

About: Mixed pain, pain that combines tissue-damage pain (nociceptive), nerve-damage pain (neuropathic), and sometimes an overly sensitive nervous system (nociplastic) in the same patient, is common, often missed, and needs to be diagnosed and treated with a combination of methods, not a single drug or single specialist. A group of international pain societies wrote 16 formal recommendations, built mostly from expert consensus (since few large trials exist), covering how to spot it, how to treat it, who should be on the care team, and how to do this ethically.

Mixed pain is under-recognized and makes patients worse off

Many chronic pain conditions, low back pain with a pinched nerve, cancer pain, pain after surgery, arthritis, actually involve more than one pain mechanism at once. Because doctors often look for only one cause, mixed pain frequently goes undiagnosed. Left unrecognized, it leads to longer-lasting pain, worse function, lower quality of life, and higher healthcare costs than pain from a single cause.

Three different pain “engines” can run at the same time

- **Nociceptive** pain comes from actual tissue injury or inflammation, causing localized, aching, or throbbing sensations. It predominates in conditions such as osteoarthritis and post-surgical pain.
- **Neuropathic** pain comes from damaged or diseased nerves, producing burning, electric, shooting, or tingling sensations. It can show up as "negative" symptoms (numbness, reduced sensation) or “positive” symptoms (allodynia, pain from things that shouldn't normally hurt, like light touch; and hyperalgesia, an exaggerated pain response to something that does hurt).
- **Nociplastic** pain comes from a nervous system that has become overly sensitive, even without ongoing tissue or nerve damage. It's frequently seen in fibromyalgia and chronic low back pain.
- A related process, **central sensitization**, involves the central nervous system becoming more reactive to pain signals, causing pain to spread beyond the original site, feel more intense, and persist even after tissue has healed. It plays a role in chronic low back pain, osteoarthritis, and post-surgical pain, and shows up clinically as hyperalgesia and allodynia.

Because these mechanisms often overlap, for example, low back pain with a pinched nerve (nociceptive plus neuropathic), cancer pain from a tumor plus chemotherapy-related nerve damage (nociceptive plus neuropathic), post-surgical pain from tissue and nerve trauma during surgery, or osteoarthritis complicated by central sensitization, treatment aimed at only one mechanism often fails.

Diagnosis needs structured tools, not just a doctor’s impression

Clinicians should combine a detailed pain history and physical exam with validated screening questionnaires (DN4, PainDETECT, or LANSS) to detect neuropathic features. Imaging (MRI) and nerve tests (EMG/NCS) should be used selectively, not routinely, since imaging

findings often don't match symptoms. Clinicians should also screen for "red flags" (signs of serious disease) and "yellow flags" (psychological and social factors that predict chronic pain).

Drug treatment should combine medicines that target different mechanisms

No single drug covers all three pain types, so the guideline recommends multimodal pharmacotherapy rather than one drug alone, for example, pairing an anti-inflammatory (NSAID or acetaminophen) with a nerve-pain drug (gabapentin, pregabalin, or duloxetine). When opioids are needed, dual-action ones (tramadol, tapentadol) are preferred over traditional opioids. Topical treatments (lidocaine, capsaicin) are favored for localized pain, especially in older or medically complex patients.

Non-drug therapies are essential, not optional extras

Physical therapy, psychological therapies (CBT, acceptance-based therapy, mindfulness), interventional procedures (nerve blocks, radiofrequency ablation, neuromodulation), occupational therapy, and patient education should all be layered in alongside medication. Evidence supports this combined approach as more effective than drugs alone.

Care works best as a coordinated team, not separate specialists

The guideline recommends an interdisciplinary team, at minimum a physician, nurse, pharmacist, physiotherapist, and psychologist, working from one shared care plan with regular communication, rather than several specialists each treating a patient in isolation. This model is linked to better pain relief, better function, and fewer unnecessary healthcare visits.

Progress should be tracked with structured tools, not just “how’s your pain today”

Regular follow-up should measure pain intensity, how much pain interferes with daily life, physical function, mood and psychological factors, and quality of life, using standardized questionnaires. Clinicians should watch for warning signs like rising opioid doses without improvement, or signs of misuse.

Treatment must be adapted to the specific patient group

Older adults need simplified, lower-dose, more topical regimens. Children need conservative, family-centered, mostly non-drug approaches. Cancer patients need mechanism-based multimodal pain control beyond the standard pain-ladder. Patients with depression or anxiety need close collaboration between pain and mental health specialists. Disadvantaged populations face access barriers that need to be actively addressed.

Ethical care means informed consent, fairness, and knowing one’s limits

Because mixed pain treatment can involve long-term medications, invasive procedures, or off-label use, patients need full information and a real say in decisions (shared decision-making). Care should be equitably accessible regardless of income or location, and

clinicians should refer complex cases to specialists rather than manage beyond their expertise. Use of digital health tools (apps, wearables, records) must follow privacy laws such as GDPR and HIPAA.

What's still missing

The recommendations are based mostly on expert consensus and indirect evidence, not large clinical trials specific to mixed pain, because that evidence largely doesn't exist yet. The authors call for better diagnostic tools (biomarkers), more research in underrepresented patient groups, and continued development of digital and personalized approaches to close these gaps.