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European Interdisciplinary Guidelines on Pain Management in Acute Pancreatitis: UEG, EPC, EDS, ESDO, EAGEN, ESPGHAN, ESGAR, and ESPCG Evidence-Based Recommendations

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ABSTRACT

Pain is often the presenting symptom of acute pancreatitis (AP) and has a prognostic significance, with poorly treated pain affecting patient outcomes. Despite this, there are currently no international recommendations for pain management in patients admitted with AP. This current guideline was developed following the United European Gastroenterology framework for the development of high-quality clinical guidelines. Nine working groups were formed to develop statements on pain management in AP from admission to discharge. After systematic literature reviews, the evidence was evaluated according to the Grading of Recommendations Assessment, Development, and Evaluation methodology, as appropriate. Statements and comments were developed by the working groups and voted using three rounds of Delphi method. The guidelines concluded that acute post-operative pain management guidelines are applicable for treating acute pain due to AP. The numerical rating scale is preferred for pain assessment because of better compliance. Opioids currently form the cornerstone of severe pain management. Potent opioids such as buprenorphine and pentazocine provide superior pain relief over non-opioid medications and decrease the need for rescue analgesia. Current evidence does not consistently demonstrate harm from opioids in AP. In patients with severe pain, safety concerns should not delay the timely use of opioids to ensure adequate pain management. Specific recommendations concerning the use of epidural analgesia, acupuncture and management of pain in the paediatric population and during pregnancy are provided based on evidence and expert opinions. Finally, the unmet needs for future research were discussed and proposed.

The complete details of the authors of European Pain in Acute Pancreatitis Multidisciplinary Group are provided in the Supporting Information S3.

Key Summary

- Summarize the established knowledge on this subject
  - Pain is the cardinal symptom of acute pancreatitis (AP) and has prognostic significance; however, until now, no international, interdisciplinary guidelines for its management have existed.
  - Clinical practice has been highly variable, often extrapolating from general acute pain management principles due to a lack of high-quality AP-specific evidence.
  - Opioids have been widely used for severe pain, but concerns about potential adverse effects on the sphincter of Oddi motility and disease severity have led to uncertainty and hesitation in their use.
  - The pathophysiology of AP pain is complex, involving nociceptive and neuropathic components, but a comprehensive understanding has been limited by a lack of human tissue studies.
- What are the significant and/or new findings of this study
  - These are the first international, multidisciplinary guidelines to provide structured, evidence-based recommendations for pain management in AP across the entire patient journey, from admission to discharge.
  - Strong opioids (e.g., buprenorphine, pentazocine) provide superior pain relief for severe AP pain compared to non-opioids, and current evidence does not consistently demonstrate harm; safety concerns should not delay their timely use to ensure adequate analgesia.
  - For the first time, specific recommendations are provided for epidural analgesia (noting its safety and efficacy profile in severe AP), complementary treatments (acupuncture and Chinese herbal medicine), and pain management in paediatric populations and during pregnancy.
  - The guidelines formally conclude that recommendations from acute postoperative pain management may be applicable to AP when specific evidence is lacking, and they identify critical unmet needs—such as the development of an AP-specific pain assessment tool and the need for high-quality RCTs on opioid safety and non-pharmacological interventions—to direct future research.

1 | Introduction

Acute pancreatitis (AP) is a common cause of emergency hospital admission worldwide, with increasing incidence [1]. Pain is often the presenting symptom and has prognostic significance [2], and specific features of pain, such as duration and severity, have been associated with severe AP [3]. Recent meta-analyses suggest that randomised controlled trials investigating pain in AP often have methodological and sample size limitations. This makes interpretation of data difficult and implementation of evidence into routine clinical practice challenging [4].

As optimal pain management is mandatory to avoid suffering and facilitate mobilisation and food intake, guidelines as to how to approach pain in AP are needed. However, there are currently no international recommendations on pain management in AP. Several AP guidelines in the last 10 years did not recommend pain management in AP [5–10](Figure 1). There are no recommendations for pain management in AP in the paediatric population. In the absence of specific guidelines, pain management in AP is often extrapolated from general management of pain from abdominal emergencies using the WHO analgesic ladder. Recent evidence suggests that there is variability in pain management in AP [11] with substantial intercontinental differences in opioid use for pain in AP. There is increased use of traditional Chinese medicine and acupuncture in China for managing pain in AP.

Therefore, the current guideline represents a concerted effort to develop interdisciplinary recommendations specific to pain management in AP to make the guidelines inclusive of regional differences in pain management.

2 | Methods

The guideline development adhered to the UEG framework for the development of high-quality clinical guidelines, as proposed by the UEG Quality of Care Taskforce [12].

2.1 | Scope and Purpose

The primary objective was to cover all aspects of pain management in AP from assessment and treatment of pain, with particular emphasis on paediatric pain management and during pregnancy, and to provide practical guidance on pain management at the time of discharge.

2.2 | Steering Committee and Supporting Societies

An initial steering committee was formed based on expertise in AP management. On behalf of the European Pancreatic Club (EPC), four EPC members constituted the Steering Committee responsible for the design of the guideline protocol and the UEG application. Two methodologists were included in the steering committee.

The European Digestive Surgery (EDS), the European Society of Digestive Oncology (ESDO), the European Association for Gastroenterology Endoscopy & Nutrition (EAGEN), the European Society for Paediatric Gastroenterology, the Hepatology and Nutrition (ESPGHAN), the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), and the European Society of Primary Care Gastroenterology (ESPCG) endorsed the UEG guideline grant application. A patient organisation (GUTS Charities, UK) endorsed the project. GUTS charities have a patient group with lived experience of acute pancreatitis and patients were asked to review the statements once finalised in addition to the final manuscript prior to submission. Their comments and opinions were considered in the manuscript. The UEG provided endorsement and financial support with a grant for the project.

The steering committee agreed on the scope of guidelines, which led to the development of working groups.

2.3 | Working Groups

Working groups (WGs) were formed with a lead as the chair for individual WGs. The steering committee and the WG leads invited experts based on their previous publications on that topic and the expertise they brought from other subspecialities, such as pediatrics, acute pain management, and anesthesia. All working group members signed the COI forms and were updated every 6 months. The first WG meeting was held during the UEG week, Copenhagen, Denmark (October 2023), where the WGs were finalized, and a lead responsible for each group was appointed (Table 1).

2.4 | Formulation of Search Questions and Literature Search

Questions included the Population, Intervention, Comparison, and Outcome (PICO) format [12], and were formulated by the WG lead in conjunction with the WG members for each group. The PICOs were proposed by the chapter leads and discussed at two consecutive meetings (EPC Santiago de Compostela, Spain (2024), and at the UEG meeting in Copenhagen (2023) by all members and were rated during the meetings on whether to include them in the final list of statements. The PICOs were further shared with the GUTS Charities UK patient group. Additional PICOs recommended by the patient group without evidence in the literature were included in a section on unmet needs in pain management in acute pancreatitis.

Literature search was then undertaken until June 2025. The search strategy and PRISMA flow charts for each chapter are summarised in supplement 1.

2.5 | Grading Quality of Evidence, and Definition of Statements and Comments

Statements for each WG were formatted using the PICO format where applicable [13]. We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [14] to appraise the quality of evidence. Where the body of evidence to support a statement was indirect, and other criteria for their development were fulfilled in a consensus within the working groups, good practice statements were considered in place of GRADE [15]. These good practice advice statements were drawn from a review of the published literature and from the consensus of expert opinion of all working groups through the Delphi process The WGs were supported by the expert methodologists throughout the process.

2.6 | Consensus Process

A dedicated Delphi consensus platform was used for all WG members to vote on [12]. An agreement of 80% or higher was deemed to be indicative of consensus based on UEG guideline recommendations. Statements with < 80% agreement were

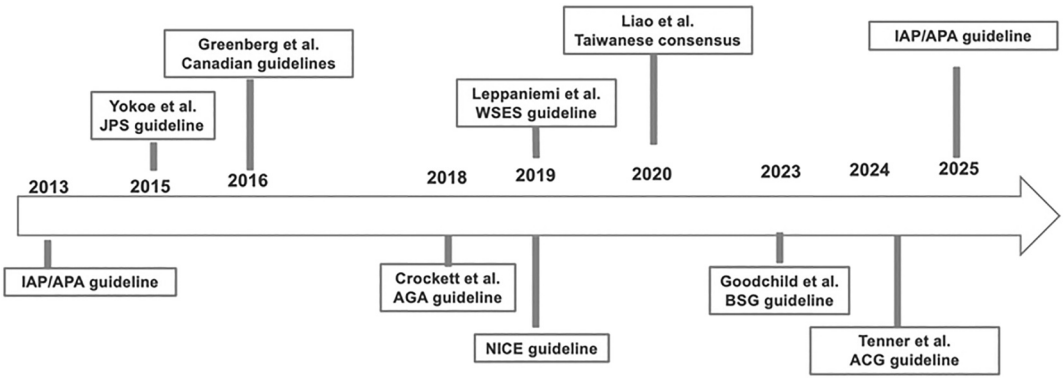

FIGURE 1 | Acute pancreatitis management guidelines timeline. ACG: American College of gastroenterology; APA: American Pancreas Association; BSG: British Society of Gastroenterology; IAP: International association of pancreatology; JPS: Japanese Pancreas Society; NICE: National Institute of Clinical Excellence; WSES: World Society of Emergency Surgery.

TABLE 1 | Overview of chapters.

	Chapter title	Chapter lead	Collaborators	Statements
Chapter 1	Acute pain management in general	Esther Pogastzi-Zahn	5	2
Chapter 2	Pathophysiology of pain in AP	Patrice Forget	6	1
Chapter 3	Assessment of pain in AP	Louise Kuhlmann	4	4
Chapter 4	Treatment of pain in AP	Cecilie Siggaard Knoph	7	6
Chapter 5	Role of epidural analgesia in AP	Karina Cárdenas-Jaén	7	4
Chapter 6	Role of complimentary treatment including acupuncture	Wei Huang	5	2
Chapter 7	Impact of lack of treatment of pain in AP	Asbjorn Mohr Drewes	6	8
Chapter 8	Paediatric AP pain management and during pregnancy	Isabelle Scheers	7	3
Chapter 9	AP pain management at discharge	Sara Regner	5	8

Note: Chair: Sanjay Pandanaboya Co-Chair: Asbjorn Mohr Drewes.

returned to the WG for revision of the statement and supporting text. The degree of consensus was indicated alongside the level of evidence for each of the statements included in the guideline. The final statements and evidence were presented at the EPC in Düsseldorf (June 2025). All statements except the chapter on Traditional Chinese Medicine and Acupuncture (Chapter 6) achieved consensus after the first round of Delphi. Chapter 6 warranted three rounds of Delphi before a consensus (> 80%) was achieved. No statements were abandoned during the Delphi process. The first draft of the manuscript was prepared and distributed to the WG leads and methodologists for their comments. The final version of the guidelines was then sent to independent expert pancreatologists representing the Indian Pancreas Club, Hungarian Pancreatitis Study Group and the American Pancreas Association. A final round of amendments was then made.

