Oncology Treatment Discovery, 2026, Volume 4, Issue 2
http://ojs.bbwpublisher.com/index.php/OTD
Online ISSN: 2981-8079
Print ISSN: 3083-4996

Cancer Pain in Adults: Contemporary Approaches to Assessment, Phenotyping, and Multimodal Management

Liying Yang[1], Mengnan Du[2,3], Huiling Liu[2,3], Yunchao Zhang[2,3,4], Wentao Li[2,3,4], Dan Yi[2,3,4]*

[1]Tianjin University of Traditional Chinese Medicine, Tianjin 301617, China
[2]First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300000, China
[3]National Clinical Research Center for Chinese Medicine, Tianjin 300000, China
[4]Tianjin Cancer Institute of Traditional Chinese Medicine, Tianjin 300000, China

***Corresponding author:** Dan Yi, 834871221@qq.com

Abstract: As one of the most prevalent and burdensome symptoms across the cancer continuum, cancer pain affects patients with active disease, those approaching the end of life, and a growing population of long-term survivors. Despite advances in supportive oncology, clinically meaningful gaps in pain control persist. These gaps increasingly reflect limitations in implementation, inequitable access to care, delayed recognition of structural pain generators, and inconsistent integration of interdisciplinary services rather than a simple lack of therapeutic options. This narrative review provides a clinically oriented synthesis of contemporary guidelines and selected high-impact evidence on adult cancer pain management. We review the pathophysiology of cancer pain, multidimensional assessment, phenotype-informed pharmacologic strategies, disease-directed interventions, and nonpharmacologic supportive approaches. We also examine the tension between rational opioid stewardship and the risk of undertreatment in the context of the opioid crisis. Contemporary cancer pain management requires individualized, mechanism-informed care that extends beyond linear analgesic escalation. Three practical themes emerge from current evidence and guideline synthesis: first, routine multidimensional assessment is needed to distinguish nociceptive, neuropathic, mixed, and temporal pain phenotypes; second, disease-directed interventions such as palliative radiotherapy should be considered early when they address the underlying pain generator; and third, proactive multidisciplinary collaboration is essential to address functional impairment, psychosocial distress, and barriers to equitable care delivery.

Keywords: Cancer pain; Palliative care; Opioid analgesics; Neuropathic pain; Breakthrough cancer pain; Survivorship

Online publication: June 30, 2026

1. Introduction

Cancer pain remains a major source of suffering despite substantial advances in oncology and supportive

care. It is strongly associated with impaired physical function, sleep disturbance, psychological distress, and reduced quality of life [1,2]. Although pain is often most prominent in advanced disease, it is also highly prevalent during active anticancer treatment and among long-term survivors [1,3,4].

Importantly, cancer pain is not a single entity but a heterogeneous clinical syndrome arising from tumor invasion, treatment-related injury, inflammation, nerve damage, and structural instability [5–7]. Nociceptive and neuropathic mechanisms frequently coexist, while temporal features such as incident pain, end-of-dose failure, and breakthrough exacerbations further shape the clinical picture. As a result, pain intensity scores alone are insufficient to define the underlying biology or guide optimal treatment [8,9].

Historically, cancer pain management has been framed by the World Health Organization analgesic ladder. While that model remains influential, contemporary practice increasingly emphasizes repeated multidimensional assessment, recognition of pain phenotypes, early treatment of reversible structural causes, and timely integration of palliative and supportive care services [8,10–12]. A particularly important component of this shift is the accurate recognition and management of breakthrough cancer pain (BTcP), which remains common, disabling, and frequently misclassified [13,14].

Despite the availability of established guidelines, meaningful gaps persist between evidence-based recommendations and routine practice [15–17]. In many settings, these gaps reflect implementation failures, inequities in access, delayed referral, and the unintended consequences of restrictive opioid policies rather than a simple lack of analgesic options. This narrative review provides an interpretive clinical synthesis of contemporary guidelines and selected high-impact literature on adult cancer pain, with a focus on pathophysiology, multidimensional assessment, phenotype-guided treatment, and major barriers to effective implementation. To provide a practical overview of the clinical framework discussed throughout this review, a proposed algorithm for adult cancer pain assessment and management is presented in **Figure 1**.

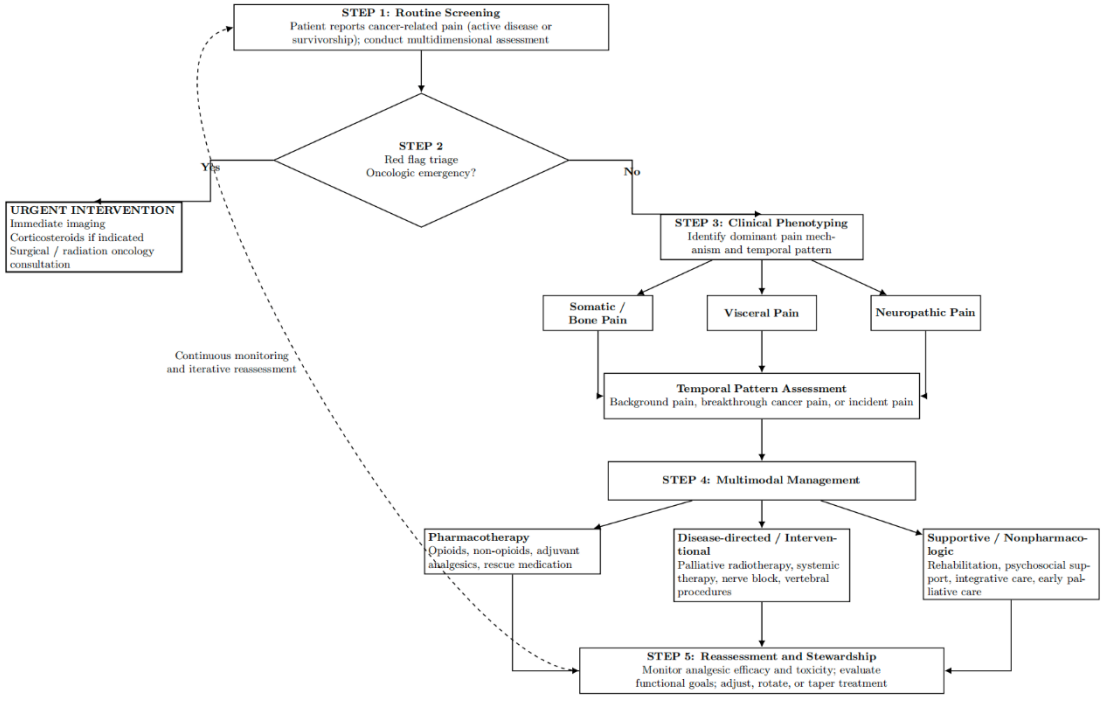

Figure 1. Proposed clinical algorithm for adult cancer pain assessment and management.

