgesia for managing postoperative pain was introduced by Kehlet and Dahl in 1993.\(^2\)\(^4\)\(^24\) Over the years, they have repeatedly promoted it in multiple publications.\(^31\) However, the implementation of such techniques in routine clinical practice is apparently challenging.\(^32\) A 2012 report from 12 surgical departments from their own institution showed surprisingly disappointing results. Their data indicated that 75% of patients were treated with opioids as first choice during the first three postoperative days and that doses of nonopioids were inadequate. The quality of pain management was unclear because pain scores were not recorded in most patients. The authors concluded that ‘... the use of multimodal opioid-sparing pain treatment was suboptimal’.\(^32\) In 2006, a group of US experts reviewed the literature and concluded that there was little evidence of any benefits of multimodal analgesia, except for the combination of paracetamol and NSAIDs.\(^33\) Eight years later, a review by one of the two originators of the concept not only came to a similar disappointing conclusion but also noted that many patients receiving combination analgesia may be at increased risk of adverse events.\(^34\) So we seem to be back to square one after 20 years of multimodal analgesia. This does not mean that we should stop combining nonopioids because the goal of avoiding strong opioids, though daunting, is still valid. It is time to shift our focus to evaluate the role of simple, local anaesthetic-based infiltrative techniques as a primary component of multimodal analgesia.

The two safest nonopioids available to us are paracetamol and local anaesthetics. The latter seem to be underused as an important component of multimodal regimens. Based on our standard protocol since 1991, every surgical patient at our hospital receives a combination of paracetamol and wound infiltration with bupivacaine (by the surgeon at the end of surgery).\(^35\) Other regional techniques, NSAIDs, opioids or intravenous morphine PCA are added as necessary. Nearly 25 years of this multimodal regimen, in tens of thousands of patients, and results of repeated audits testify to the remarkable safety
of this regimen (see ‘Acute Pain Services’ below). Wound infiltration techniques are now recommended as part of multimodal regimens by several national and international societies such as the American Society of Anesthesiologists36 and the Australian and New Zealand College of Anaesthetists.37

In conclusion, in spite of major drawbacks with the use of opioids, we have been unable to replace them as the mainstay of treatment of moderate to severe postoperative pain. In spite of much rhetoric, current evidence suggests that the advantages of combining paracetamol and NSAIDs are rather modest, the benefits of combining other nonopioids overrated, the side-effects generally ignored and the role of combining more than two nonopioids largely unknown. Future studies need to address the role of surgeon-delivered local anaesthetic-based infiltrative techniques as a first-line component of multimodal analgesia.

Regional anaesthesia techniques
In recent years, there has been an increase in the use of regional techniques for surgery and perioperative pain management, particularly in patients undergoing obstetric, orthopaedic or paediatric surgery.38 By stopping pain transmission, regional techniques with local anaesthetics can provide excellent pain control. Multiple routes of local anaesthetic administration are available. The following is a brief summary of the current status of regional techniques for postoperative pain.

Epidural techniques – ‘gold standard’ no more!
Epidural analgesia is a widely used technique to provide excellent postoperative pain after major surgery. Several earlier meta-analyses have shown that the use of the technique is also associated with other benefits such as reduced cardiovascular, pulmonary and gastrointestinal morbidity. Some studies have also shown reduced mortality. For decades, epidural techniques have been considered the ‘gold standard’ for pain management after major surgery. However, more rigorous evaluation of previous data and newer meta-analyses show less optimistic results. Several meta-analyses and data from more robust trials in patients undergoing major surgery such as aortic, colonic or gastric procedures failed to show any reduction in mortality with perioperative epidural analgesia compared with general anaesthesia and systemic opioids.39 The authors of a meta-analysis of 28 RCTs with more than 2700 cardiac surgery patients did not recommend epidural analgesia because of its poor–benefit ratio.40 The protective effect of epidural analgesia against pneumonia after abdominal or thoracic surgery has decreased over the last 35 years because of an overall reduction in baseline risk because of changes in surgical routines including early postoperative mobilisation and active physiotherapy.41 Furthermore, the debate about the pulmonary benefits of epidural analgesia is becoming less relevant with increasing use of endoscopic surgical procedures instead of open ones. A review has questioned the use of epidural analgesia in abdominal surgery.42 There are several meta-analyses showing that the far less invasive intravenous lidocaine infusion is associated with many benefits in abdominal surgery such as reduced duration of ileus, decreased pain scores, lower risk of postoperative nausea and vomiting (PONV) and shorter hospital stay.43 There are three meta-analyses showing that an even simpler and safer evidence-based method to prevent or ameliorate postoperative ileus is the use of the humble chewing gum.44–46 Chewing gum therapy is part of enhanced recovery after surgery (ERAS) protocols in many institutions.