3 | Chapter 1: Acute Pain Management in General

3.1 | Question 1.1

In patients with acute pancreatitis, can treatment guidelines of acute pain in general, as compared with pancreatitis-specific treatment regiments, be used to optimise acute pain outcome?

3.1.1 | Good Practice Statement 1.1

Recommendations from non-specific (non-AP) guidelines related to acute pain, for example, acute postoperative pain, may be applicable for treating acute pain from AP, as AP guidelines are unavailable.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 97.3%

3.1.2 | Comment

There are no studies investigating the efficacy of pain management recommended by AP guidelines compared with acute pain guidelines. Systematic reviews on acute pain in AP recommendations are similar in recommending NSAIDs ($n = 15$) [4, 16–30] and opioids as analgesics of choice ($n = 24$) [4, 16, 17, 19, 22, 24, 25, 27–29, 31–44] and recommending epidural analgesia in patients with severe pain ($n = 15$) [4, 22–25, 31, 34, 37, 38, 41–43, 45–47]. Similar recommendations have been made for acute postoperative pain in postoperative pain guidelines ($n = 4$) [48–51], of which most suggest using oral opioids if possible [48, 51]. Given that there are no specific guidelines for AP pain, recommendations that were made for acute postoperative pain may at least be considered for their suitability for managing pain after AP.

In the future, aspects such as providing education to patients with information on pain treatment options, assessing history of chronic pain, substance use disorder, and psycho-social relevant aspects for acute pain management [48, 51] should be explicitly assessed for pain related to AP.

3.2 | Question 1.2

In patients with acute pancreatitis, can escalation of treatment intensity using the same guidelines as for acute pain in general, as compared with specific pancreatitis management recommendations, be used to optimise acute pain outcome?

3.2.1 | Good Practice Statement 1.2

Escalation of treatment intensity for AP-related pain may be performed similarly to that used in other acute pain situations, for example, acute postoperative pain, if no contraindications are applicable.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 94.7%

3.2.2 | Comment

The current guidelines for acute postoperative pain recommend escalating the therapy if pain increases in intensity, with a clear recommendation for using opioids if non-opioid analgesics are not successful in treating pain [20, 25, 27, 29, 43, 52–54]. This recommendation in the AP literature is in close agreement. These explicitly provide recommendations for non-opioid analgesics to be used first line, and opioids should be added if required [48–51]. One guideline for AP emphasises the involvement of an acute pain service in patients with severe pain [54]. Although this is not based on evidence and no other AP guideline recommends this, acute pain services or similar consultations by pain specialists are recommended for acute postoperative pain as well [48, 49, 51].

Given the multidisciplinary nature of acute pancreatitis care, often involving gastroenterologists, surgeons, and intensivists, pain specialists can be integrated into the multidisciplinary care framework. Finally, one AP guideline [25] recommends the use of gabapentin and pregabalin to reduce opioid doses and mentions other adjuvants like magnesium, and ketamine. Acute postsurgical pain guidelines give more substantial recommendations for ketamine use [48–51] and are effective in reducing opioid consumption. In the future, aspects such as providing education to patients with information on pain treatment options, assessing history of chronic pain, substance use disorder, and psycho-social relevant aspects for acute pain management [48, 51] should be explicitly assessed for pain related to AP. Further research is needed to clarify strategies for escalating treatment intensity in AP. In clinical practice, treatment escalation in AP should be discussed with acute pain services and pain specialists when available.

4 | Chapter 2: Pathophysiology of Pain in Acute Pancreatitis

4.1 | Question 2.1

In adults with acute pancreatitis, what is the pathophysiology of acute pain, according to the International Association for the

Study of Pain classification of pain mechanisms (i.e., nociceptive, neuropathic, nociplastic, mixed pain)?

4.1.1 | *Good Practice Statement 2.1*

In adults with acute pancreatitis, the pathophysiology of acute pain, according to the International Association for the Study of Pain (IASP) classification of pain mechanisms, can involve nociceptive and neuropathic pain components, potentially inducing a degree of central sensitization. Pain pathophysiology is probably mixed (nociceptive and neuropathic) in many cases.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 92%

4.1.2 | *Comment*

We found indirect evidence of three potential pain mechanisms in AP: Nociceptive, neuropathic, and nociplastic. The overactivation of different pathways, and in particular the NF-κB pathway, can result in over-stimulated nociceptors and cause inflammation at both cellular and systemic levels [55, 56]. This inflammation can induce primary hyperalgesia, which can be described, in this context, as visceral hypersensitivity and is a potential factor adding to pain in AP [57].

Evidence on the damage of the central and peripheral nervous systems has been found, with an upregulation of voltage-gated ion channels, vanilloid receptors and transmembrane proteins, and neurogenic inflammation [58–60].

Secondary hyperalgesia can also occur, involving, at the periphery, the celiac plexus, and, centrally, the spinal cord, the spinothalamic tract to the thalamus, the spinoreticulothalamic pathway and the somatosensory cortex [55, 61, 62]. While neuropathic pain is difficult to confirm, the existence of neurogenic inflammation has been confirmed, as well as central sensitization [55, 63]. Nociceptive pain via an inflammatory response and neuropathic pain as a consequence of nerve damage can co-occur [64, 65].

Nociplastic pain refers to pain that arises from altered nociception. It is typically proposed in the absence of evidence of tissue damage, or disease or lesion of the somatosensory system, causing the pain. However, it is recognised that patients can have a combination of nociceptive and nociplastic pain (https://www.iasp-pain.org/resources/terminology/). In AP, we have not found direct evidence of nociplastic pain, while this has been well evidenced in chronic pancreatitis pain.

5 | Chapter 3: Assessment of Pain in Acute Pancreatitis

5.1 | Question 3.1

In patients presenting with acute pancreatitis, does a multidimensional approach compared to unidimensional pain intensity measures to assess pain and improve the accuracy of pain evaluation and clinical outcomes?

5.1.1 | *Good Practice Statement 3.1*

A multidimensional approach to pain assessment may be considered given its use in other disease processes such as chronic pancreatitis with established benefit.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 95%

5.1.2 | *Comment*

Evidence to support the use of multidimensional methods in AP is lacking. A multidimensional pain assessment may facilitate a comprehensive understanding of pain experience and enable targeted therapies [66]. Changes in pain intensity alone may not reflect a clinically meaningful patient response [67]. Evidence from acute postoperative pain shows that including multiple domains (intensity, function, analgesic use) within a core outcome set [68, 69], benefits patients by expediting recovery and enhancing satisfaction [69–71]. Current guidelines for acute pain assessment can be applied in AP [72], that is, including pain intensity, interference, physical function, and quality of life. Acute abdominal pain, the key diagnostic criterion for AP [73], varies in intensity, quality, and location, which unidimensional scales fail to capture [74, 75]. These methods inadequately address the complex nature of AP pain and its impact on physical function. A prospective study suggests that certain pain characteristics predict more severe disease progression, warranting closer monitoring [65]. Considering characteristics related to visceral and inflammatory pain may also provide insight into underlying mechanisms and guide targeted therapies [65, 75, 76]. Accurate assessment of visceral pain should incorporate gastrointestinal symptoms, autonomic responses, and psychosocial influences [76].

Recently, the PAN-PROMISE instrument has been developed and validated as a patient-reported outcome measure in acute pancreatitis [77]. PAN-PROMISE is a multidimensional symptom scale incorporating pain intensity alongside other patient-relevant domains such as gastrointestinal symptoms, fatigue, and thirst. While this represents an important step toward patient-centred outcome assessment in AP, PAN-PROMISE was designed as a global symptom burden measure rather than a dedicated multidimensional pain assessment tool, and it has not been evaluated against unidimensional pain intensity scales with respect to clinical decision-making or patient outcomes. In chronic pancreatitis, however, there is a validated comprehensive pain assessment tool available [78], taking into account (a) pain severity, (b) pain pattern, (c) factors provoking pain, (d) widespread pain, and (e) a qualitative pain-describing dimension, in addition to validation in different cultural settings [79].

5.2 | Question 3.2

In patients with acute pancreatitis, does frequent pain assessment compared with less frequent assessments lead to better pain control?

5.2.1 | *Good Practice Statement 3.2*

Evidence from acute pain in general can be used as a reference, indicating assessment frequency between every 5^{th} to 60^{th} minute, depending on pain intensity.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 95%

5.2.2 | *Comment*

There are no studies addressing pain assessment frequency in acute pancreatitis. Evidence was also limited in acute pain in general [80]. When looking into recommendations for acute pain in general, a systematic review has evaluated the optimal frequency for pain evaluation, and defines assessment every 5^{th}–15^{th} minute in severe pain (NRS $>$ 6) and every 30^{th}–60^{th} minute in moderate pain (NRS $<$ 7) [81]. Pain intensity did, however, not affect the patient's preference for assessment frequency. The mean preferred frequency was 23 min, but there were significant individual differences (5–90 min) [82].

5.3 | Question 3.3

In patients with acute pancreatitis, is the numeric rating scale as reliable as the visual analogue scale for pain assessment?

5.3.1 | *Good Practice Statement 3.3*

Both unidimensional scales are equally suited for acute pain assessment in general and can be used for AP pain. The NRS scale may be preferred due to better compliance in most studies.

Certainty of Evidence: Ungraded.

Strength of recommendation: Moderate.

Consensus agreement: 92%

5.3.2 | *Comment*

Unidimensional pain intensity assessment tools have not been compared in AP, but as pain intensity assessment is not disease-specific, this statement has been based on comparisons from acute pain in general.

5.4 | Question 3.4

In patients presenting with acute pancreatitis, is pain relief as reliable as pain intensity?