Patients with cancer-related pain should first undergo routine screening and multidimensional assessment. Red flag findings suggestive of oncologic emergencies warrant urgent evaluation and disease-directed intervention. In the absence of emergencies, pain should be phenotyped according to dominant mechanism and temporal pattern, followed by multimodal management incorporating pharmacologic, disease-directed/interventional, and supportive strategies. Continuous monitoring and iterative reassessment are required to optimize analgesia, reduce toxicity, and guide treatment adjustment.

2. Narrative review methodology

2.1. Rationale and review design

Given the breadth of adult cancer pain management—encompassing epidemiology, pathophysiology, assessment, pharmacologic treatment, interventional approaches, rehabilitation, and survivorship—a systematic review format was not considered the most appropriate design for the present article. Instead, we conducted an interpretive narrative review intended to provide a clinically focused synthesis of major contemporary guidelines and selected high-impact literature. The aim was to integrate evidence across domains and organize it into a practical framework for oncologists, palliative care clinicians, pain specialists, and supportive care teams.

2.2. Eligibility criteria

To structure the review, literature selection was guided by predefined eligibility criteria informed by the Population, Intervention, Comparison, Outcomes, and Study type [PICOS] framework. The population of interest included adults (≥ 18 years) with cancer-related pain across electronic patientreported outcomes(ePROs), the disease continuum, including active disease and survivorship; pediatric populations were excluded. Interventions of interest included pharmacologic analgesics, adjuvant agents, palliative radiotherapy, interventional pain procedures, rehabilitation, and psychosocial or integrative supportive strategies. Outcomes of interest included pain intensity, functional interference, quality of life, and treatment-related adverse effects. Priority was given to clinical practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, and clinically influential landmark studies. Basic science studies without direct clinical translation, non-indexed case reports, and pediatric-only literature were excluded.

The primary search focused on English-language publications from January 2010 through January 2025. Older landmark studies were retained selectively when they established widely used assessment instruments or foundational diagnostic criteria.

2.3. Search strategy and methodological limitations

A structured search of PubMed/MEDLINE was conducted in January 2025 using combinations of the following terms: “cancer pain,” “adult cancer pain,” “breakthrough cancer pain,” “neuropathic cancer pain,” “bone metastases pain,” “palliative radiotherapy,” “cancer survivorship pain,” “chemotherapy-induced peripheral neuropathy,” “opioid stewardship,” and “palliative care integration.” Additional targeted searches were performed on the official websites of major professional organizations, including American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), National Comprehensive Cancer Network (NCCN), and American Society for Radiation Oncology (ASTRO), to identify the most

recent clinical practice guidelines and related guidance documents [3,8,9,11,12,18]. Reference lists of included reviews and guideline documents were also screened selectively to identify major landmark studies.

As a narrative review, this article has important methodological limitations. The search relied primarily on a single bibliographic database and did not include a formal multi-database systematic screening process. Study selection was interpretive rather than protocol-driven, and no quantitative meta-analysis or formal risk-of-bias assessment was performed. Accordingly, this review should be interpreted as a clinically informed synthesis of contemporary guidelines and major studies rather than as an exhaustive systematic evidence review or a formal evidence-graded guideline.

3. Epidemiology and clinical burden

Cancer pain affects a substantial proportion of patients across the disease trajectory. Systematic review data indicate a high prevalence in advanced or terminal disease, substantial symptom burden during active anticancer treatment, and a persistent burden of post-treatment pain among survivors [1,3,4]. As cancer survivorship expands, chronic cancer-related and treatment-related pain is becoming an increasingly important component of long-term supportive care.

The burden of cancer pain extends well beyond sensory discomfort. Pain commonly interferes with mobility, sleep, mood, work, social participation, and adherence to cancer treatment, thereby contributing to overall loss of function and diminished quality of life [2,19,20]. These broader impacts underscore the need for multidimensional assessment rather than reliance on unidimensional intensity scores alone.

Despite the availability of effective pharmacologic and nonpharmacologic therapies, undertreatment remains common. Contributing factors include inadequate assessment, delayed recognition of structural or neuropathic drivers of pain, fragmented referral pathways, inequitable access to palliative and supportive care services, and clinician hesitation related to opioid prescribing [8,9,17,21].

4. Pathophysiology and clinical phenotyping

Effective management of cancer pain depends not only on symptom intensity, but also on identifying the dominant pain mechanism, associated structural drivers, and temporal pattern. In practice, this requires translating pathophysiology into clinically recognizable phenotypes that can inform targeted multimodal treatment. Rather than treating all pain exacerbations as a signal for linear opioid escalation, clinicians should evaluate whether the presentation is primarily nociceptive, neuropathic, mixed, structurally unstable, or temporally episodic [5-8].

4.1. Nociceptive syndromes

Nociceptive pain arises from activation of peripheral nociceptors by tissue injury, inflammation, or mechanical distortion. In cancer, this often reflects tumor infiltration, capsular stretch, visceral obstruction, or osseous destruction.