Epidural analgesia has been promoted as an essential component of ERAS protocols for colorectal surgery. Perioperative clinical pathways facilitate postoperative rehabilitation by optimising analgesia, early oral intake and ambulation and avoidance of fluid overload.47 ERAS programmes with a coordinated team approach in implementing the various elements of such protocols have been shown to reduce morbidity and hospitalisation times.48–50 Such pathways have been promoted for many surgical procedures, but those for colorectal surgery are the most widely studied. However, it remains difficult to demonstrate supporting evidence for individual components.49–51 On account of the mediocre to poor quality of studies, the authors of a Cochrane review did not recommend ‘fast-track’ (ERAS) as a standard of care.48 At present, there is no evidence that epidural analgesia is an essential component of ERAS protocols.49–51 Thus, it appears that the success of ERAS programmes for colorectal surgery is primarily a result of a structured, protocol-based approach and a modified attitude towards postoperative rehabilitation goals. Pain relief is important, but its role seems to be secondary, particularly in the increasingly common laparoscopic procedures. There is no convincing evidence that an epidural technique is essential or any better than simple local anaesthetic-based infiltrative techniques.39 The procedure-specific postoperative pain management (PROSPECT) group does not recommend epidural analgesia for the increasingly more common laparoscopic colonic surgery. Neither is epidural analgesia recommended as the first choice for most other abdominal procedures including laparoscopic cholecystectomy, hysterectomy, prostatectomy and caesarean section.49

The controversy about the role of epidural analgesia in influencing postoperative morbidity and mortality has resurfaced with the publication of four new reports.52–54 with meta-analyses reporting both reduced50 and increased51,52 morbidity. A literature review concluded that epidural analgesia can no longer be considered as a standard of care after routine surgery.53

Several studies (almost all retrospective) and editorials have reported that the risks of severe neurological
complications of epidural analgesia are higher than previously believed. A recent closed claims analysis from Finland reported six deaths over a period of 9 years. The risk of neuraxial haematoma was far greater with epidural analgesia (1:26 400) than spinal anaesthesia (1:775 000). A much higher risk was noted in a recent audit report of over 35 000 patients from the USA: cardiac arrest 1:5000, epidural abscess 1:27 000 and epidural haematoma 1:5400.

In making the decision to use epidural analgesia, the failure rate has to be taken into consideration. This can vary from 32% to about 50%. To be considered successful, epidurals need to facilitate the early postoperative mobilisation (‘walking epidural’) that is required for ERAS protocols and function effectively for the entire duration of treatment (typically 48 to 72 h). This has to be balanced against the costs of labour-intensive monitoring requirements; in many hospitals, such patients are still nursed in high-dependency units or ICUs. Only institutional audits can guide the clinicians as to whether their epidural analgesia risk–benefit ratios are acceptable.

Based on current evidence, the main indications for epidural analgesia could be high-risk patients scheduled for open major surgery; extensive surgery involving large areas of the body; centres wherein peripheral regional techniques have not been introduced and possible future new indications such as anticancer benefits and prevention of chronic postoperative pain. For labour analgesia, epidural analgesia remains the ‘gold standard’.