5.4.1 | *Good Practice Statement 3.4*

Pain relief has shown promise as a sensitive measure in acute pain trials, but its superiority over pain intensity in acute pancreatitis remains unproven in clinical settings. A multidimensional approach to pain assessment may be preferable but not so extensive that feasibility is compromised.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 87%

5.4.2 | *Comment*

While pain intensity is commonly used, pain relief might be a more sensitive measure in acute pain trials, but evidence is sparse [75, 83, 84]. Bova et al. omitted pain relief for pain intensity in a core outcome set for acute pain in general [72]. Furthermore, asking patients whether they want more pain medication is not a reliable indicator of pain relief, as patients may refuse additional analgesics for reasons unrelated to pain levels [85]. Patient Global Impression of Change (PGIC) captures perceived overall change and treatment benefit. However, it cannot be considered a direct measure of pain relief, particularly in acute conditions where rapid symptom fluctuation and limited baseline recall may affect its validity. Previous evidence has indicated that in rapidly evolving acute states, global change ratings show only modest correspondence with objective or domain-specific change [86, 87].

6 | Chapter 4: Treatment of Pain in Acute Pancreatitis

6.1 | Question 4.1

In patients with acute pancreatitis, will the use of the WHO ladder, as compared to the non-WHO ladder approach, improve pain control?

6.1.1 | *Statement 4.1*

We suggest that for mild to moderate pain, using the WHO ladder may be sufficient for achieving pain control in patients hospitalized with acute pancreatitis. For patients with severe pain, however, this approach may be insufficient. As such, more potent analgesics such as opioids may be warranted upon presentation. A step-down approach may be more appropriate for severe pain in acute pancreatitis, but further studies are warranted in this field.

GRADE Certainty of Evidence: Very low.

Recommendation: Weak.

Consensus agreement: 90%

6.1.2 | *Comment*

The World Health Organization (WHO) analgesic ladder could be followed for pain management in AP [88–90] where non-opioid analgesics are the first-line treatment. Opioids are used when initial treatment has been ineffective [91]. Non-opioid analgesia appears to be the primary choice for AP pain management [11]. However, a high proportion of AP patients receive opioids during admission, suggesting that patients require opioids to achieve adequate pain relief [11, 92, 93]. In AP, several factors may argue against the use of opioids, as they can exacerbate nausea and constipation and respiratory depression [94].

On the other hand, non-steroidal anti-inflammatory drugs may aggravate renal impairment and GI bleeding [95]. It is also important to note that the WHO analgesic ladder does not integrate mechanism-specific management and does not include comprehensive assessment (functional interference and psychosocial aspects) and non-pharmacological strategies. Overall, there is no direct evidence in patients with acute pancreatitis to support whether the WHO ladder is an optimal approach for managing pain and alternative strategies such as a reversed step-down approach have been suggested [96].

6.2 | Question 4.2

In patients hospitalised with acute pancreatitis, what is the effect of opioid analgesia, as compared to non-opioid analgesia, on pain control?

6.2.1 | Statement 4.2

We suggest using strong opioids, especially buprenorphine and pentazocine, in patients hospitalized with acute pancreatitis, as current evidence shows that they provide superior pain relief over non-opioid medications in terms of pain control and decreased need for rescue analgesia. However, high-level evidence from large-scale studies is warranted.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 93%

6.2.2 | Comment

Non-opioid medications, most often NSAIDs, have been compared with opioids for pain relief with variable results. Two randomised trials found similar effects for pain relief in AP comparing weak opioids (tramadol) and non-opioids (paracetamol, dexketoprofen, and diclofenac) [97, 98]. One small, randomised trial found superior pain relief with metamizole compared with morphine [98]. Recent randomised trials have found decreased need for rescue analgesia and prolonged pain-free intervals with buprenorphine and pentazocine that are mixed opioid agonists-antagonists, over NSAIDs (diclofenac) [99, 100].

Reviews and meta-analyses have concluded similar pain relief between opioids and non-opioids (predominantly NSAIDs) [4, 22, 28, 39, 101–103]. However, several of these reviews found a decreased need for supplementary analgesia with opioids [22, 28, 39, 102]. One review noted that for rescue analgesia, almost exclusively opioids are used in AP trials [103].

Evidence is limited by small sample sizes, heterogenous methodology, different choice of opioids (tramadol, morphine, buprenorphine, and pentazocine), and only a few studies were able to assess pain score and severity. Future research should focus on trials with larger samples and relevant outcomes for decision-making, such as the number of participants showing reductions in pain intensity.

6.3 | Question 4.3

In patients with acute pancreatitis, what is the effect of opioid analgesia, as compared to non-opioid analgesia, on safety?

6.3.1 | Statement 4.3

Current evidence suggests that there may not be an increased risk of adverse outcomes in AP related to opioid treatment. In patients with AP and severe pain, we suggest that safety concerns should not delay the timely use of opioids to ensure adequate pain management.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 90%

6.3.2 | Comment

The adverse effects of opioids, such as gut dysmotility, impaired gut permeability, and sphincter of Oddi spasms, have caused safety concerns regarding opioid use in AP. Results from preclinical studies in AP have been inconsistent, with some indicating worse outcomes with opioid administration [28, 104–107], whereas other studies have found improved outcomes [107–109].

Several clinical studies have demonstrated associations between opioid use and the deterioration of AP [3, 92, 110–114]. However, confounding by severity is likely in this setting, as previously proposed [3, 110, 115]. Previous meta-analyses pooling evidence from randomized trials on opioid analgesia in AP did not indicate safety issues from the administration of opioids [22, 28, 39, 102]. These meta-analyses were underpowered for evaluating safety. Another limitation of the studies is that they often compare different opioids of varying potency and category, which may not be comparable due to opioid receptor affinity differences. Finally, a recent randomized trial did not find any beneficial effect of peripheral opioid antagonism on the severity of AP [116].

Another study found no association between opioid prescriptions and early readmissions [117]. In one small study, chronic opioid use after AP was observed only in patients with recurrent AP or chronic pancreatitis [118].

6.4 | Question 4.4

In patients with acute pancreatitis, what is the effect of NSAIDs and COX-2 inhibitors, as compared to other analgesia, on clinical outcomes?

6.4.1 | Statement 4.4

NSAIDs do not increase adverse events or worsen the severity of acute pancreatitis, though studies are generally underpowered. COX-2 inhibitors (parecoxib with celecoxib/imrecoxib) may reduce the risk of progression to severe AP.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 100%

6.4.2 | *Comment*

The role of NSAIDs in acute pancreatitis remains debated, as potential anti-inflammatory benefits must be balanced against gastrointestinal, cardiovascular, and renal risks in a population prone to organ failure. Randomised trials evaluating pain relief of non-selective NSAIDs (indomethacin, diclofenac, and dexketoprofen) versus opioids or placebo found no difference in adverse events, including gastrointestinal bleeding, dyspepsia, or nausea [97–100, 119, 120]. Although underpowered, some studies reported no difference in the occurrence of pancreatic necrosis and severe acute pancreatitis [99, 100, 119, 121], which was further confirmed in a meta-analysis [30, 101]. The studies, however, were limited by small patient numbers, inconsistent methodology, and diverse outcomes.

Emerging evidence suggests COX-2 inhibitors may prevent severe acute pancreatitis [122–124]. Two randomised trials indicated that parecoxib (sequential with celecoxib or imrecoxib) reduced disease severity and organ failure in patients with predicted severe acute pancreatitis [122, 124]. No differences in renal failure or dialysis requirement were reported, though COX-2 inhibition may theoretically impair renal perfusion through reduced prostaglandin synthesis in the context of systemic inflammation and intravascular hypovolaemia [95]. It remains unclear whether the study drug was stopped upon renal deterioration. Furthermore, parecoxib currently lacks regulatory approval in many countries [125].

6.5 | Question 4.5

In patients with acute pancreatitis, will patient-controlled analgesia, as compared to intravenous or oral analgesia, improve pain control?

6.5.1 | *Statement 4.5*

Patient-controlled (intravenous) analgesia is widely used in acute pain management, but we suggest that PCA should be used with caution in the context of AP.

GRADE Certainty of Evidence: Very low.

Recommendation: Weak.

Consensus agreement: 95%

6.5.2 | *Comment*

Patient-controlled analgesia (PCA) has been used particularly for acute post-operative pain but is also used for pain control in AP. However, the evidence is sparse. A retrospective study [126] of 656 patients with AP found that those treated with PCA increased length of stay, longer time to enteral nutrition and a higher likelihood of being discharged on opioids. The study was limited by a retrospective design and the efficacy of the mode of drug delivery on pain scores was not studied.

Another randomised controlled study found that IV hydromorphone PCA resulted in a higher incidence of acute post-pancreatitis fluid collections, more opioid consumption and increased costs compared with intramuscular pethidine in AP. There were more adverse events with PCA, and the study was halted prematurely [127].

A randomised controlled trial [128]compared the use of epidural analgesia (bupivacaine and fentanyl) and patient controlled IV analgesia (fentanyl) in predicted severe AP and pain relief was better with EA compared to PCA.

Although the concept of PCA appears to be attractive and appealing, it requires careful patient selection, individualisation, and standardisation of dosages and regimens for different opioid drugs.

6.6 | Question 4.6

In patients with acute pancreatitis, what is the effect of unconventional analgesic treatments (e.g., anticonvulsants, anxiolytics), as compared to conventional analgesia, on pain control? (As measured by improvement of pain, improvement of patient-measured outcomes, improvement of quality of life, etc).

6.6.1 | *Statement 4.6*

The role of unconventional analgesics in the pain management in AP in terms of analgesia efficacy and improvement in patient-reported outcomes is only experimental, and we suggest against their use for standard clinical practice.

GRADE Certainty of Evidence: Very low.

Recommendation: Weak.

Consensus agreement: 97%

6.6.2 | *Comment*

Pathophysiology of pain in AP traditionally deals with pancreatic inflammation from local complications [129]. Recently 'neurogenic inflammation', in which different noxious substances released from the damaged acini activate the peripheral nociceptive nerve endings, has been suggested [57]. Neuropeptides attract the immune cells, leading to vasodilatation and local inflammation causing pain. Thus, interaction between the nervous system and pancreatic inflammation can offer clues to the management of AP. Data has primarily been extrapolated from studies on chronic pancreatitis. The effects of unconventional agents such as anticonvulsants, anxiolytics and others for pain management in AP come from experimental trials [60, 64].

As such, intrathecal gabapentin or NMDA receptor antagonist, along with morphine, was administered in an experimental rat model [130, 131], showing that the combination was better than either drug alone in reducing pain-related behaviours in rat models. It was speculated that N-type voltage-activated calcium

channels were involved in the visceral pain of AP [132]. Multiple randomized controlled trials exist evaluating the role of antioxidants in AP, but do not give conclusive answers on their effect on pain management.

6.7 | Question 4.7

In patients with acute pancreatitis, what is the effect of unconventional analgesic treatments (e.g., anticonvulsants, anxiolytics), as compared to conventional analgesia, on safety?