Somatic pain is typically well localized and described as aching, throbbing, or pressure-like. Bone pain is the most prominent somatic phenotype in oncology. Its pathogenesis is multifactorial, involving inflammatory mediators, osteoclast activation, microfracture, structural instability, and mechanical stress [6,22,23]. This complexity helps explain why systemic analgesics alone may be insufficient and why disease-

directed therapies, particularly radiotherapy or stabilization procedures, are often necessary components of pain control [8,12].

Visceral pain is more often diffuse, cramping, squeezing, or poorly localized. It may arise from capsular distension, hollow-organ obstruction, ischemia, or mucosal infiltration [6,23]. In selected settings, symptom relief depends not only on analgesics but also on treatment of the underlying driver, such as decompression, corticosteroids, or bowel-directed supportive measures.

4.2. Neuropathic syndromes

Neuropathic cancer pain results from injury to the somatosensory nervous system. Common causes include direct tumor invasion of nerves or plexuses, spinal cord or nerve root compression, surgery, radiotherapy, and neurotoxic chemotherapy [5,6,18,24]. Patients often describe burning, shooting, stabbing, tingling, or electric shock-like pain, sometimes accompanied by numbness, sensory loss, or allodynia [5,25].

Neuropathic features are clinically important because they are associated with greater functional impairment and may respond incompletely to opioid monotherapy [5,8]. Their recognition should prompt consideration of adjuvant analgesics and, when clinically indicated, urgent evaluation for reversible structural causes such as nerve root compression or epidural disease [8,9,26].

4.3. Sensitization and neuroimmune amplification

Persistent nociceptive and neuropathic signaling can drive both peripheral and central sensitization. Tumor cells, immune cells, and injured nerves release cytokines, growth factors, and excitatory neurotransmitters that amplify nociceptive transmission [6,7,27]. Clinically, this neuroimmune crosstalk may contribute to disproportionate pain severity, widening pain distribution, allodynia, hyperalgesia, and reduced responsiveness to standard analgesic strategies. Recognition of these processes is relevant because it helps explain why some patients with mixed or longstanding pain do poorly with opioid escalation alone and may require a broader multimodal approach.

4.4. Temporal phenotypes: Background vs. breakthrough pain

Temporal pattern is a central component of cancer pain phenotyping. Patients may present with relatively stable background pain, movement-related incident pain, end-of-dose failure, or breakthrough cancer pain (BTcP) [9,13,14]. These temporal patterns are not interchangeable and distinguishing them is essential for selecting appropriate rescue medication, adjusting baseline regimens, and identifying when disease progression or structural instability should be suspected. End-of-dose failure should not be misclassified as BTcP, because it generally indicates the need to reassess the maintenance opioid regimen rather than simply increase rescue dosing [9,13].

5. Clinical assessment framework

Comprehensive assessment is the foundation of mechanism-informed cancer pain management. Numerical intensity scores are useful but insufficient in isolation. Evaluation should include pain location, radiation, quality, temporal pattern, precipitating factors, likely mechanism, impact on function, previous analgesic response, and associated psychosocial distress [8,9,19,20]. A clinically useful assessment also distinguishes pain at rest from pain on movement, as incident pain often reflects structural pathology or instability that may

require more than medication adjustment.

Validated instruments can improve assessment consistency. The Brief Pain Inventory (BPI) captures both pain severity and functional interference [19]. The Edmonton Symptom Assessment System (ESAS) situates pain within the broader symptom context, including fatigue, nausea, anxiety, and depression [20]. The DN4 questionnaire may assist in identifying neuropathic features, although it should complement rather than replace clinical judgment [25].

A critical component of assessment is the identification of oncologic emergencies and other reversible causes of severe pain. New or rapidly worsening back pain, focal neurologic deficits, bladder or bowel dysfunction, or pain associated with suspected mechanical instability should prompt urgent evaluation for malignant spinal cord compression, epidural disease, or pathologic fracture [8,26,28,29]. More broadly, clinicians should routinely reassess whether apparent analgesic failure reflects undertreated baseline pain, a new neuropathic or structural pain generator, toxicity from prior treatment, or progressive disease.

6. Comparison of major guideline recommendations

Major professional organizations, including ESMO, NCCN, and ASCO, have issued influential guidance relevant to adult cancer pain management [3,8,9,11,18]. These documents share core principles, comprehensive assessment, individualized multimodal treatment, appropriate opioid use, and interdisciplinary care, but differ in emphasis according to target population and intended scope. NCCN provides highly operational clinical algorithms for active cancer pain, ESMO offers a broad pharmacologic and palliative framework, and ASCO has contributed particularly important guidance in survivorship, chemotherapy-induced peripheral neuropathy, and early palliative care integration [3,11,18]. **Table 1** summarizes selected cross-guideline themes.

Because these guidelines differ in methodology, update cycle, and clinical scope, they should be interpreted as complementary rather than directly interchangeable documents.

Table 1. Comparison of core cancer pain recommendations from major guidelines

Domain	ESMO (2018) [8]	NCCN (Version 2.2024) [9]	ASCO (2016, 2020) [3,18]
Assessment	Emphasizes detailed history, physical examination, and routine use of validated scales	Highly operational algorithms for comprehensive and urgent assessment	Focuses on survivorship assessment, functional interference, and CIPN
Opioid strategy	Morphine, oxycodone, hydromorphone as first-line for moderate/severe pain; detailed titration rules	Stepwise algorithms for opioid-naïve vs. opioid-tolerant patients	Recommends cautious long-term opioid prescribing for survivors; emphasizes risk assessment
Neuropathic pain	Recommends TCAs and gabapentinoids as adjuvants	Integrates adjuvants early; specific pathways for nerve compression	Strong recommendation for duloxetine in CIPN
Breakthrough pain	Advocates rapid onset transmucosal fentanyl for selected patients	Defines BTcP and end-of-dose failure; guides rescue dosing	Addressed within broader symptom management contexts
Interdisciplinary/ interventional care	Highlights palliative radiotherapy and early referral to pain specialists	Integrates interventional blocks, pumps, and neurosurgical consultation in refractory pathways	Landmark guidance on early integration of palliative care and rehabilitative strategies

Abbreviations: ASCO, American Society of Clinical Oncology; BTcP, breakthrough cancer pain; CIPN, chemotherapy-induced peripheral neuropathy; ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Cancer Network; TCA, tricyclic antidepressant.