In conclusion, the advantages of epidural analgesia are not as impressive as formerly believed and the risks are greater than estimated in the past. Epidural analgesia may have a role in high-risk patients undergoing open major vascular or cardiac surgery. In general, the role of epidural techniques has been decreasing in recent years for reasons shown in Table 1. Regional anaesthesia techniques provide the most effective postoperative pain relief. The risk–benefit equation has shifted away from epidural analgesia and in favour of less invasive but equally effective and safer regional anaesthesia techniques (Fig. 1). Epidural analgesia can no longer be considered the ‘gold standard’ as a routine method for the management of postoperative pain. The continued use of epidural analgesia at any institution can only be justified by results from its own audits. Very few institutions perform regular audits. Consequently, the success rates of epidural analgesia in each institution remain largely unknown.

**Perineural techniques – effective but underused**

It is well established that perineural techniques are highly effective and appear superior to intravenous opioid techniques. A large number of nerve block techniques have been reported for almost every part of the body. A limitation of the single-injection peripheral nerve block is the relatively short duration of analgesia. Catheter techniques allow prolonged analgesia. Regardless of the location of the catheter, continuous perineural techniques are opioid sparing and associated with a reduced risk of opioid-related side-effects such as PONV and sedation. As these techniques may be as effective as epidural analgesia but are less invasive with a better adverse effect profile, they are recommended as the first choice for major orthopaedic surgical procedures such as hip or knee replacement surgery. Several meta-analyses conclude that peripheral blocks such as femoral and sciatic are superior to epidural analgesia for knee replacement.

**Table 1: Reasons for the diminishing role of epidural analgesia in postoperative pain management**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Description</th>
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<tbody>
<tr>
<td>Re-evaluation of previous data and newer meta-analyses show less impressive outcome results regarding postoperative mortality and morbidity</td>
<td>Widespread adoption of prophylactic anticoagulant techniques by surgeons has eliminated the DVT-reducing benefits of EA while creating practical obstacles for EA catheter management</td>
</tr>
<tr>
<td>EA increasingly unnecessary because of change from open to minimally invasive endoscopic surgical techniques – also, many previous inpatient operations are now day-case or overnight stay procedures</td>
<td>Benefits of EA versus systemic opioids for postoperative pulmonary complications have decreased over the years because of overall improvements in postoperative rehabilitation and physiotherapy routines</td>
</tr>
<tr>
<td>EA failure rates can be very high (30 to 47%)</td>
<td>Risk of side-effects such as hypotension and urinary retention is relatively high, hindering postoperative mobilisation</td>
</tr>
<tr>
<td>Availability of several equally effective and far less invasive regional anaesthesia techniques (see text)</td>
<td>Monitoring requirements are labour intensive (at many institutions patients nursed in high-dependency units or ICU because of shortage of trained personnel)</td>
</tr>
<tr>
<td>Risks of serious complications (including death) greater than previously believed</td>
<td>No convincing cost-effectiveness data in spite of years of EA use</td>
</tr>
<tr>
<td>Litigation concerns because of risks of severe neurological complications</td>
<td>DVT, deep vein thrombosis; EA, epidural analgesia.</td>
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An example of how postoperative analgesic techniques for knee surgery have evolved over time. Total knee replacement is a common surgical procedure and generally considered very painful. ACB, adductor canal block; CSE, combined spinal and epidural; ERAS, enhanced recovery after surgery; LA, local anaesthetic; LIA, local infiltration analgesia.

the level of the mid-thigh has been increasingly advocated to eliminate the problem (Fig. 1).

Nevertheless, most anaesthesiologists have not been able to introduce these techniques into their clinical routines. Studies have shown that the use of perineural techniques to treat postoperative pain is very low in the USA, Europe and elsewhere. Data from the US National Center for Health Statistics showed that regional anaesthesia was used in only 8% of ambulatory cases. A French survey showed that less than 5% of inpatients received postoperative analgesia by peripheral nerve blocks and a surprisingly low 1.5% received epidural analgesia. A recent USA database report from over 400 acute care hospitals with 191,570 patients undergoing total knee arthroplasty (TKA) showed that only 12.1% of patients received postoperative analgesia with a peripheral nerve block.