6.7.1 | Statement 4.7

The current evidence remains extremely limited to delineate the safety profile of atypical/unconventional analgesic treatments in AP. We suggest against their use in routine clinical practice.

GRADE Certainty of Evidence: Very low.

Recommendation: Weak.

Consensus agreement: 100%

6.7.2 | Comment

In a systematic review of RCTs investigating the efficacy and safety of low-dose ketamine compared with morphine, no significant difference was found in reported nausea between the two groups [133]. Likewise, low-dose ketamine did not reduce rates of hypoxia However, there was a low certainty of evidence, and the studies did not exclusively investigate pain in AP. Therefore, the conclusion of the efficacy and safety in pancreatitis must be extrapolated from these preliminary findings.

6.8 | Question 4.8

In patients with acute pancreatitis, what is the effect of interventions (necrosectomy, drainage, decompression, ERCP), as compared to no intervention, on pain relief?

6.8.1 | Good Practice Statement 4.8

Several local complications may contribute to pain in acute pancreatitis. For disease management, including pain control, it remains important that these complications are identified and treated appropriately. However, current evidence is insufficient to clearly define the effect of interventional procedures on pain relief and there is a need for studies to compare the efficacy of different interventions for reducing pain in AP.

Certainty of Evidence: Ungraded.

Recommendation: Weak.

Consensus agreement: 100%

6.8.2 | Comment

Current guidelines for severe acute pancreatitis consider persistent pain an indication for intervention, particularly in sterile necrosis [6, 134, 135]. However, there is a paucity of studies directly evaluating pain relief as an outcome of different interventional procedures. Randomised trials comparing different strategies (e.g., minimally invasive vs. open necrosectomy, percutaneous vs. endoscopic drainage, ERCP with sphincterotomy) have focused on clinical outcomes such as complications, re-intervention, and mortality, without pain assessment [136–142].

In chronic pancreatitis, surgery and endoscopy have been associated with pain relief, although placebo-controlled data are scarce [143–147]. A recent sham-controlled study showed short-term pain relief with combined ESWL and ERP. Poor correlation between pancreatic morphology on imaging and pain in chronic pancreatitis suggests a role for central sensitisation, in which pain signals are amplified within the central nervous system, limiting the response to treatments directed at the periphery (pancreas) [148, 149].

In acute pancreatitis, the pain is typically acute, and central sensitisation is therefore less likely to play a major role. As such, local complications such as fluid collections, necrosis, haemorrhage, or abdominal compartment syndrome are likely to contribute to pain in this setting. Identification and treatment of complications, therefore, remain important in overall management, including pain control, despite limited direct evidence for pain relief from interventions.

7 | Chapter 5: Role of Epidural Analgesia in Acute Pancreatitis

7.1 | Question 5.1

In patients with acute pancreatitis, does epidural analgesia combined with standard of care provide better pain control than standard of care as measured by improvement of pain, improvement of patient-reported outcomes, and improvement of quality of life?

7.1.1 | Good Practice Statement 5.1

Epidural analgesia, combined with standard care, provides superior pain relief in acute pancreatitis compared with standard care alone and leads to improved patient-reported outcomes and enhanced quality of life, particularly in patients with severe AP. We recommend its use when local expertise is available.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 92%

7.1.2 | Comment

Epidural analgesia provides better analgesia than standard of care in acute pancreatitis—particularly in predicted severe disease—demonstrating lower pain scores in an RCT [128] and superior analgesia with reduced rescue medication use in meta-analyses [22]. Some studies also report improved overall clinical outcomes [45]. While one analysis showed no significant pain-score difference, epidural analgesia substantially reduced opioid requirements (15 vs. 52 mg morphine equivalents/day) [150]. Patient-reported outcomes may also improve, with fewer

post-discharge symptoms and better quality of life reported [77, 151]).

7.2 | Question 5.2

In patients with acute pancreatitis, does epidural analgesia compared with standard care reduce the incidence or severity of complications and improve hospital outcomes?

7.2.1 | Statement 5.2

Epidural analgesia in AP improved respiratory outcomes and survival in observational cohorts, but findings from RCTs are inconsistent; therefore, the overall benefit remains uncertain and we suggest against its use until further high-quality research is conducted.

GRADE Certainty of Evidence: Low.

Strength of recommendation: weak.

Consensus agreement: 94.7%

7.2.2 | Comment

Preclinical models suggest that epidural analgesia improves splanchnic perfusion, supporting a hypothesized reduction in organ failure and local complications, but clinical data remain inconclusive. Observational studies report lower ARDS/acute kidney injury and reduced mesenteric ischaemia/mortality with EA [151–153], whereas RCTs show no consistent reduction in new organ failure or local complications [128, 153, 154]. Effects on respiratory support, length of stay, and mortality are mixed across studies and meta-analyses [45, 128, 150–152, 154], with evidence largely derived from ICU cohorts, limiting generalizability to milder acute pancreatitis [150].

7.3 | Question 5.3

In patients with acute pancreatitis, does epidural analgesia offer a good safety profile compared with standard-of-care treatment?

7.4 | Statement 5.3

Epidural analgesia is a safe pain management option in AP with a low risk of serious complications. Transient hypotension is the most common issue and is usually well controlled. We suggest that epidural analgesia may be considered when expertise is available, and strict aseptic techniques and close monitoring are essential.

GRADE Certainty of Evidence: Moderate.

Strength of recommendation: strong.

Consensus agreement: 97%

7.4.1 | Comment

The most frequently reported complication after EA use was transient hypotension, usually self-limited or managed with fluid resuscitation or inotropic support [45, 151, 152, 154, 155]. Al-Leswas et al. reported it in up to 18% (133/726) patients with no long-term sequelae [45]. No severe neurological or hemorrhagic events were reported, and only one epidural abscess occurred in a high-risk polytrauma ICU patient, highlighting the need for strict aseptic catheter care [155]. Careful periprocedural management is essential, especially with anticoagulants/antiplatelets (median interruption 17 h and 2.5 days, respectively) [45]. Overall, with rigorous asepsis and close monitoring, EA remains a safe and effective analgesic strategy in AP.

7.5 | Question 5.4

In patients with acute pancreatitis, what is the effect of epidural analgesia compared to standard-of-care on the development of persistent pain after discharge (defined as the need for home analgesia and/or emergency room visits for persistent pain)?

7.5.1 | Good Practice Statement 5.4

The role of epidural analgesia in preventing chronic pain recurrence after acute pancreatitis remains unclear due to insufficient evidence. Further research is needed to explore post-discharge outcomes after epidural analgesia use in AP.

Certainty of Evidence: Ungraded.

Strength of recommendation: weak.

Consensus agreement: 86%

7.5.2 | Comment

The lack of studies on long-term outcomes of epidural analgesia in AP, particularly regarding post-discharge pain recurrence, reveals a notable gap in the literature. Further research is needed to assess the long-term efficacy and safety of this treatment in such patients.

8 | Chapter 6: Complementary Treatment (Traditional Chinese Medicine) Including Acupuncture

8.1 | Question 6.1

In patients admitted with acute pancreatitis, does sufficient pain management by Chinese herbal medicine (CHM) formulae, as compared with conventional treatment, relieve abdominal pain and improve gut function?

8.1.1 | Statement 6.1

CHM formula Chaiqin Chengqi Decoction may have positive effects on pain control and intestinal symptoms in patients with severe AP and we suggest its use. However, it may be associated with higher rates of hypernatraemia.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 81%

8.1.2 | *Comment*

Complementary treatment modalities in AP are commonly used in China and can be used in children and non-pregnant women [156]. CHM formulae are combinations of herbs guided by traditional Chinese medicine principles, such as yin-yang harmony, qi/blood regulation, and interactions between the organ systems. CHM formulae of major purgative decoctions containing key components Rhei Radix et Rhizoma (Da Huang; rhubarb) and Natrii Sulfas (Mang Xiao; mirabilite) have been widely used in China to treat patients with AP [157].

Chaiqin Chengqi Decoction (CQCQD) has been shown to decrease abdominal pain, pancreatic necrosis, systemic inflammation, and multiple organ dysfunction indices in rodent AP models [158–164]. A randomised trial investigated the administration of CQCQD on patients with predicted severe AP, including a daily visual analogue scale (VAS) score of pain as one of the secondary outcomes [165]. The CQCQD comparator was made as 10% of Decoction following a protocol suggested by a previous study for a practical reason (colour and odour) [166]. In comparison to the comparator ($n = 124$), patients receiving CQCQD ($n = 124$) had reduced VAS scores during the first 2 days, decreased intra-abdominal pressure, and more rapid resumption of oral intake. Moreover, CQCQD reduced the incidence of progression to severe AP [167]. The CQCQD group had a higher number of patients with hypernatraemia requiring treatment (19.4% vs. 0.4%), while nonfatal serious adverse events were comparable between the two groups (25% vs. 23.4%).

Of note, CQCQD is not an FDA-approved drug and is associated with a high incidence of hypernatraemia. The previous studies are from a single center in China, and the results may not be translatable.

8.2 | Question 6.2

In patients admitted with acute pancreatitis, does pain management by acupuncture as compared with conventional treatment reduce the severity of abdominal pain and improve gut function?

8.2.1 | *Statement 6.2*

We suggest that acupuncture with appropriate acupoints may be effective in relieving abdominal pain and reducing the time to oral intake without significant side effects in patients with AP and may be considered.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 82.8%

8.2.2 | *Comment*

Acupuncture includes traditional acupuncture, electroacupuncture, moxibustion, and other variants [168]. A meta-analysis of 19 RCTs [168] has shown that the top 5 used acupoints are ST36, RN12, ST25, LI4, and PC6 for acupuncture/electroacupuncture to relieve pain in AP. A randomised trial compared early administration of transcutaneous electrical acustimulation (TEA; $n = 21$) and sham-TEA ($n = 21$) in patients with AP admitted within 24 h after symptoms onset. Compared with the sham-TEA group, patients receiving TEA had significantly reduced VAS pain score and first defecation time. Another three-arm RCT ($n = 89$) [169] investigating the effect of local (abdominal acupoints: CV12 and CV13) electroacupuncture and local plus distal electroacupuncture (12 acupoints) on abdominal pain relief showed no significant change in VAS pain score at day 5. However, electroacupuncture decreased the time to food intake (median 2 vs. 3 days) without any significant adverse events.

9 | Chapter 7: Impact of Lack of Treatment of Pain in Acute Pancreatitis

9.1 | Question 7.1

In patients admitted with acute pancreatitis, will sufficient pain management as compared with suboptimal analgesia reduce the time to oral intake of solids?