7. Pharmacologic management

Pharmacologic treatment should be tailored to the pain mechanism, temporal profile, comorbidity burden, organ function, and goals of care. In contemporary practice, analgesic selection is not simply a matter of escalating drug potency; rather, it involves matching the regimen to the dominant pain phenotype while also considering whether disease-directed or interventional treatment is needed to address the underlying pain generator. The quality of evidence varies substantially across analgesic classes and clinical phenotypes, making regular reassessment essential.

7.1. Nonopioid analgesics

Nonopioid agents remain important components of multimodal analgesia. Acetaminophen may provide modest benefit in selected mixed-mechanism syndromes, although its independent analgesic effect in severe cancer pain is weak [8,30]. NSAIDs are particularly useful in inflammatory and bone-related pain phenotypes, where they may reduce opioid requirements and improve pain on movement. However, gastrointestinal, renal, and cardiovascular toxicities necessitate careful patient selection, especially in older adults and those with frailty, dehydration, thrombocytopenia, or baseline renal dysfunction [8,30].

Corticosteroids may be helpful in selected situations, including pain related to raised intracranial pressure, nerve compression, capsular distension, or malignant bowel obstruction [9,31–33]. Their use is generally best viewed as indication-specific and time-limited, given the risks of hyperglycemia, proximal myopathy, delirium, immunosuppression, and mood disturbance.

7.2. Opioids: Balancing access and the opioid crisis

Opioids remain the cornerstone of treatment for moderate to severe cancer pain, particularly when pain is clearly nociceptive or mixed and is causing substantial functional suffering [8,9,34]. Agent selection, route of administration, and formulation should be individualized according to prior opioid exposure, pain severity, swallowing ability, renal and hepatic function, and the need for rapid titration.

At the same time, contemporary oncology practice must navigate the tension between appropriate opioid stewardship and the risk of undertreatment. Policies developed in response to the broader opioid crisis have, in some settings, created unintended barriers for patients with cancer, including delayed dispensing, prior authorization hurdles, pharmacy denials, and dose-limit restrictions that do not adequately account for cancer-related suffering [15,17,21]. Clinicians should therefore practice rational opioid stewardship, using risk assessment, prescription monitoring, patient education, and careful follow-up, without allowing regulatory anxiety to normalize undertreatment of severe cancer pain [8,17,21,34]. Opioid restrictions developed for chronic non-cancer pain should not be indiscriminately applied to patients with active cancer, as undertreatment of severe pain poses a greater immediate clinical risk.

Equally important, opioid dose escalation should not substitute for mechanistic reassessment. Escalating doses in the setting of neuropathic pain, spinal instability, incident bone pain, or opioid-related neurotoxicity may worsen outcomes if the underlying structural or pharmacologic problem is not recognized [5,12,26,35,36].

7.3. Adjuvant analgesics

Adjuvant analgesics are particularly relevant for neuropathic and mixed-mechanism pain. Among these agents, duloxetine has the strongest direct evidence for painful chemotherapy-induced peripheral neuropathy (CIPN) and is specifically supported by ASCO guidance in that context [18,37].

By contrast, the evidence base for gabapentinoids in cancer-related neuropathic pain is more limited and heterogeneous than their widespread clinical use might suggest [38–40]. Gabapentin and pregabalin may still be reasonable in selected patients, particularly when neuropathic features are prominent, but clinicians should monitor carefully for sedation, dizziness, gait instability, and additive central nervous system toxicity, especially in frail or older adults [41]. Tricyclic antidepressants and other adjuvants are also used in practice, although tolerability often limits their role in medically complex oncology populations [8,24,40].

For refractory pain, particularly when systemic toxicity limits further escalation, referral for specialist pain or palliative care assessment is appropriate. In carefully selected patients, neuraxial techniques or intrathecal drug delivery may reduce systemic opioid burden and improve analgesia [8,24,43].

7.4. Safety monitoring and adverse-effect management

Analgesic therapy should be accompanied by proactive monitoring and prevention of predictable toxicities. Opioid-induced constipation is common and should generally be managed prophylactically with bowel regimens unless contraindicated [8,9,34]. Sedation, delirium, cognitive slowing, and impaired balance warrant close surveillance, particularly in older adults, patients with pre-existing cognitive vulnerability, and those receiving concomitant sedatives [35,36,41].

Opioid-induced neurotoxicity may present with myoclonus, hallucinations, agitation, or paradoxical hyperalgesia and is often precipitated by dehydration, infection, or accumulation of renally cleared metabolites [35,36]. Respiratory depression is rare with appropriate opioid titration for cancer pain, but risk increases with concurrent sedative use, renal impairment, advanced frailty, or rapid dose escalation. Regular reassessment of analgesic benefit relative to toxicity should therefore accompany all opioid prescribing [34–36].

Key pharmacologic options for adult cancer pain management, together with representative indications, limitations, and major safety considerations, are summarized in **Table 2**.

Table 2. Representative pharmacologic approaches to adult cancer pain management

Class / Intervention	Representative agents	Typical clinical role	Key cautions/limitations
Nonopioid analgesics	Acetaminophen	Adjunct for mild to moderate mixed-mechanism pain; may modestly support opioid-sparing	Limited independent efficacy in severe cancer pain; dose caution in hepatic impairment
Nonopioid analgesics	NSAIDs	Particularly useful in inflammatory and bone-related pain; may improve pain on movement	Renal, gastrointestinal, cardiovascular, and bleeding risks; caution in frailty, thrombocytopenia, dehydration
Corticosteroids	Dexamethasone, prednisone	Indication-specific use in nerve compression, capsular distension, raised intracranial pressure, malignant bowel obstruction	Hyperglycemia, delirium, proximal myopathy, mood effects, immunosuppression; generally time-limited use
Strong opioids	Morphine, oxycodone, hydromorphone	Mainstay for moderate to severe nociceptive or mixed cancer pain	Sedation, constipation, delirium, respiratory risk, dose escalation without reassessment; metabolite accumulation in renal dysfunction for some agents
Rapid-onset rescue opioids	Transmucosal fentanyl formulations	Selected opioid-tolerant patients with true BTcP characterized by rapid onset and short duration	Requires careful patient selection and education; not appropriate for opioid-naïve patients

