

Integrative chronic pain management: a narrative review

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Abstract

Chronic pain, a pervasive public health issue, significantly contributes to the opioid crisis in the United States, where opioid-related deaths have escalated dramatically since the late 1990s. This narrative review explores integrative approaches to managing chronic pain, aiming to reduce reliance on opioid medications. It synthesizes evidence from randomized controlled trials, meta-analyses, and systematic reviews, focusing on various pain etiologies, including arthritis, musculoskeletal pain, postsurgical pain, cancer-related pain, fibromyalgia, migraines, and neuropathic pain. Key findings suggest that dietary interventions, lifestyle modifications, and complementary therapies, such as acupuncture, massage, and photobiomodulation therapy, can significantly alleviate pain across multiple conditions. These integrative strategies not only manage pain but also address the pain epidemic and the opioid crisis by offering personalized, multimodal treatment plans that consider the complexity of chronic pain, its psychological and social determinants, and the need for long-term management strategies.

Keywords: Chronic pain, opioid crisis, integrative approaches, pain management, complementary therapies, dietary interventions, lifestyle modifications, acupuncture, massage therapy, photobiomodulation therapy, multimodal treatment, pain etiology, arthritis, musculoskeletal pain, postsurgical pain, cancer-related pain, fibromyalgia, migraines, neuropathic pain, psychological determinants, social determinants, long-term management

1. Introduction

The opioid crisis in the United States underscores a complex convergence of factors, with 91,799 deaths attributed to drug overdoses in 2020 (Hedegaard *et al.*, 2021). Notably, drug overdoses surpass auto accidents and gun deaths as a leading cause of death in young men (FastStats, 2023). This crisis disproportionately affects post-industrial regions of the US, where employment opportunities have dwindled (Charles *et al.*, 2019). Chronic pain affects a staggering 126.1 million Americans within three months, with 25.3 million experiencing daily pain (Nahin, 2015). Alarming, two-thirds of chronic pain sufferers in 2019 continued to experience chronic pain in 2020 (Nahin *et al.*, 2023).

Chronic pain is a global problem affecting an estimated 20% of the world's adult population (Goldberg & McGee, 2011). While pain is helpful for protection from harm, and painful stimuli can help the person avoid danger, the signal can become nonadaptive in

Chronic pain profoundly impacts employment, with sufferers being more likely to be unemployed (Giladi *et al.*, 2015). Moreover, navigating work with chronic pain proves challenging and often limiting (Adams and Salomons, no date). Fifteen percent of chronic pain patients experience high-impact chronic pain, severely constraining their activities (Von Korff *et al.*, 2020). This limitation translates into 3.7 times more missed workdays compared to those without chronic pain (Von Korff *et al.*, 2020).

Demographic factors also influence the prevalence of chronic pain. Native Americans and multiracial adults exhibit the highest pain prevalence, while Asian Americans report the lowest rates (Zajacova *et al.*, 2022). Household wealth correlates significantly with chronic pain rates, with the lowest quartile experiencing rates 3.3 times higher than those in the top two quartiles (Janevic *et al.*, 2017). Notably, two-thirds of adults with

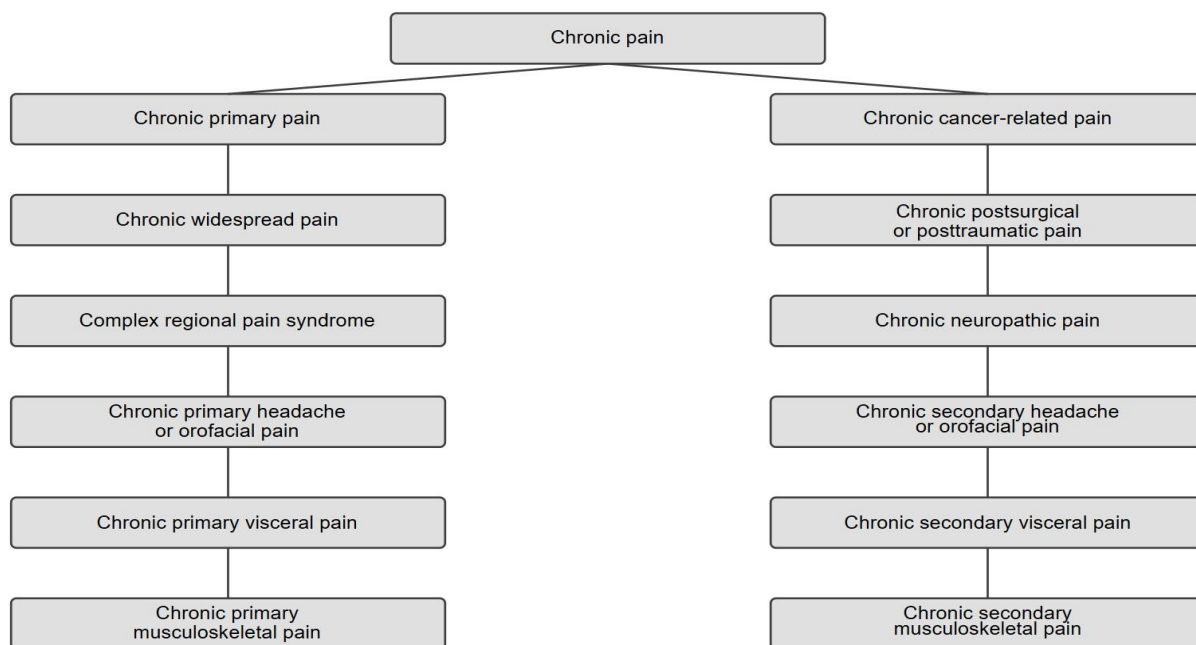


Figure 1. The taxonomy of chronic pain indications, divided into primary (left) and secondary (right) etiology. Adapted from (Treede *et al.*, 2019).

chronic pain have comorbid psychiatric diagnoses (Workman *et al.*, 2002).