9.1.1 | *Good Practice Statement 7.1*

Sufficient pain relief may prevent pain relapse during enteral refeeding and thus promote tolerance to oral feeding and reduce the time to oral intake of solid foods in patients with acute pancreatitis. Non-opioid analgesics may be preferable due to opioid side effects on the gastrointestinal system, including slow transit, nausea, and indigestion.

Certainty of Evidence: Ungraded.

Recommendation: Weak.

Consensus agreement: 95%

9.1.2 | *Comment*

Several studies have documented improved outcomes of AP with early enteral refeeding [170–172] However, enteral refeeding is often complicated by pain relapse in patients with AP [173–175]. Better pain control will result in mobilisation, and theoretically promote food intake, although no studies in AP exist [176]. A clinical study of 40 patients admitted for colorectal cancer found an increased caloric intake postoperatively in patients receiving epidural bupivacaine with low-dose morphine compared with morphine alone [177]. In this setting, pain relief from epidural analgesia has been suggested to be more effective than opioids in promoting oral food intake due to the adverse effects of opioids on the gastrointestinal tract [178, 179].

9.2 | Question 7.2

In patients admitted with predicted severe acute pancreatitis, does optimal compared with suboptimal pain management reduce the risk of single or multiple end-organ dysfunction/failure?

9.2.1 | *Good Practice Statement 7.2*

The risk of organ dysfunction failure may potentially be increased with suboptimal pain management. The organs most affected are the lungs, kidneys, and heart, although side effects from some analgesics (e.g., opioids) can cause respiratory depression, gut dysfunction, and reduced mobilisation.

Certainty of Evidence: Ungraded.

Recommendation: Weak.

Consensus agreement: 92%

9.2.2 | *Comment*

Abdominal pain in AP may limit diaphragmatic excursion and decrease functional residual capacity, resulting in hypoxaemia, ventilation-perfusion abnormalities, and respiratory failure secondary to basal atelectasis and pneumonia. These can potentially all be improved with appropriate analgesia. On the other hand, treatment with opioids in high doses has the potential to make the situation worse with respiratory depression and an increased risk of respiratory failure [180].

Thoracic epidural analgesia is an option for patients with severe AP, especially in those requiring opiates over an extended period [43]. It may also play a therapeutic role through targeted sympathectomy and improving microcirculation through splanchnic vasodilatation and dampening of the inflammatory response [181]. On the other hand, an RCT (EPIPAN) enrolling ICU patient with AP evaluated epidural analgesia and found no change in ventilator-free days and an increase in the duration of invasive ventilation. While it reduced opioid requirements, there was no effect on the biomarkers of lung and kidney injury.

Renal dysfunction is a relatively common organ dysfunction in severe AP patients, and this can be worsened with NSAID-based analgesic protocols [182]. On the contrary, insufficient analgesia may lead to long-lasting immobilisation, which can also potentially impact renal function.

Abdominal pain, especially when associated with peritonitis, reduces the mobility of a patient, increasing the risk of deep vein thrombosis and pulmonary embolism.

Suppression of cellular and humoral immune function may also increase the risk of infection [183]. Other effects of suboptimal pain management include hyperglycaemia, mental depression, sleep disturbances, prolongation of hospital admission and overall reduced quality of life.

9.3 | Question 7.3

In patients admitted with acute pancreatitis, does sufficient pain management as compared with suboptimal treatment lead to early resolution of ileus and constipation and help reduce intra-abdominal hypertension, and the risk of non-occlusive mesenteric ischaemia, deep venous thrombosis, and pulmonary embolism?

9.3.1 | *Statement 7.3*

Sufficient pain relief will help reduce the duration of ileus and augment bowel motility in acute pancreatitis and may indirectly help in the reduction of intra-abdominal hypertension. Although it does not have direct effects, it may help reduce the risk of deep venous thrombosis or pulmonary thromboembolism through early mobilisation.

GRADE Certainty of Evidence: Low.

Recommendation: Weak.

Consensus agreement: 92.5%

9.3.2 | *Comment*

One of the early signs of intestinal dysfunction in AP is the development of ileus and consequent constipation. The aetiology is multifactorial, including inflammatory stress, local complications [184], electrolyte disturbance, and endogenous opioids [185]. Early reversal is desirable as prolonged ileus can, in turn, hamper nutrition and propagate a systemic inflammatory response [186, 187]. While it is logical that sufficient pain management can help improve ileus, direct evidence in AP is lacking. Nevertheless, this fact can be extrapolated from post-operative ileus, where optimum pain management has been shown to reduce the duration of ileus and hospital stay. In a meta-analysis, Sun et al. [188] showed that IV lidocaine, when compared to controls, caused statistically significant shortening of time to first flatus pass and bowel movement. Similar findings were echoed by Vigneault et al. [189]. These motility benefits are more pronounced with thoracic epidural analgesia. Interestingly, Moselli et al. [190] showed that the use of epidural analgesia intra-operatively attenuated the pro-inflammatory response compared with intravenous analgesia. Evidently, post-operative optimum analgesia has been included as an essential component for enhanced recovery pathways after abdominal surgery in most guidelines [191, 192]. Thus, sufficient pain management will help reduce the duration of ileus and augment bowel motility in AP, similar to post-operative ileus.

Trials comparing opioids versus non-opioids for pain management in AP showed no difference in GI dysmotility [116].

Intra-abdominal hypertension can develop in patients with severe AP, and this can manifest as abdominal compartment syndrome with very high morbidity and mortality [193]. The development of intra-abdominal hypertension is multifactorial [194], with key factors contributing including paralytic ileus leading to bowel distension, ascites, and peripancreatic fluid collections. Abdominal pain in AP leads to guarding of the abdominal wall and can affect the compliance of the abdominal wall. Interestingly, this effect has been recently demonstrated in rat models of intra-abdominal hypertension to predict raised intra-abdominal pressure [195]. Thus, while direct evidence is lacking, sufficient pain management may indirectly help intra-abdominal pressure reduction by the afore-mentioned mechanisms.

In patients with severe AP, prolonged intestinal dysfunction and gut ischaemia can lead to non-occlusive mesenteric ischemia similar to critically ill intensive care patients [196]. Non-occlusive mesenteric ischaemia is not a common phenomenon of AP [197]. However, while sufficient pain management might not have any direct effects, early mobilisation from optimum pain management may help reduce the risk of the development of intra-abdominal hypertension and deep vein thrombosis/pulmonary thromboembolism.

9.4 | Question 7.4

In patients admitted with acute pancreatitis, does sufficient pain management, as compared with suboptimal treatment, result in a decrease in the frequency and/or severity of central nervous system sensitization and associated complications?

9.4.1 | Good Practice Statement 7.4

Adequate pain relief may reduce the frequency and severity of complications associated with central nervous system sensitisation in patients with acute pancreatitis, including the development of chronic pain, increased post-discharge analgesic requirements, and the risk of opioid dependency. However, further research is needed to fully evaluate these aspects, particularly due to the lack of long-term follow-up studies.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 95%

9.4.2 | Comment

Several studies indicate that patients with AP continue opioid use for over 90 day post-discharge [92, 118, 198]. Higher pain scores during hospitalisation and at discharge are risk factors for prolonged opioid use, and there may be a link between inadequate in-hospital pain management and the risk of opioid dependency [92, 126]. Hypothetically, effective pain management during the acute phase may therefore reduce the need for opioid prescriptions upon discharge, potentially mitigating the risk of prolonged opioid use and dependency.

Another potential consequence of poorly controlled acute pain is transition to chronic pain. Previous studies have shown that the presence and intensity of acute postoperative pain are significant predictors of chronic pain development [199, 200]. Effective and timely perioperative pain relief plays a significant role in preventing chronic pain, as it minimises acute pain and reduces the noxious stimuli that can lead to peripheral and central sensitisation [201, 202].

9.5 | Question 7.5

In patients with acute pancreatitis, will sufficient pain management, as compared with suboptimal treatment, increase compliance with an enhanced recovery program?

9.5.1 | Statement 7.5

We suggest taking into consideration that sufficient pain management may increase compliance with an enhanced recovery program in patients with acute pancreatitis, especially in mild disease.

Certainty of Evidence: Very low.

Strength of recommendation: Weak.

Consensus agreement: 92.5%

9.5.2 | Comment

In mild acute pancreatitis, two studies have investigated enhanced recovery pathways with the aim of determining the safety of the program as well as its potential to facilitate patient recovery [203, 204]. In one study, 60 patients with mild acute AP either followed an enhanced recovery or a traditional pathway [203]. The main result was lower costs in the enhanced recovery pathway group due to shorter length of stay. In a double-blinded trial, 46 patients were randomised to standard treatment or an enhanced recovery program, where pain control was a secondary outcome [204]. There was no difference in opioid use between the groups. In conclusion, evidence is lacking on whether sufficient pain assessment would increase compliance with an enhanced recovery program in AP.

9.6 | Question 7.6

In patients admitted with acute pancreatitis, does sufficient pain management compared with suboptimal treatment decrease the time to full mobility and reduce the impairment of daily activities, leading to a shorter time to return to work?

9.6.1 | Good Practice Statement 7.6

Sufficient pain management may help to prevent prolonged periods of pain and may also decrease the time to full mobility and reduce the impairment of daily activities. This may, in turn, result in a shorter return-to-work period for patients with acute pancreatitis.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 97%

9.6.2 | Comment

Gougol et al. reported that 41% of patients with AP exhibited significant impairment in work and daily activities 1 year after diagnosis [198]. Nevertheless, despite recommendations indicating that functional assessments are necessary in pain trials [205, 206], there is currently no data examining the influence of sufficient pain management on functional impairment in AP patients.

Higher pain intensity is associated with more significant impairment of daily activities [199, 202, 207–210], in the

context of acute and chronic conditions [211–213]. In chronic pancreatitis, there is a correlation between pain intensity and impairment of daily activities and physical activity [214]. Also, it is well documented that the experience of acute post-operative pain can result in a notable restriction of daily activities [209].

In conclusion, although the evidence is limited, it can be reasonably concluded that sufficient pain management for AP can reduce the time to full mobility, reduce impairment with daily activities, and reduce the time to return to work.

9.7 | Question 7.7

In patients admitted with acute pancreatitis, does sufficient pain management compared with suboptimal treatment improve quality of life and reduce psychological and psychosomatic stress?

