Guidelines

Peri-operative pain management in adults: a multidisciplinary consensus statement from the Association of Anaesthetists and the British Pain Society

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Summary

Background Nearly half of adult patients undergoing surgery experience moderate or severe postoperative pain. Inadequate pain management hampers postoperative recovery and function and may be associated with adverse outcomes. This multidisciplinary consensus statement provides principles that might aid postoperative recovery, and which should be applied throughout the entire peri-operative pathway by healthcare professionals, institutions and patients.

Methods We conducted a directed literature review followed by a four-round modified Delphi process to formulate recommendations for organisations and individuals.
Results We make recommendations for the entire peri-operative period, covering pre-admission; admission; intra-operative; post-anaesthetic care unit; ward; intensive care unit; preparation for discharge; and post-discharge phases of care. We also provide generic principles of peri-operative pain management that clinicians should consider throughout the peri-operative pathway, including: assessing pain to facilitate function; use of multimodal analgesia, including regional anaesthesia; non-pharmacological strategies; safe use of opioids; and use of protocols and training for staff in caring for patients with postoperative pain.
Conclusions We hope that with attention to these principles and their implementation, outcomes for adult patients having surgery might be improved.

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Recommendations

1. Every hospital should have a pain team to help ensure compliance with optimal peri-operative pain management, to educate staff, to write and implement local guidelines, and to ensure appropriate patient information documentation is available.
2. Throughout the peri-operative pathway, pain assessment should be used to guide analgesic management and should rely on measures of function, rather than unidimensional pain scores.
3. Throughout the peri-operative pathway and, where not contraindicated, multimodal analgesia should be encouraged, including paracetamol; non-steroidal anti-inflammatory drugs; α-2 adrenergic agonists; N-methyl-D-aspartate antagonists; corticosteroids; and regional analgesia.
4. Patients should be screened pre-operatively for modifiable risk factors for severe acute pain and chronic postsurgical pain. This includes the use of high doses of opioids; frailty; anxiety; depression; and lifestyle factors (weight, smoking, alcohol and drug use).
5. Pre-operative shared decision-making and expectation management should include a discussion of the risks and benefits of peri-operative pain management strategies, including regional anaesthetic techniques.
6. Analgesia should be multimodal and be of sufficient duration to extend analgesia to the postoperative period.
7. Intra-operative pain management should take a personalised medicine approach and use evidence-based procedure-specific recommendations.
8. When analgesics, including opioids, are used, the lowest effective dose and oral routes should be used when possible, and initial doses should be age-appropriate.
9. Modified-release formulations and compound opioid preparations should not be used routinely for acute postoperative pain.
10. There should be local protocols for the prescription of discharge medicines after surgery, of no greater than 7 days duration, with guidance for patients on how to seek support for any ongoing pain management needs after 7 days.

What other guidelines are available on this topic?

The last comprehensive UK guidance on managing pain after surgery was in 1990 [1]. In contrast, the American Pain

Society published guidance on the management of postoperative pain in 2016 [2] and other US organisations have published guidance on the interventions that need to occur across the peri-operative pathway [3, 4]. The Royal College of Anaesthetists has produced Guidelines for the Provision of Anaesthetic Services (GPAS) for Inpatient Pain Management, and this outlines the standards that a hospital and a pain team should uphold [5]. The procedure-specific postoperative pain management (PROSPECT) group publishes procedure-specific guidance for the management of postoperative pain after specific procedures [6]. They use evidence-based research methodology to develop the best available consensus recommendations in a clinically useful format. However, their guidance mainly focuses on the intra-operative and postoperative stages of that specific procedure. There is also an international consensus statement on the prevention of opioid-related harm in adult surgical patients, UK guidelines for the peri-operative use of opioids [7, 8], and Canadian guidance on the prescription of analgesic medicines at discharge after elective adult surgery [9].

Why were these guidelines developed?

There was a need for contemporary, balanced, patient-centred principles of peri-operative pain management for organisations and clinicians. This consensus statement was developed to produce one unified document that includes recent knowledge and interventions that contribute to the optimal management of peri-operative pain.

How does this statement differ from existing guidelines?

This multidisciplinary consensus statement differs from existing guidelines by using contemporary evidence aiming to facilitate enhanced recovery, effective analgesia and organisational change in multiple domains of peri-operative care.

Introduction

Acute pain occurs following tissue injury associated with surgery. Although preventing and alleviating postoperative pain are prime responsibilities for healthcare professionals, patients continue to experience significant postoperative pain. In a 2016 cross-sectional, observational study of over 15,000 UK patients undergoing surgery, 11% reported severe pain and 37% reported moderate pain in the first 24 postoperative hours [10]. This is underscored by Peri-operative Quality Improvement Programme data showing that postoperative pain is still common [11].

Postsurgical pain is often inappropriately managed using outmoded tools, including the World Health Organization (WHO) analgesic ladder [12]; the administration of opioids according to numerical pain scores; and the discredited `Pain as the 5th vital sign´ (P5VS) campaign [13, 14]. These strategies work on the premise that humanitarian pain relief is the sole goal of postoperative pain management, while in fact there are multiple goals [15] (Fig. 1), including the promotion of recovery.

This consensus statement considers the institutional and analgesic interventions for various stages of the integrated collaborative peri-operative care pathway, is applicable to all healthcare professions in each stage (including after hospital discharge) and aims to aid postoperative recovery for adults. We refer to previous guidelines on reducing the adverse consequences of opioids but do not make recommendations for the management of chronic postsurgical pain. We hope that this consensus statement will improve the quality of care for adult patients having surgery by optimising pain management.

Methods

We aimed to produce a multidisciplinary consensus statement directed by a steering committee and a diverse authorship who were invited based on their clinical and/or academic expertise in the area. Authors included surgeons; anaesthetists; physicians (including pain specialists); clinical psychologists; physiotherapists; pharmacists; nurse specialists (including pain specialists); and patients with lived experience. Recommendations were formulated using a multi-round modified Delphi process. An initial long list of recommendations was produced following directed literature reviews for all relevant phases of patient care throughout the peri-operative pathway, including pre-admission; admission; intra-operative; post-anaesthesia care unit (PACU); ward; intensive care unit; preparation for discharge; and post-discharge. Further recommendations for organisational and generic principles were also formulated. In the first round, these recommendations were distributed among all authors who anonymously rated each as `include´, `exclude´; or `revise´, as well as provided anonymised comments onto a Microsoft Excel spreadsheet (Microsoft Inc., Redmond, WA, USA). Recommendations with ≥ 75% inclusion decisions proceeded unchanged into the second round; those with 50–74% underwent revision; and those with < 50% inclusion decisions were removed from the recommendations. Second and third remote voting rounds proceeded, with anonymised comments and full voting results shared after each round, and the

Figure 1 Goals of postoperative pain management.

same thresholds adhered to. In the third round, authors were also asked to vote on whether each remaining recommendation should be a top 10 recommendation. Following these three remote voting rounds, any recommendation with ≥ 75% agreement for inclusion remained unchanged in the manuscript, and any with 50–74% entered a fourth and final round of a virtual round table for final voting.

Results

The role of the hospital organisation

Achieving the multiple goals of optimal postoperative pain relief requires multidisciplinary input and support. This should include hospital Trust executives and divisional directors; integration between surgical directorates; peri-operative services; waiting list services; anaesthetic departments; in-patient pain team; psychology services; outpatient or specialist pain services; pharmacy; and business intelligence, information technology and administration teams. Traditionally acute pain services have focused on inpatients only. However, the future remit of the inpatient pain team will need to encompass the entire patient journey through pre-operative assessment, peri-operative admission and after discharge. There are benefits for institutions to have an appropriately resourced pain team to coordinate required interventions within integrated pain pathways [16]. Adequately resourced pain teams (in terms of both time and equipment) can: co-ordinate necessary interventions; ensure compliance with optimal peri-operative pain management; educate staff; lead on quality and service improvement; write and implement local guidelines; and ensure appropriate patient information documentation is available throughout the peri-operative pathway.

Implementing the clinical practice recommended in guidelines and consensus statements is both a science and an art, that is crucial to facilitating improvements in both healthcare delivery and improving clinical outcomes. Stakeholders should familiarise themselves with the principles [17, 18], so that patients undergoing surgery may benefit from optimal peri-operative pain management. Moreover, inpatient pain teams, led by named individuals, could play an important role in ensuring the optimal use of electronic health records for monitoring and alerting patients at high risk of peri-operative pain complications. Pain teams should be multidisciplinary, with input from anaesthetists, nurse specialists, and other key stakeholders.

- **Every hospital should have a pain team to help ensure compliance with optimal peri-operative pain management, to educate staff, to write and implement local guidelines, and to ensure appropriate patient information documentation is available.**

General principles of peri-operative pain management

Achieving the objectives of peri-operative pain relief (Fig. 2) requires interventions at the various stages of an integrated collaborative peri-operative care pathway. Many of these interventions and principles are applicable to the whole of the pathway.