Chronic pain prevalence is highly age-stratified (Fayaz *et al.*, 2016). Individuals above 75 years old in the United Kingdom experience chronic pain rates between 46% and 62%, compared to rates of 31% to 32% among those aged 25 to 34 (Parsons *et al.*, 2007; Elliott *et al.*, 1999). Chronic pain remains a pervasive issue, with one in nine young adults in the US affected (Murray *et al.*, 2022). Women, older individuals, Caucasians, and non-Hispanic populations are at increased risk of chronic pain (Newman *et al.*, 2017).

Opioid prescriptions for chronic nonmalignant pain pose risks, with 3.3% of chronic pain patients developing abuse or addiction behaviors (Fishbain *et al.*, 2008). Effective management of chronic pain requires a multifaceted approach aimed at prevention and providing support for those grappling with opioid use disorders (OUDs). Another adverse effect of opioid use to treat chronic pain is the well-known fact that opiates increase the incidence and recurrence of cancer (Szczepaniak *et al.*, 2020). In the whole USA, opioid deaths were 3.2x higher in 2016 than in 1999 (Hedegaard *et al.*, 2021), and opioids are responsible

for 2/3 of drug overdose deaths (Seth *et al.*, 2018). Chronic pain is a massive drain of resources, as chronic pain patients visit clinics at 3.4 times the rate of the general population (Kay *et al.*, 2017), and pain complaints comprise 40 to 50% of primary care consultations (Frießem, Willweber-Strumpf and Zenz, 2009). One Australian grey literature report determined the average cost per year of people living with chronic pain to be AUS\$23000 to \$43000 (\$17000 to \$32000 in 2021 US dollars) when non-financial costs were considered¹.

Apart from fatalities, opioid addiction engenders numerous harms, including criminal activities driven by the need to procure opioids (Q. Chen *et al.*, 2022). Volumes of illegal opiates entering Canada and the USA have significantly increased since 2019 (Krausz *et al.*, 2021) and are used in the majority of overdose deaths. The Iranian and Chinese examples set the historical precedent for the current opioid crisis.

In conclusion, chronic pain lies at the heart of the opioid crisis, spurring both legal and illegal opioid use. While opioids manage chronic pain in the short term, their misuse and adverse effects underscore the urgency of exploring alternative pain management strategies.

1. Reducing the Motivation for Opiates: Addressing Chronic Pain

As chronic pain is the proximal reason that people take opiates, addressing the opiate epidemic involves finding alternative treatments for chronic pain. The most recent update to the International Classification of Diseases (ICD-11) codes used in medical billing has separated pain into primary and secondary indications (Treede *et al.*, 2019). Secondary pain occurs as a result of another condition, whereas primary pain is the indication itself. The secondary indications are divided into several categories, and we address the main contributors to secondary chronic pain (Figure 1)

Chronic pain has many sources, as included in Table 1. Table 1 below summarizes the main contributors to chronic pain, their ICD-11 codes, their prevalence within the population, the prevalence of opioid use in the patient population, and the proportion of those prescribed opioids who go on to develop opioid use disorders (OUDs).

Identifying the sources of chronic pain presents challenges, with postsurgical patients experiencing chronic pain one year after surgery at rates up to 12% (Fletcher *et al.*, 2015). Arthritis and back problems emerge as leading causes of chronic pain, with arthritis affecting 48% and back problems 29% of chronic pain patients, respectively (Henderson *et al.*, 2013). Additionally, other conditions contribute to chronic pain in 28% of respondents, with over 10% reporting multiple causal conditions (Henderson *et al.*, 2013). These results are consistent with other literature: a UK study found 32% of those experiencing chronic pain reported back pain, and a Latin American survey of 400 chronic pain patients showed 25% were in pain due to a herniated disk (Castro *et al.*, 2009).

In the UK, chronic pain rates rose from 41% in the 1990s to 45% between 2010 and 2015 (Fayaz *et al.*, 2016). The economic toll of chronic pain in the US alone amounts to an estimated \$560 billion annually, with prevalence estimates ranging from 11% to 40% (Kuehn, 2018). Approximately 50.2 million US adults, or 20.5% of the adult population, experience pain on most or every day (Yong *et al.*, 2022). Major causes of chronic pain are arthritis, injuries, low back pain, surgical procedures, cancer, fibromyalgia, bowel pain, migraines, neuropathy, and headaches and migraines. Their prevalence is included in Table 1.

Before examining the specific causes of chronic pain, we first examine interventions that show promise in reducing chronic pain levels generally.

Minimally processed whole foods diets decreased chronic pain levels in a recent trial, and minimally processed ketogenic diets performed better still at lowering pain levels (Field *et al.*, 2022).

Another meta-analysis of ketogenic diets and their impact on neurological and inflammatory outcomes summarized the effects of ketogenic diets on neurological outcomes (Field *et al.*, 2023). Of the studies on neurological outcomes, 83% showed improvement, and of the studies on inflammatory biomarkers, 71% reported a reduction in inflammation. Anti-inflammatory diets have been shown to result in significant decreases in pain.

Other dietary factors have been studied for their effects on chronic pain; a recent review found five trials for caloric restriction and/or fasting, two trials for diets enriched in polyunsaturated fatty acids, five trials for plant-based diets, one trial for a high protein diet, seven trials for elimination diets, nine trials for diets enriched in antioxidant vitamins and minerals, four trials for diets rich in fruits and fibers and five trials studying the effect of prebiotics and probiotics (Dragan *et al.*, 2020).