In conclusion, there is convincing evidence about the efficacy and feasibility of peripheral nerve blocks to manage pain. Catheter techniques can prolong the duration of analgesia for an unlimited time. Ultrasound-guided blocks have reduced failure rates and encouraged more anaesthesiologists to use such techniques. However, routine use of these techniques still remains restricted to a relatively small percentage of institutions. In ambulatory surgery patients, perineural catheter techniques for pain management will most likely be restricted to an even smaller number of institutions because of safety concerns in the medically unsupervised patient at home.

**Infiltrative techniques – growing and evolving, the way forward**

Epidural and perineural catheter techniques are very effective in controlling postoperative pain, but these techniques require the expertise of an anaesthesiologist, are associated with technical failures and catheter management can be labour intensive. In recent years, several infiltrative techniques have received increasing attention as simple and less invasive local anaesthesia-based alternatives either alone or as part of multimodal regimens to treat postoperative pain. These techniques can be single dose or catheter techniques and are usually surgeon administered.

The ease of use and safety of local anaesthetics has been well recognised for decades. Collectively, they serve as one of the most important classes of drugs in perioperative pain management. The main advantage of local anaesthetics is that they directly act on the tissue to which they are applied and do not have the adverse effects of opioids. Consequently, they should be evaluated further as component of multimodal techniques.
Simple surgeon-delivered techniques such as wound infiltration, preperitoneal/intraperitoneal administration, transversus abdominis plane (TAP) block and local infiltration analgesia (LIA) as single administration or with catheters placed under direct vision and in collaboration with anaesthesiologists and the APS can play a significant role in improvement of postoperative care. A meta-analysis concluded that even a simple instillation of local anaesthetic in the peritoneal cavity can provide effective analgesia, albeit for only about 6 h postoperatively after gynaecological laparoscopy. As some of these techniques are relatively new and others still evolving, there is a need for further studies to address the many unanswered questions.

**Wound infiltration and catheter infusion techniques – surprisingly effective**

Direct application of local anaesthetics to the surgical site is a rational approach to block pain transmission from afferent nociceptive barrage. Local anaesthetics also inhibit the inflammatory response to injury and may, therefore, reduce the risk of hyperalgesia. The technique is simple and inexpensive, and has a good safety profile with few side-effects. It can be used alone or as part of multimodal regimens depending on the severity of postoperative pain. Surgeon-administered wound infiltration at the end of surgery is a simple and effective technique, and is used routinely in many hospitals.

Wound catheter infusions (WCIs) should preferably be called surgical-site catheter infusions because the catheters are not always strictly in the surgical wound. The technique involves catheters placed in a number of sites including subcutaneous, subfascial, preperitoneal, intraperitoneal, subacromial, intraosseous, intra-articular and others. A systematic review of 44 RCTs showed that WCI techniques provided effective pain relief at rest and movement, and reduced opioid use and increased patient satisfaction, with some limited evidence for shorter hospital stay. No major adverse effects were reported, and the rates of wound infection were very low (0.7%) and similar to those in the control group. WCI was effective across a variety of surgical procedures (abdominal, cardiothoracic, orthopaedic and others).

A more recent meta-analysis of 14 RCTs (756 patients) focused on ropivacaine for WCI, the authors noting consistent evidence of effective analgesia and opioid sparing in a wide range of surgical procedures such as total knee or hip replacement, and major abdominal and cardiac surgery. Similarly, a meta-analysis of intra-articular techniques (WCI, TAP, intraperitoneal) versus placebo for routine analgesia for colorectal surgery concluded that the infiltrative techniques were associated with lower pain scores, reduction of opioid requirements, shorter length of stay and no increase in complications.

