



- **FACT SHEET No. 19**

New Treatment Opportunities for Joint Pain

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Osteoarthritis (OA) remains an increasing source of pain, distress, and disability for the world's aging population. OA affecting weight-bearing joints, in particular the knee or hip, limits mobility and physical activity, while that affecting the upper limbs affects activities of daily living. Arthritis pain results from complex interactions between joint pathology, neuronal processing, and psychological context. Combination approaches are often necessary for adequate pain management. Treatments might relieve joint pain by modifying the underlying disease (for example with biologic agents used for rheumatoid arthritis), whereas often such disease modifying drugs are not currently available and symptomatic treatment remains the priority.

Several published guidelines have summarized the current evidence of benefits for a range of OA treatments. Exercise, orthotic devices, topical or systemic analgesic drugs, intra-articular injections, psychological approaches, and joint replacement surgery can each offer benefit to at least some people with OA pain. Despite this, many people with OA use few, or sometimes none, of these treatments.

Low treatment uptake might reflect difficulties with access to treatment or inadequate information on which to base choices. Decisions to commence or continue a specific treatment are always influenced by the balance between observed or anticipated benefit and adverse events. Low efficacy or unpleasant and sometimes medically serious side effects might limit treatments as well. Considerable research effort is currently being invested in improving treatment adherence, reducing adverse events. For example, new opiates might achieve more sustained benefit with less gastrointestinal or cognitive disturbance or risk of dependency. The way in which analgesic treatments are administered is pivotal in



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optimizing outcomes. Systemic adverse events might be avoided by local administration. Analgesic benefits of intra-articular glucocorticoid injections, for example, can be prolonged. Topical cyclooxygenase inhibitors have a lower propensity for gastrointestinal or cardiovascular adverse events than do oral preparations and yet can offer useful analgesia for knee or hand OA.

Recently published clinical trials of blocking antibodies directed to nerve growth factor (anti-NGF) support the proposed importance of peripheral sensitization in OA pain and illustrate the potential of biologic therapies for OA pain. These agents have poor penetration into the central nervous system, and targeting peripheral pain mechanisms might avoid adverse events such as somnolence and nausea associated with some centrally acting analgesics such as opioids. A contribution of subchondral bone turnover to OA pain has also been supported by a recent clinical trial consistent with analgesic benefits from osteoclast inhibition using bisphosphonates.

OA pain is commonly described using words characteristically associated with neuropathic pain, raising the possibility that a neuropathic component might contribute to OA symptoms. Nerve damage might follow joint surgery, explaining some persistent pain after knee arthroplasty, although neuropathic-like symptoms might also result from shared mechanisms between OA and neuropathic pain. Duloxetine displayed efficacy for both neuropathic and OA pain. Less convincing results in OA for other neuropathic pain treatments might suggest that shared pain mechanisms apply only to a subset of OA patients. Improved pain phenotyping has the potential to select patient groups for whom existing treatments might have greater benefit than would be suggested by randomized controlled trials with nonselective recruitment.

Psychological approaches can help patients manage OA pain and might reduce pain intensity. Psychological distress can increase both the perception and impact of pain, and cognitive behavioral therapies (CBT) similar to those efficacious for distress can also facilitate pain management. Psychological distress is also a key predictor of poor surgical outcomes, and CBT might facilitate positive responses to non-psychological interventions. Recent developments in psychological pain-management approaches, including Acceptance and Commitment Therapy, might also have a place in the management of OA pain.

A consistent finding from most randomized controlled trials aiming to reduce OA pain is that placebo interventions can also provide substantial analgesic benefit. Placebo response has been estimated to contribute approximately half of the benefit from medical analgesics in OA trials. Placebo responses in clinical trials reflect the context in which treatments are used, and context similarly has the potential to modulate response to analgesic treatments in clinical practice. Key contextual factors might include patients' beliefs about OA, pain and medications, psychological distress, concurrent or sequential treatments, and comorbidities. Optimizing this context in order to maximize analgesic benefit from existing treatments has the potential to further relieve suffering from OA.

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