It is now recognised that the sole use of the numerical pain score to guide analgesic interventions may lead to harm through overuse of opioids, leading to oversedation and increasing the risks of opioid use disorder [19]. There is uncertainty regarding the comparative efficacy of unidimensional pain assessment tools, and it is increasingly recognised that pain assessment used to guide analgesic management should be based on function [20]. While functional scoring systems exist, for example, the functional activity scale, validation of such scores is scarce within peri-operative populations [21]. For certain groups, such as people living with dementia, there are valid and reliable tools that can be used [22, 23]. Currently, self-reported pain scores remain the mainstay of care, with the numerical rating scale and verbal rating scale examples of commonly used tools. Simple pain scores may be useful in assessing pain trajectories in individual patients, signifying surgical complications, neuropathic pain or psychological distress [20, 24]. However, these scoring systems need to be interpreted according to context, as people use pain scores to communicate a variety of concerns, including to request medicines [25], and they may be influenced by other factors, such as mood, sleep or other medicines [21, 26].

To help achieve optimal pain relief that meets all analgesic goals (Fig. 1), a variety of analgesic interventions should be considered throughout the integrated peri-operative pathway, encompassing multimodal analgesia (including safe opioid use) and non-pharmacological strategies. The principle of multimodal analgesia is that improved pain relief can be achieved by combining analgesics with different mechanisms of action that work synergistically. This may allow lower effective doses of each drug, potentially reducing adverse effects compared with the use of single drugs [27]. A range of drug classes can be used, including paracetamol; non-steroidal anti-inflammatory drugs (NSAIDs); α-2 adrenergic agonists; N-methyl-D-aspartate (NMDA) receptor antagonists; corticosteroids; lidocaine; and regional analgesia (Table 1) [21, 28–30]. Multimodal analgesia also includes non-pharmacological elements, which may be low risk, have potential analgesic benefits and may reduce both the necessary dose and possible adverse effects of drugs used. While robust evidence for the role of some of these interventions is still evolving, examples include peri-operative education [31, 32]; humanistic communication [33, 34]; avoidance of nocebo [35]; mindfulness and meditation [36]; cognitive behavioural therapy [37, 38]; pre-operative [39–41] and postoperative

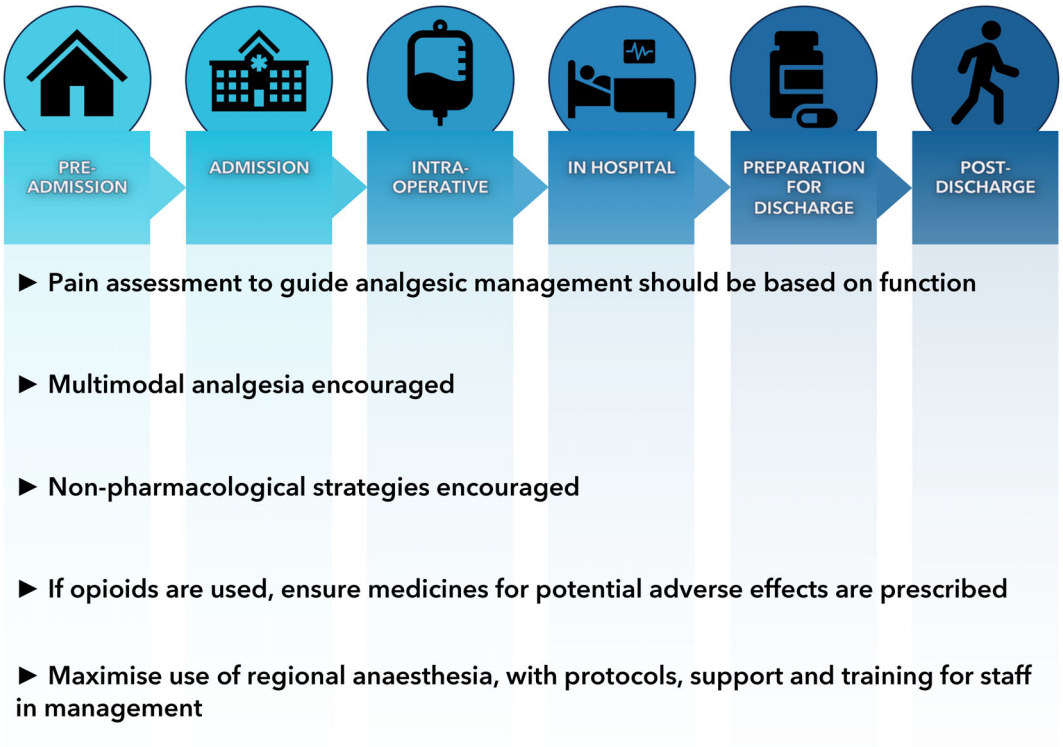

Figure 2 General principles of peri-operative pain management.

physiotherapy, activity and exercise [42–44]; acupuncture [45–47]; and transcutaneous electrical nerve stimulation (TENS) [48] (Table 2).

Opioids continue to have a pivotal role in peri-operative pain management. Despite well-documented analgesic benefits, opioid-related adverse drug events remain common. Principles for reducing the risk and management of opioid-induced ventilatory impairment and persistent postoperative opioid use are described elsewhere [7]. As well as opioid-induced ventilatory impairment and persistent postoperative opioid use, other opioid-related adverse drug events such as constipation and nausea and vomiting are common [49]. Up to 60% of patients receiving opioids for non-cancer pain experience constipation, and 15–40% experience nausea and vomiting, with the odds ratio (95%CI) of nausea and vomiting associated with postoperative opioid use being 1.4 (1.2–1.6) [50]. Given the frequency at which these particular complications occur, co-prescription of laxatives and anti-emetics, for prevention and/or treatment, is imperative. Contemporary data on opioid-induced ventilatory impairment are unclear, but current estimates suggest an incidence of 5% [50]. Given the potential implications of opioid-induced ventilatory impairment, a `rescue´ prescription of naloxone can also be recommended for this group of patients [51].

Regional anaesthesia includes local and regional analgesia and encompasses local infiltration; peripheral nerve blocks; fascial plane blocks; and central neuraxial blockade. We see regional anaesthesia as an integral element of multimodal analgesia, with a range of outcome benefits reported in a multitude of peri-operative settings [52–56]. With the increasing use of regional anaesthesia to facilitate recovery and manage postoperative pain, there is a recognition that safe management requires well-trained staff, as well as institutionally agreed and implemented protocols [57]. These protocols may facilitate the assessment of regional blockade, management of failed blockade and management of complications of regional anaesthesia. Furthermore, staff who care routinely for patients following surgery are often the first to detect complications. Without appropriate training, recognition and initial management of complications, such as local anaesthetic systemic toxicity [58] or persistent neurological injury after peripheral nerve blocks or central neuraxial blockade [59, 60] could be missed, with potentially devastating consequences.

Table 1 Summary of systemic non-opioid analgesics that can be used as part of multimodal analgesia. This does not include adjuncts for regional anaesthesia.

Class of drug and examples	Impact on postoperative pain	Comments
Paracetamol (acetaminophen)	• Effective analgesia • Opioid-sparing • Reduce ORADEs	• Fewer adverse effects than NSAIDs • Oral preparations are preferred as they are equally efficacious as intravenous, less expensive, have a smaller carbon footprint, do not tether patients to the bedside, and thus promote mobilisation
Nonselective NSAIDs, e.g. ibuprofen, diclofenac	• Effective analgesia • Opioid-sparing • Reduce ORADEs	• Use limited by drug interactions, drug-disease interactions and adverse effects • Oral form is preferred. • Synergistic with paracetamol
Selective NSAIDs, e.g. celecoxib and parecoxib	• Effective analgesia • Opioid-sparing • Reduce ORADEs	• Short-term use (< 7 days) of parecoxib does not cause gastritis in older patients • Long-term use associated with gastritis and cardiovascular complications • No impairment of platelet function
Alpha-2 agonists, e.g. clonidine and dexmedetomidine	• Effective analgesia • Opioid-sparing • Reduce ORADEs	• Clonidine does not reduce pain scores but does reduce opioid consumption while dexmedetomidine reduces both pain scores and opioid consumption • Use is limited by sedation and hypotension
NMDA antagonists, e.g. ketamine and magnesium	• Effective analgesia • Opioid-sparing • Reduce ORADEs • Reduce PONV	• Low dose intra-operative intravenous ketamine is not significantly associated with dissociative syndromes • Low dose intravenous and oral ketamine can be used postoperatively for patients with intractable pain • Intra-operative intravenous magnesium can lead to hypotension and there are concerns regarding synergism/addition to neuromuscular blocking drugs increasing residual paralysis • Useful in patients who are opioid tolerant and limiting the acute tolerance/opioid-induced hyperalgesia that is associated with remifentanil use • Ketamine and magnesium are synergistic due to the multiple effect site actions of magnesium
Corticosteroids, e.g. dexamethasone	• Effective analgesia • Reduce ORADEs • Reduce rebound pain after regional anaesthesia	• Increasingly recommended and used for analgesic effect as well as established role of PONV prophylaxis • Minimal effect on blood glucose in patients with well-controlled diabetes or without diabetes
α-2-delta ligands (gabapentinoids), e.g. gabapentin and pregabalin	• Opioid-sparing • Reduce ORADEs • Reduce phantom limb pain • Attenuate opioid-induced hyperalgesia/tolerance in opioid-tolerant patient	• Concerns of sedation, dizziness, postural hypotension and risk of opioid-induced ventilatory impairment • The routine use in gabapentinoid-naïve patients cannot be recommended
Lidocaine	• Effective analgesia • Opioid-sparing	• Evidence only in abdominal surgery • Risk of local anaesthetic toxicity • Use cannot be recommended without organisational support and specific consent from patient

NSAIDs, non-steroidal anti-inflammatory drugs; ORADEs, opioid-related adverse drug events; NMDA, N-methyl-D-aspartate; PONV, postoperative nausea and vomiting.