Of the five trials for caloric restriction and/or fasting, all showed an improvement in pain symptoms (Riecke *et al.*, 2010; Messier *et al.*, 2013; Michalsen *et al.*, 2013; Di Lorenzo *et al.*, 2015; Marum *et al.*, 2016). It should be noted that for two of these trials, the impact on pain may have been mediated by weight loss, resulting in less stress on the knee joints. (Riecke *et al.*, 2010; Messier *et al.*, 2013) One trial used a specialized, low in fermentable oligo-, di-, or monosaccharides and polyols (low FODMAP) diet, albeit calorie consumption was reduced by 41% in the treatment group. Sources of pain in these trials varied, including migraine³⁷ knee joint pain (Messier *et al.*, 2013; Riecke *et al.*, 2010), fibromyalgia 39, and gastrointestinal (Marum *et al.*, 2016). So, fasting and caloric restriction for pain treatment may be less effective for generalized pain management.

Two trials covered enriched polyunsaturated fatty acid diets, which were for the treatment of headaches (Ramsden *et al.*, 2013; Soares *et al.*, 2018). Patient pain improved in the (Ramsden *et al.* 2013), and mi-

Table 1: An overview of the major sources of chronic pain and the rates of opioid use and abuse emerging from each source of pain.

Pain Source	Population Prevalence	Risk Factors	Opioid use prevalence inpatient population	Opioid abuse prevalence in opioid using population
Rheumatoid Arthritis	0.6% (Almutairi <i>et al.</i> , 2021)	Smoking (Oliver & Silman, 2006) Latin American Indigenous background (Peláez-Ballestas <i>et al.</i> , 2018) Female (Otón & Carmona, 2019)	85% (Machado-Duque <i>et al.</i> , 2020)	25% using opioids every month throughout duration of 7 year study (Machado-Duque <i>et al.</i> , 2020)
Injuries	13% [†] (Gupta <i>et al.</i> , 2015)	Male (Rivara <i>et al.</i> , 1982) Occupational danger exposure (Mock <i>et al.</i> , 2017) Young age (rate of injury) (Fife <i>et al.</i> , 1984) Old age (injury severity) (Fife <i>et al.</i> , 1984)	27% to 6% (Riva <i>et al.</i> , 2020)	16% (Alghnam & Castillo, 2017)
Low Back Pain	33% (Calatayud <i>et al.</i> , 2020)	Female, Obesity, Smoking, Strenuous work, Sedentary Transport (Shiri <i>et al.</i> , 2019)	42% (Ivanova <i>et al.</i> , 2011)	43% (Martell <i>et al.</i> , 2007)
Postsurgical pain	8% [‡] (Johansen <i>et al.</i> , 2012)	Genetic factors, Psychological disposition, Young age (Bruce & Quinlan, 2011)	37% (Sabatino <i>et al.</i> , 2018)	26% (Boscarino <i>et al.</i> , 2010)
Cancer pain	0.1%** (Pisani <i>et al.</i> , 2002)	Young age (Poleshuck <i>et al.</i> , 2006), Obesity, Education, chemotherapy, hormone therapy (Leysen <i>et al.</i> , 2017)	35% of cancer patients (Y. Chen <i>et al.</i> , 2022)	19% (Yennurajalingam <i>et al.</i> , 2021)
Fibromyalgia	3% (Queiroz, 2013) to 5% (Jones <i>et al.</i> , 2015)	Female (Queiroz, 2013)	14% (Wolfe <i>et al.</i> , 1997), 22% (Berger <i>et al.</i> , 2008), 32% (Fitzcharles <i>et al.</i> , 2011)	39% (Kim <i>et al.</i> , 2013; Halpern <i>et al.</i> , 2016) to 45% use opioids after 1 year
Bowel Pain	13% (Icks <i>et al.</i> , 2002)	Younger age (Icks <i>et al.</i> , 2002)	13% (Edwards <i>et al.</i> , 2001)	23% to 38%* (Edwards <i>et al.</i> , 2001)
Headaches and Migraines	12% (Yeh <i>et al.</i> , 2018) to 16% (Smitherman <i>et al.</i> , 2013)	Female (Smitherman <i>et al.</i> , 2013)	30% (Buse <i>et al.</i> , 2012)	17% (for dependence) (Buse <i>et al.</i> , 2012)
Neuropathy	7% to 8% (Torrance <i>et al.</i> , 2006; Bouhassira <i>et al.</i> , 2008)	Older age, Female, Manual occupation and social deprivation (Smith & Torrance, 2012)	7% (Dieleman <i>et al.</i> , 2008)	3%-19% (General chronic pain population) (Fishbain <i>et al.</i> , 1992)

* Based on 3% of IBD patients and 5% of Crohn's disease (CD) patients being addicted to narcotics out of the 13% of IBD patients using opiates, (Edwards *et al.*, 2001)

[†]Nepalese survey, which may be nonrepresentative (Gupta *et al.*, 2015).

[‡]Based on a 24% three-year prevalence of surgery (Johansen *et al.*, 2012).

** Based on 1.5% five-year incidence of cancer (Pisani *et al.*, 2002) and chronic pain in 40% of cancer patients.

graine headaches became less frequent in the (Soares *et al.* 2018) trial of 51 subjects (Soares *et al.*, 2018). Enriched polyunsaturated fatty acid diets may be important in reducing the need for opiates, as 36% of survey respondents using prescription medication either actively used opioid medications or kept them on hand (Lipton *et al.*, 2020). Omega3 FA tends to reduce inflammation and pain via the arachidonic acid pathway (Calder, 2010). Specialized pro-resolving mediators (SPMs) can be even more effective at resolving inflammation and pain (Chávez-Castillo *et al.*, 2021; Leuti *et al.*, 2021).

While seemingly contradictory, low-fat plant-based diets were also successful at reducing patient pain scores for pain from diabetic neuropathy (Bunner *et al.*, 2015), migraines (Ferrara *et al.*, 2015), fibromyalgia (Martinez-Rodriguez *et al.*, 2018), nonalcoholic mild pancreatic disease (Maruki, *et al.*, 2013), and musculoskeletal pain (Towery *et al.*, 2018). One double-blind, randomized controlled trial (RCT) of a high-protein diet showed substantial improvement in chronic back pain. 53

Gluten elimination showed beneficial improvements in fibromyalgia patients (Rodrigo *et al.*, 2013; Slim *et al.*, 2017). Elimination of monosodium glutamate (MSG) improved symptoms in patients with irritable bowel syndrome (IBS) and fibromyalgia (Holton *et al.*, 2012), whereas another study of fibromyalgia (but not IBS) patients did not show improvement when MSG and aspartame were eliminated (Vellisca & Latorre, 2014). Restriction of lactose improved abdominal pain in lactose intolerant individuals (Savaiano *et al.*, 2013; Magiera *et al.*, 2014), though this result may be considered trivial.