9.7.1 | Good Practice Statement 7.7

Sufficient pain management in patients with acute pancreatitis may significantly improve quality of life and reduce psychological and psychosomatic stress. Effective pain relief may also reduce the need for additional analgesics and prevent complications associated with inadequate pain management, which can considerably reduce psychological stress.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 85%

9.7.2 | Comment

Several studies have documented the positive impact of effective pain management during AP. It is essential to address the psychological aspects of pain management, as patients with AP often experience significant psychological stress [210]. A comprehensive review has highlighted various pain management strategies and their effectiveness in improving the quality of life and reducing stress [55]. However, the role of sufficient pain relief in improving the quality of life and reducing stress is still not completely understood.

9.8 | Question 7.8

In patients admitted with acute pancreatitis, can sufficient pain management, as compared with suboptimal treatment, potentially reduce the length of hospitalisation and decrease the rate of readmissions?

9.8.1 | Statement 7.8

We suggest taking into account that sufficient pain relief may improve patients' comfort, possibility to undertake physical activity, and may further reduce complications in acute pancreatitis. How this relates to the length of hospitalisation and readmission data in acute pancreatitis is still contradictory.

GRADE Certainty of Evidence: Low.

Strength of recommendation: Weak.

Consensus agreement: 95%

9.8.2 | Comment

In AP, when pain is effectively controlled, patients are more likely to mobilise early, resume normal activities, and tolerate oral intake sooner, facilitating a faster transition from intravenous to oral nutrition [22]. In a meta-analysis of Cai et al. [22] of 12 randomised controlled trials in AP, it was shown that treatment with analgesics versus controls significantly reduced VAS scores and the need for rescue analgesia, but not the length of hospital stay [22, 120, 122, 215]. Similar results were found for patients with AP and pain when they are treated with opioids compared with treatment with non-opioids [97–99, 216–218]. Ushe et al. showed a positive impact of a pain management consult compared to no consultation in AP with reduced pain scores, opioid usage, and hospital stay [219]. Stevens et al. compared fentanyl versus placebo as pain treatment in AP and showed a significant reduction in pain experienced and length of hospital stay [220].

Proper pain management in acute pancreatitis can decrease the likelihood of readmissions. Poor pain control is a significant predictor of recurrent hospital visits due to ongoing discomfort and the risk of complications. Despite supporting evidence on the relationship between adequate pain control and a smaller chance of readmission in pancreatic and colorectal surgery [192, 221], there is no evidence in supporting these observations in AP.

10 | Chapter 8. Paediatric AP Pain Management, and During Pregnancy

10.1 | Question 8.1

In children with AP, what is the impact of non-opioid analgesic medication compared with opioids on length of stay or intensive care unit admission?

10.1.1 | Statement 8.1

In children with AP, the type of administered analgesics (opioid vs. non-opioid) does not appear to affect length of stay or admission in intensive care.

GRADE Certainty of Evidence: Very low.

Strength of recommendation: Weak.

Consensus agreement: 84%

10.1.2 | Comment

Gorbunova et al. carried out a retrospective study in 224 children hospitalized with AP, comparing intensive care unit admission rates and length of stay (LOS) between children who received non-opioid analgesics and those who received opioids [222]. Most children (71%) had received opioids, including 29%

as part of multimodal analgesia (paracetamol or NSAID combined with opioids).

In multivariate analysis, children who received opioids within the first 48 h of admission did not experience a significant increase in length of stay or intensive care admission compared with those who received non-opioid analgesics.

10.2 | Question 8.2

In children with acute pancreatitis, what is the impact of feeding compared to fasting on pain severity scores and on length of stay?

10.2.1 | Statement 8.2

In children with AP, oral feeding does not significantly increase pain, and we suggest that oral feeding may be considered. Length of stay was similar in patients who kept fasting than in those allowed to eat within the first 24h.

GRADE Certainty of Evidence: Low.

Strength of recommendation: Weak.

Consensus agreement: 84%

10.2.2 | Comment

Ledder et al. performed a randomized controlled trial in children with mild to moderate AP to compare early feeding ($n = 18$) to initial fasting and intravenous fluid therapy ($n = 15$) on LOS [223]. Both groups had similar LOS, pain scores, and times to pain-free status.

Bukowski et al. [224] performed a randomized study in children with mild AP to compare the impact of very early (< 24h of admission, $n = 42$) to early feeding (> 24h of admission, $n = 33$) on inflammatory markers. Although pain and LOS were not primary or secondary study outcome points, the authors did not find any difference in terms of the severity of pain or LOS between the 2 groups.

Abu-El-Haija et al., in a retrospective study, showed that pain severity scores did not differ significantly between children receiving any form of oral nutrition and those who remained fasting [225]. Patients kept nil per oral during the first 24h had a similar LOS to those who were allowed to eat within 24h of admission.

10.3 | Question 8.3

In children with acute pancreatitis, would utilization of the multidisciplinary approach to pain management, compared with traditional opioid therapy, lead to improved patient outcomes?

10.3.1 | Good Practice Statement 8.3

The utilization of a multidisciplinary approach to pain management can be extrapolated from the postoperative setting, which has been shown to decrease postoperative opioid use and may be considered.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 94.1%

10.3.2 | Comment

The use of a combination of opioids, non-opioids, interventional procedures, and behavioural pain management interventions is well-established as the gold standard for acute paediatric pain management [226]. Despite this, there continues to be a paucity of studies examining this approach in paediatric patients with AP on pain-associated outcomes. Current recommendations are derived from expert opinions [227, 228].

Gorbounova et al. noted there was a trend toward increased use of multimodal analgesia with concomitant decrease in opioid use in the treatment of AP in paediatric patients [222]. Rich et al. reviewed the role of cognitive behavioural therapy in the treatment of pancreatitis pain, emphasizing the role behavioural health specialists can play in intervening on a patient's functional disability and mood disturbances that may have developed as a result of the severity of disease and associated treatments [229]. A systematic review of psychological interventions in managing acute postoperative pain in children found that they were effective in reducing postoperative pain compared with standard of care.

In summary, factors that influence the analgesic type, the impact of analgesic modality on the post-pancreatitis outcome and long-term analgesic use constitute a knowledge gap. Future studies are needed to inform analgesic use in paediatric AP [230].

10.4 | Question 8.4

In pregnant women with acute pancreatitis, what are the effects of epidural analgesia compared with intravenous opioids on pain intensity and maternal and foetal outcomes?

10.4.1 | Statement 8.4

In pregnant women with AP, there is limited evidence suggesting that epidural anesthesia may be more effective than opioid, fentanyl, or tramadol infusions in relieving pain. Maternal and foetal outcomes appear to be similar between the groups.

GRADE Certainty of Evidence: Very low.

Strength of recommendation: Weak.

Consensus agreement: 84%

10.4.2 | Comment

Studies reporting on pain management and maternal and foetal outcomes are scarce. The use of NSAIDs is contraindicated in the third trimester of pregnancy. Dogra et al. conducted a retrospective study in 12 pregnant women who developed AP during the second or third trimester [231]. Seven patients received IV opioids. Two of them were treated with continuous

fentanyl, whereas 5 others received tramadol. In 5 other patients, epidural analgesia with ropivacaine was administered. Pain scores, decreased more in patients with epidural analgesia compared with those receiving fentanyl or tramadol. Maternal and foetal complications were comparable between the groups.

Similar results were obtained by Khan et al., where pain scores decreased more in patients with epidural analgesia compared with those receiving fentanyl or tramadol [232]. Maternal complications included premature caesarean section or vaginal delivery (3 in the fentanyl, 7 in the tramadol, and 9 in the epidural analgesia group). Foetal outcomes included NICU admissions related to prematurity (2 in fentanyl, 3 in tramadol, and 6 in epidural analgesia group) and neonatal jaundice (3 in epidural analgesia group).

11 | Chapter 9: Recommendations for Pain Management at Discharge and Follow-Up

11.1 | Question 9.1

In patients with persistent, recurrent, or escalating pain after discharge for AP, what is the difference between scheduled and non-scheduled follow-up on readmissions/new hospital visits and quality of life?

11.1.1 | Good Practice Statement 9.1

There is insufficient evidence to suggest that specifically scheduled visits in patients discharged with pain after AP can reduce the risk of readmission or ameliorate quality of life. Further research is needed to assess the impact of scheduled follow-up on readmissions.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 100%

11.1.2 | Comment

Persistent and/or recurrent pain occurs in about 20% of patients discharged for AP and quality of life is worse than in the control population [198, 233, 234]. There are no data on the association between the scheduled and non-scheduled follow-up visits and risk of readmission and quality of life. Furthermore, there are no studies investigating the association between follow-up visits with a pancreatic specialist or a non-pancreatic specialist and the risk of readmission and quality of life.

11.2 | Question 9.2

In patients with persistent, recurrent, or escalating pain after discharge in AP, what is the role of routine follow-up imaging and no follow-up imaging in identifying the cause of pain?

11.2.1 | Good Practice Statement 9.2

There is insufficient evidence to suggest that specifically scheduled imaging in patients discharged with pain after AP can identify the cause of pain. In recurrent or escalating pain after AP, there might be a clinical indication for imaging to rule out complications although there are no specific studies reporting on its usefulness in this cohort.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 89.5%

11.2.2 | Comment

Persistent and/or recurrent pain occurs in about 20% of patients discharged for AP [198]. Changes in pancreatic morphology can be observed in some patients after discharge in children and adults [235, 236]. There are no data on the association between routine follow-up imaging and no follow-up imaging in the identification of the cause of pain.

11.3 | Question 9.3

In patients with persistent, recurrent, or escalating pain after discharge in AP, what is the role of endoscopic ultrasound (EUS) in identifying the cause of pain?

11.3.1 | Good Practice Statement 9.3

There is insufficient evidence to suggest EUS for identifying the cause of pain after AP. EUS can be considered to investigate the etiology of pancreatitis in patients with inconclusive imaging examinations.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 84.2%

11.3.2 | Comment

Persistent and/or recurrent pain occurs in about 20% of patients discharged for AP, and in up to 30% of patients, the etiology of acute pancreatitis remains undetermined [198]. There are no strong data supporting the role of EUS or other diagnostic imaging in patients with recurrent pain [237]. However, in a retrospective study, EUS showed a 63% diagnostic gain on the etiology of AP in comparison to contrast-enhanced CT or MRI with MRCP [238].

11.4 | Question 9.4

In patients with persistent, recurrent, or escalating pain after discharge in AP, what is the role between CT follow-up imaging and other (EUS/MRCP) follow-up imaging in identifying the cause of pain?