It must be emphasised that all studies with wound infiltration are not positive. A Cochrane review concluded that the beneficial effects of wound infiltration were modest in patients undergoing laparoscopic cholecystectomy. Meta-analysis has also shown modest benefits of wound infiltration in patients undergoing mastectomy and those undergoing spinal surgery.

**Local infiltration analgesia – game changer in orthopaedic practice**

The LIA technique was introduced by Kerr and Kohan mainly for controlling pain after total hip arthroplasty (THA) and TKA. In spite of its name, the original LIA technique is not just infiltration of local anaesthetic but a multicomponent optimisation package. In addition to infiltration with a mixture of ropivacaine, adrenaline and ketorolac into all tissues subject to surgical trauma, it includes extensive preoperative patient education, minimally invasive surgery, accelerated postoperative rehabilitation and structured follow-up care. This is combined with an intra-articular catheter for analgesic top-ups, allowing the blockade to last as long as 36 h. Ice packs and compression bandages are also a part of the technique. Surgery is performed under spinal anaesthesia. Thrombosis prophylaxis consists of aspirin only. Postoperative analgesia is provided by paracetamol and ibuprofen with morphine as a rescue analgesic. Postoperative mobilisation is started about 4 h after surgery.

In a case series of 325 patients, more than half of those undergoing surgery could be discharged on the first postoperative day and most of the remainder were discharged on the following day. Postoperative pain scores were low and there were very few thromboembolic complications. The details of the infiltration technique and the other components of LIA technique are described elsewhere. The LIA technique has achieved widespread acceptance by orthopaedic surgeons, especially in the Scandinavian countries, UK, Australia and some other countries. Much of the literature is from Denmark, Sweden, Norway, UK, USA and Australia, although none of these studies has been able to replicate the 1 to 3 days discharge times reported by Kerr and Kohan. In general, the discharge times are in the range of 3 to 5 days, which is still much shorter than the pre-LIA hospitalisation times of 6 to 10 days. The 2014 report of the Swedish Knee Arthroplasty Register showed that almost every patient (97.3%) received LIA for TKA in 2013. However, the intra-articular catheter was used in only 25.6% of patients.

The LIA technique has shown favourable results when compared with traditional methods of pain relief such as epidural analgesia and intrathecal morphine for both THA and TKA, and also with femoral nerve block for TKA. In comparison with epidural for TKA, LIA was not only more effective but was also associated with superior knee function, lower cumulative morphine dose, faster mobilisation and shorter hospital stay. LIA with a catheter for TKA was not only associated with similar

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pain scores as with epidural, but also the opioid consumption was reduced and hospital stay was 2 days shorter in the LIA group.99

A literature review concluded that LIA may be useful for TKA but not for THA if nonopioid multimodal analgesia is used.85 However, no evidence was provided to support this claim. Furthermore, another systematic review of LIA for THA disagreed and concluded that the technique was an effective method for THA.90 Two editorials concluded that LIA for TKA is promising but that further studies are necessary.89,97

Analgesia for TKA is a good example of how regional techniques have evolved in recent years. As shown in Fig. 1, the femoral block was shown first to be an effective alternative to epidural analgesia49,99 and now there is increasing evidence that ACB with LIA may be an effective alternative to femoral block within the framework of ERAS programmes for TKA.64,85,87 LIA was associated with effective analgesia, improved ambulation and ability to climb stairs. Combining ACB with LIA was associated with further increases in ambulation and more rapid discharge home.98

In conclusion, LIA is a major recent development in lower extremity joint replacement surgery. In some institutions, it has been a game changer. In Sweden, almost every TKA is performed in association with a LIA technique. Although controlled trials are necessary to address the many unanswered questions such as the role of intra-articular catheters and the most appropriate drug combinations, the technique is here to stay. The results of ongoing studies with ultra long-acting local anaesthetics are eagerly awaited.