Class / Intervention	Representative agents	Typical clinical role	Key cautions/limitations
Short-acting rescue opioids	Immediate-release morphine, oxycodone, hydromorphone	Rescue dosing for episodic pain after optimization of background regimen	Overuse may signal uncontrolled baseline pain, end-of-dose failure, or a new structural pain generator
Adjuvant analgesics for neuropathic pain	Duloxetine	Best-supported option for painful CIPN; may help selected neuropathic phenotypes	Nausea, fatigue, drug interactions; not universally effective for all neuropathic cancer pain
Adjuvant analgesics for neuropathic pain	Gabapentin, pregabalin	Commonly used for neuropathic features or mixed pain	Sedation, dizziness, gait instability, cognitive adverse effects; renal dose adjustment often required
Adjuvant analgesics for neuropathic pain	TCAs	Occasionally used in selected neuropathic syndromes	Anticholinergic effects, orthostasis, arrhythmia risk; often poorly tolerated in older or frail patients
Specialist analgesic strategies	Neuraxial analgesia, intrathecal drug delivery	Refractory pain or systemic toxicity limiting conventional escalation	Requires specialist expertise, careful selection, and procedural resources

Abbreviations: BTcP, breakthrough cancer pain; CIPN, chemotherapy-induced peripheral neuropathy; NSAIDs, nonsteroidal anti-inflammatory drugs; TCA, tricyclic antidepressant.

8. Breakthrough Cancer Pain (BTcP) management

BTcP is typically defined as a transient exacerbation of severe pain occurring despite relatively controlled background pain [13,14]. Episodes may be spontaneous or precipitated by predictable triggers such as movement, swallowing, coughing, or procedures. They are often rapid in onset and short in duration, although substantial interpatient variability exists [13,14].

Accurate characterization is essential because not all pain flares represent BTcP. Clinicians should distinguish true BTcP from end-of-dose failure, uncontrolled baseline pain, and pain caused by new structural progression [9,13]. Apparent “breakthrough” episodes that occur predictably before the next scheduled opioid dose usually indicate inadequate baseline coverage rather than a separate rescue-only phenomenon. Similarly, recurrent movement-evoked flares may signal unstable bone metastases or other treatable mechanical causes.

Once background pain is reasonably optimized, rescue treatment may include short-acting oral opioids or, in appropriately selected opioid-tolerant patients, rapid-onset transmucosal fentanyl formulations [9,34]. Choice of rescue agent should be guided by the onset, predictability, and duration of episodes, along with patient-specific factors such as route tolerance, prior opioid exposure, and safety risk.

9. Disease-directed and interventional strategies

Analgesia should not distract from the need to treat the underlying pain generator whenever feasible. In many patients, effective pain control depends on combining pharmacologic treatment with disease-directed or structurally targeted interventions.

Palliative radiotherapy is a key example and should be considered early for painful bone metastases, particularly when pain is localized and attributable to a radiographically defined lesion [12,42]. Single-fraction regimens provide meaningful relief for many patients and offer practical advantages in convenience and treatment burden [12,42]. Radiotherapy is therefore best understood not as a late salvage option, but as an important analgesic modality in its own right.

Mechanical instability requires urgent recognition. New back pain in the setting of spinal metastases

should prompt assessment for epidural extension, vertebral collapse, or neoplastic instability, with tools such as the Spinal Instability Neoplastic Score helping to structure decision-making [26,28]. Depending on neurologic status and structural findings, patients may require urgent imaging, corticosteroids, surgical consultation, decompression, or stabilization [26,28,29].

Selected interventional procedures can also provide meaningful opioid-sparing benefits. For example, celiac plexus neurolysis may reduce pain burden in pancreatic cancer, while neuraxial or intrathecal approaches may be appropriate in refractory cases managed by experienced teams [24,43,44].

10. Nonpharmacologic and supportive interventions

Nonpharmacologic approaches should be viewed as integral components of comprehensive cancer pain care rather than optional adjuncts reserved for refractory cases. Their greatest value often lies in reducing pain interference, improving coping, restoring function, and addressing the psychological and behavioral dimensions of suffering.

10.1. Rehabilitation and physical therapy

Rehabilitation remains underused in cancer pain management. Physical therapy, graded activity, gait training, mobility aids, and targeted exercise can reduce pain interference and improve function, particularly in patients with deconditioning, altered biomechanics after surgery, lymphedema, postural instability, or chronic post-treatment pain syndromes [3,4]. In survivorship settings, rehabilitation is especially important because the therapeutic goal often shifts from short-term symptom suppression to long-term functional restoration.

10.2. Psychological interventions

Pain and psychological distress are bidirectionally reinforcing. Cognitive behavioral therapy, coping-skills training, relaxation techniques, and other psychologically informed interventions may help reduce distress, catastrophizing, sleep disruption, and pain-related interference [2,4]. These approaches are best understood as adjunctive rather than substitutive therapies: they do not replace pharmacologic treatment for severe nociceptive pain, but they can substantially improve the overall experience and manageability of cancer-related suffering.

10.3. Integrative therapies

Selected integrative therapies may serve as safe adjuncts within an evidence-based supportive care framework. Acupuncture, for example, has shown potential benefit for some cancer-related pain symptoms and treatment-related arthralgias, although effect sizes and study quality remain variable across populations and indications [45]. Such interventions may be most useful when integrated into a broader multimodal plan rather than presented as stand-alone alternatives to established analgesic care.

10.4. Early palliative care integration

Early integration of palliative care improves symptom control, communication, care planning, and quality of life [10,11]. In the context of cancer pain, palliative care can facilitate opioid titration, management of complex adverse effects, clarification of goals of care, and coordination with radiation oncology, pain medicine, rehabilitation, and psychosocial services. Importantly, palliative care should be delivered alongside active

oncologic treatment when needed and should not be reserved for the final stages of life [10,11].