11.4.1 | Good Practice Statement 9.4

There is insufficient evidence to suggest specifically scheduled CT imaging in patients discharged with pain after AP. Imaging follow-up can be suggested in unexplained aetiology of acute

pancreatitis or persistent, recurrent, or escalating pain after discharge where complications after AP are suspected.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 84%

11.4.2 | *Comment*

Persistent and/or recurrent pain occurs in about 20% of patients discharged for AP [198]. Small retrospective studies of patients with CT follow-up after acute pancreatitis (not related to pain) reported the diagnosis of pancreatic cancer, increased size of pancreatic collection, or newly developed pancreatic collection in 4%–21% of patients [239, 240]. A single-phase CT scan has been reported sufficient to monitor AP severity and complications in the short-term follow-up in retrospective studies [241, 242].

11.5 | Question 9.5

In patients with persistent, recurrent, or escalating pain after discharge in AP, what is the role between MRCP and other (EUS/CT) follow-up imaging in identifying the cause of pain?

11.5.1 | *Good Practice Statement 9.5*

There is insufficient evidence to propose follow-up imaging in patients discharged with pain after AP. MRCP can help to assess the cause of pancreatitis related to duct anomalies.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 92.1%

11.6 | Question 9.6

In patients discharged for AP, does alcohol as etiology versus biliary (and/or other) increase the risk for being on opioid treatment after discharge?

11.6.1 | *Good Practice Statement 9.6*

Although evidence suggests that more patients with alcoholic etiology are prescribed opioids during admissions for acute pancreatitis, and studies on opioid prescription at discharge are limited to only a few, no studies have found increased prescription of opioids at discharge or prolonged opioid use in patients with alcoholic etiology. Hence, opioids may be considered to ensure adequate pain relief for both alcohol and biliary etiology AP at discharge.

Certainty of Evidence: Ungraded.

Strength of recommendation: Weak.

Consensus agreement: 84.1%

11.6.2 | *Comment*

Knoph et al. have found that patients with biliary disease are less likely to require opioids during admission (OR 0.69) [11]. This aligns with results from Wu et al., where alcoholic etiology was associated with an increased risk of opioid prescription during admission (OR 1.11) [92]. However, neither Knoph et al. nor Ahmed et al. found that any etiology was associated with an increased risk of opioid prescription at discharge [11, 118].

11.7 | Question 9.7

In patients discharged for AP, does recurrent acute pancreatitis, compared with first-time acute pancreatitis, increase the risk for being on opioid treatment after discharge?

11.7.1 | *Statement 9.7*

Although only based on a few studies, evidence suggests that patients with recurrent AP may have a higher risk of having pain requiring opioid treatment at discharge. Further studies are needed to confirm these findings and explore whether nociplastic changes in pain processing contribute to this difference.

GRADE Certainty of Evidence: Very low.

Strength of recommendation: Weak.

Consensus agreement: 89.4%

11.7.2 | *Comment*

Yang et al. found a borderline significant difference between the number of patients with opioid prescription at discharge between recurrent acute pancreatitis and first-time acute pancreatitis, whereas there was a significant difference between the groups in the study by Ahmed et al. [118, 243]. Both studies showed an increased number of opioid prescriptions in the recurrent acute pancreatitis group [118, 243].

11.8 | Question 9.8

In patients discharged for AP, does acute on chronic versus acute pancreatitis increase the risk for being on opioid treatment after discharge?

11.8.1 | *Statement 9.8*

There was no significant difference in new opioid prescriptions at discharge between opioid-naive patients with acute-on-chronic pancreatitis and patients with AP.

GRADE Certainty of Evidence: Very low.

Strength of recommendation: Weak.

Consensus agreement: 89.4%

11.8.2 | *Comment*

There was no significant difference in opioid prescriptions at discharge between opioid-naive patients with acute-on-chronic

TABLE 2 | Summary of consensus statements.

Chapter		Statement	Certainty of evidence	Recommendation strength	Consensus (%)
1. Acute pain management in general	1.1	Recommendations from non-specific acute pain guidelines may be applied to AP as disease-specific guidelines for AP are lacking.	Good practice statement-ungraded	Weak	97.3
	1.2	Escalation of analgesic therapy in AP can follow principles used in other acute pain conditions.	Good practice statement-ungraded	Weak	94.7
2. Pathophysiology	2.1	Pain in AP involves mixed mechanisms (nociceptive and neuropathic), with possible central sensitization.	Good practice statement-ungraded	Weak	92
3. Pain assessment	3.1	Multidimensional pain assessment may be considered given its established benefit in chronic pancreatitis.	Good practice statement-ungraded	Weak	95
	3.2	General acute pain practices can be used with respect to assessment frequencies (every 5–60 min depending on intensity).	Good practice statement-ungraded	Weak	95
	3.3	Numeric rating scale (NRS) may be preferred over VAS due to better patient compliance however, both scales are equally suited for acute pain management in general.	Good practice statement-ungraded	Moderate	92
	3.4	Pain relief may be a useful outcome metric, though superiority over pain intensity is unproven.	Good practice statement-ungraded	Weak	87
4. Pharmacological treatment	4.1	WHO analgesic ladder may be sufficient for mild–moderate pain; opioids may be required early in severe AP, and a step-down may be warranted upon presentation.	Very low	Weak	90
	4.2	Strong opioids such as buprenorphine and pentazocine provide better pain relief and reduce the need for rescue analgesia compared to non-opioid medications like NSAIDs in patients hospitalized with AP.	Low	Weak	93
	4.3	Opioids are not associated with increased adverse outcomes and should not be delayed due to safety concerns to ensure adequate severe pain control.	Low	Weak	90
	4.4	NSAIDs do not seem to worsen the severity of AP, and COX-2 inhibitors may reduce progression to severe disease.	Low	Weak	100
	4.5	Patient-controlled analgesia should be used cautiously and is not routinely recommended in AP	Very low	Weak	95
	4.6	We suggest against the use of unconventional analgesics in standard clinical practice, as their role in analgesic efficacy and improvement in patient-reported outcomes is only experimental.	Very low	Weak	97
	4.7	Safety profile of unconventional analgesics remains unclear; we suggest against their use in standard clinical practice.	Very low	Weak	100

(Continues)

TABLE 2 | (Continued)

Chapter		Statement	Certainty of evidence	Recommendation strength	Consensus (%)
	4.8	Local complications may contribute to pain in AP, and these should be actively identified and managed.	Good practice statement-ungraded	Weak	100
5. Epidural analgesia	5.1	We recommend epidural analgesia combined with standard care over standard care alone, as it improves patient-reported outcomes and quality of life, particularly in severe acute pancreatitis, provided local expertise is available.	Good practice Statement-ungraded	Weak	92
	5.2	Epidural analgesia may improve respiratory outcomes and survival; however, we suggest against its routine use due to inconsistent evidence.	Low	Weak	94.7
	5.3	Epidural analgesia is a safe option with appropriate monitoring and aseptic technique and may be considered for AP pain management where local expertise is available.	Moderate	Strong	97
	5.4	The role of epidural analgesia in preventing chronic pain after acute pancreatitis remains unclear, and further research is needed.	Good practice statement-ungraded	Weak	86
6. Complementary therapies	6.1	CHM formula chaiqin chengqi decoction may improve symptoms but has limited evidence and potential risks	Low	Weak	81
	6.2	Acupuncture may reduce abdominal pain and time to oral intake without significant side effects	Low	Weak	82.8
7. Impact of pain control	7.1	Adequate pain control may improve tolerance to enteral feeding and reduce time to oral intake; non-opioid analgesics may be preferable due to opioid-related gastrointestinal side effects.	Good practice statement-ungraded	Weak	95
	7.2	Suboptimal pain control may increase risk of organ dysfunction (lungs, kidneys, heart) and reduce mobilization.	Good practice statement-ungraded	Weak	92
	7.3	Pain relief reduces ileus, which in turn helps lower intra-abdominal hypertension and indirectly reduces thromboembolic risk through earlier mobilization.	Low	Weak	92.5
	7.4	Adequate pain control may reduce risk of complications associated with central nervous system sensitisation such as chronic pain and opioid dependence.	Good practice statement - ungraded	Weak	95
	7.5	Effective pain management may improve compliance with enhanced recovery pathways especially in mild AP	Very low	Weak	92.5
	7.6	Adequate pain control may shorten recovery time and improve return to daily activities and return to work periods.	Good practice statement-ungraded	Weak	97
	7.7	Adequate pain control improves quality of life and reduces psychological stress.	Good practice statement-ungraded	Weak	85

(Continues)

TABLE 2 | (Continued)

Chapter		Statement	Certainty of evidence	Recommendation strength	Consensus (%)
	7.8	Adequate pain relief may improve comfort and mobility and reduce complications. However, its impact on length of stay and readmissions remains unclear	Low	Weak	95
8. Special populations	8.1	In children, we suggest the type of analgesics (opioid vs. non-opioid) used does not affect outcomes such as length of stay or intensive care admission.	Very low	Weak	84
	8.2	We suggest considering early oral feeding in children, as it does not worsen pain or length of stay.	Low	Weak	84
	8.3	Multidisciplinary pain management can be extrapolated from postoperative settings and may be considered in paediatric AP	Good practice statement-ungraded	Weak	94.1
	8.4	Epidural analgesia may be more effective than opioids in pregnancy in relieving AP pain, though evidence is limited.	Very low	Weak	84
9. Discharge & follow-up	9.1	There is insufficient evidence that scheduled follow-up visits improve the risk of readmissions or quality of life after discharge. Further research is warranted	Good practice statement-ungraded	Weak	100
	9.2	Routine scheduled imaging is not recommended for patients discharged with pain after acute pancreatitis; however, imaging should be considered in cases of recurrent or escalating pain to exclude complications.	Good practice statement - ungraded	Weak	89.5
	9.3	EUS may be considered when aetiology remains unclear.	Good practice statement-ungraded	Weak	84.2
	9.4	Routine CT follow-up is not recommended unless clinically indicated or in unexplained aetiology.	Good practice statement-ungraded	Weak	84
	9.5	MRCP may be useful to assess the cause of pancreatitis related to ductal anomalies and routine follow-up MRCP is not recommended.	Good practice statement-ungraded	Weak	92.1
	9.6	No strong evidence linking alcoholic aetiology to increased opioid use at discharge; opioids may be considered to ensure adequate pain relief at discharge in both alcohol and biliary AP	Good practice statement-ungraded	Weak	84.1
	9.7	Recurrent AP may increase likelihood of opioid requirement post-discharge; more research is warranted to explore contribution of nociplastic changes in pain processing.	Very low	Weak	89.4
	9.8	To consider no difference in new opioid prescriptions at discharge between AP and acute-on-chronic pancreatitis	Very low	Weak	89.4

Abbreviations: AP: Acute pancreatitis; CHM: Chinese Herbal Medicine; COX-2: Cyclooxygenase 2; EUS: endoscopic Ultrasound; MRCP: Magnetic resonance cholangiopancreatography; NSAIDs: Non-steroidal anti-inflammatory drugs.

pancreatitis and patients with AP in a single-centre study [243]. More research is needed to further elucidate this issue.