**Intra-peritoneal local anaesthetics for abdominal surgery – site of catheter placement may be key**

In a meta-analysis of 30 RCTs, intra-peritoneal use of local anaesthetic in laparoscopic cholecystectomy was shown to reduce pain, opioid use and the need for rescue analgesia.90 Literature is now appearing in which WCI has been compared with other regional techniques. A meta-analysis of nine RCTs compared WCI with epidural analgesia in abdominal surgery including liver resection, colorectal and aortic aneurysm repair concluded that WCI was associated with comparable pain scores both at rest and during movement up to 48 h, and with less urinary retention.91 With increasing published literature, certain aspects of WCI are becoming clearer. For example, the importance of catheter positioning was demonstrated in two studies in patients undergoing open colorectal surgery. Ropivacaine infusion through a preperitoneally placed catheter provided effective analgesia, less PONV and accelerated postoperative recovery.92–94 The technique has been demonstrated to be superior to epidural analgesia in terms of analgesia and reduction of hospital stay.93,94 For caesarean section, the most appropriate position is subfascial rather than subcutaneous and in this position, WCI was as effective as epidural analgesia95 or better.90 This catheter placement is recommended by the PROSPECT group.49

**Transversus abdominis plane blocks – increasing evidence of efficacy**

Owing to the ease of administration and efficacy, TAP infiltration has been used successfully in bowel surgery, appendicectomy, hernia repair, umbilical surgery and gynaecological surgery.97 There is a substantial quantity of safety and efficacy data which has allowed several meta-analyses98–100 and a Cochrane review.101 Another meta-analysis has shown TAP block to be effective for pain after caesarean section,102 and it is also recommended by the PROSPECT group.49

**Current management guidelines are ‘one size fits all’ – need for procedure-specific recommendations**

All pain management guidelines advocate generalised ‘one size fits all’ recommendations for the use of analgesic drugs and techniques. Such guidelines are derived from different surgical procedures with varying pain characteristics such as type (visceral versus somatic), location, intensity and duration. The efficacy of an analgesic can vary depending on a surgical procedure.103 Also, even similar high pain intensities may be associated with widely different postoperative morbidity, for example dental extraction pain versus open thoracotomy or upper abdominal surgery, the latter procedures are associated with considerable pulmonary dysfunction.26 In clinical practice, it is well recognised that there are clear differences in perception of pain intensity and its consequences across different surgical procedures, for example thoracotomy versus hysterectomy, or knee replacement versus hip replacement. Furthermore, the consequences of surgical technique (open versus endoscopic surgery) on postoperative pain and morbidity will influence the choice of analgesic technique and its risk–benefit ratio. For example, although epidural analgesia is very effective for analgesia, it may not have risk–benefit advantages in thoracoscopic versus thoracotomy and laparoscopic versus laparotomy procedures. Thus, there is a need for surgical procedure-specific recommendations.

PROSPECT guidelines are such a source of evidence-based, procedure-specific recommendations from an international group of anaesthesiologists and surgeons. The PROSPECT recommendations are based on systematic reviews of the literature for a particular surgical procedure and include randomised studies that evaluate the role of analgesic drugs and techniques and also the role of anaesthetic and surgical techniques on postoperative pain. The recommendations also take into consideration clinical routines and risk–benefit aspects. For
example, the PROSPECT group does not recommend epidural analgesia as first-line treatment for a number of surgical procedures (laparoscopic cholecystectomy, hysterectomy, laparoscopic colorectal surgery, THA, TKA, caesarean section) in spite of its documented analgesic efficacy in all these procedures. Readers are presented with algorithms and different alternatives to help with clinical decision making. Implementation of procedure-specific protocols has been shown to be associated with significant improvement in pain management. PROSPECT recommendations are freely available online (www.postoppain.org). At present, the following procedures are online: cholecystectomy; hip replacement; knee replacement; thoracotomy; hysterectomy; prostatectomy; inguinal hernia surgery; haemorrhoidectomy; and mastectomy. The latest procedure to go online is caesarean section. Among the evidence-based (Level of Evidence 1, Grade of Recommendation A) recommendations are preoperative gabapentin, Joel-Cohen and similar transverse incisions (superior to the commonly used Pfannenstiel incision), nonclosure of peritoneum, infiltrative techniques such as wound infiltration including WCI, iliohypogastric and ilioinguinal blocks, and TAP block. This again illustrates that the PROSPECT group also evaluates the role of surgical techniques in improving postoperative pain. It is proposed that 15 to 20 of the most common surgical procedures will be included. The recommendations are updated regularly. At present, PROSPECT is funded and administered by a grant from the European Society of Regional Anaesthesia and Pain Therapy.