Table 2 Summary of non-pharmacological interventions that can be used as part of peri-operative multimodal analgesia.

Domain	Intervention	Comments
Psychological	Pre-operative education	Pre-operative procedural and pain management information might improve pain control and shorten recovery time
	Postoperative education	Emerging evidence that postoperative education on analgesic use reduces both pain scores and opioid consumption
	Humanistic patient-centred discussions	Pre-operative empathetic discussions have might reduce postoperative pain, recovery time and duration of stay
	Avoidance of nocebo effect	Avoiding negative suggestions or negatively valenced words resulting in unpleasant or undesirable effects of an intervention. Evidence that nocebo communication may be associated with worse pain scores
	Mindfulness and meditation	Current evidence suggests that it may lead to lower postoperative pain scores and may be opioid sparing
	Cognitive behavioural therapy	Current evidence suggests that it may lead to lower postoperative pain scores and facilitates recovery but does not appear to be opioid sparing
Physical therapy	Pre-operative physiotherapy	Might reduce pain, risk of avoidance behaviour, and improve quality of life and physical activity levels before surgery
	Postoperative physiotherapy, activity and exercise	Effective in promoting recovery from surgery, but robust evidence of impact on pain scores and opioid use is modest
Passively applied physical approaches	Cryotherapy	Some evidence of analgesic efficacy in knee surgery, but not superior to compression in arthroplasty
	Acupuncture and acupressure	Some evidence in specific settings for analgesic benefit
	Transcutaneous electrical nerve stimulation (TENS)	Reduces acute pain compared with no TENS after a range of surgical procedures

- **Throughout the peri-operative pathway, pain assessment should be used to guide analgesic management and be based on function, rather than numerical pain scores.**
- **Throughout the peri-operative pathway, and where not contraindicated, multimodal analgesia should be encouraged, including paracetamol; NSAIDS; α-2 adrenergic agonists; NMDA antagonists; corticosteroids; and regional analgesia.**
- **Throughout the peri-operative pathway non-pharmacological strategies to reduce the risk and severity of postoperative pain should be encouraged.**
- **If opioids are used at any stage of the peri-operative pathway, medicines to manage the adverse effects should also be prescribed, such as laxatives, anti-emetics and naloxone.**
- **Regional anaesthesia should be used wherever possible.**
- **Protocols and support for managing regional anaesthesia should be available throughout the hospital.**
- **Staff should be trained to identify and manage the complications of regional anaesthesia.**

Before admission to hospital

The time between listing for surgery and the operation provides an important opportunity to optimise the patient and reduce postoperative complications such as risk of long-term pain and/or opioid dependence [61]. Prehabilitation includes screening for risk factors for severe acute pain and chronic post-surgical pain [62], and applying the following key non-pharmacological interventions, namely the use of empathic communication skills to improve the patient's knowledge of surgery (procedural instruction) [34]; setting realistic expectations for postoperative pain management; and avoid instilling the nocebo effect. This narrows the possible gap between the patient's expectation of complete pain relief and the true effectiveness of postoperative pain treatment [63] and will include setting the expectation that acute pain can be managed well and will settle after surgery [64]. In addition, pre-operative patient education combined with better patient preparation has been shown to reduce postoperative opioid consumption [32, 65].

Prehabilitation also includes optimisation with exercise and nutrition to improve frailty [66, 67] (specific guidelines for people living with frailty are published elsewhere [68]); psychological interventions to reduce pain `catastrophising´; and to attenuate the stress response to surgery [69, 70]. Patients should be signposted to surgery schools [71] and non-pharmacological self-management techniques to practice as prehabilitation while waiting for surgery. This `self-control´ should include behavioural stress

reduction techniques (e.g. diaphragmatic breathing and relaxation exercises), cognitive strategies to recognise and challenge any catastrophic thinking and motivational techniques for creating hope and empowering self-efficacy.

- **Patients should be screened pre-operatively for modifiable risk factors for severe acute pain and chronic postsurgical pain. This includes the use of high doses of opioids; frailty; anxiety; depression; and lifestyle factors (weight, smoking, alcohol and drug use).**
- **Pre-operative shared decision-making and expectation management should include discussion of the risks and benefits of peri-operative pain management strategies, including regional anaesthetic techniques.**
- **Where possible, patients taking high doses of opioids should be referred for pre-admission opioid tapering.**
- **Patients should be provided with deprescribing advice and realistic expectations of peri-operative pain. All information should be given both orally and in written format as a reminder of the discussion.**
- **Patients at risk of persistent postoperative opioid use, pre-existing chronic pain and high risk of severe postoperative pain should be identified pre-operatively and a multidisciplinary analgesic plan developed between the acute pain service, surgical and anaesthetic teams, and the patient.**

Admission

Admission to hospital for surgery occurs increasingly on the day of surgery. In general, there are likely to be few interventions that can provide meaningful and sustained changes in analgesic outcomes. However, generic principles of peri-operative pain management should be considered for this phase of patient care.

Intra-operative

The aims of intra-operative analgesia are to: reduce the surgical stress response; ensure a patient is comfortable at the end of surgery and on emerging from anaesthesia; and ensure pain relief for the immediate postoperative period and transition to ward-based care. The overall goal is to optimise analgesia to ensure patient comfort that will promote recovery. While pain is a biopsychosocial experience, and management involves using both pharmacological and non-pharmacological strategies, during the intra-operative period, pharmacological management is key.

Intra-operative multimodal analgesia mitigates the surgical stress response [72]; improves postoperative pain and functional outcomes [73]; and reduces postoperative opioid requirements and opioid adverse effects [74, 75]; and reduces complications [27]. Combinations of different drugs need to be chosen accounting for patient characteristics; comorbidities; pre-existing analgesic use; drug interactions; and the surgery being undertaken [76]. This should involve systemic and regional/local analgesia, and during the postoperative phase may include non-pharmacological techniques. There is level 1 evidence to support the effectiveness of paracetamol; NSAIDs; NMDA antagonists (ketamine and magnesium); steroids; and α-2 adrenergic agonists (clonidine and dexmedetomidine) [21]. Intra-operative analgesia primarily based on short-acting agents such as remifentanil may be associated with poor pain outcomes, including opioid-induced hyperalgesia and opioid tolerance [77–79]. Therefore, intra-operative analgesia should be multimodal and extend into the postoperative period. Notably, there is no robust evidence that reducing intra-operative opioid use is associated with a reduction of postoperative opioid administration [80].

Data have shown that acute pain [52]; morbidity [53]; functional [54]; and, in some settings, chronic pain outcomes [55], are improved when regional analgesic techniques are added to multimodal peri-operative analgesic regimens [56]. Although the evidence in properly implemented enhanced recovery after surgery (ERAS) protocols is unclear [81–83], the analgesic and functional gains across a range of surgical procedures has cemented the role of regional anaesthesia in such protocols and other procedure-specific recommendations [84–86]. Recent efforts to enhance the ability and confidence of anaesthetists in performing regional techniques have included the introduction of fascial plane techniques [87]; increased emphasis on regional anaesthesia in the anaesthetic training curriculum [88]; and introduction of the concept of `Plan A Blocks´—involving the selection, training and pathway implementation of a limited number of high-value blocks to increase patient access to regional anaesthesia [89]. Therefore, procedure-specific regional anaesthesia should be considered an essential element of multimodal analgesia where feasible. Importantly, a `one-size-fits-all´ approach to peri-operative pain management is rarely possible. Rather, intra-operative pain management should take a personalised medicine approach utilising evidence-based, procedure-specific recommendations. Of note, rebound pain after single-shot peripheral nerve block is a recognised phenomenon in up

to half of patients [90, 91], which might be mitigated with pre-emptive multimodal analgesia and patient education and expectation management [92, 93].

- **Intra-operative analgesia should be multimodal and extend into the postoperative period.**
- **Procedure-specific regional anaesthesia should be considered an essential element of multimodal analgesia where feasible.**
- **Intra-operative pain management should take a personalised medicine approach utilising evidence-based, procedure-specific recommendations.**

Post-anaesthesia care unit (PACU)

The PACU is designed to provide care for patients recovering from general anaesthesia, sedation, regional anaesthesia or local anaesthesia. The Royal College of Anaesthetists' Guidelines for the Provision of Anaesthesia Services recommend that patients should remain in the PACU until they are stable and unlikely to need immediate support from an anaesthetist [5]. As well as general guidance published elsewhere, analgesia constitutes an important element of care in the PACU. Generic principles of peri-operative pain management elsewhere in this document should be considered for this phase of patient care.

- **Anaesthetic staff must be contactable and available in and out of daytime working hours to support provision of analgesia in the PACU.**

Ward

The aim of ward care before and after surgery is to manage both anticipated and unanticipated postoperative medical or surgical issues, in parallel with promoting rehabilitation and ensuring timely discharge planning. The focus of pain management on wards is to promote comfort and facilitate function while minimising the associated risks of delirium; deconditioning; pain-related distress; resultant medical morbidity (e.g. postoperative pulmonary complications); longer-term opioid dependency; and delayed discharge. Promoting timely mobilisation and optimising pulmonary function requires attending to patients' fear of movement. In addition, patient and staff expectations need to be managed so that there is an appreciation that mobilisation and physiotherapy may not be pain free.