Antioxidant-rich diets have been shown to improve pain or quality of life in several trials, as reported in the 2020 review by Dragon *et al.* (Dragan *et al.*, 2020). The agents studied varied, including separate formulations with multiple antioxidant components, which have been found to improve migraine pain (Gaul *et al.*, 2015) and abdominal pain in chronic pancreatitis. 61 One study of a custom antioxidant formulation, including vitamin D3, on musculoskeletal pain due to breast cancer showed no change in musculoskeletal symptoms (Khan *et al.*, 2017). Vitamin D2 was effective at lowering musculoskeletal pain levels in breast cancer due to chemotherapy (Rastelli *et al.*, 2011). In Vitamin D-deficient patients with chronic low back pain, Vitamin D3 supplementation improved function and reduced

pain intensity (Ghai *et al.*, 2017; Brady *et al.*, 2019). Vitamin D3 supplementation also decreased migraine frequency in a double-blind, randomized controlled trial (RCT) of 48 subjects. Another study of paclitaxel (chemotherapy) induced peripheral neuropathy showed improvements in quality of life scores when patients were given omega-3 fatty acids and vitamin E (Anoushirvani *et al.*, 2018).

Dietary interventions that increase the fruit and fiber content of patient diets were successful in reducing musculoskeletal pain (Brain *et al.*, 2019; Du *et al.*, 2019) and bowel pain (Romano *et al.*, 2013; Cassettari *et al.*, 2019). For abdominal pain, probiotic supplementation improved pain scores (Cassani *et al.*, 2011; Guerra *et al.*, 2011; Waitzberg *et al.*, 2013). Patients with neck and shoulder stiffness and headaches experienced some pain alleviation with probiotic supplementation, as indicated by a 76% reduction. However, one study of fibromyalgia patients given a probiotic supplement did not show improvement (Roman *et al.*, 2018).

Botanicals, including curcumin and Boswellia serrata, are effective for pain relief (Haroyan *et al.*, 2018; Rudrappa *et al.*, 2022; Sethi *et al.*, 2022). Ginger (Rondanelli *et al.*, 2020) and other herbs (Walker *et al.*, 2002; Wegener & Lüpke, 2003; Warnock *et al.*, 2007; Majid & Al-Mashhadani, 2014; Lin *et al.*, 2023) may have benefits in the adjunctive setting.

More equivocal, albeit positive, results exist for photobiomodulation (PBM) therapy for postsurgical pain. Mouse models show a significant reduction in inflammatory pain using red LED light (Pigatto *et al.*, 2019), and another mouse study demonstrated reductions in pain sensitivity after photobiomodulation using 808nm wavelength light (de Andrade *et al.*, 2017). One human trial of PBM demonstrated a decrease in the inflammatory biomarker prostaglandin E2 but no reduction in pain levels after PBM at 90 minutes. Another meta-analysis from the same group shows non-clinically significant decreases in pain (Tomazoni *et al.*, 2020). However, an adequate dose of PBM therapy showed improvement when given as part of a regimen that included exercise, compared to exercise alone. Moxibustion may help alleviate chronic pain and can even be self-administered.

The next section of this manuscript focuses on the specific causes of pain and their integrative treatment, including arthritis, musculoskeletal pain (injuries,

postsurgical pain, and low back pain), cancer-associated pain, fibromyalgia, migraines and headaches, bowel pain, and neuropathy.

Cannabis has been investigated as a potential agent for reducing the use of opioids, as cannabis can also help lower pain severity (Fine & Rosenfeld, 2013; Ueberall et al., 2019; Boehnke et al., 2022).

2.1 Arthritis

As mentioned before, arthritis (ICD-11 codes FA00-FA25) is the most common cause of chronic pain, responsible for pain in 48% of chronic pain patients (Henderson et al., 2013). Interventions to address arthritis can decrease reliance on opioids for pain management. Forty percent of rheumatoid arthritis patients use opioids regularly (Curtis et al., 2017; Day & Curtis, 2019), and opioid users often have worse physical outcomes (Hayes et al., 2018; Bodden et al., 2021).

Rheumatoid arthritis can be addressed through multiple medical and integrative approaches (Table 2).

Table 2. Interventions for arthritis related pain.

Intervention	Effect
Anti-inflammatory diet	Improvement in pain and lowering of inflammatory markers (Matsumoto et al., 2021; Schönenberger et al., 2021)
Traditional Chinese Medicine	Reduction in tender joint count (Xing et al., 2020)
Combination of electroacupuncture, moxibustion, and massage	Reduction in pain (Kwak et al., 2022)
Tripterygium wilfordii Hook. F combined with methotrexate	Combination was superior to methotrexate in isolation (Lv et al., 2015)
Omega-3 fatty acids	Reduction in non-steroidal anti-inflammatory (NSAID) medication and tender joint count (Lee et al., 2012) Favorable effect (Senftleber et

	al., 2017)
Fasting	Improvement in symptoms compared to control group when combined with a vegetarian diet (Sköldstam et al., 1979; Kjeldsen-Kragh et al., 1991)
Cat's Claw	Some benefit (Rosenbaum et al., 2010)
Mediterranean diet	Improvement (Petersson et al., 2018)
Ginger	Improvement (Funk et al., 2009)
Feverfew	Grip strength improvement (Pareek et al., 2011)

2.2 Musculoskeletal pain, postsurgical pain, and injuries

In a Dutch survey of men and women aged 25 to 64 years, 39% of men and 45% of women reported chronic musculoskeletal pain in any body location (Wijnhoven, de Vet and Picavet, 2006). In a study of 76 men and 83 women (149 subjects overall) experiencing spinal pain, 53% used opiates (Martinez-Calderon et al., 2021).