Major nonpharmacologic, supportive, and interdisciplinary strategies that complement pharmacologic treatment are summarized in **Table 3**.

Table 3. Nonpharmacologic, supportive, and interdisciplinary strategies in adult cancer pain management

Strategy	Representative components	Main clinical objectives	Typical settings/comments
Rehabilitation and physical therapy	Graded activity, strength and balance training, gait training, mobility aids, posture optimization	Reduce pain interference, improve mobility and function, decrease fall risk, support survivorship recovery	Especially useful in deconditioning, altered biomechanics, chronic post-treatment pain, and lymphedema-associated functional limitation
Psychological interventions	Cognitive behavioral therapy, coping-skills training, relaxation, sleep-focused support	Reduce distress, catastrophizing, insomnia, and pain-related disability; improve coping and self-efficacy	Best used as adjuncts within multimodal care rather than substitutes for analgesia in severe nociceptive pain
Integrative therapies	Acupuncture, mind-body interventions, selected supportive complementary therapies	Adjunctive symptom relief, improved coping, reduction in pain-related burden	Evidence varies by indication; best integrated into evidence-based supportive oncology programs
Early palliative care integration	Symptom management, goals-of-care discussions, care coordination, caregiver support	Improve symptom control, communication, treatment alignment, and quality of life	Should occur alongside active oncologic care when indicated, not only at end of life
Palliative radiotherapy	Single-fraction or multifraction radiotherapy for painful lesions	Treat underlying pain generator, especially bone metastasis-related pain; reduce analgesic burden	Should be considered early when pain is localized to a treatable lesion
Interventional pain procedures	Celiac plexus neurolysis, nerve blocks, neuraxial techniques, intrathecal systems	Opioid-sparing analgesia, refractory pain control, targeted treatment of specific syndromes	Requires expertise and careful patient selection
Multidisciplinary supportive care	Coordination among oncology, palliative care, pain medicine, rehabilitation, nursing, and psychosocial teams	Improve comprehensive assessment, streamline referral, and address complex physical and psychosocial contributors	Particularly important in refractory pain, frailty, survivorship, and high symptom burden

11. Special populations

11.1. Older adults

Pain management in older adults with cancer is particularly complex because frailty, polypharmacy, renal decline, sensory impairment, cognitive vulnerability, and fall risk amplify the harms of standard analgesic regimens [30,35,41]. At the same time, undertreated pain contributes to immobility, delirium, sleep disruption, and loss of independence. Management requires cautious titration, close monitoring for adverse effects, frequent medication review, and active involvement of caregivers when appropriate [41]. A “start low, go slow” approach is often prudent, but should not be misapplied as a rationale for persistent undertreatment.

11.2. Cancer survivors

Long-term survivors represent a distinct cancer pain population with needs that differ from those of patients with advanced progressive disease. Common syndromes include chemotherapy-induced peripheral neuropathy, persistent postsurgical pain, musculoskeletal dysfunction, and radiation-related fibrosis [3,4,7,18].

These pain states often persist long after curative-intent treatment has ended and may be associated with substantial functional limitation.

Management in survivorship should prioritize functional restoration, rehabilitation, psychosocial support, and mechanism-based nonopioid or adjuvant therapy [3,4]. Although opioids may still be appropriate in selected cases, long-term opioid therapy warrants particular caution in this population because the balance of benefit, tolerance, dependence risk, and functional goals differs from that in advanced cancer care [3,21,17]. When opioids are used, treatment plans should include clear functional targets, review intervals, and consideration of tapering or exit strategies.

Persistent pain in cancer survivors is increasingly recognized as a longterm functional issue rather than a transient symptom. These chronic syndromes often require prolonged rehabilitation, mechanismbased nonopioid analgesia, and adjuvant therapy rather than repeated opioid escalation. Prioritizing functional recovery, mobility, and longterm tolerability helps align pain management with the unique needs of survivorship, balancing effective relief with safety and quality of life.

11.3. Patients with renal dysfunction and clinical frailty

Renal dysfunction and frailty substantially complicate analgesic prescribing. Accumulation of active opioid metabolites may increase the risk of sedation, delirium, myoclonus, and neurotoxicity, particularly in dehydrated or cachectic patients [35,36]. NSAID use may also be limited by renal vulnerability, gastrointestinal risk, or thrombocytopenia. In such settings, analgesic choice should be individualized, doses adjusted conservatively, and reassessment performed frequently, especially during acute illness or rapid clinical decline.

12. Implementation barriers and global equity

Global inequities further compound these implementation challenges across resourcelimited and resourceabundant settings alike. Persistent failures in cancer pain control are increasingly systemic rather than purely pharmacologic. Common barriers include fragmented care pathways, inconsistent pain assessment in routine oncology visits, delayed referral to palliative care or pain specialists, limited access to rehabilitation and psychosocial services, and insufficient recognition of oncologic emergencies or treatable structural pain syndromes [8,11,15-17]. In some settings, payer restrictions and pharmacy-level barriers further delay timely access to appropriate opioid therapy or adjuvant medications [21,17].

At a global level, disparities are even more profound. In many low- and middle-income countries, patients still lack reliable access to oral morphine, palliative radiotherapy, trained clinicians, and basic supportive infrastructure [12,15]. These gaps are not merely technical shortcomings; they represent major inequities in health systems and in the distribution of relief from suffering. Addressing them will require policy reform, opioid availability safeguards, workforce training, radiotherapy capacity, and incorporation of symptom relief into universal health coverage agendas [15].

13. Future directions

Future progress in cancer pain care will depend not only on new analgesics but also on better translation of mechanism-based science into clinically useful treatment pathways. Phenotype-enriched trials are needed

to determine which patients benefit most from specific adjuvant agents, early radiotherapy, interventional procedures, or combination strategies [5-7,23,27]. In parallel, pragmatic studies should evaluate whether earlier multidisciplinary intervention improves outcomes compared with conventional stepwise analgesic escalation.