Staff on surgical wards manage postoperative pain and pain-related distress. In these settings, accurately assessing and recording pain with a focus on facilitating function rather than treating a numerical pain score is an important consideration. This will help minimise tethering to medical devices, oversedation and immobility. In addition, an appropriate validated tool may be required in specific circumstances (e.g. in people living with dementia) [22, 23, 94].

As with the generic principles, multimodal analgesia should be prescribed, with simple analgesia including paracetamol and NSAIDs, if suitable. However, if opioid analgesia is required in the acute setting, then immediate-release opioids should be used for rapid and titratable analgesia rather than modified-release or compound formulations. Evidence suggests that analgesic efficacy is inferior, and adverse events and development of persistent postoperative opioid use are more frequent, with modified-release formulations [95]. Thus immediate-release opioids should be used to facilitate function rather than treat pain intensity, as it is functional recovery that is important. Avoiding compound preparations (e.g. opioids mixed with paracetamol) is beneficial as two constituent drugs can have different analgesic profiles and hinder opioid weaning [7]. Where possible, the oral route is preferred, and the lowest effective dose should be given. Sedation score monitoring is advisable in patients receiving opioids to alert the ward staff to early opioid-induced ventilatory impairment [96–98]. In addition, the co-administration of other sedative drugs can increase the risk of opioid-induced ventilatory impairment and should be avoided if possible. If this is unavoidable, the lowest doses possible should be given, for the shortest possible duration, with the patient monitored carefully to detect signs of opioid-induced ventilatory impairment. Where possible, non-pharmacological techniques to reduce opioid demand and minimise distress are important considerations. Finally, following any intervention, pain should be reassessed.

While many patients' postoperative analgesic management onwards may be straightforward, for those patients not following an expected pain trajectory and/or who require advanced analgesic techniques, the involvement of the hospital pain team will be necessary. Furthermore, pain may be a presenting feature of an unexpected complication of surgery, such as nerve injury or compartment syndrome, which may be identified and communicated to surgical teams by hospital pain teams.

- **Immediate-release opioids should be prescribed, to facilitate function rather than treating pain intensity.**
- **Modified-release formulations and compound opioid preparations should not be used routinely for acute postoperative pain.**

- **When analgesics, including opioids, are used, the lowest effective dose and oral routes should be used when possible, and initial doses should be age-appropriate.**
- **The co-administration of sedative medicines should be avoided if possible or, if unavoidable, use the lowest doses possible for the shortest duration and monitor patients carefully for signs of opioid-induced ventilatory impairment.**
- **For patients receiving opioids, ensure sedation is monitored with the vital signs to alert to early opioid-induced ventilatory impairment.**
- **Involve pain teams for patients not following the expected pain trajectory or requiring advanced analgesic techniques.**

Preparation for discharge from hospital

To reduce the risk of opioid-related adverse drug events after discharge, and to facilitate recovery, patients and their carers need guidance on how to use, store and dispose of analgesic medicines within the community. Persistent postoperative opioid use continues to be a concern globally and is associated with worse postoperative health outcomes and increased mortality rates [99–102]. Consequently, UK regulatory guidance now recommends that healthcare professionals inform patients that prolonged use of opioids may lead to drug dependence and addiction, even at therapeutic doses and that, before starting treatment, a plan for ending the opioid treatment is agreed [103]. During preparation for the discharge of patients on opioids, there is an opportunity to educate patients and carers to prevent, recognise and/or manage other opioid-related adverse drug events, such as opioid-induced ventilatory impairment, constipation, nausea, and vomiting. Moreover, patients and carers should be advised of the legal and safety consequences of discharge opioid prescriptions, such as drug driving (driving a motor vehicle while taking opioids) [104], which has been shown to be a risk factor for motor vehicle accidents [105–107]. Patients should also be counselled regarding opioid diversion, and all opioids should be stored securely and disposed of safely when no longer needed [108, 109]. Information should also be provided on the possible adverse effects of non-opioid analgesics prescribed at discharge, such as gastrointestinal and bleeding complications with NSAIDs, and dizziness and somnolence with gabapentinoids.

Patients and their carers also need to be advised on how to use non-pharmacological techniques and when to seek help. Therefore, patient education is a key part of the peri-operative analgesic plan, which has benefits if it is drawn up as a collaboration between the patient, carers and the multidisciplinary team of clinicians. In the elective setting, this could commence when a patient is scheduled for surgery and considered at each stage of the pathway, e.g. at pre-operative assessment (to encompass both physical and medical needs); admission to hospital; and, importantly, re-enforced on discharge. Patient information leaflets, such as that from the British Pain Society [110], can facilitate these concepts and can improve patient understanding of postoperative pain management and opioid stewardship [111].

Plans for discontinuing analgesia are fundamental. The concept of the `reverse pain ladder´ can be useful for reducing and stopping opioids and hence mitigating the risk of persistent postoperative opioid use. Suggesting regular simple analgesia and restricting opioids to `as needed´ use to aid mobilisation [112], is followed next by stopping NSAIDs, and finally stopping the regular paracetamol. Pre-operative analgesics can be weaned off in a controlled manner if the patient has had a pain-relieving procedure e.g. joint arthroplasty. By educating patients on appropriate de-escalation of analgesia, with a particular focus on using it for mobilisation, there may be reduced risks of persistent postoperative opioid use and analgesic dependence.

Complications may occur from the use of nerve blocks, such as persistent neurological injury, or, more frequently, rebound pain. To mitigate the risk and allow early management, patients and their carers should be provided with information on expected trajectories, as well as when and how to seek help.

- **Before prescribing opioids at discharge, discuss with the patient the risks and features of tolerance, dependence and addiction, and agree together a treatment strategy and plan for the end of treatment.**
- **There should be local protocols for the prescription of discharge medicines after surgery, of no greater than 7 days duration, with guidance for patients on how to gain support for any ongoing pain management needs after 7 days.**
- **Patient information should be available, with advice on self-administration, weaning analgesia, disposing of unused analgesic medicines and the dangers of driving/operating machinery while taking opioid medicines. If patients have received regional nerve blocks, specific patient information leaflets for these should be provided.**
- **The discharge summary must explicitly state the recommended opioid, indication, dose and duration.**

After discharge

Following discharge from hospital, ongoing postoperative pain is generally managed in primary care. Repeat prescriptions of opioids are associated with increases in risk of opioid misuse; opioid dependence; abuse; and overdose [113]. Each additional week of opioids taken raising the risk of misuse by 20% [114]. Moreover, there is increasing evidence of an association between the duration of postoperative opioid administration [80] and household opioid diversion, with a substantial proportion of people who have developed opioid addiction commencing this from household opioid diversion [49]. Some patients may have ongoing postoperative pain that limits function, posing challenges to primary care teams to manage. In these settings, referral back to the surgical team may allow re-assessment to exclude complications, and an opportunity to engage pain expertise in subsequent management.

- **Clinicians should avoid issuing repeat prescriptions, and advise patients to avoid drug driving, beware of opioid diversion, and use safe storage and disposal of opioid principles.**
- **If postoperative pain is unmanageable in the community, the primary care team should refer patients back to the surgical care team for review.**

Intensive care unit

There are evidence-based guidelines outlining the management of pain in critical care [115]. Pain assessment and management is advocated as part of the ICU Liberation `ABCDEF bundle´ that supports the ICU inter-professional team to provide high-quality acute care, generating the best outcomes for patients following ICU discharge [116]. Self-reporting of pain remains the standard for assessment in ICU. For patients unable to express pain in words, behavioural pain scales specifically validated for ICU populations are recommended. The Behavioural Pain Scale (BPS) [117] and Critical Care Pain Observation Tool (CPOT) currently have the most evidence of reliability and validity to support their use [118]. Procedural pain is common, particularly due to: turning and repositioning; tracheal suctioning; wound and chest drain removal; and arterial cannulation, and requires pre-emptive analgesia [119]. Opioids are recommended as first-line analgesics in ICU for analgosedation or `analgesia first´ protocols [115]. There is limited evidence to support the superiority of one opioid over another with respect to analgesic efficacy in ICU [120–122]. However, increasingly the evidence highlights the negative consequences of opioid use in ICU patients. These include immunosuppression; gastrointestinal complications [123]; delirium [124]; respiratory depression; withdrawal syndromes [125]; as well as a potential independent risk of persistent opioid use [126–128]. To enable opioid sparing, multi-modal analgesia is advocated, although evidence for specific agents or techniques in the ICU is limited. Two systematic reviews considering dexmedetomidine, clonidine, paracetamol, NSAIDs, gabapentinoids, carbamazepine, ketamine and magnesium, mostly in surgical patients, concluded that any such adjuvant was associated with reduced opioid consumption and a small decrease in pain scores 24 h after admission, compared with opioids alone [129, 130], but were unable to evaluate short (e.g. hypotension) and long term (e.g. delirium) adverse effects. While used commonly, evidence supporting local/regional analgesia in ICU is limited. Epidural analgesia can cause hypotension, although it is usually feasible to give vasopressor support as the patient is in a critical care environment. Due to the severity of illness and associated immunosuppression and coagulopathy commonly encountered by patients in the ICU, the risk of infection and/or bleeding within the vertebral canal associated with indwelling catheters may also be higher.