Acute pain services still ‘work in progress’ 25 years on
The establishment of an Acute Pain Service has been accepted as an important tool in the improvement of postoperative pain management on surgical wards and in providing safe analgesia with the use of more advanced techniques such as intravenous opioid PCA, epidural analgesia and other regional techniques. APS with a multidisciplinary team approach has received widespread formal acceptance from national and international organisations. It is generally accepted that the problem of undertreated postoperative pain is best addressed by having an appropriate APS organisation. Worldwide, the number of hospitals with an APS seems to be increasing. However, a prevalence of APSs does not mean much in the absence of established standards for structure and function of an APS. There is evidence that many APSs provide only a token service because of financial constraints and low priority. A literature review concluded that most APSs worldwide did not meet basic quality criteria, defined as regular recording of pain scores at least once a day, written protocols, dedicated personnel and policies for pain management during nights and weekends (Table 2). In Norway and Denmark, the APS numbers have decreased in recent years, apparently because of increasing implementation of ERAS programmes. An editorial made a connection between this reduction in APSs with increased deaths because of opioid overdose on Norwegian surgical wards and concluded that APSs and ERAS programmes are not mutually exclusive and that ERAS programmes should complement, not replace, APSs.

Various APS models, with significant differences in structure and function, have been reported. The main models include the model described above with 24-h cover by an anaesthesiologist, and a ‘low-cost’ specialist nurse-based APS supervised by anaesthesiologists. A literature review showed that physician-based APSs were more common than the nurse-based APSs. Whichever the model selected, an APS should have a collaborative interdisciplinary approach to managing postoperative pain. Table 2 shows the requirements that are generally accepted for a good APS. It is beyond the scope of this review to debate the pros and cons of the APS models and how to implement APSs; these have been addressed elsewhere. In any model of an APS, the role of ward nurses needs to be upgraded if postoperative pain management is to improve on surgical wards. Even today, in most institutions and countries, ward nurses are not allowed to administer opioids through intravenous lines or local anaesthetics through epidural or perineural catheters. A 2012 US survey of APSs in 301 hospitals showed that PCA was the most common method to treat pain and was managed by surgeons in 75% of hospitals. Notably, ward nurses were not allowed to adjust PCA in 38% of hospitals, epidural analgesia in 57% of hospitals and perineural techniques in 79% of hospitals. Similar disappointing results were reported from European surveys. There is very little information from low-resource countries, and it is probably even more disappointing. In physician-based APSs, surgical ward nurses are required to call the APS anaesthesiologist

Table 2 Requirements* for establishing an organised Acute Pain Service (APS) team