Opioid use in musculoskeletal pain often results in the persistence and enhancement of chronic musculoskeletal pain, as pain signals are upregulated (hyperalgesia) (Crofford, 2010). The use of opioids usually negatively impacts the treatment outcomes in low back pain (Lin et al., 2020). Chronic pain prevalence after spinal cord injury is 68% (Hunt et al., 2021).

General pain decreased after the use of the Emotional Freedom Technique (EFT), which involves tapping acupressure points (Bach et al., 2019).

2.3 Injuries

While injuries are as varied as the stories leading into them, it is difficult to talk about statistical aggregates of injuries. The prevalence of prolonged opioid use after musculoskeletal injury ranges between 27% for patients with high rates of prior substance use disorder and 6% for low-risk populations (Riva et al., 2020). A separate survey found a 4% opioid abuse rate in users with no previous history of opioid use (Durand et al.,

2019). This is similar to other estimates of 3×10^8 . For workplace injuries, 16% of people prescribed opioids were still using opioids one year later, with increasing doses on average (Franklin *et al.*, 2009).

Opioids can increase the risk of falls and associated injuries, contributing possibly to a self-reinforcing cycle (Yoshikawa *et al.*, 2020). Interventions for injury-related pain are included below in **Table 3**.

Table 3. Interventions for chronic pain resulting from injuries.

Interventions	Effect
CBT	Patient improvement (Knoerl <i>et al.</i> , 2016)
Massage	Improvement in pain levels (Tiidus, 2015)

2.4 Postsurgical Pain

Notoriously, the case for the alleged lack of addictive potential of opioids was made based on a five-sentence letter published in the New England Journal of Medicine, which proposed to examine hospital records for records of narcotic addiction, finding only four out of a patient population of 11,882 patients receiving narcotics².

The letter was uncritically cited to support the hypothesis that narcotics were not highly addictive, despite the original letter only looking at cases of hospital-prescribed narcotics, which are supervised and time-bound, limiting the abuse potential (Leung *et al.*, 2017).

More accurate data has since been collected; in a Canadian study, the rates of opioid use 1-year post-operation were 0.4% (Soneji *et al.*, 2016). Rates for opioid use 90 days post surgery are 3.1% (Soneji *et al.*, 2016). A meta-analysis calculated 7% of patients using opioids more than 3 months after surgery (Lawal *et al.*, 2020), consistent with another estimate of 6% to 7% (Brummett *et al.*, 2017).

Alternatives to reduce opioid use for postsurgical pain are included in **Table 4** below (Maindet *et al.*, 2019; Bakker *et al.*, 2020; Sakallı & Kara, 2022). Acupuncture, among other interventions, is promising in reducing postoperative pain (Wu *et al.*, 2016).

Table 4. Interventions to treat postoperative pain.

Intervention	Effect
Acupuncture	Reduced postoperative pain (Wu <i>et al.</i> , 2016)
Complementary and Integrative Methods	Management of Postoperative Pain (Sakallı & Kara, 2022)
Guided imagery	Improved pain (Carpenter <i>et al.</i> , 2017)
Integrative medicine	Reduce pain and increase quality of life (Dusek <i>et al.</i> , 2021)
Relaxation therapy	Reduced pain (Felix <i>et al.</i> , 2019)
Integrative Korean Medicine	Reduced the incidence of postoperative pain (Ahn <i>et al.</i> , 2021)

Prevention emerges as a crucial strategy for addressing low back pain (LBP). Exercise, coupled with education, reduces the risk of LBP episodes by 45%, while exercise alone diminishes episodes by 35% (Steffens *et al.*, 2016). Several meta-analyses highlight the combined preventive effects of exercise and education. (Shiri *et al.*, 2018; de Campos *et al.*, 2021) Conversely, product-based interventions like back belts and shoe insoles exhibit limited or no effectiveness in preventing LBP (Steffens *et al.*, 2016).

Several risk factors contribute to LBP, including obesity (Croft *et al.*, 1999), sports participation (Croft *et al.*, 1999), and lifting heavy loads exceeding 25lbs (Macfarlane *et al.*, 1997; Taylor *et al.*, 2014). Office workers exhibit the highest prevalence of LBP, according to a German survey (Schneider *et al.*, 2006). Strengthening lower limb muscles emerges as a protective measure against LBP (Cho *et al.*, 2014; de Sousa *et al.*, 2019). Notably, a 3-day/week strength training program reduces one-year recurrence rates to 8.3%, representing a 75% reduction compared to the control group (Calatayud *et al.*, 2020). Complementary interventions offer promising avenues for managing LBP. Yoga demonstrates a positive impact on long-term LBP reduction (Chang *et al.*, 2016).

While evidence regarding medical cannabis remains of low quality, necessitating further investigation (First *et al.*, 2020; Lee *et al.*, 2023). Psychological approaches such as cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR) yield improvements in LBP (Petrucci *et al.*, 2022). Lessons in the Alexander Technique (Alexander, 1932), focusing on posture coaching, effectively decreases LBP incidence (Little *et al.*, 2008; Hafezi *et al.*, 2022a).

Although with lower confidence, modalities like massage (Furlan *et al.*, 2015a), spinal manipulation, and transcutaneous electrical stimulation show potential in reducing LBP (Edzard Ernst, 1999). Acupuncture also presents a favorable effect (Furlan *et al.*, 2015a).

Additionally, dietary interventions offer avenues for managing chronic back pain. A double-blind, randomized controlled trial (RCT) reveals substantial improvement with a high-protein diet (Shell *et al.*, 2016). Weight loss through dieting and adopting low-inflammatory diets can alleviate LBP (Shin *et al.*, 2022; Torlak *et al.*, 2022). Conversely, alcohol consumption may exacerbate LBP (Liu *et al.*, 2023).