- **Frequent assessment of pain should be conducted in the critical care setting using pain scales validated for use in the ICU (including the Behavioural Pain Scale and the Critical Care Pain Observation Tool where patients are not able to self-report).**
- **Pain should be considered as a cause of agitation or delirium in patients who are critically ill.**
- **Patients on opioid infusions for ≥ 72 h should be reviewed and monitored for opioid withdrawal.**
- **Pain-generating procedures in ICU should have pre-emptive analgesia administered accordingly.**
- **The lowest possible opioid dose to achieve adequate analgesia should be utilised by performing frequent, validated assessment of pain and opioids adverse effects, in those patients receiving opioid infusions.**

Discussion

Postoperative pain continues to threaten patients' experience, recovery and morbidity, as well as posing societal and institutional burdens. This multidisciplinary consensus statement provides principles for peri-operative pain management to improve patient outcomes after surgery. Interventions and modifications to care throughout the peri-operative pathway can be considered, along with generic principles and institutional policies and procedures. Implementation of these recommendations requires

multidisciplinary engagement, education and practice change from anaesthetists; surgeons; nurses; pain specialists; pharmacists; physiotherapists; psychologists; and hospital managers and administration teams. Hospital organisations, in particular, have an important role in funding, supporting and directing safe peri-operative pain management, including ensuring well-managed pain teams.

There are several areas representing opportunities for future research work. Although postoperative pain assessment is standard practice, it remains unclear which tools to use, particularly given the importance of using analgesia to facilitate function, rather than simply to reduce postoperative pain [28]. The role of physiotherapy in managing postoperative pain continues to evolve. Rebound pain remains a challenge to avoid and manage, and work is required to understand the most effective methods for reducing its risk and consequences.

This consensus statement has limitations. Our methodology did not include a full systematic review with quantitative or qualitative synthesis, nor grading of recommendations, due to the breadth of the topic and expected heterogeneity in evidence. Indeed, many of the recommendations are supported by modest evidence. The recommendations focus on UK practice, but principles are generalisable beyond. Some of the recommendations are aspirational, but most should be considered readily implementable by clinicians. The role of trainees in mitigating peri-operative pain has not been considered. Finally, surgical techniques and management may have a substantial impact on pain outcomes, but, due to the complexity of each type of surgical procedure, we did not make recommendations in this area.

Nearly half of patients having surgery experience moderate or severe postoperative pain. Insufficient pain management hinders postoperative function, may be associated with adverse outcomes and can lead to longer-term problems. This consensus statement provides principles to be applied throughout the entire peri-operative pathway by healthcare professionals, institutions and patients. We hope putting these recommendations into practice will improve outcomes for patients having surgery and the longer-term health of the population in general.

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References

1. Working Party on Pain After Surgery, Spence A. *Commission on the Provision of Surgical Services. Report of the Working Party on Pain after Surgery*. 1990.
2. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee and Administrative Council. *J Pain* 2016; **17**: 131–57. https://doi.org/10.1016/j.jpain.2015.12.008.
3. Mariano ER, Dickerson DM, Szokol JW, et al. Multisociety organizational consensus process to define guiding principles for acute perioperative pain management. *Reg Anesth Pain Med* 2022; **47**: 118–27. https://doi.org/10.1136/rapm-2021-103083.
4. Hyland SJ, Brockhaus KK, Vincent WR, Spence NZ, Lucki MM, Howkins MJ, Cleary RK. Perioperative pain management and opioid stewardship: a practical guide. *Healthcare* 2021; **9**: 333. https://doi.org/10.3390/healthcare9030333.
5. Royal College of Anaesthetists. Guidelines for the Provision of Anaesthetic Services. 2022. https://rcoa.ac.uk/safety-standards-quality/guidance-resources/guidelines-provision-anaesthetic-services (accessed 12/06/2024).
6. Joshi GP, Albrecht E, Van de Velde M, Kehlet H, Lobo DN. PROSPECT methodology for developing procedure-specific pain management recommendations: an update. *Anaesthesia* 2023; **78**: 1386–92. https://doi.org/10.1111/anae.16135.
7. Levy N, Quinlan J, El-Boghdadly K, et al. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. *Anaesthesia* 2021; **76**: 520–36. https://doi.org/10.1111/anae.15262.
8. Srivastava D, Hill S, Carty S, et al. Surgery and opioids: evidence-based expert consensus guidelines on the perioperative use of opioids in the United Kingdom. *Br J Anaesth* 2021; **126**: 1208–16. https://doi.org/10.1016/j.bja.2021.02.030.
9. Clarke HA, Manoo V, Pearsall EA, et al. Consensus statement for the prescription of pain medication at discharge after elective adult surgery. *Can J Pain* 2020; **4**: 67–85. https://doi.org/10.1080/24740527.2020.1724775.
10. Walker EMK, Bell M, Cook TM, Grocott MPW, Moonesinghe SR. Patient reported outcome of adult perioperative anaesthesia in the United Kingdom: a cross-sectional observational study. *Br J Anaesth* 2016; **117**: 758–66. https://doi.org/10.1093/bja/aew381.
11. Armstrong RA, Fayaz A, Manning GLP, Moonesinghe SR, et al. Predicting severe pain after major surgery: a secondary analysis of the Peri-operative Quality Improvement Programme (PQIP) dataset. *Anaesthesia* 2023; **78**: 840–52. https://doi.org/10.1111/anae.15984.
12. Crush J, Levy N, Knaggs RD, Lobo DN. Misappropriation of the 1986 WHO analgesic ladder: the pitfalls of labelling opioids as weak or strong. *Br J Anaesth* 2022; **129**: 137–42. https://doi.org/10.1016/j.bja.2022.03.004.
13. Mularski RA, White-Chu F, Overbay D, Miller L, Asch SM, Ganzini L. Measuring pain as the 5th vital sign does not improve quality of pain management. *J Gen Intern Med* 2006; **21**: 607–12. https://doi.org/10.1111/j.1525-1497.2006.00415.x.