Digital symptom monitoring and electronic patient-reported outcomes (ePROs) also offer important opportunities to detect pain deterioration earlier, identify rescue-medication overuse, and trigger timely evaluation for structural emergencies or uncontrolled symptoms between clinic visits [16]. Finally, implementation science will be essential: advances in evidence generation will have limited impact unless health systems can reliably deliver guideline-concordant, equitable, and timely pain care [15-17].

14. Conclusions

Cancer pain is a heterogeneous clinical syndrome that cannot be managed adequately through intensity-based analgesic escalation alone. Contemporary care requires multidimensional assessment, recognition of pain mechanisms and temporal phenotypes, timely identification of structural emergencies, and integration of pharmacologic, disease-directed, interventional, rehabilitative, and psychosocial strategies. Opioids remain essential for many patients, but their use should be embedded within a broader framework of mechanism-informed, reassessed, and function-conscious care. The major challenge in modern cancer pain management is increasingly one of implementation: translating existing evidence and guideline principles into timely, equitable, and multidisciplinary clinical practice across the cancer continuum.

15. Clinical practice points

(1) Use routine multidimensional assessment rather than pain intensity scores alone; include functional interference, temporal pattern, analgesic response, and psychosocial distress.

(2) Differentiate nociceptive, neuropathic, mixed, and temporal pain phenotypes, as this distinction often determines whether opioid escalation, adjuvant therapy, imaging, radiotherapy, or procedural referral is most appropriate.

(3) Consider disease-directed interventions early, especially for painful bone metastases, mechanical instability, nerve compression, or other identifiable structural pain generators.

(4) Distinguish true breakthrough cancer pain from end-of-dose failure and uncontrolled background pain before intensifying rescue opioid prescribing.

(5) Practice opioid stewardship without normalizing undertreatment; cancer-specific clinical context should remain central when balancing access, safety, and regulatory requirements.

(6) In survivorship, emphasize functional restoration, rehabilitation, and mechanism-based long-term management rather than default continuation of opioid escalation strategies used in advanced disease.

(7) Monitor proactively for constipation, sedation, delirium, neurotoxicity, gait instability, and respiratory risk, particularly in older adults and patients with renal dysfunction or frailty.

Funding

Scientific Research Project of the Tianjin Municipal Education Commission (Project No.: 2025ZD058)

Disclosure statement

The authors declare no conflict of interest.

References

[1] van den Beuken-van Everdingen MHJ, Hochstenbach LMJ, Joosten EAJ, et al., 2016, Update on Prevalence of Pain in Patients with Cancer: Systematic Review and Meta-Analysis. J Pain Symptom Manage, 51(6): 1070–1090. e9.

[2] Syrjala KL, Jensen MP, Mendoza ME, et al., 2014, Psychological and Behavioral Approaches to Cancer Pain Management. J Clin Oncol, 32(16): 1703–1711.

[3] Fallon M, Giusti R, Aielli F, et al., 2018, Management of Cancer Pain in Adult Patients: ESMO Clinical Practice Guidelines. Ann Oncol, 29(suppl 4): iv166–iv191.

[4] National Comprehensive Cancer Network, 2024, Adult Cancer Pain. Version 2.2024. National Comprehensive Cancer Network, Plymouth Meeting, PA.

[5] Paice JA, Portenoy R, Lacchetti C, et al., 2016, Management of Chronic Pain in Survivors of Adult Cancers: ASCO Clinical Practice Guideline. J Clin Oncol, 34(27): 3325–3345.

[6] Denlinger CS, Ligibel JA, Are M, et al., 2014, Survivorship: Pain, Version 1.2014. J Natl Compr Canc Netw, 12(4): 488–500.

[7] Bennett MI, Kaasa S, Barke A, et al., 2019, The IASP Classification of Chronic Pain for ICD-11: Chronic Cancer-Related Pain. Pain, 160(1): 38–44.

[8] Portenoy RK, 2011, Treatment of Cancer Pain. Lancet, 377(9784): 2236–2247.

[9] Leysen L, Adriaenssens N, Nijs J, et al., 2017, Chronic Pain in Breast Cancer Survivors: Nociceptive, Neuropathic, or Central Sensitization Pain? Pain Physician, 20(3): E561–E580.

[10] Temel JS, Greer JA, Muzikansky A, et al., 2010, Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer. N Engl J Med, 363(8): 733–742.

[11] Ferrell BR, Temel JS, Temin S, et al., 2017, Integration of Palliative Care into Standard Oncology Care: ASCO Clinical Practice Guideline Update. J Clin Oncol, 35(1): 96–112.

[12] Lutz S, Balboni T, Jones J, et al., 2017, Palliative Radiation Therapy for Bone Metastases: Update of an ASTRO Evidence-Based Guideline. Pract Radiat Oncol, 7(1): 4–12.

[13] Davies AN, Dickman A, Reid C, et al., 2009, The Management of Cancer-Related Breakthrough Pain: Recommendations of a Task Group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland. Eur J Pain, 13(4): 331–338.

[14] Davies A, Buchanan A, Zeppetella G, et al., 2013, Breakthrough Cancer Pain: An Observational Study of 1000 European Oncology Patients. J Pain Symptom Manage, 46(5): 619–628.

[15] Knaul FM, Farmer PE, Krakauer EL, et al., 2018, Alleviating the Access Abyss in Palliative Care and Pain Relief—An Imperative of Universal Health Coverage: The Lancet Commission Report. Lancet, 391(10128): 1391–1454.

[16] Basch E, Deal AM, Kris MG, et al., 2016, Symptom Monitoring with Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J Clin Oncol, 34(6): 557–565.

[17] Paice JA, 2018, Cancer Pain Management and the Opioid Crisis in America: How to Preserve Hard-Earned Gains in Improving the Quality of Cancer Pain Management. Cancer, 124(12): 2491–2497.

[18] Loprinzi CL, Lacchetti C, Bleeker J, et al., 2020, Prevention and Management of Chemotherapy-Induced

Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. J Clin Oncol, 38(28): 3325–3348.