Integrative approaches for LBP can reduce the need for opioid medications. Interventions for treating LBP are summarized below in **Table 5** (Kizhakkeveetil *et al.*, 2014)

Table 5. Integrative treatments for Low Back Pain and evidentiary basis.

Intervention	Effect
Integrative treatment	Improvement in pain and enhance quality of life (Eisenberg <i>et al.</i> , 2012; Wayne <i>et al.</i> , 2018)
Spinal manipulative therapy	Improvement in low back pain (Kizhakkeveetil <i>et al.</i> , 2017)
Chiropractic and integrative care	Pain reduction (Bronfort <i>et al.</i> , 2022)
Yoga	Reducing long-term lower back pain (Cramer <i>et al.</i> , 2013; Chang <i>et al.</i> , 2016; Wieland <i>et al.</i> , 2017)

Cognitive behavioural therapy (CBT) and mindfulness	Stress reduction can improve LBP (Petrucci <i>et al.</i> , 2022)
Alexander Technique	Reduced the incidence of LBP (Little <i>et al.</i> , 2008; Hafezi <i>et al.</i> , 2022b)
Massage	Reduced pain (Furlan <i>et al.</i> , 2015b)
Dieting	Weight loss can reduce Lower back pain (Torlak <i>et al.</i> , 2022)
Spinal manipulation and transcutaneous electrical stimulation	Reduced pain (E. Ernst, 1999)
Acupuncture	Positive impact (Furlan <i>et al.</i> , 2015b)
Theramine (amino acid supplement)	Positive impact (Shell <i>et al.</i> , 2016)

2.6 Cancer

Cancer and its treatment can be sources of chronic pain, even long after its successful treatment. Approximately 35% of cancer survivors experience chronic pain, while 16% experience high-impact chronic pain, which is more debilitating, amounting to 5.4 million and 2.5 million cancer survivors in the USA, respectively (Jiang *et al.*, 2019).

Pain prevalence varies depending on the stage of cancer and treatment. After treatment, pain prevalence is 39%, and is 55% during anticancer treatment and 66% in advanced, metastatic, or terminal disease (van den Beuken-van Everdingen *et al.*, 2016).

The prevalence of opioid use disorder in those with cancer-related chronic pain is 8%, and the risk of use disorder is 24% (Preux *et al.*, 2022).

There is a pressing need to reduce the need for opioids, as opioids can increase the risk of cancer (Szczepaniak *et al.*, 2020). Interventions for treating cancer pain are available in **Table 6** (Cassileth & Keefe, 2010; Mao *et al.*, 2022; Shkodra & Caraceni, 2022).

Table 6. Interventions for cancer-related chronic pain and evidentiary basis.

Intervention	Effect
Acupuncture	Associated with pain reduction in palliative care of patients with cancer (Bae et al., 2015 ; Chen et al., 2017 ; Yang et al., 2021)
Yoga	Reduction in cancer pain (165–167)
Guided imaginary and PMR	Reduction in general cancer pain (Sloman et al., 1994 ; Charalambous et al., 2016)
Reflexology	Reduction in general cancer pain (Stephenson et al., 2007 ; N, S and I, 2017 ; Dikmen & Terzioglu, 2019 ; Rambod et al., 2019 ; Sikorskii et al., 2020)
Massage	Reduction in general cancer pain (Shin et al., 2016 ; Pinheiro da Silva et al., 2019) and pain during palliative care (Post-White et al., 2003 ; Ernst, 2009)
Electrical nerve stimulation	Trend for efficacy in patients with cancer pain (Lee et al., 2016)
Hypnosis	Benefit on pain relief for advanced breast cancer (Goodwin et al., 2001 ; Butler et al., 2009)
Laxation, meditation, imagery, music therapy, virtual reality	Relieved depression, stress, anxiety, and other mood disturbances associated with pain (Greenlee et al., 2017 ; Deng, 2019)
Education and communication	Improvement in quality of life (Maindet et al., 2019)
NMDA Antagonists	Improved management of neuropathic pain (Chizh & Headley, 2005)
Cannabis	Improved management of cancer pain (Blake et al., 2017)
Tetrodotoxin	Treatment of uncontrolled moderate to severe cancer-related pain (Hagen et al., 2017)
Botulinum Toxin Type A (BoNT-A)	Improvement in nociceptive and neuropathic cancer pain(Finnerup et al., 2015 ; Reyes-Long et al., 2021)
TRPM8 Activator Menthol	Improvement in localized cancer-related neuropathic pain (Fallon et al., 2015)
Growth Factors Inhibitors	Decreased metastatic cancer-related bone pain (Sopata et al., 2015)
Lemairamin	Antinociceptive effects in pain hypersensitivity (Wang et al., 2020)
Physical exercise	Positive impact on pain when combined with cognitive-behavioral therapies (CBT) or lifestyle programs (Basen-Engquist et al., 2006 ; Rajotte et al., 2012)
Emotional dimension (Supportive-expressive group therapy Music therapy)	Improved cancer pain scores (Kwekkeboom et al., 2010)
Mindfulness mediation	Positive effects on some chronic pain conditions (Rosenzweig et al., 2010)

2.7 Fibromyalgia

Fibromyalgia is characterized by widespread body pain and affects roughly 5% of the US adult population (Jones *et al.*, 2015). It affects women significantly more often than men, and the ratio of

Table 7. Interventions for the treatment of fibromyalgia pain.