14. The Joint Commission. R3 Report Issue 11: pain assessment and management standards for hospitals. 2017. https://www.jointcommission.org/standards/r3-report/r3-report-issue-11-pain-assessment-and-management-standards-for-hospitals/ (accessed 12/06/2024).
15. Simpson A, Keane E, Levy N. The prescribed opioid crisis as an impetus to improve postoperative pain management. *Anaesthesia* 2023; **78**: 1062–6. https://doi.org/10.1111/anae.16054.
16. Al-Saidi I, Russell A, Dizdarevic A. The acute perioperative pain service: impact, organization, and future directions. *Curr Pain Headache Rep* 2023; **27**: 399–405. https://doi.org/10.1007/s11916-023-01133-2.
17. National Institute for Health and Care Excellence. Principles for putting evidence-based guidance into practice. https://intopractice.nice.org.uk/principles-putting-evidence-based-guidance-into-practice/index.html (accessed 12/06/2024).
18. The Health Foundation. Quality improvement made simple. What everyone should know about health care quality improvement. April 2021. https://www.health.org.uk/publications/quality-improvement-made-simple?gad_source=1&gclid=Cj0KCQjwpZWzBhC0ARIsACvjWRMaLrVyP7ir_BNsThz7hTcFnM_sWNySpH7nKIU7NCIujJJSmar-Nd8aAsFOEALw_wcB (accessed 12/06/2024).
19. Vila H, Smith RA, Augustyniak MJ, et al. The efficacy and safety of pain management before and after implementation of hospital-wide pain management standards: is patient safety compromised by treatment based solely on numerical pain ratings? *Anesth Analg* 2005; **101**: 474–80. https://doi.org/10.1213/01.ANE.0000155970.45321.A8.
20. Baamer RM, Iqbal A, Lobo DN, Knaggs RD, Levy NA, Toh LS. Utility of unidimensional and functional pain assessment tools in adult postoperative patients: a systematic review. *Br J Anaesth* 2022; **128**: 874–88. https://doi.org/10.1016/j.bja.2021.11.032.
21. Schug S, Palmer G, Scott D, et al. *Acute Pain Management: Scientific Evidence* (5th Ed). 2020. https://www.anzca.edu.au/resources/college-publications/acute-pain-management/apmse5.pdf (accessed 12/06/2024).
22. Lichtner V, Dowding D, Esterhuizen P, Closs SJ, Long AF, Corbett A, Briggs M. Pain assessment for people with dementia: a systematic review of systematic reviews of pain assessment tools. *BMC Geriatr* 2014; **14**: 138. https://doi.org/10.1186/1471-2318-14-138.
23. Schofield P. The assessment of pain in older people: UK national guidelines. *Age Ageing* 2018; **47**: i1–i22. https://doi.org/10.1093/ageing/afx192.
24. Mariano ER, El-Boghdadly K, Ilfeld BM. Using postoperative pain trajectories to define the role of regional analgesia in personalised pain medicine. *Anaesthesia* 2021; **76**: 165–9. https://doi.org/10.1111/anae.15067.
25. Bosdet L, Herron K, de Williams AC. The exploration of hospital inpatients' use of the verbal rating scale of pain. *Front Pain Res* 2021; **2**: 723520. https://doi.org/10.3389/fpain.2021.723520.
26. Pogatzki-Zahn EM, Liedgens H, Hummelshoj L, et al. Developing consensus on core outcome domains for assessing effectiveness in perioperative pain management: results of the PROMPT/IMI-PainCare Delphi meeting. *Pain* 2021; **162**: 2717–36. https://doi.org/10.1097/j.pain.0000000000002254.
27. Kehlet H, Dahl J. The value of ``multimodal'' or ``balanced analgesia'' in postoperative pain treatment. *Anesth Analg* 1993; **77**: 1048–56. https://doi.org/10.1213/00000539-199311000-00030 PMID: 8105724.
28. Bova G, Domenichiello A, Letzen JE, et al. Developing consensus on core outcome sets of domains for acute, the transition from acute to chronic, recurrent/episodic, and chronic pain: results of the INTEGRATE-pain Delphi process. *eClinicalMedicine* 2023; **66**: 102340. https://doi.org/10.1016/j.eclinm.2023.102340.
29. Doleman B, Mathiesen O, Sutton AJ, Cooper NJ, Lund JN, Williams JP. Non-opioid analgesics for the prevention of chronic postsurgical pain: a systematic review and network meta-analysis. *Br J Anaesth* 2023; **130**: 719–28. https://doi.org/10.1016/j.bja.2023.02.041.
30. Foo I, Macfarlane AJ, Srivastava D, et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. *Anaesthesia* 2021; **76**: 238–50. https://doi.org/10.1111/anae.15270.
31. Liu S, Genel F, Harris IA, et al. Effectiveness of pharmacological-based interventions, including education and prescribing strategies, to reduce subacute pain after total hip or knee arthroplasty: a systematic review of randomized controlled trials. *Pain Med* 2022; **23**: 1476–88. https://doi.org/10.1093/pm/pnac052.
32. Horn A, Kaneshiro K, Tsui BCH. Preemptive and preventive pain psychoeducation and its potential application as a multimodal perioperative pain control option: a systematic review. *Anesth Analg* 2020; **130**: 559–73. https://doi.org/10.1213/ANE.0000000000004319.
33. Canales C, Strom S, Anderson CT, et al. Humanistic medicine in anaesthesiology: development and assessment of a curriculum in humanism for postgraduate anaesthesiology trainees. *Br J Anaesth* 2019; **123**: 887–97. https://doi.org/10.1016/j.bja.2019.08.021.
34. Ellingsen D-M, Isenburg K, Jung C, et al. Brain-to-brain mechanisms underlying pain empathy and social modulation of pain in the patient-clinician interaction. *Proc Natl Acad Sci USA* 2023; **120**: e2212910120. https://doi.org/10.1073/pnas.2212910120.
35. Arrow K, Burgoyne LL, Cyna AM. Implications of nocebo in anaesthesia care. *Anaesthesia* 2022; **77**: 11–20. https://doi.org/10.1111/anae.15601.
36. Roberts RL, Hanley AW, Garland EL. Mindfulness-based interventions for perioperative pain management and opioid risk reduction following surgery: a stepped care approach. *Am Surg* 2022; **90**: 939–46. https://doi.org/10.1177/00031348221114019.
37. Gorsky K, Black ND, Niazi A, et al. Psychological interventions to reduce postoperative pain and opioid consumption: a narrative review of literature. *Reg Anesth Pain Med* 2021; **46**: 893–903. https://doi.org/10.1136/rapm-2020-102434.
38. Nicholls JL, Azam MA, Burns LC, et al. Psychological treatments for the management of postsurgical pain: a systematic review of randomized controlled trials. *Patient Relat Outcome Meas* 2018; **9**: 49–64. https://doi.org/10.2147/PROM.S121251.
39. Vasileiadis D, Drosos G, Charitoudis G, Dontas I, Vlamis J. Does preoperative physiotherapy improve outcomes in patients undergoing total knee arthroplasty? A systematic review. *Musculoskelet Care* 2022; **20**: 487–502. https://doi.org/10.1002/msc.1616.
40. Lindbäck Y, Tropp H, Enthoven P, Abbott A, Öberg B. PREPARE: presurgery physiotherapy for patients with degenerative lumbar spine disorder: a randomized controlled trial. *Spine J* 2018; **18**: 1347–55. https://doi.org/10.1016/j.spinee.2017.12.009.
41. Domínguez-Navarro F, Igual-Camacho C, Silvestre-Muñoz A, Roig-Casasús S, Blasco JM. Effects of balance and proprioceptive training on total hip and knee replacement rehabilitation: a systematic review and meta-analysis. *Gait Posture* 2018; **62**: 68–74. https://doi.org/10.1016/j.gaitpost.2018.03.003.
42. Reeve J, Stiller K, Nicol K, McPherson KM, Birch P, Gordon IR, Denehy L. A postoperative shoulder exercise program

improves function and decreases pain following open thoracotomy: a randomised trial. *J Physiother* 2010; **56**: 245–52. https://doi.org/10.1016/S1836-9553(10)70007-2.
43. Bogaert L, Thys T, Depreitere B, et al. Rehabilitation to improve outcomes of lumbar fusion surgery: a systematic review with meta-analysis. *Eur Spine J* 2022; **31**: 1525–45. https://doi.org/10.1007/s00586-022-07158-2.
44. Jonsson M, Ahlsson A, Hurtig-Wennlöf A, Vidlund M, Cao Y, Westerdahl E. In-hospital physiotherapy and physical recovery 3 months after lung cancer surgery: a randomized controlled trial. *Integr Cancer Ther* 2019; **18**: 153473541987634. https://doi.org/10.1177/1534735419876346.
45. Usichenko TI, Henkel BJ, Klausenitz C, Hesse T, Pierdant G, Cummings M, Hahnenkamp K. Effectiveness of acupuncture for pain control after cesarean delivery. *JAMA Netw Open* 2022; **5**: e220517. https://doi.org/10.1001/jamanetworkopen.2022.0517.
46. Zhang W, Liu H, Le X, et al. Acupuncture for postoperative pain of lumbar disc herniation: a systematic review and meta-analysis. *Medicine* 2022; **101**: e32016. https://doi.org/10.1097/MD.0000000000032016.
47. Wu M-S, Chen K-H, Chen I-F, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One* 2016; **11**: e0150367. https://doi.org/10.1371/journal.pone.0150367.
48. Johnson MI, Paley CA, Howe TE, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database Syst Rev* 2015; **2015**: CD006142. https://doi.org/10.1002/14651858.CD006142.pub3.
49. Hudgins JD, Porter JJ, Monuteaux MC, Bourgeois FT. Prescription opioid use and misuse among adolescents and young adults in the United States: a national survey study. *PLoS Med* 2019; **16**: e1002922. https://doi.org/10.1371/journal.pmed.1002922.
50. Coyne KS, Margolis MK, Yeomans K, King FR, Chavoshi S, Payne KA, LoCasale RJ. Opioid-induced constipation among patients with chronic noncancer pain in the United States, Canada, Germany, and the United Kingdom: laxative use, response, and symptom burden over time. *Pain Med* 2015; **16**: 1551–65. https://doi.org/10.1111/pme.12724.
51. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain—United States, 2022. *Morb Mortal Wkly Rep Recomm Rep* 2022; **71**: 1–95. https://doi.org/10.15585/mmwr.rr7103a1.
52. Kumar K, Kirksey MA, Duong S, Wu CL. A review of opioid-sparing modalities in perioperative pain management. *Anesth Analg* 2017; **125**: 1749–60. https://doi.org/10.1213/ANE.0000000000002497.
53. Memtsoudis SG, Sun X, Chiu Y-L, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology* 2013; **118**: 1046–58. https://doi.org/10.1097/ALN.0b013e318286061d.
54. Aitken E, Jackson A, Kearns R, Steven M, Kinsella J, Clancy M, Macfarlane A. Effect of regional versus local anaesthesia on outcome after arteriovenous fistula creation: a randomised controlled trial. *Lancet* 2016; **388**: 1067–74. https://doi.org/10.1016/S0140-6736(16)30948-5.
55. Weinstein EJ, Levene JL, Cohen MS, et al. Local anaesthetics and regional anaesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children. *Cochrane Database Syst Rev* 2018; **6**: CD007105. https://doi.org/10.1002/14651858.CD007105.pub4.
56. Hutton M, Brull R, Macfarlane AJR. Regional anaesthesia and outcomes. *BJA Educ* 2018; **18**: 52–6. https://doi.org/10.1016/j.bjae.2017.10.002.
57. Kelly FE, Frerk C, Bailey CR, et al. Implementing human factors in anaesthesia: guidance for clinicians, departments and hospitals. *Anaesthesia* 2023; **78**: 458–78. https://doi.org/10.1111/anae.15941.
58. Macfarlane AJR, Gitman M, Bornstein KJ, El-Boghdadly K, Weinberg G. Updates in our understanding of local anaesthetic systemic toxicity: a narrative review. *Anaesthesia* 2021; **76**: 27–39. https://doi.org/10.1111/anae.15282.
59. Lemke E, Johnston DF, Behrens MB, Seering MS, McConnell BM, Swaran Singh TS, Sondekoppam RV. Neurological injury following peripheral nerve blocks: a narrative review of estimates of risks and the influence of ultrasound guidance. *Reg Anesth Pain Med* 2023; **49**: 122–32. https://doi.org/10.1136/rapm-2023-104855.
60. Cook TM, Counsell D, Wildsmith JAW. Major complications of central neuraxial block: report on the third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth* 2009; **102**: 179–90. https://doi.org/10.1093/bja/aen360.
61. Levy N, Selwyn DA, Lobo DN. Turning `waiting lists´ for elective surgery into `preparation lists´. *Br J Anaesth* 2021; **126**: 1–5. https://doi.org/10.1016/j.bja.2020.08.021.
62. Vasilopoulos T, Wardhan R, Rashidi P, et al. Patient and procedural determinants of postoperative pain trajectories. *Anesthesiology* 2021; **134**: 421–34. https://doi.org/10.1097/ALN.0000000000003681.
63. Aglio LS, Mezzalira E, Mendez-Pino L, et al. Surgical prehabilitation: strategies and psychological intervention to reduce postoperative pain and opioid use. *Anesth Analg* 2022; **134**: 1106–11. https://doi.org/10.1213/ANE.0000000000005963.
64. Villa G, Lanini I, Amass T, et al. Effects of psychological interventions on anxiety and pain in patients undergoing major elective abdominal surgery: a systematic review. *Perioper Med* 2020; **9**: 38. https://doi.org/10.1186/s13741-020-00169-x.
65. Khorfan R, Shallcross ML, Yu B, et al. Preoperative patient education and patient preparedness are associated with less postoperative use of opioids. *Surgery* 2020; **167**: 852–8. https://doi.org/10.1016/j.surg.2020.01.002.
66. Drewniok N, Kiselev J, Daum N, Mörgeli R, Spies C, Schaller SJ. Concepts for exercise therapy in prehabilitation for elderly people with frailty or pre-frailty prior to elective surgery. A scoping review. *J Bodyw Mov Ther* 2023; **36**: 74–82. https://doi.org/10.1016/j.jbmt.2023.05.004.
67. Schaller SJ, Kiselev J, Loidl V, et al. Prehabilitation of elderly frail or pre-frail patients prior to elective surgery (PRAEP-GO): study protocol for a randomized, controlled, outcome assessor-blinded trial. *Trials* 2022; **23**: 468. https://doi.org/10.1186/s13063-022-06401-x.
68. Centre for Perioperative Care, British Geriatrics Society. Guideline for Perioperative Care for People Living with Frailty Undergoing Elective and Emergency Surgery. 2021. https://www.bgs.org.uk/cpocfrailty (accessed 12/06/2024).
69. Lotzke H, Jakobsson M, Brisby H, et al. Use of the PREPARE (PREhabilitation, Physical Activity and exeRcisE) program to improve outcomes after lumbar fusion surgery for severe low back pain: a study protocol of a person-centred randomised controlled trial. *BMC Musculoskelet Disord* 2016; **17**: 349. https://doi.org/10.1186/s12891-016-1203-8.
70. Powell R, Davies A, Rowlinson-Groves K, French DP, Moore J, Merchant Z. Impact of a prehabilitation and recovery programme on emotional well-being in individuals undergoing cancer surgery: a multi-perspective qualitative study. *BMC Cancer* 2023; **23**: 1232. https://doi.org/10.1186/s12885-023-11717-1.
71. Fecher-Jones I, Grimmett C, Carter FJ, Conway DH, Levett DZH, Moore JA. Surgery school—who, what, when, and how: results of a national survey of multidisciplinary teams