[19] Cleeland CS, Ryan KM, 1994, Pain Assessment: Global Use of the Brief Pain Inventory. Ann Acad Med Singap, 23(2): 129–138.

[20] Bruera E, Kuehn N, Miller MJ, et al., 1991, The Edmonton Symptom Assessment System (ESAS): A Simple Method for the Assessment of Palliative Care Patients. J Palliat Care, 7(2): 6–9.

[21] Enzinger AC, Ghosh K, Keating NL, et al., 2021, US Trends in Opioid Access Among Patients with Cancer Near End of Life. J Clin Oncol, 39(26): 2941–2952.

[22] Falk S, Dickenson AH, 2014, Pain and Nociception: Mechanisms of Cancer-Induced Bone Pain. J Clin Oncol, 32(16): 1647–1654.

[23] Schmidt BL, 2014, The Neurobiology of Cancer Pain. Neuroscientist, 20(5): 546–562.

[24] Fallon MT, 2013, Neuropathic Pain in Cancer. Br J Anaesth, 111(1): 105–111.

[25] Bouhassira D, Attal N, Alchaar H, et al., 2005, Comparison of Pain Syndromes Associated with Nervous or Somatic Lesions and Development of a New Neuropathic Pain Diagnostic Questionnaire (DN4). Pain, 114(1–2): 29–36.

[26] Loblaw DA, Perry J, Chambers A, et al., 2005, Systematic Review of the Diagnosis and Management of Malignant Extradural Spinal Cord Compression: The Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. J Clin Oncol, 23(9): 2028–2037.

[27] Mantyh PW, 2006, Cancer Pain and Its Impact on Diagnosis, Survival and Quality of Life. Nat Rev Neurosci, 7(10): 797–809.

[28] Fisher CG, DiPaola CP, Ryken TC, et al., 2010, A Novel Classification System for Spinal Instability in Neoplastic Disease: An Evidence-Based Approach and Expert Consensus from the Spine Oncology Study Group. Spine (Phila Pa 1976), 35(22): E1221–E1229.

[29] Coleman RE, 2006, Clinical Features of Metastatic Bone Disease and Risk of Skeletal Morbidity. Clin Cancer Res, 12(20 Pt 2): 6243S–6249S.

[30] Mercadante S, Giarratano A, 2013, The Long and Winding Road of Nonsteroidal Anti-Inflammatory Drugs and Paracetamol in Cancer Pain Management: A Critical Review. Crit Rev Oncol Hematol, 87(2): 140–145.

[31] Haywood A, Good P, Khan S, et al., 2015, Corticosteroids for the Management of Cancer-Related Pain in Adults. Cochrane Database Syst Rev, (4): CD010756.

[32] Anthony T, Baron T, Mercadante S, et al., 2007, Report of the Clinical Protocol Committee: Development of Randomized Trials for Malignant Bowel Obstruction. J Pain Symptom Manage, 34(1 Suppl): S49–S59.

[33] Laval G, Marcelin-Benazech B, Guirimand F, et al., 2014, Recommendations for Bowel Obstruction with Peritoneal Carcinomatosis. J Pain Symptom Manage, 48(1): 75–91.

[34] Caraceni A, Hanks G, Kaasa S, et al., 2012, Use of Opioid Analgesics in the Treatment of Cancer Pain: Evidence-Based Recommendations from the EAPC. Lancet Oncol, 13(2): e58–e68.

[35] King S, Forbes K, Hanks GW, et al., 2011, A Systematic Review of the Use of Opioid Medication for Those with Moderate to Severe Cancer Pain and Renal Impairment: A European Palliative Care Research Collaborative Opioid Guidelines Project. Palliat Med, 25(5): 525–552.

[36] Mercadante S, Arcuri E, 2004, Opioids and Renal Function. J Pain, 5(1): 2–19.

[37] Smith EML, Pang H, Cirrincione C, et al., 2013, Effect of Duloxetine on Pain, Function, and Quality of Life Among Patients with Chemotherapy-Induced Painful Peripheral Neuropathy: A Randomized Clinical Trial. JAMA, 309(13): 1359–1367.

[38] Bennett MI, Rayment C, Hjermstad M, et al., 2012, Prevalence and Aetiology of Neuropathic Pain in Cancer Patients: A Systematic Review. Pain, 153(2): 359–365.

[39] Wiffen PJ, Derry S, Bell RF, et al., 2017, Gabapentin for Chronic Neuropathic Pain in Adults. Cochrane Database Syst Rev, 6(6): CD007938.

[40] van den Beuken-van Everdingen MHJ, de Graeff A, Jongen JLM, et al., 2017, Pharmacological Treatment of Pain in Cancer Patients: The Role of Adjuvant Analgesics, A Systematic Review. Pain Pract, 17(4): 409–419.

[41] Mohile SG, Dale W, Somerfield MR, et al., 2018, Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology. J Clin Oncol, 36(22): 2326–2347.

[42] Chow E, Zeng L, Salvo N, et al., 2012, Update on the Systematic Review of Palliative Radiotherapy Trials for Bone Metastases. Clin Oncol (R Coll Radiol), 24(2): 112–124.

[43] Deer TR, Smith HS, Burton AW, et al., 2011, Comprehensive Consensus Based Guidelines on Intrathecal Drug Delivery Systems in the Treatment of Pain Caused by Cancer Pain. Pain Physician, 14(3): E283–E312.

[44] Wyse JM, Carone M, Paquin SC, et al., 2011, Randomized, Double-Blind, Controlled Trial of Early Endoscopic Ultrasound-Guided Celiac Plexus Neurolysis to Prevent Pain Progression in Patients with Newly Diagnosed, Painful, Inoperable Pancreatic Cancer. J Clin Oncol, 29(26): 3541–3546.

[45] Chiu HY, Hsieh YJ, Tsai PS, 2017, Systematic Review and Meta-Analysis of Acupuncture to Reduce Cancer-Related Pain. Eur J Cancer Care (Engl), 26(2): e12457.