Intervention	Effect
Acupuncture	Improving sleep, global well-being and fatigue and in the reduction of pain and stiffness (Pereira <i>et al.</i> , 2021)
Heart Rate Variability Biofeedback	Related to decreased pain (Reneau, 2020)
Mindfulness	Contribute to symptom management in chronic pain conditions (Gordon <i>et al.</i> , 2023)
Education + Cognitive Behavioral Therapy	Improvement in patient pain (Lladser <i>et al.</i> , 2021)
Pilates	Beneficial effects on pain and quality of life of individuals (Cordeiro <i>et al.</i> , 2020)
Pain Neuroscience Education, Exercise Therapy, Psychological Support, and Nature Exposure	Improvement in affective valence, arousal, dominance, fatigue, pain, stress, and self-efficacy (Serrat <i>et al.</i> , 2020)
Photobiomodulation	Treat chronic pain syndromes (White <i>et al.</i> , 2018)
Exercise and Massage	Improvement in pain and other symptoms (Maffei, 2020)

women to men with fibromyalgia is at least 2.3 to 1, depending on diagnostic criteria (Jones *et al.*, 2015). Of patients with diagnosed fibromyalgia, 31% used opioids regularly or at high doses, while 27% used opioids intermittently or at lower doses (Turner *et al.*, 2016). Forty-two percent reported minimal or no use of opioids, leaving 58% of fibromyalgia patients using opioids to treat their pain.

One survey found that 32% of those referred to a fibromyalgia clinic used opioids (Fitzcharles *et al.*, 2011), despite limited evidence for efficacy, benefits outweigh risks (Bruce *et al.*, 2021). Interventions for FM are included in the table below (Table 7) (Maffei, 2020).

2.8 Bowel Pain

Of those with inflammatory bowel disease (IBD) presenting to a clinic, 13% used opiates (Edwards *et al.*, 2001). Additionally, 3% of IBD patients and 5% of Crohn’s disease (CD) patients were addicted to narcotics (Edwards *et al.*, 2001). One estimate from 1988 found that 30% of IBD patients referred for psychiatric consultation were addicted to narcotics (Kaplan & Korelitz, 1988).

Table 8. Interventions to reduce the symptom burden of abdominal pain.

Intervention	Effect
Apheresis therapy (Adsorptive granulocyte/monocyte apheresis)	Reduce the local inflammatory response by isolating and absorbing one or more specific leukocytes in the peripheral blood (Naganuma <i>et al.</i> , 2020)
Antibiotics, probiotics, prebiotics, postbiotics, synbiotics, and fecal microbiota transplantation	Improvement of Intestinal Microecology (Cai <i>et al.</i> , 2021)
Cell therapy (haematopoietic stem cells (HSCs), mesenchymal stem cells (MSCs), and intestinal stem cells (ISCs))	Promote the regeneration of injured tissue and help restore specific tissue functions, thus restoring the integrity of the intestinal mucosal barrier (Jin, 2017)
Exosome Therapy	Maintaining intestinal barrier function (Petit <i>et al.</i> , 2012)
Diet (diet of low-FODMAP)	Symptom relief and improvement of life quality (Cox <i>et al.</i> , 2020; Chey <i>et al.</i> , 2021)
Mood and Psychology training	Reduction in recurrence of the disease (Cai <i>et al.</i> , 2021)

Bowel pain may be the result of specific intolerances, including gluten sensitivity or celiac disease (Sainsbury *et al.*, 2013) and lactose intolerance (Gremse *et al.*, 2003). Interventions and their studied effects are available in **Table 8** (Billings *et al.*, 2021; Cai *et al.*, 2021).

2.9 Migraines

Migraines are painful headaches, impacting many people and even featuring heavily in the philosophy of the great Friedrich Nietzsche, who suffered from migraines since childhood and throughout his adult life (Hemelhoet *et al.*, 2008). Migraines are estimated to affect 12% (Yeh *et al.*, 2018) to 16% (Smitherman *et al.*, 2013) of the general population. Migraines are more common in younger individuals, women, and those with lower socioeconomic status. Over one-quarter of women aged 18 to 54 years experienced a severe migraine or headache in the past three months, compared to roughly 12% of men in the same age range (Smitherman *et al.*, 2013).

Migraines are typically treated with triptans and isometheptene, together comprising 99% of antimigraine prescriptions (Smitherman *et al.*, 2013). Triptans have been shown to relieve headaches within 2 hours of ingestion in 42 to 76% of patients, but headache relief at 24 hours dropped to 29 to 50% of patients (Cameron *et al.*, 2015). Other medications, including ergots, also have some evidentiary basis (Clinch & Kesler, 2006) but comprise <1% of antimigraine prescriptions (Smitherman *et al.*, 2013). Dietary and lifestyle factors may play a role in migraine prevention, as noted in a superb 2018 review by Rehman *et al.* (2019). **Table 9** below summarizes the interventions that can be used to treat bowel pain.

Currently, there is limited evidence to make solid recommendations. Riboflavin, magnesium, and Coenzyme Q10 may reduce the pain severity from migraines (Gaul *et al.*, 2015). Vitamin D markedly reduces the frequency of migraine attacks per month but has a non-significant impact on migraine severity (Hu *et al.*, 2021). Among obese adolescents, a weight loss program focusing on dietary education and exercise significantly lowered headache frequency and intensity (Verrotti *et al.*, 2013). The herb Tanacetum may decrease migraine pain, especially when combined with acupuncture (Ferro *et al.*, 2012). Together, integrative techniques may reduce the incidence and severity of migraines and headaches, which often cause people to turn to opioids.

Table 9. Interventions for the treatment of migraine or headache-related pain.