delivering group preoperative education. *Perioper Med* 2021; **10**: 20. https://doi.org/10.1186/s13741-021-00188-2.
72. Cusack B, Buggy DJ. Anaesthesia, analgesia, and the surgical stress response. *BJA Educ* 2020; **20**: 321–8. https://doi.org/10.1016/j.bjae.2020.04.006.
73. Geng Z, Bi H, Zhang D, et al. The impact of multimodal analgesia based enhanced recovery protocol on quality of recovery after laparoscopic gynecological surgery: a randomized controlled trial. *BMC Anesthesiol* 2021; **21**: 179. https://doi.org/10.1186/s12871-021-01399-2.
74. Memtsoudis SG, Poeran J, Zubizarreta N, Cozowicz C, Mörwald EE, Mariano ER, Mazumdar M. Association of multimodal pain management strategies with perioperative outcomes and resource utilization: a population-based study. *Anesthesiology* 2018; **128**: 891–902. https://doi.org/10.1097/ALN.0000000000002132.
75. Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Non-opioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. *Br J Anaesth* 2017; **118**: 22–31. https://doi.org/10.1093/bja/aew391.
76. Gritsenko K, Khelemsky Y, Kaye AD, Vadivelu N, Urman RD. Multimodal therapy in perioperative analgesia. *Best Pract Res Clin Anaesthesiol* 2014; **28**: 59–79. https://doi.org/10.1016/j.bpa.2014.03.001.
77. Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia—when is enough too much? A review of opioid-induced tolerance and hyperalgesia. *Lancet* 2019; **393**: 1558–68. https://doi.org/10.1016/S0140-6736(19)30430-1.
78. Kim SH, Stoicea N, Soghomonyan S, Bergese SD. Remifentanil—acute opioid tolerance and opioid-induced hyperalgesia. *Am J Ther* 2015; **22**: e62–74. https://doi.org/10.1097/MJT.0000000000000019.
79. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. *Br J Anaesth* 2014; **112**: 991–1004. https://doi.org/10.1093/bja/aeu137.
80. Santa Cruz Mercado LA, Liu R, Bharadwaj KM, et al. Association of intraoperative opioid administration with postoperative pain and opioid use. *JAMA Surg* 2023; **158**: 854–64. https://doi.org/10.1001/jamasurg.2023.2009.
81. El-Boghdadly K, Jack JM, Heaney A, et al. Role of regional anesthesia and analgesia in enhanced recovery after colorectal surgery: a systematic review of randomized controlled trials. *Reg Anesth Pain Med* 2022; **47**: 282–92. https://doi.org/10.1136/rapm-2021-103256.
82. McIsaac DI, Cole ET, McCartney CJL. Impact of including regional anaesthesia in enhanced recovery protocols: a scoping review. *Br J Anaesth* 2015; **115**: ii46–56. https://doi.org/10.1093/bja/aev376.
83. Ibrahim M, Elnabtity AM, Hegab A, Alnujaidi OA, El Sanea O. Combined opioid free and loco-regional anaesthesia enhances the quality of recovery in sleeve gastrectomy done under ERAS protocol: a randomized controlled trial. *BMC Anesthesiol* 2022; **22**: 29. https://doi.org/10.1186/s12871-021-01561-w.
84. Feray S, Lubach J, Joshi GP, Bonnet F, van de Velde M, the PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy. PROSPECT guidelines for video-assisted thoracoscopic surgery: a systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia* 2022; **77**: 311–25. https://doi.org/10.1111/anae.15609.
85. Beverly A, Kaye AD, Ljungqvist O, Urman RD. Essential elements of multimodal analgesia in enhanced recovery after surgery (ERAS) guidelines. *Anesthesiol Clin* 2017; **35**: e115–43. https://doi.org/10.1016/j.anclin.2017.01.018.
86. Roofthooft E, Joshi GP, Rawal N, van de Velde M, the PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy and supported by the Obstetric Anaesthetists' Association. PROSPECT guideline for elective caesarean section: updated systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia* 2021; **76**: 665–80. https://doi.org/10.1111/anae.15339.
87. Chin KJ, Mariano ER, El-Boghdadly K. Advancing towards the next frontier in regional anaesthesia. *Anaesthesia* 2021; **76**: 3–7. https://doi.org/10.1111/anae.15321.
88. Royal College of Anaesthetists. Curriculum for a CCT in Anaesthetics 2023. 2021. https://www.rcoa.ac.uk/documents/2021-curriculum-cct-anaesthetics/introduction (accessed 30/03/2023).
89. Turbitt LR, Mariano ER, El-Boghdadly K. Future directions in regional anaesthesia: not just for the cognoscenti. *Anaesthesia* 2020; **75**: 293–7. https://doi.org/10.1111/anae.14768.
90. Barry GS, Bailey JG, Sardinha J, Brousseau P, Uppal V. Factors associated with rebound pain after peripheral nerve block for ambulatory surgery. *Br J Anaesth* 2021; **126**: 862–71. https://doi.org/10.1016/j.bja.2020.10.035.
91. Hade AD, Okano S, Pelecanos A, Chin A. Factors associated with low levels of patient satisfaction following peripheral nerve block. *Anaesth Intensive Care* 2021; **49**: 125–32. https://doi.org/10.1177/0310057X20972404.
92. Muñoz-Leyva F, Cubillos J, Chin KJ. Managing rebound pain after regional anesthesia. *Korean J Anesthesiol* 2020; **73**: 372–83. https://doi.org/10.4097/kja.20436.
93. Jlala HA, French JL, Foxall GL, Hardman JG, Bedforth NM. Effect of preoperative multimedia information on perioperative anxiety in patients undergoing procedures under regional anaesthesia. *Br J Anaesth* 2010; **104**: 369–74. https://doi.org/10.1093/bja/aeq002.
94. Georgiou E, Hadjibalassi M, Lambrinou E, Andreou P, Papathanassoglou EDE. The impact of pain assessment on critically ill patients' outcomes: a systematic review. *Biomed Res Int* 2015; **2015**: 1–18. https://doi.org/10.1155/2015/503830.
95. Liu S, Athar A, Quach D, et al. Risks and benefits of oral modified-release compared with oral immediate-release opioid use after surgery: a systematic review and meta-analysis. *Anaesthesia* 2023; **78**: 1225–36. https://doi.org/10.1111/anae.16085.
96. Overdyk F, Dahan A, Roozekrans M, der Schrier R, Van AL, Niesters M. Opioid-induced respiratory depression in the acute care setting: a compendium of case reports. *Pain Management* 2014; **4**: 317–25. https://doi.org/10.2217/pmt.14.19.
97. Gupta K, Prasad A, Nagappa M, Wong J, Abrahamyan L, Chung FF. Risk factors for opioid-induced respiratory depression and failure to rescue. *Curr Opin Anaesthesiol* 2018; **31**: 110–9. https://doi.org/10.1097/ACO.0000000000000541.
98. Lee LA, Caplan RA, Stephens LS, Posner KL, Terman GW, Voepel-Lewis T, Domino KB. Postoperative opioid-induced respiratory depression. *Anesthesiology* 2015; **122**: 659–65. https://doi.org/10.1097/ALN.0000000000000564.
99. Santosa KB, Priest CR, Oliver JD, Kenney B, Bicket MC, Brummett CM, Waljee JF. Long-term health outcomes of new persistent opioid use after surgery among medicare beneficiaries. *Ann Surg* 2023; **278**: e491–5. https://doi.org/10.1097/SLA.0000000000005752.
100. Sitter T, Forget P. Persistent postoperative opioid use in Europe. *Eur J Anaesthesiol* 2021; **38**: 505–11. https://doi.org/10.1097/EJA.0000000000001346.
101. Adams TJ, Aljohani DM, Forget P. Perioperative opioids: a narrative review contextualising new avenues to improve