12 | Discussion

The current guidelines have proposed an important set of recommendations on the management of AP pain, including the role of opioids in pain relief, epidural analgesia, complementary treatments, and pain management in the paediatric population. The statements are summarised in Table 2.

The recommendations from acute postoperative pain guidelines are applicable for treating acute pain due to AP, and escalation of treatment intensity for AP-related pain can be performed similarly to that used in other acute pain situations if no contraindications are applicable. The numerical rating scale is preferred for pain assessment because of better compliance. For mild to moderate pain, simple analgesics may be sufficient for achieving pain control. For severe pain, opioids may be warranted upon presentation. Strong opioids, especially buprenorphine and pentazocine, provide superior pain relief over non-opioid medications in terms of pain control and decreased need for rescue analgesia. There does not appear to be an increased risk of adverse outcomes in AP related to opioid treatment. Safety concerns should not delay the timely use of opioids to ensure adequate pain management.

Acupuncture appears to be effective in relieving abdominal pain and reducing the time to oral intake without significant side effects in patients with AP and should be considered where expertise is available. Consideration of Traditional Chinese Medicine and Acupuncture outside China may not be feasible due to lack of regulatory approvals, implementation barriers and definite lack of proven efficacy from randomised controlled trials Epidural analgesia appears to be a safe and effective pain management option in AP and may provide superior pain relief compared to standard care alone. In children with AP, the type of administered analgesics (opioid vs. non-opioid) does not appear to affect length of stay or admission in intensive care. In children, a multidisciplinary approach to pain management, including the use of simple analgesics, opioids, interventional procedures, and behavioural pain management interventions should be considered.

Statements from various working groups have also identified several areas of unmet needs in pain management in AP.

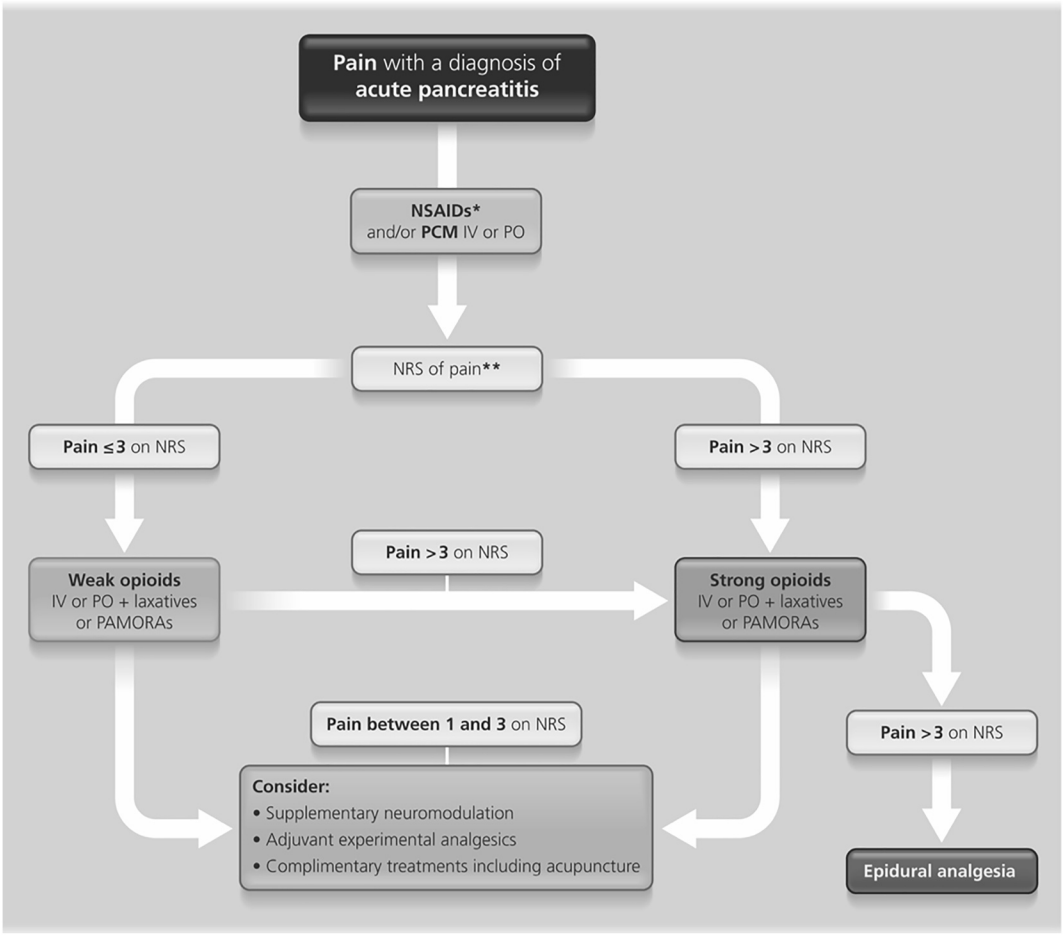

FIGURE 2 | Treatment algorithm for acute pancreatitis pain management. NRS: Numerical rate scale of intensity (0–10); PCM: Paracetamol; NSAID: Nonsteroidal anti-inflammatory drugs; PAMORA: peripheral acting μ-opioid receptor antagonist; Neuromodulation: acupuncture and transcutaneous electrical nerve stimulation. Epidural anesthesia can be used instead of strong opioids where available. *Recent data have shown that COX2-selective NSAIDS may offer better pain relief and reduce severity. **In the near future, a specific questionnaire developed to assess pain in AP(CAPPOS) may replace NRS.

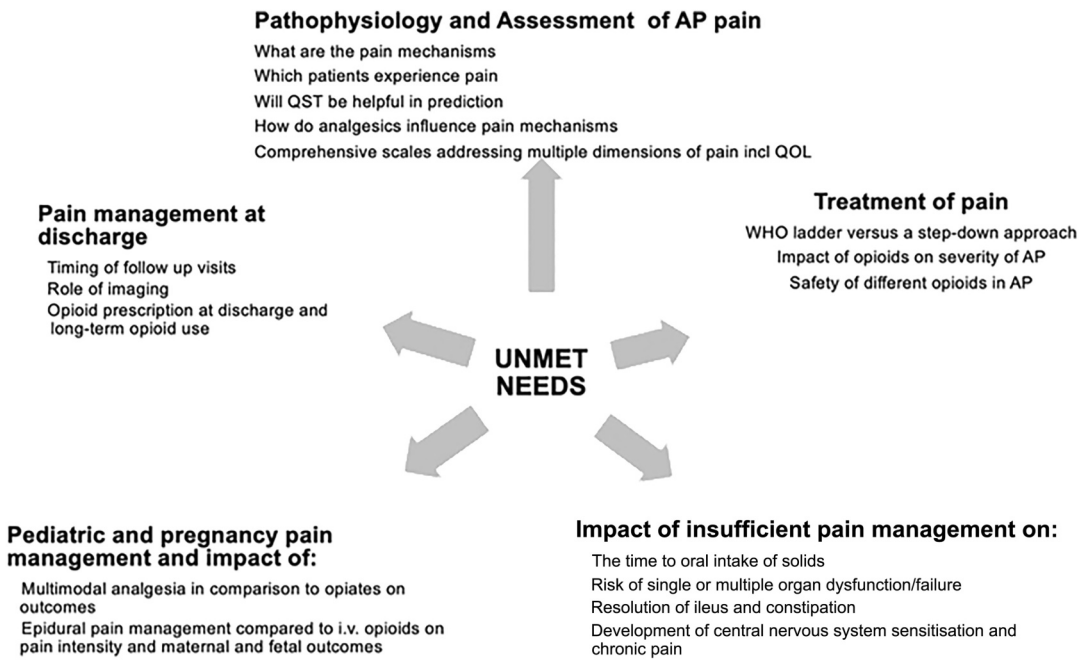

FIGURE 3 | Unmet needs in acute pancreatitis pain research.

Several domains of acute pain, such as psychological impact and impact on quality of life during hospitalisation and after discharge, have not been explored in AP pain. This is further reflected in the lack of an AP-specific pain assessment score. The 'CAPPOS initiative' to develop a multidimensional pain assessment instrument specific to AP is a step forward to address this unmet need [244].

Pain management is another area that needs further evidence to explore the role of, for example, a step-down approach for pain management as opposed to the conventional step-up approach based on the WHO ladder. Recent RCT data on the use of COX-2 inhibitors for improving pain and reducing the severity of AP [124] is an important addition to the pain literature. This was not fully addressed in the current guidelines, as the data were published post-completion of the guidelines. It also remains to be studied whether optimal pain management can improve the outcome via indirect effects on mobilisation, food intake, and renal and lung function. However, for ethical reasons, such studies will be difficult to design. Pain management post-discharge is another area with significant paucity of data. In patients with persistent or worsening pain, it is important to ensure adequate analgesic treatment and to investigate potential complications or alternative causes of the pain. When opioid therapy is required, a clear follow-up plan should be in place to minimize the risk of prolonged and harmful use. The frequency of follow-up for the assessment of pain, long-term opioid use, and the role of imaging in diagnosing post-pancreatitis complications may predict the need for pain medication. Post-pancreatitis complications are frequent after moderately severe and severe AP and are likely to worsen pain. Increasing pain and obstructive symptoms are often the indications for drainage of walled of necrosis. Although it seems logical that endoscopic or percutaneous interventions could alleviate pain, evidence to support this hypothesis in the literature is lacking. Furthermore, the impact of ongoing pain at the time of discharge on the development of chronic pain is unknown. Based on the available evidence, we propose a treatment algorithm for pain management for health care providers when patients are admitted with painful AP, based on the evidence published so far (Figure 2). It is important to acknowledge that the evidence to support the algorithm is low quality and clinicians should apprise themselves with emerging evidence to assist pain management in AP. The unmet needs are further summarised in (Figure 3).

13 | Conclusion

The guidelines systematically reviewed all aspects of pain management AP. Consensus was reached on all the statements. The guidelines process also identified unmet needs in all statements, emphasising the priority areas for future research in pain management in AP.

These guidelines will be reviewed and revised within 5 years or as new evidence emerges in pain management in AP.

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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Disclaimer

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

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