Intervention	Effect on Migraine
Vitamin D	Symptom improvement (Gazerani <i>et al.</i> , 2019; Hu <i>et al.</i> , 2021)
Multivitamin (2 mg of folic acid, 25 mg of vitamin B₆, and 400 µg of vitamin B₁₂)	Improvement (Lea <i>et al.</i> , 2009)
Magnesium	Oral magnesium alleviates the frequency and intensity of migraine (Chiu <i>et al.</i> , 2016)
Vitamin B2	Improvement (Y.-S. Chen <i>et al.</i> , 2022)
Folic acid with pyridoxine	Decrease in headache severity (Askari <i>et al.</i> , 2017)
Probiotic	No effect (Parohan <i>et al.</i> , 2022)
Feverfew	Low quality evidence for preventative effect (Wider <i>et al.</i> , 2015)
Butterbur	Preventative effect (Diener <i>et al.</i> , 2004) but possible health issues (Prieto, 2014)
Meditation	Improved pain tolerance (Wachholtz <i>et al.</i> , 2017)
Yoga	Reduced headache frequency (Wu <i>et al.</i> , 2022)
Tai Chi	Decreased stress in Chinese women with migraines (Wang <i>et al.</i> , 2022)
Melatonin	Low quality evidence for improvement (Liampas <i>et al.</i> , 2020)
Ginger	Better treatment efficacy when used adjunctively with ketoprofen (Martins <i>et al.</i> , 2019) Similar efficacy to drug sumatriptan (Maghbooli <i>et al.</i> , 2014)

2.10 Common elements

Some interventions are suitable for pain emerging from multiple sources. These are summarized in **Table 10** next page.

Table 10. For those interventions acting on pain emerging from multiple sources, which types of pain are they effective against. + indicates a positive treatment effect. n.s. not significant. * Impact on quality of life.

\Intervention Pain Source\	Omega-3	Anti-inflammatory Diet	Acupuncture	Photobiomodulation	Massage
Chronic pain	+(Prego-Dominguez <i>et al.</i> , 2016)	+(Sala-Climent <i>et al.</i> , 2023)	+(Ju <i>et al.</i> , 2017)	+(animal model) (Balbinot <i>et al.</i> , 2021)	+(Keeratitanont <i>et al.</i> , 2015; Crawford <i>et al.</i> , 2016)
Rheumatoid Arthritis	+(Lee <i>et al.</i> , 2012)	+(Vadell <i>et al.</i> , 2020)	+(Wang <i>et al.</i> , 2008; Chou & Chu, 2018) n.s. (Lee <i>et al.</i> , 2008)	+(animal model) (Ryu <i>et al.</i> , 2023)	+(Field <i>et al.</i> , 2013, 2014; Sahraei <i>et al.</i> , 2022)
Injuries or Injury risk	+(running injury risk)(Davinelli <i>et al.</i> , 2023)	Unknown	+(case series) (Lee <i>et al.</i> , 2020)	+(Neto <i>et al.</i> , 2020; Ferlito <i>et al.</i> , 2023)	+(Poppendieck <i>et al.</i> , 2016)
Low Back Pain	+(Zhou <i>et al.</i> , 2022)	+(Shin <i>et al.</i> , 2022)	+(Manheimer <i>et al.</i> , 2005; Yuan <i>et al.</i> , 2008; Lee <i>et al.</i> , 2013)	n.s. (Tomazoni <i>et al.</i> , 2020)	+(Kumar <i>et al.</i> , 2013; Furlan <i>et al.</i> , 2015b)
Postsurgical pain	n.s. (Mohsen <i>et al.</i> , 2023)	+(animal model) (Guillemot-Legris <i>et al.</i> , 2018)	+(Sun <i>et al.</i> , 2008)	+(Ezzati, Fekrazad and Raoufi, 2019)	+(Boyd <i>et al.</i> , 2016; Liu <i>et al.</i> , 2022)
Cancer pain or chemotherapy pain	n.s.*(Lustberg <i>et al.</i> , 2018; Tawfik <i>et al.</i> , 2023)	n.s.† (Long Parma <i>et al.</i> , 2022)	+(Choi <i>et al.</i> , 2012; He <i>et al.</i> , 2020) n.s. (Paley <i>et al.</i> , 2015)	+(de Pauli Paglioni <i>et al.</i> , 2019)	+(Lee <i>et al.</i> , 2015; Boyd <i>et al.</i> , 2016)
Fibromyalgia	n.s. (Rastmanesh <i>et al.</i> , 2022)	+(Correa-Rodríguez <i>et al.</i> , 2020; Silva <i>et al.</i> , 2022)	+(Deare <i>et al.</i> , 2013; Valera-Calero <i>et al.</i> , 2022; Zheng & Zhou, 2022) n.s. (Mayhew & Ernst, 2007; Bai <i>et al.</i> , 2014)	+(Navarro-Ledesma <i>et al.</i> , 2022)	+(Kalichman, 2010; Li <i>et al.</i> , 2014; Yuan <i>et al.</i> , 2015)
Neuropathic pain	+(case series) (Ko <i>et al.</i> , 2010)	+(Allison <i>et al.</i> , 2016)	+(Feng <i>et al.</i> , 2023; Li <i>et al.</i> , 2023)	+(da Silva <i>et al.</i> , 2023; Korada <i>et al.</i> , 2023)	Partial response (Norrbrink & Lundeberg, 2011)
Migraine	+(reduction in migraine duration) (Maghsoumi-Norouzabad <i>et al.</i> , 2018)	+(Ghoreishy <i>et al.</i> , 2022)	+(Linde <i>et al.</i> , 2005; Da Silva, 2015)	+(Gomes <i>et al.</i> , 2022)	+(Lawler & Cameron, 2006; Chaibi <i>et al.</i> , 2011)

Conclusion

Chronic pain is currently a significant health challenge at the population level, albeit a tractable one. This review summarizes possible integrative treatments for chronic pain, aiming to reduce dependence on opioid medications, as many people prescribed opioids to treat their chronic pain go on to develop opioid use disorders.

This approach minimizes the reliance on opioids and allows people agency in resolving their pain issues. Awareness of integrative approaches to pain can yield an empowered population less reliant on costly pharmaceutical interventions and medical treatments. Future knowledge development can shape these collections of varied interventions into well-defined protocols, which can be administered with supervision, thereby improving access to chronic pain prevention and relief. This manuscript is intended to be built upon by developing rigorous trials of interventions and then disseminating the findings to the public.

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Conflicts of Interest Statement

The authors declare no conflicts of interest.

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