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Description</th>
<th>Notes</th>
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<tr>
<td>Designated personnel responsible for 24-h service</td>
<td>Regular pain assessment at rest and movement and maintaining scores below predetermined threshold</td>
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<tr>
<td>Documentation of pain scores before and after intervention</td>
<td>Documentation of side-effects</td>
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<tr>
<td>Active cooperation with surgeons to implement analgesic protocols as part of</td>
<td>Ongoing cooperation and support from anaesthesiologist, intervention by ward nurses, avoidance of analgesic protocols that are inappropriate for the patient</td>
<td></td>
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<tr>
<td>ERAS programmes to achieve preset goals for postoperative rehabilitation</td>
<td>Ongoing cooperation with surgeons to implement analgesic protocols as part of ERAS programmes to achieve preset goals for postoperative rehabilitation</td>
<td></td>
</tr>
<tr>
<td>Ongoing teaching programmes for ward nurses (drugs and modalities used,</td>
<td>ERAS, enhanced recovery after surgery; PCA, patient-controlled analgesia. *Irrespective of the APS model selected, these are considered to be the essential requirements (see text for details).</td>
<td></td>
</tr>
<tr>
<td>‘standard orders’, PCA pump programming, regional anaesthesia catheter</td>
<td></td>
<td></td>
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<tr>
<td>techniques, recognition and management of adverse effects, monitoring</td>
<td></td>
<td></td>
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<tr>
<td>routines)</td>
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<td>Patient education regarding their right to good analgesia and treatment</td>
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<td></td>
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<tr>
<td>options</td>
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<td></td>
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<tr>
<td>Policies and procedures for continuous quality improvement</td>
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every time the patient needs dose adjustments for PCA or epidural. The patient remains in pain until the physician arrives, and it is not uncommon that this physician is relatively inexperienced.\textsuperscript{110} This system seems time-consuming, cost-ineffective and inhumane.

Specialist nurse-based, anaesthesiologist-supervised APS models which cover all patients undergoing surgery (not just those requiring hi-tech services) address the above issues by allowing ward nurses to administer intravenous opioids on demand, programme PCA pumps and adjust PCA, epidural and perineural techniques as necessary. Details of this model, including the responsibilities of the APS anaesthesiologist, APS nurses, ‘section anaesthesiologist’, surgeon, ward nurse and ‘pain representative’ nurse and surgeon on each ward are described elsewhere.\textsuperscript{108–110} Since the implementation of this model at our hospital in 1991 and based on audit results, many changes have taken place over the years. Some of the key changes have been the change from intramuscular or subcutaneous to titrated doses of intravenous morphine administered by ward nurses on every surgical ward; patient information brochures in 16 languages and video; regular pain assessment at rest and on movement (every 3 h in awake patients) and documentation of pain scores; pain assessment tool changed to numerical rating scale from visual analogue scale; increase from one to three APS nurses (two of this time period) although the total number of operations decreased gradually from 20 000 to about 15 000 per year; annual audit feedback to surgeons and ward nurses; epidural PCA mode instead of continuous infusion to allow better mobilisation with ‘walking epidural’; modified analgesic routines to adapt to surgical ERAS protocols; increased use of perineural techniques on surgical wards; electronic recording of pain scores; and the use of hand-held computers by APS nurses to prospectively collect audit data and joining the PAIN OUT international database for benchmarking of our APS.\textsuperscript{111} The general principles of this APS model have been recommended for Swedish hospitals by the Swedish Medical Association (Svenska Läkaresällskapet) in 2001\textsuperscript{112} and have also been implemented in several other countries.\textsuperscript{2,109,113}

This ‘office hours only’ APS nurse-based model does not provide direct hands-on patient care, nor does it provide out of hours cover. This model is a resource for education and training and promotion of good clinical practice. It relies on the on-call anaesthesiologist being consulted during nights and weekends. The number of times these anaesthesiologists are consulted has decreased over the years; at present, this only happens occasionally.

In conclusion, it is increasingly clear that the decades-old problem of undertreated postoperative pain is not because of lack of effective drugs or techniques but to a lack of an organised, multidisciplinary approach (APS) which uses existing treatments. Irrespective of the APS model, teaching programmes to upgrade the role of ward nurses, standardised protocols and regular audits are necessary to address the problem. The role of the last of these to improve outcomes cannot be overstated.

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References


89 Mariano ER, Perlas A, Adductor canal block for total knee arthroplasty. The perfect recipe or just one ingredient? Anesthesiology 2014; 120:530–532.