prescribing. *Br J Anaesth* 2023; **130**: 709–18. https://doi.org/10.1016/j.bja.2023.02.037.
102. Liu S, Stevens JA, Collins AE, et al. Prevalence and predictors of long-term opioid use following orthopaedic surgery in an Australian setting: a multicentre, prospective cohort study. *Anaesth Intensive Care* 2023; **51**: 321–30. https://doi.org/10.1177/0310057X231172790.
103. Medicines and Healthcare products Regulatory. *Drug Safety Update*, Volume 14, Issue 2. September 2020. 2020. https://assets.publishing.service.gov.uk/media/5f6b4dda8fa8f55f35107768/Sept-2020-DSU-PDF.pdf (accessed 12/06/2024).
104. Faculty of Pain Medicine. Taking opioids for pain. 2016. https://www.fpm.ac.uk/opioids-aware-information-patients/taking-opioids-pain (accessed 12/06/2024).
105. Wickens CM, Mann RE, Brands B, et al. Driving under the influence of prescription opioids: self-reported prevalence and association with collision risk in a large Canadian jurisdiction. *Accid Anal Prev* 2018; **121**: 14–9. https://doi.org/10.1016/j.aap.2018.08.026.
106. Monárrez-Espino J, Laflamme L, Rausch C, Elling B, Möller J. New opioid analgesic use and the risk of injurious single-vehicle crashes in drivers aged 50–80 years: a population-based matched case–control study. *Age Ageing* 2016; **45**: 628–34. https://doi.org/10.1093/ageing/afw115.
107. Rudisill TM, Zhu M, Kelley GA, Pilkerton C, Rudisill BR. Medication use and the risk of motor vehicle collisions among licensed drivers: a systematic review. *Accid Anal Prev* 2016; **96**: 255–70. https://doi.org/10.1016/j.aap.2016.08.001.
108. Neuman MD, Bateman BT, Wunsch H. Inappropriate opioid prescription after surgery. *Lancet* 2019; **393**: 1547–57. https://doi.org/10.1016/S0140-6736(19)30428-3.
109. Lee BH, Wu CL. Educating patients regarding pain management and safe opioid use after surgery: a narrative review. *Anesth Analg* 2020; **130**: 574–81. https://doi.org/10.1213/ANE.0000000000004436.
110. British Pain Society. Managing your pain after surgery. 2022. https://www.britishpainsociety.org/static/uploads/resources/files/pain_management_print-ready_atwork_2.pdf (accessed 12/06/2024).
111. Rose P, Sakai J, Argue R, Froehlich K, Tang R. Opioid information pamphlet increases postoperative opioid disposal rates: a before versus after quality improvement study. *Can J Anesth* 2016; **63**: 31–7. https://doi.org/10.1007/s12630-015-0502-0.
112. Huxtable CA, Roberts LJ, Somogyi AA, Macintyre PE. Acute pain management in opioid-tolerant patients: a growing challenge. *Anaesth Intensive Care* 2011; **39**: 804–23. https://doi.org/10.1177/0310057X1103900505.
113. Young JC, Dasgupta N, Chidgey BA, Stürmer T, Pate V, Hudgens M, Jonsson Funk M. Impacts of initial prescription length and prescribing limits on risk of prolonged postsurgical opioid use. *Med Care* 2022; **60**: 75–82. https://doi.org/10.1097/MLR.0000000000001663.
114. Brat GA, Agniel D, Beam A, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study. *Br Med J* 2018; **360**: j5790. https://doi.org/10.1136/bmj.j5790.
115. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med* 2018; **46**: e825–73. https://doi.org/10.1097/CCM.0000000000003299.
116. Pun BT, Balas MC, Barnes-Daly MA, et al. Caring for critically ill patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. *Crit Care Med* 2019; **47**: 3–14. https://doi.org/10.1097/CCM.0000000000003482.
117. Payen JF, Bru O, Bosson JL, et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. *Crit Care Med* 2001; **29**: 2258–63. https://doi.org/10.1097/00003246-200112000-00004.
118. Gélinas C, Johnston C. Pain assessment in the critically ill ventilated adult: validation of the critical-care pain observation tool and physiologic indicators. *Clin J Pain* 2007; **23**: 497–505. https://doi.org/10.1097/AJP.0b013e31806a23fb.
119. Puntillo KA, Max A, Timsit J-F, et al. Determinants of procedural pain intensity in the intensive care unit. The Europain® Study. *Am J Respir Crit Care Med* 2014; **189**: 39–47. https://doi.org/10.1164/rccm.201306-1174OC.
120. Casamento AJ, Serpa Neto A, Young M, et al. A phase II cluster-crossover randomized trial of fentanyl versus morphine for analgosedation in mechanically ventilated patients. *Am J Respir Crit Care Med* 2021; **204**: 1286–94. https://doi.org/10.1164/rccm.202106-1515OC.
121. Hu A-M, Shan Z-M, Zhang Z-J, Li H-P. Comparative efficacy of fentanyl and morphine in patients with or at risk for acute respiratory distress syndrome: a propensity score-matched cohort study. *Drugs R&D* 2021; **21**: 149–55. https://doi.org/10.1007/s40268-021-00338-3.
122. Wang W, He Q, Wang M, et al. Associations of fentanyl, sufentanil, and remifentanil with length of stay and mortality among mechanically ventilated patients: a registry-based cohort study. *Front Pharmacol* 2022; **13**: 13. https://doi.org/10.3389/fphar.2022.858531.
123. Yan Y, Chen Y, Zhang X. The effect of opioids on gastrointestinal function in the ICU. *Crit Care* 2021; **25**: 370. https://doi.org/10.1186/s13054-021-03793-1.
124. Duprey MS, Dijkstra-Kersten SMA, Zaal IJ, et al. Opioid use increases the risk of delirium in critically ill adults independently of pain. *Am J Respir Crit Care Med* 2021; **204**: 566–72. https://doi.org/10.1164/rccm.202010-3794OC.
125. Duceppe M-A, Perreault MM, Frenette AJ, et al. Frequency, risk factors and symptomatology of iatrogenic withdrawal from opioids and benzodiazepines in critically ill neonates, children and adults: a systematic review of clinical studies. *J Clin Pharm Ther* 2019; **44**: 148–56. https://doi.org/10.1111/jcpt.12787.
126. Tollinche LE, Seier KP, Yang G, et al. Discharge prescribing of enteral opioids in opioid naïve patients following non-surgical intensive care: a retrospective cohort study. *J Crit Care* 2022; **68**: 16–21. https://doi.org/10.1016/j.jcrc.2021.10.021.
127. Karamchandani K, Pyati S, Bryan W, Pepin M, Lehman EB, Krishnamoorthy V, Raghunathan K. New persistent opioid use after postoperative intensive care in US veterans. *JAMA Surg* 2019; **154**: 778–80. https://doi.org/10.1001/jamasurg.2019.0899.
128. von Oelreich E, Eriksson M, Sjölund K-F, Discacciati A, Larsson E, Oldner A. Opioid use after intensive care: a nationwide cohort study. *Crit Care Med* 2021; **49**: 462–71. https://doi.org/10.1097/CCM.0000000000004896.
129. Zhao H, Yang S, Wang H, Zhang H, An Y. Non-opioid analgesics as adjuvants to opioid for pain management in adult patients in the ICU: a systematic review and meta-analysis. *J Crit Care* 2019; **54**: 136–44. https://doi.org/10.1016/j.jcrc.2019.08.022.
130. Wheeler KE, Grilli R, Centofanti JE, et al. Adjuvant analgesic use in the critically ill: a systematic review and meta-analysis. *Critical Care Explor* 2020; **2**: e0157. https://doi.org/10.1097/CCE.0000000000000157.